Case report

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GULLO´S SYNDROME (BENIGN PANCREATIC HYPERENZYMEMIA)

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BACKGROUND-AIM

Gullo´s syndrome or Benign Pancreatic Hyperenzymemia (BPH) is a new and rare entity described by Dr. Lucio Gullo in 1986. It is a hyperenzymemia maintained over time, with elevations, large fluctuations and transient normalization of pancreatic enzyme values, in absence of any evidence of clinical or morphological pancreatic disease. It appears in healthy individuals.

METHODS

Due to the rarity of this disorder and the novelty of the investigations, we consider interesting its review through the study of this case: 38-year-old male, without medical history.

RESULTS

Routine analysis: High values of amylase (221U/L [10-125]) and lipase (178.9U/L [13-60]). Acute pancreatitis was suspected. Other parameters were normal.
Emergency Department: Asymptomatic. Physical examination and pancreas imaging were normal. Analysis was repeated and lipase had almost normalized: 109.7U/L.
2 weeks later: Pancreatic enzyme control analysis showed again an increase in amylase (313U/L) and lipase (344.8U/L), without further alterations. Later on, a new analysis showed normalized values of amylase (127U/L) and lipase (48U/L). The veracity of these results was questioned, and determinations of both samples were repeated by different analytical equipment. The results, showing an intense fluctuation and normalization of the pancreatic enzymes within 8 hours, were confirmed.
It was decided to keep the patient under follow-up to study his evolution.

CONCLUSIONS

Elevated pancreatic enzymes generally mean pancreatic disease. However, BPH is characterized by a persistent increase in pancreatic enzymes (amylase and lipase), without any evidence of disease. It occurs sporadically or familiarly. Its molecular mechanism is unknown.
Laboratory is essential to confirm the results obtained and to reassure the clinician about its veracity and the reliability of the biochemical analysis equipment, given that the fluctuation of pancreatic enzymes in such a short period of time could be non-expected.
The diagnosis of BPH is important as it is a benign syndrome without pancreatic disease, which means that the performance of completely dispensable examinations, treatments and hospitalizations should be avoided, in order to prevent patients from suffering unnecessary worry and anxiety.

Case report

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SRY-NEGATIVE 46,XX TESTICULAR DISORDER OF SEX DEVELOPMENT WITH COMPLETE MASCULINIZATION

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BACKGROUND-AIM

46,XX testicular disorder of sex development (DSD) is a rare disease in men with 46,XX karyotype, also known as De la Chapelle syndrome. There is a disagreement between chromosomal sex (female) and gonadal sex and phenotype (male). It affects 1/20,000 men and represents 2% of cases of male infertility.

METHODS

13-year-old boy, studied by pediatric endocrinology service for his puberty. Important hypospadias, operated 4 times.

RESULTS

Physical examination: Male phenotype without dysmorphism, height 153.7cm, weight 63kg.
Hormonal study: Follicle-stimulating hormone 31.9U/L [1.7-11]; luteinizing hormone 12.2U/L [0.5-6]; testosterone 2.08ng/mL [2.4-10.7]. Further analysis confirmed hypergonadotropic hypogonadism.
Genetic study: 46,XX karyotype. After carrying out FISH, the absence of SRY gene was observed. SRY-negative 46,XX testicular DSD was confirmed. In order to determine the origin of the disease, a molecular study of SOX9 gene was performed. The patient did not present abnormalities in the analyzed regions, so the pathology is due to another cause not yet determined.

CONCLUSIONS

This disorder is characterized by the presence of male external genitalia ranging from normal to ambiguous, absence of Müllerian structures, small testes, testosterone deficiency, azoospermia, gynecomastia, short stature, obesity, cryptorchidism and hypospadias.
Diagnosis is established by combining clinical findings, endocrinological study and cytogenetic analysis showing hypergonadotropic hypogonadism (high gonadotropin hormones and low testosterone) and 46,XX karyotype.
Patients are divided into two groups: those who have SRY gene translocated from Y chromosome to X, that actives male sexual differentiation, and those who do not. 80-90% of cases are SRY-positive. As our case, an increasing number of published cases describe SRY-negative 46,XX patients (10-20%) with male phenotype, which would indicate the implication of other genes linked to X chromosome as the cause of DSD: SOX9, SOX3, RSOP1, etc.
Treatment consists in the progressive administration of testosterone to avoid the consequences of the hormonal deficiency. Genetic counselling and psychological assessment are always necessary. With an adequate hormonal treatment, the chance of carrying a good quality of life is high.

Case report

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MARSHALL´S SYNDROME (PFAPA SYNDROME)

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BACKGROUND-AIM

Recurrent episodes of fever are pathologies with difficult manage and a broad differential diagnosis in the healthcare system. Marshall's or PFAPA (periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis) syndrome is a pediatric periodic disease characterized by recurrent febrile episodes with head and neck symptoms, characteristic blood tests and poor response to conventional treatment.

METHODS

6-year-old child. She has monthly recurrent febrile episodes, tonsillitis and cervical adenitis lasting 3-5 days, always with similar analysis results. Asymptomatic between episodes.

RESULTS

Analysis: Leukocytosis 18.3*103/µL [4.5-13.5]; neutrophilia 12.7*103/µL [1.7-8.0]; high C-reactive protein (CRP) 59.8mg/L [0-5]; high immunoglobulin E (IgE) 980kUA/L [0-5]. Rest of parameters are normal.
Rapid antigen detection test for group-A β-hemolytic streptococcus: Negative.
Treatment: Little success with antibiotics and antipyretics. Good corticosteroid response.
PFAPA syndrome is confirmed.

CONCLUSIONS

Marshall´s is probably the most frequent autoinflammatory syndrome. It appears during early childhood with recurrent episodes of fever lasting 3-5 days and constitutional symptoms in the absence of respiratory infection. It is usually repeated approximately once a month and resolves spontaneously before 10 years of age. During healthy periods, patients grow normally.
Its origin is unknown: it could occur due to an abnormal adaptive immune response to an infectious agent, probably localized in lymphoid organs, capable to induce a rapid activation of natural immunity cells. Differential diagnosis includes other diseases characterized by periodic fevers: familial Mediterranean fever, hyper-IgD syndrome, cyclic neutropenia...
Laboratory studies help in the diagnosis: leukocytosis; neutrophilia; elevated CRP and IgE. Other parameters are normal. Oral culture swabs are negative for infection and patients fail to respond to antipyretic or antibiotic treatment. A dose of corticosteroid is enough to treat it.
It is important to determine the diagnosis quickly. Its monthly recurrence produces school absenteeism and interferes in the patient's quality of life, but as it is a benign and self-limited illness that resolves spontaneously, its final prognosis is excellent.

Case report

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TWO METABOLIC LIVER DISEASES IN A CHILD

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BACKGROUND-AIM

A number of metabolic conditions involve liver. The three most common are hereditary hemochromatosis (HH), alpha-I antitrypsin deficiency (AATD) and Wilson disease (WD). These inherited pathologies can cause important aftermath and lead to death. In addition, they can present themselves along with other liver diseases. Therefore, diagnosis, early treatment and genetic counselling are essential.

METHODS

The interest of this case lies in the coincidence of diagnosing two metabolic diseases in the same patient thanks to laboratory studies.
7-year-old boy, with normal physical examination, evaluated for self-limiting diarrhea of 4 months of evolution.

RESULTS

Stool test: Negative. Infectious origin is ruled out.
1stbiochemical-analysis: Slightly elevated transaminases: aspartate transaminase (AST) 48U/L [0-46], alanine transaminase (ALT) 45U/L [0-39]. Liver disease is suspected.
Serology: Hepatitis A, B, C virus: negative.
Immunology: Antinuclear, anti-LKM, antimitochondrial antibodies: negative.
2ndanalysis: Hypertransaminasemia confirmed: AST 44U/L, ALT 47U/L; ceruloplasmin <0.03g/L [0.15-0.3]; copper (Cu) in blood 12 µg/dL [80-160]; alpha-I antitrypsin 0.77g/L [0.9-2].
Genetic study: 2 metabolic liver diseases confirmed: WD, c.1934T>G mutation in homozygosis in the ATP7B gene and AATD, carrier of the Pi*Z allele in heterozygosis.

CONCLUSIONS

In case of recurrent diarrhea, infectious or malabsorptive origin must be ruled out first. Then, due to elevated transaminases, identify the most common causes that can induce it: hepatitis by alcohol, drugs, B or C virus; autoimmune; celiac disease; HH; WD; AATD; etc.
In this child, WD and AATD were diagnosed. Both are rare genetic diseases with liver involvement. In WD Cu accumulates in the liver, brain, eyes and other organs. Sometimes, it can cause asymptomatic liver failure with mild hypertransaminasemia. AATD is characterized by low serum levels of alpha-1-antitrypsin protein that often causes emphysema in adults and liver disease at any age.
Laboratory findings were essential to guide the diagnosis and perform genetic counselling. It allowed the rapid implantation of the zinc treatment to prevent Cu absorption. He has not repeated episodes of diarrhea and his quality of life has improved.

Case report

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HOOK EFFECT IN FERRITIN IN A PATIENT WITH HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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BACKGROUND-AIM

Hook or prozone effect is an interference of immunological techniques. The effectiveness of antibodies to form immune complexes is affected when concentrations of the antigen or antibody are very high. The formation of immune complexes stops increasing with greater concentrations and then decreases with extremely high concentrations, producing a hook shape on a graph of measurements and resulting in false negatives or inaccurately low results.
The following is a case of the prozone effect in ferritin.

METHODS

71-year-old woman with haemophagocytic lymphohistiocytosis (HLH) has discomfort, asthenia and fever.

RESULTS

Analysis: Pancytopenia; hyponatremia; abnormal liver function test (alkaline phosphatase, transaminases); disseminated intravascular coagulation; elevated D-dimer, triglycerides, lactate dehydrogenase, C-reactive protein, ferritin.
Hyperferritinemia [30-400] day to day: 22592µg/L; 288080µg/L; 836µg/L; 196265µg/L.
These hemogram, biochemistry and coagulation results are normal analytical findings of HLH activity, but the decreased ferritin value in day 3 is striking. Its determination is repeated in the equipment, obtaining similar values (878.4µg/L).
When doubting its veracity, serial dilutions of the sample are made until reaching a concentration within the equivalence interval. Real ferritin result: 546320µg/L (1/1000 dilution). Hook effect is confirmed.

CONCLUSIONS

The interest of the case lies in the importance of detecting this immunologic phenomenon.
The typical dose-response curve is linear up to a determined concentration, in which a plateau occurs. If the prozone effect happens, the curve starts a negative slope until it reaches low values.
As the ferritin concentration is so high, the immunoturbidimetric test antibodies become saturated, the precipitation and measurement signals decreases and the results are falsely low. The amount of precipitate formed is inversely proportional to the concentration of present antigen. This can lead to possible error by underestimating ferritin and to make erroneous clinical decisions.
Clinical validation is important: it is the only way to detect this interference. When suspected, serial dilutions of the sample should be made to reach a concentration within the equivalence range and correct the result.

Case report

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INCREASED COBALAMIN CONCENTRATION DUE TO MACROCOMPLEXES-B12

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BACKGROUND-AIM

A 73-year-old woman showed persistently increased cobalamin concentrations during the last 2 years, without toxic habits. Physical and neurological examinations were normal. The last fasting biochemical control showed a normal complete blood count, and a normal general metabolic panel, including iron profile, liver panel, folate and glomerular filtration rate. Serum cobalamin was quantified using a chemiluminiscent microparticle immunoassay on the Architect i2000 platform (Abbott Diagnostics), yielding a result of >1476pmol/L (normal: 134–651pmol/L). No supplementation was reported.
Given the persistent elevation of serum cobalamin, tumor biomarkers, serologies and autoimmunity panels were requested. Moreover, the laboratory manager also decided to perform an interference study in order to rule out a spurious cobalamin result.

METHODS

Not applicable

RESULTS

Different pathologies have been associated with high levels of cobalamin, such as myeloproliferative syndromes, autoimmune lymphoprolipherative syndrome and fibrolaminar hepatocellular carcinoma. Other pathologies with a likely association are cancer and metastasis of unknown origin, liver or kidney disease.
Tumor biomarkers, the tests for autoimmune diseases and the serologies were all negative, and her medical records did not reflect any alteration in liver tests or kidney function.

CONCLUSIONS

In order to rule out analytical errors, the test was repeated and quantified using an alternative methodology (enzimoimmunoanalysis, Elecsys, Roche), yielding the same result. The blockage and removal of possible heterophilic antibodies led to the same cobalamin result. In addition, the negative result for the rheumatoid factor in our patient allowed ruling out such interference. Finally, all possible interfering antibodies or macrocomplexes were removed by precipitation with polyethylene glycol. 8 samples of patients with cobalamin supplementation were selected as a negative control. The mean recovery obtained in these controls was 80.8%. In our case, cobalamin recovery was <5%. The cause of the hypervitaminemia was concluded to be the existence of macrocomplexes-B12, which may interfere in some commercially available cobalamin assays, resulting in falsely elevated cobalamin levels.

Case report

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PERNICIOUS ANAEMIA MANIFESTED BY SEVERE HAEMOLYSIS

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BACKGROUND-AIM

Anaemia is one of the most common problems faced in clinical practice. It is defined as a reduction in any of the main red blood cell measurements: haemoglobin, haematocrit and red blood cell count.

METHODS

A patient visits her primary care physician because of a "strange urine smell". Follow-up laboratory tests were requested.
Clinical history: hypothyroid, morbid obesity, hypotension and dyslipidaemia.

RESULTS

Laboratory results:
Biochemistry: LDH: 1752 U/L; total bilirubin: 0.6 mg/dL; haptoglobin: <1 mg/dL.
CBC: red blood cells: 1.9 x106/mcL; haemoglobin: 7.7 g/dL; mean corpuscular volume: 130.5 fL;
red cell dispersion: 20.1%; platelets: 101 x103/mcL.
In view of the blood count, LDH and haptoglobin values, haemolysis was confirmed. Haemolytic anaemia vs. megaloblastic anaemia was suspected, so additional tests were performed. In addition, the patient is contacted to go to the emergency department for assessment by a haematologist:
Complementary tests:
Biochemistry: vitamin B12 (vitB12): 149 pg/mL. Folic acid normal.
Peripheral blood smear: anaemia without spherocytosis. Platelet microaggregates.
Direct Coombs negative.
Reticulocytes: 13.2 x103/mcL and 4.9 x103/mcL, in a second determination after 4 days.
The negative Coombs' test eliminates the presence of autoimmune haemolysis. Low vitB12 levels plus low reticulocyte count are indicative of a vitB12 deficiency, with further testing to indicate the cause:
Complementary tests:
IgG anti-parietal cell IgG antibody titre: 1/640.
IgG anti-intrinsic factor antibodies: 10,6 U/mL

CONCLUSIONS

The positivity of both antibodies confirms the diagnosis of pernicious anaemia. The patient is treated with intramuscular vitB12 and monitored for treatment efficacy.
Pernicious anaemia is an autoimmune disease that affects the gastric mucosa, altering the absorption of vitB12. Symptoms manifest insidiously and rarely arouse clinical suspicion, but mainly peripheral neuropathy and megaloblastic anaemia.
Rarely, as in the present case, it manifests as haemolytic anaemia, with normal or low reticulocytes, due to this bone marrow production inefficiency caused by vitB12 deficiency.

Case report

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COMPOSITE LYMPHOMA IN A PATIENT WITH A HISTORY OF HODGKIN LYMPHOMA

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BACKGROUND-AIM

Composite lymphomas are very rare diseases where two different lymphomas are present in the same anatomical tissue. The diagnosis can be challenging as the predominant lymphoma, often the most aggressive one, can mask the other.

METHODS

We present the case of a 54-year-old male patient with a history of obstructive myocardial hypertrophy, chronic hepatitis c and smoker that was diagnosed with a lymphocyte-rich classical Hodgkin Lymphoma, stage IV-B. He received 8 cycles of a doxorubicin (Adriamycin), bleomycin, vinblastine and dacarbazine regimen and achieved complete remission.
During the medical follow-up a positron emission tomography–computed tomography (PET-TC) revealed multiple supraclavicular, axillar, para aortic, porto-cava, iliac and inguinal adenopathies. With a suspected relapse, a blood analysis and a left axillary lymph node biopsy were performed.

RESULTS

Analysis revealed a strictly normal hemogram (leucocyte 9.69x109/L, lymphocytes 1.98x109/L, haemoglobin 163 g/L, platelet 166x109/L). Otherwise, flow cytometry (FC) analysis of the lymph node revealed 2 distinct B-cell populations. The first population comprised 70% of the B-cells and expressed CD19, CD20, CD22, FMC7 and CD10 with a kappa light chain restriction. This population was negative to CD5, CD23, CD38, CD103, CD123 and CD11c. The second population comprised 30% of the B-cells and expressed CD19, CD20 dim, CD22 dim, CD5, CD23, CD79b dim with a lambda light chain restriction. This smaller population was negative to CD10, FMC7, CD38, CD103, CD123 and CD11c.
Initially the cyto-histopathology study confirmed the presence of a B-cell population forming nodular patterns that expressed BCL2, CD10, BCL6 i MUM1. Furthermore, taking into account the FC findings, it was possible to detect a second B-cell population that expressed CD5, CD23 and BCL2.
Study of immunoglobulin gene rearrangements detected two monoclonal peaks at the FR1, FR2, FR3 and DH locus. FISH study was negative to BLC2 and C-MYC but positive to BCL6 rearrangements.

CONCLUSIONS

Given the immunophenotype, histopathology and molecular findings, the patient was diagnosed with a composite follicular lymphoma and a chronic lymphocytic lymphoma. The flow cytometry analysis was the key to suspect a composite lymphoma in a complex case of a patient with a Hodgkin lymphoma history.

Case report

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GENETIC DIAGNOSIS OF MODY 3. A CASE REPORT

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BACKGROUND-AIM

MODY (Maturity Onset Diabetes of the Young) is an inherited form of diabetes, which comprises a heterogeneous group of monogenic diseases characterized by dysfunction of beta cells of the pancreas. MODY 3 is caused by mutations in the HNF1A gene and is characterized by progressive damage of insulin-producing cells and decreased insulin secretion. Unlike MODY 2 diabetes, there are usually elevated glucose levels, and the severity of hyperglycemia increases with the time of disease progression.

METHODS

We present the case of a 44-year-old patient in whom basal hyperglycemia is detected 3 years before, without being overweight, establishing the diagnosis of Type 2 Diabetes Mellitus (DM) and starting treatment with metformin. The mother was diagnosed with DM-2 and the brothers had no glycidic disorder. In the last months, the symptoms increase, and the patient loses weight progressively. Due to the evolution in recent years, LADA (Latent Autoimmune Diabetes in Adults) diabetes is suspected, is requested, therefore, determination of C-peptide and GADA autoantibodies (glutamic acid anti-decarboxylase), IA2 (membrane anti-tyrosine phosphatase), and IAA (anti-insulin), all with values in the normal range. Because of this, autoimmune diabetes is ruled out and a genetic study of the patient's monogenic DM is requested

RESULTS

By direct analysis of the genes contained in the panel MODY NextGeneDx, a change is detected in the heterozygous HNF1A gene, consisting of a transition of adenine for guanine (c.586A> G), that level protein causes the change of the threonine at position 196 by an alanine (p.Thr196Ala). This change is already described as a pathogenic change associated with MODY 3, so it comes down to the final diagnosis of the patient.

CONCLUSIONS

The patient carries, heterozygous, of the pathogenic change c.586A> G (p.Thr196Ala) in HNF1A gene. The results of the study are consistent with the clinical diagnosis of MODY 3. It is advisable to study the pathogenetic change c.586A> G in the HNF1A gene in the progenitors of the patient to know whether inherited or de novo, as well as other family members at risk of being carriers.

Case report

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LEVELS OF INFLIXIMAB AND ANTI-INFLIXIMAB ANTIBODIES IN THE MANAGEMENT OF ULCERATIVE COLITIS

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BACKGROUND-AIM

The incidence of inflammatory bowel disease in the pediatric age has increased in the last decades. Infliximab (IFX) is a chimeric antibody against tumor necrosis factor-alpha (TNF-a), a cytokine with a critical role in the pathogenesis of inflammatory diseases. This drug can cause immunogenicity, leading to the formation of anti-infliximab antibodies (Ac), whose presence has been associated with lack or loss of response.

METHODS

A 13-year-old female patient was admitted to our hospital for left coxalgia of 5 months evolution. During her stay, diarrheal stools with pathological products and abdominal pain reappeared, and she was diagnosed with ulcerative colitis.

RESULTS

After several days on corticosteroids, treatment was switched to infliximab, whose therapeutic serum concentration range is 3-7 mcg/mL. Three induction doses of 5 mg/kg were prescribed at an 8-week interval, followed by three maintenance doses of 10 mg/kg intravenously at another 8-week interval. At that time, the patient was still in clinical remission and she was receiving concomitant oral immunosuppressive treatment (azathioprine and mesalazine). Given the apparent healing of the mucosa and the favorable drug levels (8,8 mcg/mL) reached in the middle of the cycle, infliximab was continued and immunosuppressive treatment was suspended. In the next blood test the biopharmaceutical concentration was undetectable (<0,01 mcg/mL) and the anti-IFX Ac levels were high (261 U/mL). Finally, due to the new antibody positivity (73,2 U/mL) in the middle of this cycle and the excellent clinical response of the patient at that time, it was decided to suspend treatment with infliximab and to restart azathioprine administration.

CONCLUSIONS

This clinical case is a clear example of the immunogenicity that can be generated during treatment with biopharmaceuticals, being of vital importance the determination of the levels of both drug and anti-drug antibodies to optimize the therapeutic strategy and achieve a good clinical management of these patients.

Case report

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GENETIC DIAGNOSIS OF MCARDLE DISEASE. A CASE REPORT

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BACKGROUND-AIM

McArdle disease or glycogen storage disease type V is a metabolic myopathy characterized by exercise intolerance that is inherited in an autosomal recessive manner. Onset during childhood, the disease is caused by mutations in the PYGM gene, located on chromosomal region 11q13, which codes for muscle glycogen phosphorylase. The absence of the enzyme glycogen phosphorylase results in an inability to utilize glycogen stores.

METHODS

A 15-year-old female patient who comes for consultation due to weakness in the lower limbs and muscle contractures after physical exertion. In the analysis performed, creatine kinase (3500 U/I) and fructose-bisphosphate aldolase (34 U/I) were elevated, without myoglobinuria. Subsequently, an exercise intolerance test was performed and a flat lactate curve was observed, so type V glycogenosis was suspected and a genetic study was requested.

RESULTS

A molecular study was performed for the analysis of small deletions/insertions and point mutations in the coding region and splicing sites of the PYGM gene. By direct analysis of the above gene, a transition from a cytosine to a thymine (c.148C>T) was detected in the patient, which at the protein level produces the change of the arginine at position 50 to a premature stop codon (p.Arg50*). This change has been previously described as the most frequent pathogenic change associated with type V glycogenosis in the European population. With the above genetic results, it was confirmed that the patient was a carrier, apparently in homozygosis, of the c.148C>T change (p.Arg50*) in the PYGM gene, being compatible with her clinical diagnosis of McArdle's disease.

CONCLUSIONS

After analyzing the PYGM gene in the patient's parents, it was concluded that both were heterozygous carriers of the genetic change c.148>T (p.Arg50*), the patient being a homozygous carrier of this change. Although there is no curative treatment for this disease, the patient was recommended to perform moderate aerobic physical exercise routinely, after increasing carbohydrate intake.
This clinical case is a clear example of how laboratory tests are essential, since the diagnosis of many patients is guided by the exercise intolerance test and confirmed by the genetic study.

Case report

M187

ROLE OF THE LABORATORY IN THE IDENTIFICATION AND CHARACTERIZATION OF TYPE I CRYOGLOBULINEMIA: A CASE REPORT

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BACKGROUND-AIM

Cryoglobulins are immunoglobulins (Ig) that precipitate at temperatures below 37˚C and dissolve again upon rewarming. According to immunochemical analysis, they are classified into: type I (monoclonal IgM, IgG or IgA, mostly associated with haematological disorders); type II (monoclonal IgM with Rheumatoid Factor (RF) activity combined with polyclonal IgG); and type III (polyclonal IgM with RF activity combined with polyclonal IgG). Type II and III (mixed cryoglobulinemia) are associated with infections, particularly hepatitis C, and autoimmune diseases. Clinical manifestations are heterogenous, highlighting ischemic lesions with vascular obstruction due to precipitation of immunocomplexes.

METHODS

A 42-year-old woman, no previous pathologies, came to emergency department due to abdominal pain of 2 months of evolution. Suspecting intestinal ischemia, she underwent surgery with the finding of jejunum erythema, which improved with hot serum lavages.
Laboratory analysis: serum biochemistry (including renal function, liver enzymes, calcium, albumin, C-reactive protein), blood count, coagulation, tumor markers, RF, ANAs, ENAs, ANCAs, CMV, VIH, EBV and hepatitis virus were within normal limits or negatives. Initial serum protein capillary electrophoresis (CE, Capillarys-2 Sebia®) without visual alterations. Complement C4 low. Positive cryoglobulins: total quantification of 13 mg/dL [0-3.7] and the immunofixation electrophoresis (IFE, Hydragel-Hydrasys Sebia®) of precipitate showed an IgM-Kappa monoclonal component.

RESULTS

Given the laboratory finding of cryoglobulins, serum protein study was expanded: increased IgM 494 mg/dL [40-230], and CE and subsequent IFE confirmed an IgM-Kappa monoclonal protein. Therefore, after bone marrow study, the clinical diagnosis was IgM monoclonal gammopathy and the patient has started treatment with plasmapheresis and Bortezomib.

CONCLUSIONS

Type I Cryoglobulinemia is associated with lymphoproliferative disorders, predominantly symptoms of the underlying haematological disease and those secondary to blood hyperviscosity. In this case, the early and correct detection of cryoglobulins allowed anticipation before the patient had a typical symptomatology and provided guidance for the etiological diagnosis and treatment options.

Case report

M188

OVERLAP SYNDROME AIH- PBC IN 73 YEARS OLD PATIENT

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BACKGROUND-AIM

Autoimmune hepatitis (AIH) is a chronic liver disease characterized by inflammation and necrosis of liver cells. Anomalous serologic tests are usually found.
Approximately between 7% and 10% of autoimmune disease have the same features of primary biliary cholangitis (PBC). This condition which shares features of at least two more widely recognised disorders are called overlap syndrome.
This study aims to describe a case report of overlap syndrome.

METHODS

73 years-old female diagnosed of multiple sclerosis and followed up by neurology department, presented with complaints of abdominal pain, diarrhoea, vomiting. Computed Tomography Scan (CT) findings correlated with colitis.
The patient had dehydration and Acute Renal Failure and she was treated with IV fluids and antiemetics to control symptomatology.
The first diagnosis was colitis on the descending colon.
The patient after days admitted and in treatment, was not feeling better and blood samples (from March 18, February 23,18,15) showed transaminitis and cholestasis. Results were: ALT (46, 44, 45, 66 U/L), AST (26, 43, 45,73 U/L), GGT (435, 416,448,499 U/L), ALP (181, 192, 200, 260 U/L).
An abdominal ultrasound performed revealed uniform liver, suggestive of hepatic steatosis. There was a suspicious 9 mm nodule, and it was suggestive of hepatic haemangioma. A hepatic biopsy was considered.
The histology demonstrated inflammatory cell infiltrate without a clear diagnosis of cholestasis.

RESULTS

The patient showed Antinuclear (ANA) pattern AC21 (1/320) (IFI on Hep-2) anti-smooth muscle (ASMA, 1/80) and antimitochondrial antibodies (AMA, 1/40) IFI triple Tissue). Immunobloting showed positivity for f- antiactin and E2 subunits of 2-oxoacid dehydrogenase complexes (nPDc, BCOADC-E2).
Although, biopsy was showed inflammatory cell infiltrate (typical of AIH) biochemical profile reflects cholestasis more than hepatitis.
These results suggest overlap syndrome AIH-PBC.

CONCLUSIONS

Overlap syndrome AIH- PBC is very infrequent disease and more prevalent in females. Usually, unspecific symptoms and laboratory tests could be hepatitis or cholestasis profile. Their identification is important because its clinical relevance, normally more aggressive and with less therapeutic response than others autoimmune diseases.

Case report

M189

SUSPICION OF ASPECIFIC TROPONIN I ELEVATION: A CASE REPORT OF TWO INTENSIVE CARE PATIENTS

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BACKGROUND-AIM

Although the ESC has recommended the use of ultrasensitive Troponin (Tn) I or T, the assay is curently debated because of potentiel lack of specificity. Our work illustrates the biological exploration of two patients from the intensive care unit of the University Hospital of Liege (Belgium) whose Tn results were concerning.

METHODS

In 2021, a 70-year-old man was admitted to the emergency department (ED) for dyspnea. He later underwent surgery for thromboendarterectomy, triple bypass surgery and aortic valve replacement. Following it, the patient displayed a Tn concentration increase with a maximum of 42,524 ng/L. The second patient was 47 years old and was admitted to the ED for cardiorespiratory arrest. One week later, an acute peripheral ischaemia (API) was diagnosed. TnI results of the patient increased up to 12.639 ng/L following the embolectomy procedure. In our laboratory, the Alinity Abbott® analysers are used for this assay. Atellica from Siemens®, Cobas 8000 from Roche® and Vitros from Ortho clinical Diagnostic® were used for external analysis.

RESULTS

A significant Tn rise is expected after cardiac surgery and depends on the type of surgery performed. As the value was considered inadequate by the intensivists, it was explored. The result was confirmed by others methods, except the Vitros analyser which showed lower values (22,300 ng/L). In order to determine if this elevation should be considered abnormal, all the causes of Tn elevations observed in our hospital have been checked during a month (n=66). The median of postoperative value was about 20,000ng/L. Then, a test for anti-heterophilic antibodies was performed and found negative. The elevated Tn T value (2,391ng/L) is an additional argument in favour of a mycoardial injury. In conclusion, the exploration leads us to believe that this Tn increase was the consequence of the postoperative period. As with the first patient, the biological investigation confirmed the initial result for the second one. The hypothesis is that the API which is responsible of rhabdomyolysis also caused myocardial injury on a heart already weakened.

CONCLUSIONS

There are still some pitfalls in the interpretation of ultrasensitive Tn. In our cases, the Tn elevation was specific to the heart muscle but the cause was either surgery or rhabdomyolysis.

Case report

M190

MTHFR GENETIC VARIANTS AND VACCINE-INDUCED THROMBOTIC THROMBOCYTOPENIA: TWO CASE REPORTS

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BACKGROUND-AIM

Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been rapidly developed in order to limit the infection spread. Noteworthy, recipients of vaccines can develop adverse effects, ranging from local pain to systemic effects. Among these, vaccine-induced thrombotic thrombocytopenia (VITT) leading to death has been described worldwide in individuals who received the ChAdOx1 nCov-19 vaccination. Although the underlying causes of VITT are actually unclear, several hypotheses have been proposed, including a genetic predisposition.
We report two cases of patients who died within 21 days after receiving the ChAdOx1 nCov-19 vaccine.

METHODS

Patient 1 was a thirty-seven years old woman admitted to the Emergency Department (ED) in a drowsy state. She had an occlusive thrombus in the superior sagittal venous sinus and a very large haemorrhage in the frontal cerebral lobe. Patient 2 was a fifty years old man admitted to the ED for abdominal pain. He had portal vein thrombosis with smaller thrombi in the splenic and upper mesenteric veins. Then, the patient also developed extensive intra-cerebral haemorrhage.

RESULTS

Both patients had decreased platelet count, increased D-Dimer levels and were positive for antibodies against platelet factor 4 heparin. The genetic thrombophilia screening was also assessed: both patients were wild type for the main polymorphisms on FV and FII genes, while for C677T methylenetetrahydrofolate reductase (MTHFR) polymorphism (rs1801133) patient 1 was homozygotes and patient 2 was heterozygotes.

CONCLUSIONS

Although the role of rs1801133 is debated for its frequency in the general population, recently, it has been significantly correlated with the risk of deep vein thrombosis and pulmonary embolism. Even if the assessment of MTHFR polymorphisms is not recommended in the routine, it could be relevant in conditions associated with an increased risk of thrombotic events, such as the vaccine administration. Thus, it may be useful to evaluate the genetic predisposition to thrombophilia before initiating the vaccination plan? It is desirable to collect all data of fatal cases after ChAdOx1 nCov-19 vaccination in order to confirm or exclude this association.

Case report

M191

PERITONEAL CARCINOMATOSIS: RELEVANCE OF THE STUDY OF THE ASCITIC FLUID CYTOMORPHOLOGY AT THE EMERGENCY LABORATORY

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BACKGROUND-AIM

Peritoneal carcinomatosis is a diffuse dissemination of tumour cells from a primary tumour into the ascitic fluid (AF). It appears during the most advanced stage of extension of the tumour, in metastatic disease. The urgent study of the AF cytomorphology at the emergency laboratory stands as a fast, simple and low-cost tool for the early evaluation of patients with suspected tumour infiltration into serous cavities such as peritoneum.

METHODS

We present a case report of a patient with peritoneal carcinomatosis. An ascitic fluid sample was analysed with Sysmex technology at the emergency laboratory and, afterwards, cytocentrifugation, stain and optical microscope analysis of the sample was performed.

RESULTS

82-year-old man with cardiac, respiratory, renal and urological comorbidities and personal history of bladder carcinoma pT1G2 in 2003 came to the Emergency Services due to abdominal distension and respiratory distress. The abdominal X-ray confirmed the abdominal distension and an echography-guided paracentesis was performed, indicating mild ascites without hepatopathy nor portal hypertension. The results of the analysis of the AF at the emergency laboratory were: 2731 cells/μL, 9% polymorphonuclear cells, 91% mononuclear cells, 43.4% high fluorescence cells, CEA 18363 ng/mL, Ca15.3 1167 UI/mL and Ca19.9 6.29 UI/mL. We proceed to the cytocentrifugation and stain of the sample, which showed a large amount of big size cells, with a low nucleus/cytoplasm ratio, rounded nucleus, abundant basophile cytoplasm and plenty of vesicles and some double-nucleated cells. Besides, cell nests were present. All of these results were suggestive of malignancy. The cytology of the AF showed atypical cells suspected of low-differentiated carcinoma. Given these results, the patient underwent an abdominal CT scan with contrast and a biopsy was taken, confirming the diagnosis of peritoneal carcinomatosis, with suggestive lesions of hepatic and colonic implants, remaining the location of the primary tumour unknown, suspected of ureteral malignancy.
The Oncology Department took care of the patient and informed him about the diagnosis, prognosis and incurability of the disease, the antineoplastic treatment options, the low probability of benefit and high toxicity and finally it was agreed to use symptomatic-palliative treatment. Subsequently, the patient presented poor clinical control and a fast deterioration, with dyspnea at rest, asthenia and anorexia. Consequently, palliative sedation was initiated and the patient finally died four months after diagnosis.

CONCLUSIONS

The cellular content of AF is normally below 250 cells/μL. Above 500 cells/μL and presenting at least 5% of high fluorescence cells, the performance of a cytocentrifugation, stain and cytological study of the fluid is recommended. The morphology of the cells present in the AF allows us to detect the presence of severe diseases, such as solid malignancies or severe hematological diseases. Malignant cells show specific morphological characteristics depending on the type of tumour and cytoplasmatic vesicles and cells undergoing mitosis are frequently found. Moreover, hematological malignant cells do not form nests in AF, in contrast to solid malignancies. In the case of detecting the presence of malignant cells in the AF at the emergency laboratory, it will be necessary to confirm these results with a cytological study.

Poster Abstracts – EuroMedLab Munich 2021 – Munich, April 10–14, 2022 • DOI 10.1515/cclm-2021-5013
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Case report

M192

GENETIC DIAGNOSIS OF NEUROFIBROMATOSIS TYPE 1. PURPOSE OF A CASE

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BACKGROUND-AIM

Neurofibromatosis type 1 is a genetic disorder that is transmitted in an autosomal dominant manner with complete penetrance and variable clinical expressiveness. The most characteristic clinical features are the presence of café-au-lait spots and cutaneous neurofibromas. Diagnostic criteria have been established that require at least 2 of the following clinical manifestations: café-au-lait spots, neurofibromas, axillary or inguinal epelids, optic glioma, iris hamartomas, and bone lesions. The disease is due to deletions or duplications that affect one or more exons of the NF1 gene

METHODS

A boy was admitted to Pediatrics at the age of 6 years, with suspicion of NF1; he reported generalized pruritus and paresthesias in the lower limbs. He is readmitted for seizures and decreased visual field. Family history includes café-au-lait spots in the paternal family.
On examination, café-au-lait spots are observed all over the body surface, palpation of a nodule on the back not attached and painful on mobilization. It is evaluated by Internal Medicine for the study of suspected NF1.
A CT scan of the skull was requested, showing lesions compatible with multiple neurofibromas in the retroorbital areas and small nodules on the antero-medial aspect of the left orbit. Cranial MRI with cortical thickenings in the left occipital lobe and both temporal. The CT scan of thighs revealed multiple plexiform neurofibromas involving the bilateral femoral nerves.

RESULTS

Genetic study is requested. Direct analysis detects a change in heterozygosity in the NF1 gene, consisting of a transition from an A to a G (c.4662-2A> G) at the splicing acceptor site of intron 34. This This change affects the correct processing of the mRNA since it is found in the splicing acceptor canonical site and has not been described in population databases.

CONCLUSIONS

This disease does not contemplate specific treatment. In this case, as the patient presents a stability in the progress of his disease, he does not require treatment other than annual check-ups, the retroorbital neurofibromas being very important.
Analysis of the c.4662-2A> G change is recommended in the parents of the patient indicated above in order to determine whether it is a de novo or inherited change, as well as in the rest of the relatives at risk.

Case report

M193

DIAGNOSIS OF HEMOGLOBINOPATHY S HOMOZYGOTE IN A PATIENT WITHOUT SYMPTOMATOLOGY

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BACKGROUND-AIM

Hemoglobin S (Hb S) is a type of structural hemoglobinopathies generated by a mutation in 6th position of the Hb βglobin gene, where Glutamic Acid is replaced by Valine (β6Glu->Val). Increasing the rigidity and viscosity of the erythrocyte membrane, and promotes a change in morphology (''sickle'' shape), causing episodes of vessel occlusion and hemolytic anemia. Sickle cell syndromes present great clinical heterogeneity. High performance liquid chromatography (HPLC) is the reference method for diagnosis.
Describe the unexpected finding and diagnosis of hemoglobinopathy S homozygote in an asymptomatic patient.

METHODS

Case description.

RESULTS

A 28-year-old man from Senegal underwent a control test and the following findings were revealed: Red blood cells 2.82 x10^6/µl(4.3-5.75x10^6/µl), Hb 8.6g/dl (13.5-16.5g/dl), Hematocrit 24.8%(39.5-50%), mean corpuscular volume 88fl (80-101fl), mean corpuscular Hb 30.7pg (27-34pg), mean corpuscular Hb concentration 34.8 g/dl(31.5-36g/dl), reticulocytes 9.63 %(0.5-2.8%), Glucose 100mg/dl (74-106mg/dl), Total Bilirubin 1.74mg/dl (0.3-1.2mg/dl), Indirect Bilirubin 1.37 mg/dl(0- 0.75mg/dl), Lactate dehydrogenase 319 U/L(208-378 U/L). Glycosylated Hb(HbA1c): HPLC(Horiba®) determination was performed and no band was observed for Hemoglobin A(HbA1c: 0%) and the chromatogram indicated the presence of an anomalous band. A consultation was conducted with Hematology for suspected haemoglobinopathy. The Hb fractions were determined with the equipment in β-thalassemia mode: HbA0 0%, HbA2 2.6%(0-3.8%), Hb Fetal(F) 12.6 %(0-2%), Hb S 84.8 %(0-0.5%). Positive sickle cell test. The sample was sent away to confirm by capillary electrophoresis and the results were confirmed: HbA0 0%, Hb A2 2.6%, Hb F 13.1% and Hb S 84.3%. The outcomes are compatible with homozygous haemoglobinopathy S.

CONCLUSIONS

In HbA1c analysis by HPLC, abnormal Hb can be detected and serve as a ''diagnostic screening'' for patients with hemoglobinopathy. With the data from the Hb analysis using the two methodologies and the positive sickle cell test, the diagnosis of homozygous SS haemoglobinopathy is confirmed. The protocol established between Clinical Analysis and Hematology allows for the early diagnosis of these patients and more rapid implementation of the necessary clinical actions.

Case report

M194

ANTI-MULLERIAN HORMONE AS A TUMOR MARKER: A CASE REPORT.

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BACKGROUND-AIM

Anti-mullerian hormone (AMH) is a glycoprotein known for its role during sexual differentiation. The production of AMH in the female foetus starts in the 36th week and reaches a maximum around the age of 25. Later, secretion gradually declines throughout the reproductive years until menopause, becoming indetectable soon after. The measurement of AMH levels in the laboratory has several recognized clinical applications: prediction of the age of menopause onset, evaluation of ovarian reserve, use in personalized ovarian stimulation, diagnosis and monitoring of pathologies such us polycystic ovarian syndrome, among others.

METHODS

We present the case of an 84-year-old woman who is admitted to the hospital due to a pelvic mass. She has a history of ovarian neoplasia. The patient undergoes a general biochemical analysis that results slightly altered and a hormonal analysis. The main hormonal tests were realized in the cobas e 801 analyzer (Roche Diagnostics), an immunochemistry module that performs a broad range of immunoassay tests using the ElectroChemiLuminescence technology.

RESULTS

The result of the pituitary-gonadal hormones does not fit with the expected values according to the age of the patient (postmenopausal woman): FSH: 0.3 mUI/mL (26 – 135); LH: 0.3 mUI/mL (7.7 - 59); Estradiol: 165 pg/mL (5 – 138). In light of these results, the laboratory performs complementary measurements to clarify the results: AMH and some tumor markers. The obtained values are pathologically high: AMH: 45.90 ng/mL (< 0.01); CA 125: 96.5 U/mL (5 – 35); CA 19.9: 59.9 U/mL (2 – 37); CEA: 5.11 ng/mL (0.1 – 5). The elevated AMH result, above all, along with other medical examinations led to the diagnosis of a granulosa cell tumor, a rare type of ovarian malignancy belonging to the family of “sex cord-stromal tumors”.

CONCLUSIONS

In addition to its well-known clinical utilities, an increasing number of studies are describing the AMH as a potential biomarker of some tumors such us adult granulosa cell tumor. In our case report we confirm the diagnostic value of this hormone in granulosa cell tumor in an 84-year-old woman, and we also demonstrate the fundamental role that the clinical laboratory plays in aiding the diagnosis and follow-up of important pathologies.

Case report

M195

EDWARDS AND DOUBLE Y SYNDROMES

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BACKGROUND-AIM

Double Y syndrome is considered an underdiagnosed entity. No specific ultrasound markers or abnormalities in the biochemical parameters used in prenatal screening have been described. The etiology is paternal meiotic nondisjunction and presents a wide clinical spectrum, from asymptomatic men with normal intelligence and tall stature (due to the existence of 3 copies of the SHOX gene located in the PAR 1 pseudoautosomal regions), to men with neurological disorders. cognitive and behavioral. These patients are at increased risk for hyperactivity and attention problems.
Edwards syndrome (chromosome 18 trisomy) is the second most common chromosomal disease in humans (incidence: 1 in 3,000 to 8,000 live newborns). It can affect both sexes, although 80% with trisomy 18 are women, with better survival. The etiology is meiotic nondisjunction, more frequent in meiosis II, in 90% of cases it occurs in maternal meiosis. The prognosis for life is not good. They present cardiovascular alterations: ventricular septum defects (94%), ductus (77%), atrial septum defects (68%); brain abnormalities: cerebellar hypoplasia (32%), cerebral edema (29%), large cisterna magna (26%) and choroid plexus abnormalities (19%); mental and legal retardation; ocular abnormalities (microphthalmia and corneal opacities); gastrointestinal abnormalities: esophageal atresia (26%), imperforate anus and diaphragmatic hernia; bone abnormalities: small pelvis, short sternum, rib abnormalities, syndactyly and polydactyly -which is usually postaxial- and radioelectric aplasia; genital abnormalities: hypospadias and cryptorchidism; and omphalocele in 5% of cases. They usually have their hands closed with the second and fifth fingers superimposed on the third and fourth. 63% of affected fetuses usually die in utero.

METHODS

A case of a 22-week pregnant woman with suspected fetal malformation syndrome after ultrasound evaluation is presented. She underwent genetic amniocentesis to study the fetal karyotype.

RESULTS

This cytogenetic study in amniotic fluid (resolution 400 bands) showed an additional Y chromosome and a trisomy 18. No other numerical or structural abnormalities were observed.
Chromosomal formula: 48, XYY (double Y syndrome) + trisomy 18 (Edwards syndrome).
In this case, the ultrasound phenotype of the fetus was mainly correlated with Edwards syndrome. The IVE (voluntary termination of pregnancy) rate is 80%. In this case, the pregnant woman terminated the pregnancy.

CONCLUSIONS

What is interesting about the case is the description of a double aneuploidy involving a sex chromosome trisomy and an autosomal trisomy (incidence <1 in every 30,000 births), combining non-meiotic function in two chromosomes. After reviewing the literature, we only found three cases with 48, XYY + trisomy 18 karyotype. Cytogenetic study in amniotic fluid was the definitive diagnostic test.

Case report

M196

A CASE REPORT: FAMILIAL DIFFERENTIATED (OR NON-MEDULLARY) THYROID CARCINOMA

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BACKGROUND-AIM

Familial differentiated (or non-medullary) thyroid carcinoma is defined by the presence of this neoplasm in two or more first-degree relatives in the absence of other predisposing factors. It accounts for almost 10% of all thyroid cancers. It is a polygenic disorder associated with multiple susceptibility genes, with low to moderate and incomplete penetrance. At least three distinct clinical presentations have been reported, the rarest being the familial syndromic form that is associated with non-thyroid diseases such as Gardner syndrome (APC gene), Cowden syndrome (PTEN gene), Werner syndrome (WRN gene) or Carney complex (PRKARI gene) and accounts for 5% of cases.

METHODS

Case report
46-year-old woman with multifocal follicular variant papillary carcinoma, with a family history of mother and two sisters affected. She underwent total thyroidectomy one year ago. She was referred from endocrinology for genetic study.
A clinical exome panel of genes associated with hereditary cancer and familial non-medullary thyroid cancer such as APC, PTEN, PRKARI, WRN, DICER1 and other susceptibility genes such as HABP2, SRGAP1, FOXE1 TITF-1, MAP2K5 was performed on the Illumina NextSeq 500 platform.

RESULTS

The study showed two variants of uncertain significance in heterozygosis: ATM gene, NM_000051.3: c.7018G>T, pV2340F; and APC gene, NM_000038.5: c.757G>T, pG253C. The APC gene is related to Familial Adenomatous Polyposis Syndrome and 2 to 12% of cases develop thyroid carcinoma, which is usually papillary and more frequent in women. The ATM gene, which participates in DNA repair processes through the ATM-BRCA4-CHEK pathway, has been associated with an increased risk of papillary thyroid cancer in Caucasians and in other studies it has a protective role. The familial genetic study found the same variants in one of the sisters as in the index case and in the other sister and the mother the variant in the ATM gene.

CONCLUSIONS

The results of the study reveal a certain relationship with the pathology under study, although due to the controversies encountered, the clinical significance of these alterations remains unclear. As this disease is not very prevalent and its evidence is limited, it presents a challenge due to the lack of knowledge of its hereditary determinants.

Case report

M197

BILOTHORAX SECONDARY TO CHEST TRAUMA

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BACKGROUND-AIM

Pleural effusions can be a clinical manifestation of pleuropulmonary pathologies or extrapulmonary alterations. Pleural fluids with high concentrations of bile are called bilothorax. In most cases, they are a rare complication of hepatobiliary diseases. Pleural fluid analysis can help determine its origin and appropriate treatment.

METHODS

A 60-year-old man who underwent cholecystectomy in 2004 and with no other relevant history, was admitted due to a crisis of paroxysmal self-limited nocturnal dyspnea and a dry cough without fever. Three days earlier, he was discharged from another center where he was admitted for several rib fractures secondary to left chest trauma. The chest radiograph showed congestive signs, a voluminous left pleural effusion and passive atelectasis with multiple previously reported rib fractures.

RESULTS

A diagnostic thoracentesis was performed to analyze the pleural fluid. According to Light's criteria, it was classified as a predominantly mononuclear exudate. Given the greenish-brown appearance of the fluid, it was decided from the emergency laboratory to measure the hematocrit, obtaining a value of 0.9% with blood values of 37%. In addition, total bilirubin in liquid and serum were 4.37 and 0.5 mg/dL respectively, being diagnosed from the laboratory as a bilothorax. Given the patient's clinical history, direct and indirect bilirubin was quantified resulting in 0.17 and 4.20 mg/dL respectively, thus ruling out the biliary origin of bilirubin and guiding to hemolysis of a possible evolved hematoma secondary to the previous trauma. The patient was treated with an endothoracic drainage tube to evacuate the entire effusion and progressed favorably.

CONCLUSIONS

The most widely used biochemical profile for the analysis of pleural fluids encompasses only the differential count of leukocytes and the determinations of glucose, proteins and LDH. However, other markers could contribute to facilitating its etiology. In this case, by extending the hematocrit determination from the laboratory, the hemothorax could be ruled out, and with the quantification of total and direct bilirubin it was possible to verify that it was a bilothorax at the expense of indirect bilirubin, which led to a hemolytic origin of pleural effusion.

Case report

M198

DABIGATRAN MONITORING BY VISCOELASTOMETRY IN CARDIAC SURGERY

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BACKGROUND-AIM

Direct-acting oral anticoagulant (DOAC) such as dabigatran currently constitute an alternative to classical anticoagulation with coumarin derivatives. Patients undergoing treatment with dabigatran who are to undergo urgent surgical intervention may require immediate reversal with idarucizumab. The techniques for global evaluation of hemostasis have been used to rapidly detect and treat the existence of an alteration in coagulation. However, they cannot detect the presence of DOACs specifically. The ClotPro, a new generation viscoelastometry analyzer, has several tests to overcome this limitation.

METHODS

A 60-year-old male patient with hemophilia A, anticoagulated with dabigatran for atrial fibrillation and advanced heart failure secondary to dilated cardiomyopathy, who is going to undergo heart transplantation surgery

RESULTS

Prior to the intervention, dabigatran quantification was carried out using the chromogenic ecarin test, obtaining blood levels of 342 ng/mL (reference values: 90-184 ng/mL). With the patient in the surgical area, a study was performed using ClotPro viscoelastometry. The result showed an elongated clotting time (CT) in all tests, especially the ecarin test (ECA-test), a thrombin activator derived from the venom of the saw-scaled viper (Echis carinatus) that activates prothrombin from the blood sample. These data are compatible with the presence of dabigatran, for which 5 g. of idarucizumab and 4,000 IU factor VIII for the treatment of hemophilia was administered intravenously. Subsequently, the ClotPro study was repeated, showing the corrected CT in all tests. The patient had a rapid reversal of the coagulation disorder with no evidence of bleeding during heart transplant surgery.

CONCLUSIONS

The monitoring of DOACs can be carried out by indirect and/or direct methods. However, the prolongation of the times in the coagulation study lacks specificity, and the quantification of the anticoagulant levels does not determine their degree of influence on coagulation. Therefore, the implantation of viscoelastometry technology in the surgical area with tests that allow detecting coagulation alterations due to DOACs, can prevent and/or improve the management of bleeding and thrombotic complications in the surgical patient.

Poster Abstracts – EuroMedLab Munich 2021 – Munich, April 10–14, 2022 • DOI 10.1515/cclm-2021-5013
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Case report

M199

DIFFERENTIAL DIAGNOSIS OF CHYLOUS EFFUSION IN BIOLOGICAL FLUID

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BACKGROUND-AIM

The laboratory can support the clinician in identifying the origin and characteristics of biological fluids. In this case, advice was sought on the presence of lymph in a biological fluid extracted from a drain in a patient with carcinoma of the tongue, who had undergone surgery in previous days.
We were referred to the emergency laboratory with a greyish-brown liquid which, after centrifugation, showed a milky sediment and a brown supernatant. We were informed that it was a fluid extracted from a neck drainage of a patient operated on a week ago for a carcinoma of the tongue in which a resection with lymphadenectomy had been performed. They suspect possible contamination with fluid from the thoracic duct vs infection, due to a change in the macroscopic appearance of the drainage fluid and in the patient's symptoms.

METHODS

Based on the SEQC (Spanish Society of Clinical Chemistry) biological quantities commission document "Identification of biological fluids of unknown origin" and the literature, we compare our values with those expected in lymph.

RESULTS

Our fluid has a total protein of 5.1 g/dL, a cholesterol of 108 mg/dL, triglycerides of 222 mg/dL, LDH greater than 4500 U/L and ADA of 192 U/L and an amylase of 12 U/L.
Liquid results // Serum results //Lymph composition // Diagnostic criteria
in pleural fluid
Triglycerides 222 // 141 // >Serum // >110
(mg/dL)
Cholesterol
(mg/dL) 108 // 146 // 65-220 // <200
We were guided by the criteria used for the diagnosis of chylothorax and by the criteria for differentiation of exudates and transudates.

CONCLUSIONS

Analysing the values of the fluid, we can state that it is a fluid of mixed origin.
Exudate in terms of LDH and proteins. The high ADA values can be explained by the empyema, the high leukocytosis that we observed confirms this idea.
On the other hand, the triglyceride and cholesterol values and the appearance after centrifugation allow us to affirm that there was also fluid of lymphatic origin.
This case demonstrates one of the advantages of our hospital's routine emergency laboratory and the importance of the laboratory physician in interpreting the results and performing certain tests after justification.

Case report

M200

BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM WITH CONCOMITANT CHRONIC MYELOMONOCYTIC LEUKEMIA AND INITIAL CEREBROSPINAL FLUID INFILTRATION

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BACKGROUND-AIM

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematological malignancy. Usually, it is characterized by an aggressive clinical course and poor prognosis. We present a case of BPDCN with cerebrospinal fluid (CSF) infiltration and concomitant chronic myelomonocytic leukemia (CMML) in a 70-year old male patient.

METHODS

The standard analytical methods in the workup of hematological malignancies were performed (automated blood count, cytological and histological analyses, flow cytometry, cytogenetic and molecular genetic analyses).

RESULTS

The patient was diagnosed with BPDCN based on a skin biopsy from a lesion on his trunk. He was admitted to our hospital for hematological workup. He showed a pancytopenia with leucocytes of 3.74 (reference range: 3.90-9.90) x109/L, hemoglobin (Hb) of 9.9 (13.5-17.5) x109/L and a platelet count of 102 (140-440) x109/L. The monocyte count was 1.40 (0.20-1.00) x109/L accounting for 37% of all leucocytes. Morphologically, they appeared atypical with several promonocytes. In addition, very few blasts with fine cytoplasmatic vacuolization were detected. In the bone marrow, an infiltration with blasts showing a variety of nuclear shapes and containing fine vacuoles was observed. The flow cytometric immunophenotyping revealed a population of cells positive with CD4, CD56 and CD123 of about 30% of all nucleated cells. This is a typical pattern for blasts from BPDCN. 6% monocytic cells were detected. Based on these results the patient was diagnosed with BPDCN and CMML. Prior to therapy, a lumbar puncture was performed. The cytolomorphological and flow cytometric evaluation revealed an infiltration with the described BPDCN-blasts. Chemotherapy was started and partial remission was achieved. After short time, a relapse occurred and the patient died six months after the diagnosis.

CONCLUSIONS

In this case, the clinical presentation and the flow cytometric analysis were the diagnostic guardrails. Both showed typical features of BPDCN leading to the diagnosis. The concomitant occurrence of BPDCN and CMML has been described. It is assumed to originate from a shared clonal evolution of precursor cells. Involvement of the CSF is especially known for relapsed BPDCN. However, the infiltration of the CSF with blasts before initial therapy is an uncommon finding.

Case report

M201

SOLE DEPENDENCE ON RADIOLOGICAL IMAGING FOR THE LOCALIZATION LEADING TO MISDIAGNOSIS OF A MULTIFOCAL INSULINOMA

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BACKGROUND-AIM

Insulinomas are neuroendocrine tumours that show clinical symptoms mainly due to the autonomous endocrine activity rather than the primary malignancy itself. The localization of a tumour is conventionally done by radiological imaging, but being functional tumours that secret hormones, invasive venous sampling is another means of localization available for insulinomas. However, they are smaller in size at presentation, making localization by imaging a challenge.

METHODS

The patient was clinically and biochemically assessed during the presentation and later subjected to invasive venous sampling for further evaluation.

RESULTS

A 30-year-old divorced woman with three children was referred to the psychiatric unit to evaluate episodic fainting attacks with depressive symptoms worsening for 3-months. She complained of significant weight gain (10kg), and her recurrent fainting attacks fulfilled Whipple's triad. Her basic investigations were within normal limits except for low fasting plasma glucose (2.61 mmol/L; normal: 3.3-5.6). An endogenous organic hyperinsulinemia was confirmed by elevated fasting insulin (1287 pmol/L; normal <174) and C-peptide (1.42 nmol/L; normal: 0.26-1.03) with increased amended insulin-to-glucose ratio (1170 pmol/mmol; normal >53.6). She was subjected to partial resection of the pancreas upon radiological localization of a neoplastic lesion (11x10 mm) at the pancreatic head without pursuing further investigation by selective intraarterial calcium stimulation test (SICST). However, she presented with recurrence of symptoms 3-weeks later, despite the absence of any lesions on postoperative CT. Therefore, a SICST was performed, which revealed a rise of insulin secretion in the proximal splenic artery territory, indicating residual autonomous insulin secretion from the preserved pancreatic body area. Although the patient initially refused repeat surgery, she later agreed due to increasing symptoms and underwent complete resection of the remaining pancreatic mass.

CONCLUSIONS

As surgical excision of the tumour is usually curative in the absence of metastasis, accurate localization of the tumour is of paramount importance in the management. However, sole dependence on radiological imaging for the localization of functional tumours can lead to misdiagnosis of multifocal tumours, as observed in this case, resulting in suboptimal surgical resection. This case highlights the importance of invasive venous sampling in the accurate localization of functional tumours such as insulinoma and detrimental outcomes in the sole dependence on imaging to localize functional tumours.

Case report

M202

ROLE OF S100 IN THE DIAGNOSIS OF BONE MARROW METASTASIS FROM GLIOBLASTOMA: A CASE REPORT

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BACKGROUND-AIM

Glioblastoma (GBM) is the most aggressive central nervous system (CNS) tumor-associated with high mortality. Since systemic treatment often leads to drug-induced toxicity, therapeutic decisions should consider the benefit vs. the impact on the patient's quality of life. For this purpose, the diagnosis of progressive disease is crucial, but it can be difficult due to treatment-induced imaging changes and the lack of reliable non-invasive biomarkers. The S100B protein (S100) is a well-established tumor marker (TM) in the follow-up of melanoma patients. It has also emerged as a biomarker to detect brain injury. However, to date, there is scarce information on circulating S100 concentrations in patients with CNS tumors and their prognostic value.

METHODS

We described the case of a 68-year-old male, diagnosed with GBM, treated with Bevacizumab, who presented an exacerbation of chronic lumbar pain (14 months after the initial diagnosis).

RESULTS

The laboratory tests showed pancytopenia and increased LDH=7112 U/L [<234U/L]. The TMs profile revealed an extremely high concentration of S100=61.93µ/L [<0.20µ/L] and NSE=293ng/mL [<25ng/mL], the rest of TMs (ProGRP, SCC, AFP, PSA, CA 125, CA 15.5, CA 19.9, CYFRA 21.1, TAG 72 and CEA) were within the normal range. The patient did not have kidney failure or liver disease, and other possible causes of false positives were excluded. Both altered TMs are expressed in CNS, indicating the high probability of progression. Thoraco-abdominal CT scan did not show evidence of disease progression, but bone marrow aspiration smear indicates the absence of normal hematopoiesis and marked infiltration of non-hematological cells. Finally, the anatomopathological study characterized the malignant cells (PFAG and OLIG2 positive), confirming the clinical suspicion of metastasis from GBM.

CONCLUSIONS

This case report illustrates the challenging diagnosis of GBM progression. Most patients develop local relapse or neuraxis spread, but extra-neural metastases are extremely rare. To date, only 16 cases of bone marrow metastasis have been reported in the literature. However, this possibility should be considered, and the measurement of serum TMs expressed in CNS (S100 and NSE) may help to early identification of disease progression.

Case report

M203

DETECTION OF PLASMA CELL LEUKEMIA WITHOUT RENAL INSUFFICIENCY. CASE REPORT

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BACKGROUND-AIM

Multiple myeloma (MM) is a mature B cell neoplasm with a monoclonal proliferation of plasma cells in the bone marrow (BM) which synthesize immunoglobulins known as M-component. The clinical features are anemia, renal insufficiency, pathological fractures and hypercalcemia. The patients have increased susceptibility to infections. Following the diagnostic criteria of the World Health Organization (WHO, 2016), it is essential to determine three specific biomarkers: M-component, clonal BM plasma cells and presence of focal lesions on magnetic resonance imaging. These biomarkers are associated with different stages of the disease, ranging from mild forms to symptomatic or even to very progressive and aggressive forms that can evolve into plasma cell leukemia (PCL).

METHODS

Case Report

RESULTS

53-year-old male who in a routine blood analysis: hemoglobin (Hb) 12 g/dl, leucocytosis; total proteins 10.2 g/dl, total calcium 9.7 mg/dl, creatinine 1 mg/dl with a gamma monoclonal peak of 3 g/dl. In the peripheral blood (PB) a viscous layer was observed with the presence of reactive lymphocytes and monocytes.
Few months later, patient was admitted in the hospital with a big laterocervical tumefaction and dyspnea. Then: Hb 9.7 g/dl, leucocytosis and Rouleaux formation in PB. Total proteins were 9.5 g/dl, total calcium 9.2 g/dl, creatinine 1 mg/dl, beta 2 microglobuline 5.82 mg/dl with a gamma monoclonal peak of 4.8 g/dl. Urine showed proteins of 1.660 mg/24h with monoclonal free kappa chain. BM showed a 20% of atypical plasma cells. Diagnosis: MM in transformation on PCL
MM and PCL are diseases characterized by an abnormal proliferation of clonal BM plasma cells and production of monoclonal immunoglobulins. PCL may occur as the terminal phase of MM. It is a much aggressive form with a poor prognosis. The diagnostic criteria is based by the presence of more than 20% circulating plasma cells and more than 2000/ul in PB.

CONCLUSIONS

In this case the patient only had anemia with M-component of 3g/dl. According to WHO criteria, it would not be sufficient enough for MM diagnosis. Although it should be noted that not sufficient test were made to discharge all the diagnostic criteria. Several months later, the patient was diagnosed by PCL as a terminal phase of the MM that he had from the beginning.

Case report

M204

POSTPARTUM HAEMORRHAGE: GUIDED THERAPY USING THROMBOELASTOMETRIC TESTS AT POINT-OF-CARE TESTING DEVICES

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BACKGROUND-AIM

Massive bleeding of any aetiology is a medical emergency that should be treated as soon as possible and in the most targeted manner possible, thus reducing patient morbidity and mortality and the cost of therapy. The performance by the Clinical Laboratory of thromboelastometric tests at Point-of-Care Testing (POCT) devices has been a revolution in aiding the diagnosis of possible associated coagulation disorders and in the targeted therapy of massive bleeding.

METHODS

A 39-year-old pregnant woman of 38+6 weeks was followed up for low birth weight for gestational age. Induction of labour was scheduled, during which emergency caesarean section was performed due to risk of loss of foetal well-being (sustained foetal bradycardia associated with uterine hypertonia that did not respond to intravenous therapy). After the operation and birth of the child, the patient presented postpartum haemorrhage, which was found to be due to disseminated intravascular coagulation (DIC) and suspected amniotic fluid embolism, being in haemorrhagic shock and in need of vasoactive support. She was transfused due to anaemia (Hb 7.9 g/dL) and a thromboelastometric study was requested.

RESULTS

The results of the thromboelastometric study were as follows:
Clotting time of the intrinsic pathway: 529 s (100-240)
Clotting time of the extrinsic pathway: 517 s (38-79)
Maximum clot firmness: 10 mm (50-72)
Fibrin-deficient clot formation
Thus, guided by the thromboelastometry results, clotting factors were replenished with fresh plasma and fibrinogen as well as platelets on up to two times. In total, 6 units of pooled red blood cell, 5 units of fresh frozen plasma, 2 units of pooled platelets, 4 g fibrinogen and tranexamic acid (procoagulant drug) were administered, following the algorithm approved by the Hospital's Multidisciplinary Committee.
At 18 hours, a new thromboelastometric study was performed, the results of which were normal, thus correcting the alteration in coagulation parameters.

CONCLUSIONS

The use of the POCT device for thromboelastometric tests by the Clinical Laboratory has made it possible to confirm the presence of DIC in the patient and to guide the replacement of blood products, allowing its efficient use and correcting the coagulation alteration.

Case report

M205

ACUTE PANCREATITIS INDUCED BY CICLOSPORIN IN HEMATOPOIETIC STEM CELL GRAFT PATIENT.

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BACKGROUND-AIM

A case of tacrolimus-induced acute pancreatitis related to high triglycerides levels has been recently reported. However, underlying mechanisms remain misunderstood. We present here an original case of ciclosporin-induced acute pancreatitis related to high triglyceride levels.

METHODS

Plasma lipase and triglyceride levels were measured by colorimetric enzymatic assay on Cobas 8000 analyzer. Plasma ciclosporin levels were measured by microparticulate chemiluminescence immunoassay on Architect i2000sr.

RESULTS

A 61-year-old male patient received immunosuppressive therapy by ciclosporin following hematopoïetic stem cell graft. Immediate complication included graft-versus-host reaction treated with corticosteroid therapy. Sixteen day after graft, the patient was admitted to the emergency department for confusion and poor condition. Laboratory results revealed elevated plasma lipase levels (4604 U/l), hypertryglyceridemia (33.64 g/l) and major hyperglycemia (13.49 g/l). An abdominal ultrasound showed gall-bladder lithiasis but no main or accessory bile duct dilatation. An abdominal computed tomography scan showed acute necrotizing pancreatitis. These finding led to a diagnosis of acute biliary pancreatitis. Ciclosporin-induced acute pancreatitis was also suspected. A continuous insulin infusion was administered (also aimed at stimulating lipoprotein lipase activity) and ciclosporin was replaced by mycophenolate mofetil, plasma lipase and lipid normalized within 1 week. On Day 28, patient was switched to tacrolimus. Plasma lipase and lipid levels remained within normal values.

CONCLUSIONS

Ciclosporin and tacrolimus are both calcineurin inhibitor immunosuppressants, ciclosporin via cyclophilin-A and tacrolimus via tacrolimus-binding-protein-12. Both cases of pancreatitis induced by these immunosuppressive therapies are related to high triglycerides levels. Hence, this could suggest a mechanism related to calcineurin and lipoprotein lipase inhibition. Considering the widespread use of ciclosporin, it is necessary to be mindful about ciclosporin-induced complications. Further studies are needed to confirm and quantify the risk of ciclosporin-induced acute pancreatitis.

Case report

M206

MULTIFOCAL PHEOCHROMOCYTOMA/PARANGANGLIOMA AND SDHD MUTATION

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BACKGROUND-AIM

Paraganglioma (PGL) and pheocromocytoma (PCC) are rare disorders derived from the neural crest chromaffin tissues. They have a reported anual incidence of 1 in 300000. Germline mutation is detected in up to 40% of patients with paraganglioma/pheocromocytoma (PPGL). The succinate dehydrogenase complex subunit D (SDHD) gene has been implicated as one of the pathogenic genes. SDHD mutations were demonstrated to be associated with sporadic and familiar pheochromocytoma (PGL1). This syndrome is characterized by parasympathetic head and neck PGL (89.0%), sympathetic thoracic PGL (16.0%), and/or PCC (10.5%), with a high incidence of multiple tumors (66.9%) and recurrence of new tumors (58.2%). PGL1 almost always manifests when the SDHD mutation is paternally inherited (imprinted in the father).

METHODS

Urinary Metanephrines and Cathecolamines by High Performance Liquid Chromatography (HPLC) (Agilent® 1100 series).

RESULTS

This case below describes multifocal paraganglioma diagnosed in a 44-years-old male with a history of pain on the right of the neck associated with dizziness during one year. On physical examination, two painful masses on both sides of the neck were obsserved. Biochemical results showed urinary metanephrines and cathecolamines levels in normal range. A contrast-enhanced CT scan revealed two hypervascularized bilateral masses on the bifucartion carotid. These findings were compatible with non secretory paragangliomas. Patient was submitted to genetic testing. The results showed the presence of a heterozygous germline variant in the SDHD gene (c.191_192delTC/p.leu64ProfsX4).
At control, patient presented with uncontrolled arterial hypertension and facial flushing. The biochemical analysis revealed an increase in 24-hour urine Noradrenaline level: 253µg/24h (12-85µg/h). Magnetic Resonance Imaging (MRI) confirmed a mass on the right of adrenal medulla.

CONCLUSIONS

Despite their predominantly benign behavior, SDHD-related PGLs are usually multiple, rare and require a multimodal approach. Genetic testing is recommended in all patients with PPGL to identify disease-causing mutations. These results have implications for diagnosis and prognostication. As SDHD mutation lead generally to develop new PPGLs is important to undergo annual biochimical and imaging examination.

Poster Abstracts – EuroMedLab Munich 2021 – Munich, April 10–14, 2022 • DOI 10.1515/cclm-2021-5013
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Case report

M207

A CASE REPORT: THE IMPORTANCE OF BLOOD GAS IN A SAMPLE FROM THE CORPORA CAVERNOSA FOR DIFFERENTIAL DIAGNOSIS OF PRIAPISM

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BACKGROUND-AIM

Priapism is an urological emergency characterized by a prolonged penile erection in the absence of sexual desire that could have serious long term effects to penile tissue if diagnosis is delayed. It is classified as ischemic, due to venous cavernosal occlusion, and non-ischemic (high-flow), caused by an increased arterial blood flow in them. Blood gas analysis in a sample collected from the corpora cavernosa is required for the differential diagnosis of this condition.

METHODS

A 48-year-old male, cocaine user and without relevant data in clinical records admitted to the emergency department with a 12-hour sustained and painful erection. He didn't take drugs such as phosphodiesterase type 5 inhibitors and had no traumas. Patient reported a previous episode that dissapeared spontaneously.

RESULTS

Blood-gas analysis of blood collected from the corpora cavernosa revealed a pH of 6.812, pCO2 of 115 mmHg, pO2 of 19 mmHg and lactate level of 21 mmol/L, data consistent with hypoxia, ischemia and acidosis.
On treatment, under the benefits of a dorsal penile block, the patient was treated with cavernosal aspiration and irrigation not achieving detumescence. Then he was injected adrenaline, which was successful.

CONCLUSIONS

Sickle cell disease is the most common cause of ischemic priapism. Other causes include solid tumours, neurological disorders and medication such as antipsychotics, as well as drugs such as cocaine and cannabis. Although the use/abuse of cocaine has been associated with priapism in the literature, this association could not be confirmed in our case.
Ischemic priapism is an emergency disease that urgently requires management, sometimes surgical, to reduce pressure in the corpora cavernosa. In our case, penile cavernosal blood data showed acidosis and hypoxia. Thus he was diagnosed with ischemic priapism. STAT laboratory plays a critical role in the differential diagnosis of priapism with the analysis of blood gas of blood aspirated from the corpora cavernosa.

Case report

M208

CLARKSON'S DISEASE IN A PATIENT WITH COVID-19: IMPORTANCE OF THE CLINICAL LABORATORY IN THE DIAGNOSIS OF INFLAMMATORY CARDIOVASCULAR DISEASES

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BACKGROUND-AIM

With coronavirus disease 2019 (COVID-19) pandemic, we are discovering that severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has properties to induce a dysregulated immune response that exceed the simple respiratory infection. Several cases of immune diseases have been reported concomitantly with SARS-CoV-2 infection such as systemic capillary-leak-syndrome (SCLS), also known as Clarkson's disease, is a rare immune disorder that evolves with episodes of shock. We report a patient who presented a COVID-19 infection concomitantly with a SCLS.

METHODS

A 38-year-old man with no medical history was referred to the emergency department for diffuse abdominal pain and malaise. The patient reported diffuse myalgias, shortness of breath, with intense pain in both legs. Asthenia and anorexia that have been increasing, generalized abdominal pain, predominantly in the epigastrium. Generalized edema. No nausea, vomiting, diarrhea, no other symptoms. His condition quickly progressed to shock, with blood pressure of 86/57mmHg, respiration rate 28pm, 123bpm and a body-temperature of 38ºC. The patient was admitted in ICU.

RESULTS

Laboratory tests revealed lactic-acidosis (pH 7.21 and lactate 40mg/dL) and acute kidney failure (creatinine 3.8mg/dL, calcium 8.7mg/dL and phosphorus 10.3mg/dL). A blood count showed haemoconcentration (haemoglobin 23.6g/L and haematocrit 70.0%). Leukocytosis (36.5x109/L), D-Dimer (1342ng/mL) and thrombocytopenia. Low levels of total-protein (3.5g/dL) and albumin (1.7g/dL) with high levels creatine-kinase (39.000U/L) and rhabdomyolysis. Echocardiography showed normal myocardial function with signs of hypovolaemia. Chest-CT-scan revealed a few ground glass opacities. SARS-CoV-2 infection was confirmed by RT-PCR assay by means of an oropharyngeal swab. Bacterial blood cultures: negatives.

CONCLUSIONS

Diagnosis of SCLS was made by the association of hypotension, hypovolaemia, haemoconcentration and hypoalbuminemia in the context of COVID-19 pandemic. SCLS is a rare disorder that can be secondary to blood malignancies, immune disorders, toxics, medication, infections (especially viruses responsible for respiratory-tract-infections) or idiopathic. Recently a SCLS during the SARS-CoV-2 infection has been described. SCLS is the consequence of secretion of inflammatory mediators triggered in response to SARS-CoV-2 leading to an increase in vascular permeability via disruption of adherens junctions that disjoin endothelial cells.

Case report

M209

TEMPORAL ASSOCIATION BETWEEN HAMPTON´S HUMP PULMONARY EMBOLISM AND FIRST-DOSE CHADOX1 NCOV-19 VACCINE IN A PATIENT WITH ACTIVATED PROTEIN C RESISTANCE

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BACKGROUND-AIM

The ongoing coronavirus disease 2019 (COVID-19) pandemic has devastated economies and caused unprecedented challenges to healthcare and food systems around the world. In March 2021, vaccination using the ChAdOx1 nCov-19 vaccine (Oxford-AstraZeneca) was paused in several European countries because of unusual thrombotic events observed after vaccine administration, sharing distinct clinical features (thrombosis in uncommon locations, thrombocytopenia, predominantly observed in young adults and women). Subsequently, vaccine-induced immune thrombotic thrombocytopenia (VITT), a variant of heparin-induced thrombocytopenia (HIT), was identified as a cause of thrombosis in these patients.

METHODS

Here, we report on the radiological and laboratory diagnostic workup of an otherweise healthy 58-year-old man with extensive pulmonary thromboembolism (PE) 18 days following the first dose of the ChAdOx1 nCov-19 vaccine.

RESULTS

A 58-year old man presented to his practitioner with right-sided pleuritic chest pain, dyspnoea, and fatigue 18 days following the first dose of the ChAdOx1 nCov-19 vaccine. At the time of anamnesis we could not identify risk factors for venous thromboembolism, however, chest auscultation revealed a reduced air entry over the right lower quadrant. A chest radiograph was done, followed by computed tomography pulmonary angiography (CTPA), with the latter showing a prominent Hampton´s hump in the right lower lobe indicative of subpleural pulmonary infaction. The only abnormal blood tests reported where a mild leukocytosis of 11.62 G/L (normal range 4.00-10.00 G/L), a markedly elevated D-dimer level of 7.53 µg/mL (normal range < 0.5 µg/mL), and a previoulsy unknown activated protein C (APC) resistance of 1.3 (normal range >= 1.8). Of note, neither thrombocytopenia nor antibodies against platelet factor 4-polyanion complexes (PF4) could be observed. Furthermore, we failed to demonstrate Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection as indicated by repeatedly negative nasopharyngeal swab testing.

CONCLUSIONS

Here we report on the temporal association between the first dose of the ChAdOx1 nCov-19 vaccine and extensive PE in an otherwise healthy patient with APC resistance, however, further investigation is needed to prove causality.

Case report

M210

A CASE REPORT ON GROSSLY ELEVATED ALKALINE PHOSPHATASE IN A PREGNANT WOMAN WITH PREECLAMPSIA AND GESTATIONAL DIABETES

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BACKGROUND-AIM

Alkaline phosphatase (ALP) is a ubiquitous membrane-bound ectoenzyme with several isoforms in the liver, bone, intestine, and placenta. Liver isoform mainly contributes to the serum ALP activity in a healthy adult. However, ALP gradually increases during pregnancy, owing to the placental ALP isoenzyme that typically mounts to 2-3 times its pregestational value, rendering it less useful as a hepatobiliary indicator in pregnant women.

METHODS

The patient was clinically and biochemically assessed during the presentation and later subjected to fractionated ALP analysis.

RESULTS

A 29-year-old mother of one child with gestational diabetes was admitted to the obstetrics unit to induce labour at 40-weeks of gestation. She had a blood pressure of 140/100mmHg on admission prompting, screening for preeclampsia. Her initial investigations were within normal limits except for the grossly elevated ALP [2125 IU/L (38-229)], while other liver and bone parameters were found to be normal. The fractionated ALP analysis based on heat-stability revealed a 93% residual ALP activity following the incubation of serum at 600C for 30 minutes, indicating significant contribution by heat-stable placental isoenzyme to serum ALP activity (2125x0.93=1979 IU/L). She had an uncomplicated vaginal delivery of a healthy baby with no postnatal complications. The mother's ALP level was serially monitored and noted to fall gradually during the postpartum period, which reached normal limits for non-pregnant women within 10-weeks (79 IU/L).

CONCLUSIONS

About 3% of women develop a liver disease during pregnancy (hyperemesis gravidarum to eclampsia or acute fatty liver). Therefore, it is essential to differentiate between benign and pathological causes of liver enzyme derangements in cases with gross ALP elevation. Hypotheses suggest a correlation of elevated ALP to large-for-gestational-age, preterm delivery, gestational diabetes, preeclampsia, and possible placental insufficiency. However, the impact of marked elevation of placental ALP on the overall pregnancy outcome remains elusive. Thus, active identification of extreme elevation of placental ALP and close monitoring of fetomaternal sequalae can unmask the underlying pathologies not yet well understood.

Case report

M211

A CASE REPORT ON INCONSISTENT POSTMORTEM THYROID FUNCTIONS BETWEEN FEMORAL BLOOD AND VITREOUS FLUID BIOCHEMISTRY

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BACKGROUND-AIM

Postmortem biochemistry can provide important information in determining the cause of death (COD). Out of postmortem specimens, vitreous fluid is ideal for postmortem biochemical analysis, as it is relatively isolated and less affected by postmortem changes (redistribution, hemoconcentration). However, equilibration of some analytes between blood and vitreous fluid can be affected by its anatomical location, as observed in this case, where postmortem femoral blood and vitreous fluid thyroid functions were used to conjecture premortem thyroid status of the patient in the absence of premortem values.

METHODS

The postmortem specimens of femoral blood and vitreous fluid were obtained during the autopsy and analysed for thyroid hormones in the absence of premortem thyroid hormone values.

RESULTS

A 28-year-old pregnant woman admitted at 26-weeks of gestation due to tachypnea and palpitations for 3-days. She had tachycardia (200bpm), with supraventricular-tachycardia on electrocardiogram, and poor left-ventricular function on echocardiography. She underwent an emergency hysterotomy to terminate her pregnancy but suffered a sudden death 6-hours after surgery. During the postmortem to ascertain her COD, vitreous biochemistry revealed a hyperthyroid picture with suppressed TSH and elevated free-T3 [TSH: 0.108mIU/L(0.465-4.68), free-T4: 13.22pmol/L(10-28.2), free-T3: 12.74pmol/L(4.26-8.1)], while femoral blood had a euthyroid picture [TSH: 1.32mIU/L, free-T4: 13.3pmol/L, free-T3: 4.54pmol/L]. Postmortem thyroid histology showed detached follicular-epithelial-cells (autolytic changes), excluding autoimmune thyroiditis causing hyperthyroidism thus supraventricular-tachycardia as the COD. Her COD was confirmed as acute on chronic myocarditis by postmortem cardiac histology.

CONCLUSIONS

Based on the clinical presentation, hyperthyroidism was a differential diagnosis in this case leading to postmortem thyroid investigations. T3-toxicosis on vitreous biochemistry was confounding with detached follicular-epithelial-cells mimicking lymphocytes, misleading towards autoimmune thyroiditis. Differences in thyroid hormone transportation between compartments explain the inconsistency of thyroid status between femoral blood and vitreous fluid. This case highlights the need to interpret postmortem biochemistry cautiously and arrive at conclusions with a holistic approach. Due to the lack of literature on the correlation of postmortem to premortem biochemistry, the postmortem specimen type best representative of premortem thyroid function requires further research.

Case report

M212

MONOCLONAL GAMMOPATHY DEBUTING WITH THROMBOTIC MICROANGIOPATHY IN RENAL TRANSPLANT PATIENT

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BACKGROUND-AIM

Thrombotic Microangiopathy (TMA) is a not very prevalent heterogeneous group of clinical syndromes that can cause organ damage (e.g. renal), being secondary to vascular endothelial injury. It's usually diagnosed on the basis of its peripheral manifestations (mainly microangiopathic haemolytic anaemia, schistocytosis and thrombocytopenia), but definitive diagnosis requires renal biopsy. Monoclonal gammopathy of renal significance (MGRS) may act as a trigger for an underlying genetic predisposition for development of TMA.

METHODS

A 53-year-old male with chronic kidney disease of unknown aetiology, right and left nephrectomy for clear cell and papillary renal carcinoma respectively, with haemodialysis and renal transplant.
In 2020, creatininaemia and proteinuria increased markedly and patient was studied.

RESULTS

The most important analytical results were:
- Peripheral blood smear: schistocytes (1.5%)
- LDH 444 U/L (0-250)
- IgA 1044 mg/dL (40-350)
- Monoclonal peak (0.6 g/dL) in beta region (serum capillary electrophoresis) and monoclonal bands IgA and lambda (serum immunofixation electrophoresis)
- Free light chains (FLC): kappa 19.9 mg/dL (0.33-1.94)
lambda 89.6 mg/dL (0.57-2.63)
lambda/kappa 4.5
- Proteinuria 4.966 g/24h (0-150)
- Negative: Bence-Jones proteinuria, autoimmunity and complement studies

Differential diagnoses included: typical/atypical haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, drug nephrotoxicity, lymphoproliferative syndrome, active acute renal damage due to antibodies and obstructive component.
Biopsy of the renal graft showed TMA in 15.6% of the 32 glomeruli biopsied.
The bone marrow aspirate showed plasma cell infiltration (11.5%; 99.5% pathological phenotype) and the rapid increase in proteinuria suggested TMA as secondary to a MGRS.
In renal transplant patient, the definitive differential diagnosis of TMA requires tissue's examination by electron microscopy.
Finally, TMA was assumed to be associated to MGRS. So, patient began targeted therapy for monoclonal disease.

CONCLUSIONS

This is a particular case of a highly complex patient in which the involvement of the Clinical Laboratory is important as it helps to make differential diagnoses, monitoring FLC, and to guide the treatment.

Case report

M213

HEAVY METAL INTOXICATION IN AN INDIVIDUAL WITH ANEMIA AND NEUROPSICHYATRIC SYMPTOMS

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BACKGROUND-AIM

Lead poisoning is the most common metal intoxication and may appear with toxicity symptoms of variable severity depending mostly on whether exposure is acute or chronic. The main sources reported in our area are lead-based paint and water pipes in old houses, ceramics or clay products (leaded glazes) and game meat consumption.
Lead is absorbed into the body mainly through the lungs or gastrointestinal tract and is excreted through the kidneys. Symptomatology may vary from anaemia and abdominal pain to arthralgia, fatigue, neuropsychiatric symptoms.

METHODS

Clinical case description.

RESULTS

A 53-year-old man attended the Emergency Room for abdominal pain during the last two months, fatigue, dysuria, important weight loss and anaemia (Hb: 8.8 g/dL; MCV: 87.3 fL). Also, red blood cells presented basophilic stippling, which indicated a possible lead poisoning.
Blood lead was measured by inductively coupled plasma mass spectroscopy (ICP-MS NexION 300X, PerkinElmer) using Rh as internal standard. Its concentration was 332.4 µg/dL. Urine porphyrins were also measured, yielding a concentration of 608 nmol/mmol creatinine. Other heavy metals were not found.
Treatment with EDTA and dimercaprol was started. The patient referred being a regular consumer of fermented tea of Asian origin. A high concentration of lead in that tea was found, while undetectable concentrations were found in the vessel or drinking water. His wife and two children had also blood lead measured, yielding high results: 135.0 µg/L (wife), 55.2 µg/L, 48.7 µg/L (children), although none of them presented any related symptom. A periodic analytical follow-up was carried out both in whole blood and urine.

CONCLUSIONS

Clinical manifestations due to lead poisoning are highly variable as well as the different sources of exposure. Lead represents the most common metal intoxication, which makes it of special interest in individuals with unspecific neuropsychiatric symptoms and anaemia, since it is toxic to zinc–dependent enzymatic systems and interferes with calcium metabolism. This way, a good anamnesis and analytical determination are essential for the rapid action towards eliminating the source of exposure along with its treatment with chelating agents, if appropriate.

Case report

M214

DIAGNOSIS OF MALIGNANT NEOPLASIA IN PLEURAL FLUID

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BACKGROUND-AIM

Pleural fluid is found in the pleural cavity and serves as a lubricant for lung movement during breathing. Under physiological conditions, is an ultrafiltrate of plasma clear in appearance that occupies a volume between 1 -10 ml. When there is an imbalance between its formation and reabsorption, it accumulates causing a pleural effusion. One type of pleural effusion in 15-35% of cases, usually caused by increased vascular permeability, is malignat.

METHODS

A 75 years-old man came to the emergency room with progressive dyspnea and right pleural effusion which, given his history, was interpreted as a decompensation of heart failure. Despite treatment, no radiological improvement was observed during hospitalization, so the study was completed with a thoracic CT scan that suggested primary pulmonary neoplasic pathology.
It was decided to complete the study with a thoracentesis sent to the laboratory for biochemical and microbiological analysis and a cell count.

RESULTS

In the laboratory a hematic pleural fluid, which does not depend on the puncture technique, was processed by the hematology analyzer. This showed 680.000 red blood cells/μL later confirmed by microscopic cell counts and resulting in a hematocrit of 7%. The low hematocrit (<10% of total blood) rules out the possibility of hemothorax (it should be >50%) and suggests the possibility of pulmonary infarction or malignant neoplasm, so it is decided to perform a pleural biopsy.
In pathological anatomy the complementary studies are positive CAM5.2, CK7, P40 and CK5/6 showing atypical cells compatible with squamous cell carcinoma. This abundant right pleural effusion with multiple pseudonodular and nodular thickenings suggest metastasis and finally diagnosing a stage IVa pulmonary epidermoid neoplasm.

CONCLUSIONS

Biochemical and microscopic analysis of pleural fluids provides valuable information for the diagnosis of different pathologies. In addition, knowing the hematocrit makes it possible to rule out and confirm diseases.
It is essential that the laboratory suggest a possible cause of the pleural effusion, to guide the relevant diagnostic test, to detect an unsuspected tumor pathology reducing the search time and implementing the therapy as soon as possible.

Case report

M215

LATE-ONSET CONGENITAL ADRENAL HYPERPLASIA: A CASE REPORT

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BACKGROUND-AIM

Case report of late-onset congenital adrenal hyperplasia (LOCAH), based on clinical, biochemical and genetic diagnosis.

METHODS

Congenital adrenal hyperplasia (CAH) is one of the most common diseases in pediatric endocrinology. It is a family of autosomal recessive disorders due to defects in one of the enzymatic steps required for cortisol synthesis. Deficiency of the 21-hydroxylase enzyme accounts for 95% of cases and results in accumulation of precursors proximal to the blockage (progesterone and 17-OH-progesterone) and shunting towards androgen production. The severity of the disease correlates with the degree of enzyme involvement, which depends on the type of mutation occurring in the CYP21A2 gene. In LOCAH, enzyme activity is reduced but is sufficient to maintain normal glucocorticoid and mineralocorticoid secretion at the expense of excessive androgen production. The clinical picture is variable: early pubarche, hirsutism, oligoamenorrhea, acne and accelerated growth with tall stature in childhood, although early closure of the epiphyses producing short stature.

RESULTS

A six years old girl presented to her pediatrician for the appearance of acne, bilateral breast enlargement, vaginal discharge, pubic hair and pronounced increase in height. An anteroposterior radiograph of the wrist showed bone age of 8 years and 10 months, and abdominal-pelvic ultrasound showed uterus and ovaries of adequate size for the chronological age of the patient. Suspecting precocious puberty, LHRH test was requested, obtaining a LH/FSH ratio of 0.43 (<1) at 60 min, which ruled out the diagnosis. The patient was then screened for CAH. Baseline 17-OH-progesterone determination was elevated: 9.36 ng/ml (> 5). Likewise, the ACTH test revealed a peak of 17-OH-progesterone > 25 ng/ml (>10-15). Both values were indicative of 21-hydroxylase deficiency. After biochemical diagnosis, the presence of the Val281Leu mutation in homozygosis was confirmed by sequencing of the CYP21A2 gene, both parents being heterozygous.

CONCLUSIONS

Currently, in addition to the clinical and biochemical diagnosis of CAH, molecular diagnosis has been consolidated as a tool for the confirmation of this clinical entity, since genotyping is essential to detect mild forms of the disease and to provide genetic counseling. However, the gene is highly polymorphic and adequate interpretation of the variants detected by sequencing must be ensured.

Case report

M216

LIQUID RUBBER INTOXICATION: A CASE REPORT

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BACKGROUND-AIM

Waterproofers are water isolators and are used in surface coatings or to seal leaks. Currently liquid waterproofing is one of the most widely used systems due to its simple application. Liquid rubber is a type of waterproof agent, in its composition there are mixtures of organic compounds such as xylene(30-50%), ethylbenzene(0-10%), and isobutanol(0-1%) among others.

METHODS

A case is presented of a 53-year-old man who lost consciousness while performing septic tank waterproofing with liquid rubber. Approximate exposureof 1h30'. The patient was oxygenated and ventilated at the scene of the accident; hydroxycobalamin was administered and he was transferred to the hospital.

RESULTS

The acute poisoning protocol includes physical examination, regular blood analysis, urine drug profile, radiological tests and electrocardiogram. Laboratory findings: leukocytosis with a predominance of polynucleated cells (13.21*10^9/L,[4.80-10.80]), slightly increased glycemia (112mg/dL[74-100] and uremia (56mg/dL [10-50]). Arterial O2 saturation 97.8%[95-99], lactate 2.3 mmol/L[0.5-2.2], other blood gas parameters within normality. Urine sample: dark purple color, all parameters of the strip altered and presence of abundant calcium oxalate crystals. A negative result for urine drug test was obtained. Analytical control after 12h showed normalization of the parameters. No presence of acidosis, kidney or liver failure so he is discharged.

CONCLUSIONS

The determination of organic compounds in blood/urine in intoxications is complicated, mainly due to the lack of knowledge of the responsible substances and because it must be performed within the first hours of exposure due to their rapid elimination, so these tests are generally not available in emergency laboratories. At high concentrations, the action of isobutanol vapors is mainly narcotic and can cause unconsciousness. The alteration of urinary parameters and the presence of oxalate crystals is due to the interference of hydroxycobalamin (intense red color), which makes the correct assessment impossible. Cyanokit (hydroxocobalamin) should be administered when cyanide poisoning is suspected (fires, ingestions) while is not useful in other poisonings.

Case report

M217

THYROID HORMONE RESISTANCE DUE TO A THRß GENE MUTATION. A CASE REPORT.

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BACKGROUND-AIM

Mutations affecting the THRß gene, encoding the nuclear receptor for triiodothyronine (T3), are the most frequent cause of thyroid hormone resistance (THR). Both, pituitary thyrotropic cell and other organ receptors can be affected, sometimes presenting thyroid dysfunction with elevated peripheral levels of thyroid hormones (TH) and unsuppressed thyrotropin (TSH).

METHODS

A 40-year-old woman presented to our hospital with swelling on the right side of her neck and no personal history of interest suggestive of multinodular goiter after examination.

RESULTS

Blood tests showed a minimally elevated free thyroxine (fT4) 1.8 ng/dL [0.85-1.85] and a normal TSH 1.8 mU/mL [0.3-4.20]. Thyroid ultrasound showed a nodule in the right thyroid lobe compatible with a cyst and no signs of malignancy after cytological study. A week later a new thyroid function test was performed, which showed a similar pattern to the previous one, and the pituitary hormone study was completed (including free alpha subunit) without findings of interest. The gamma scan revealed an image compatible with an overactive goiter and a 'cold' nodule in the lower right lobe. A total thyroidectomy was performed six months after the initial visit. Substitutive treatment with levothyroxine was subsequently initiated, initially with a dose of 137 μg/day, achieving TSH levels of 46 mU/mL; the dose was increased to 175 μg/day, but TSH remained between 15.8 and 26.8 mU/mL with fT4 levels between 1.8 and 2.3 ng/dL. When the previous thyroid function pattern persisted, the protocol established in the laboratory to detect analytical interferences of TSH was applied and resulted negative. In view of THR suspicion, a genetic study was performed and confirmed the presence of a heterozygous mutation c.1286G>A; in exon 10 of the THRß gene.

CONCLUSIONS

The diagnosis of THR is not simple since there are several known mutations in the THRß gene that cause pituitary or peripheral resistance with variable clinical presentation. The present case is of an asymptomatic patient with goiter (the most common initial finding in THR) and TH elevation with unsuppressed TSH. Given the characteristics of goiter, she underwent a total thyroidectomy, but previously, in view of the thyroid function tests profile, the laboratory completed an analytical study to rule out an autoimmune process or TSH-producing tumor. The difficulty of adjusting the substitutive treatment increased the suspicion of a possible THR; previously, the laboratory had to rule out analytical interferences in a reliable way. The mutation detected in the index case is already known, with a dominant transmission pattern, so thyroid function was analyzed in first-degree relatives; four showed a hormonal profile compatible with THR and the genetic study confirmed the presence of the mutation in heterozygosis in three of them. In the affected members it will be necessary to perform a clinical and individualized follow-up of thyroid function since it has been described that the same mutation can cause different clinical manifestations.

Case report

M218

MINERALOCORTICOID HYPERTENSION: A CASE REPORT

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BACKGROUND-AIM

Hypertension, hypokalemia and metabolic alkalosis should make us suspect an excess of mineralocorticoids and is known as mineralocorticoid hypertension. The most common cause is probably primary aldosteronism, but the differential diagnosis included also renal artery stenosis, Liddle's syndrome (LS), Cushing's syndrome (CS), 11ß or 17α-hydroxylase deficiency, adrenal tumour, ectopic ACTH secretion, etc. A case that debuted with this triad is presented and discussed from the laboratory's point of view.

METHODS

Cas report.

RESULTS

33-year-old woman, with no relevant history, who visits her family doctor for generalized discomfort of a few months of evolution and edema in the lower extremities. She detected hypertension (147/105 mmHg) and was referred to Nephrology for study. In the general analysis, hypokalemia and metabolic alkalosis are observed, echo-Doppler rules out renal artery stenosis and is oriented as hyperaldosteronism versus LS.
In the preliminary study of the adrenal glands, serum aldosterone was at the lower limit of normal, and renin and metanephrines were normal. Hyperaldosteronism was thus ruled out and, due to the age of the patient, and, although there was no family history of hypertension or hypokalemia, LS was diagnosed and treated as such. Later, when she reported weight gain, menstrual irregularities and some degree of hirsutism, an extended hormonal analysis revealed low ACTH, increased serum and urinary cortisol, as well as an excess of serum deoxycorticosterone. The patient was questioned about the administration of exogenous corticosteroids and it was ruled out. Two consecutive cortisol suppression tests were then performed, with 1 mg and 8 mg dexamethasone (DXM), respectively, without observing suppression, and imaging tests were requested.

CONCLUSIONS

In this case, before the definitive diagnosis by computed tomography and histology (adrenal carcinoma), the lab data could already hint at it: the hormonal profile indicated a glucocorticoid-secreting adrenal tumour, since normal aldosterone and renin ruled out hyperaldosteronism and LS; low ACTH levels ruled out Cushing's disease, ectopic ACTH secretion, and 11ß or 17α-hydroxylase deficiency; and the excess of steroid precursors in a strange pattern could suggest us malignancy.

Case report

M219

D-LACTIC ACIDOSIS IN SHORT BOWEL SYNDROME - A CASE REPORT

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BACKGROUND-AIM

D-lactic acidosis is a rare complication seen in patients with short bowel syndrome (SBS) or other malabsorption syndromes. It is due to bacterial fermentation of unabsorbed carbohydrates in the colon and the change in intestinal flora that produce D-lactate. The main clinical is characterized by neurological symptoms and metabolic acidosis. Treatment includes bicarbonate, restriction of carbohydrates, and antibiotics to eliminate intestinal bacteria that produce D-lactic acid.

METHODS

We report the case of a 41-years-old man with SBS secondary to acute intestinal ischemia with a significant loss of absorptive surface area of the gut. Following surgery, patient was discharged with parenteral nutrition at home.
In a medical review the blood test revealed metabolic acidosis. Despite this, the patient did not present any neurological symptoms. Clinical history and lab tests led to suspect D-lactic acidosis secondary to SBS, although diagnosis should be confirmed with D-lactate levels.

RESULTS

Laboratory tests showed metabolic acidosis and elevated anion gap: ph 7.258 (7.35-7.45), HCO3 16.9 mmol/l (26-32), pCO242 mmHg (41-51), anion GAP 15.79 mEq/L (7-14).
L-lactic concentration was normal and other findings were not detected.
Lactic acid exits as two enantiomers, D (dextrorotatory) and L (levorotatory), although is L-lactate the main form involved in lactic acidosis in human because of the lack of the enzyme D-lactic acid dehydrogenase. Both D and L-lactate can be produced by the microbiota in the gastrointestinal tract depending of different bacterial species. The reason of the production of D-lactate in patients with SBS is the loss of absorption of most simple carbohydrates which are fermented by bacterial flora.
Normally, in routine lab exist assay to analyze L-lactate. The method to measure D-lactate is a special enzymatic assay which contain D-lactate dehydrogenase. The result obtained in this patient was 0.72 mmol/L (< 0.25 mmol/L) and this confirmed the diagnostic of D-lactic acidosis.

CONCLUSIONS

D-lactic acidosis should be suspected in a patient with SBS and elevated anion GAP metabolic acidosis and normal L-lactate levels.
Special assays are require to measure levels of D-lactate. However, early identification is very important for an appropriate treatment to correct metabolic acidemia and prevents further recurrences.

Case report

M220

CASE OF SEVERE HYPOCALCEMIA AS DEBUT OF COELIAC DISEASE

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BACKGROUND-AIM

Hypocalcemia is a relatively common finding in medical practice. Sometimes the cause is obvious, other times its identification requires an exhaustive study. We describe a case of a severe hypocalcemia as a marker of coeliac disease.

METHODS

Outpatient of 39 years – old puerperal woman, with a prior history of persistent iron deficiency anaemia, folate and vitamin B12 low levels, sciatic and low back pain, pelvic girdle weakness and postural instability for gaiting suffering paresthesias in lips, hands and feet, eyelids tremor and occasional speech difficulties is referred to be follow up by our Hospital's Neurosurgery Department. In the analysis we detected a critical result of calcium: 1,32 mmol/L (reference range (RF): 2,12 – 2,62 mmol/L) with normal albumin level: 4,3 g/dL (RF: 3,4 – 4,8 g/dL) which was notified, accordingly to our protocols, to her doctor.

RESULTS

In a second analysis we found: hypocalcemia (<1,25 mmol/L), mild hypomagnesaemia (0,66 mmol/L; RF: 0,74 – 1,07 mmol/L), low ferritin (8 ng/mL; RF: 15 – 200 ng/mL), deficient calcidiol (<10 nmol/L; sufficient >50 nmol/L), high PTH level (0,014 pmol/L; RF: 0,0002 – 0,0009 pmol/L), low prothrombin time (73,6%; RF: 80 – 100%) and a factor X deficiency (47%; normal: 65– 135%). Physical examination revealed positivity in the Trousseau manoeuvre. She denied diarrheal syndrome or intestinal discomfort only reported sporadic gastric reflux episodes in the last few months. Reviewing the patient's medical history, the doctor suspected that both iron deficiency such as severe hypocalcemia may be a result of malabsorption due to probable coeliac disease.
In a complementary study: bone densitometry was significant for osteoporosis, bone scan confirmed osteomalacia, IgA antitransglutaminase antibodies (IgA anti-tTG) were positive and the duodenal biopsy was subjective of coeliac disease and Helicobacter pylori infection was detected.
After 6 months of gluten – free diet, the level of IgA anti-tTG suffered a marked reduction and calcium and the rest of laboratory parameters normalized.

CONCLUSIONS

The case presented is a clear example that in the face of a severe hypocalcemia with a persistent iron deficiency and osteomalacia, a malabsorption syndrome should be suspected being coeliac disease one of the most frequent causes.

Case report

M221

CETUXIMAB-INDUCED ANAPHYLAXIS – THE IMPORTANCE OF MEASURING IMMUNOGLOBULIN E α-GAL: TWO CASE REPORTS

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BACKGROUND-AIM

Cetuximab is a chemotherapeutic drug used for colorectal cancer. Allergic reactions, ranging from mild to severe, even causing anaphylaxis, have been reported. Therefore, it is of utter importance to recognize these allergic reactions in order to prevent anaphylaxis and other severe complications that may end fatally. Cetuximab-specific immunoglobulin E (IgE) directed towards galactose-α-1,3-galactose (α-Gal) which is part of both Fab segments of cetuximab-specific antibodies, may be found in patients not receiving cetuximab, because of the normal presence of α-Gal in nonprimate mammals tissue. These antibodies are produced after meat consumption that contain glycans, hence causing allergic reactions after cetuximab administration. Hereby we present two cases of cetuximab-induced anaphylaxis from the period when specific IgE α-Gal was not routinely measured prior to cetuximab application.

METHODS

Two male patients, aged 68 (P1) and 62 years (P2) developed serious complications after cetuximab application. P1 experienced a cardiorespiratory arrest after the first cetuximab application, while P2 developed an anaphylactic shock after the fifteenth application. Blood samples were drawn few weeks after the anaphylaxis occured, collected in 5-mL serum tubes with clot activator and centrifuged at 3040 g for 10 minutes. Specific IgE α-Gal antibodies (ImmunoCAP^{TM} Specific IgE) were determined by fluoroenzyme immunoassay on the Phadia 100 analyzer (Phadia AB, Uppsala, Sweden). Value of 0.35 kU/L is recommended as the cut-off.

RESULTS

Specific α-Gal IgE antibodies were present in serum of both patients. Specifically, for P1 specific IgE α-Gal was 1.34 kU/L (grade=2), while for P2 specific IgE α-Gal was 6.30 kU/L (grade=3).

CONCLUSIONS

Anaphylactic reaction in both patients was caused by the presence of specific α-Gal IgE antibodies. These cases emphasize the importance of measuring cetuximab-specific IgE antibodies prior to drug application, in order to prevent side-effects, which can be life-threatening. Therefore, in our hospital setting, in agreement with physicians, prior to cetuximab application, all patients are tested for the presence of α-Gal IgE antibodies. In the case of an initial negative antibodies result and no signs of allergic reaction, measurement is repeated after the third, sixth, ninth and twelfth cetuximab application. In patients with positive α-Gal IgE antibodies, cetuximab is contraindicated.

Case report

M222

BURNING MUSCLE – A CLINICAL CASE OF HEATSTROKE WITH RHABDOMYOLYSIS

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BACKGROUND-AIM

Heatstroke is a life-threatening injury requiring neurocritical care, characterized by central nervous system dysfunction, multiorgan failure, and extreme hyperthermia, in the setting of exposure to hot weather or extreme physical exertion.
AIM: Case report presentation.

METHODS

CLINICAL REPORT: 16-year-old boy was admitted in the Paediatrics Emergency Room for malaise, tiredness and increase of his dyskinesias crisis with 1-day evolution, after spending a day at a river beach. Past history of Psychomotor Development Retardation, movement disturbance with dyskinetic crises. He had been hospitalized twice with dyskinetic crises complicated by Acute Kidney Injury (AKI) and rhabdomyolysis. Clinical observation revealed dehydration, high fever and upper limb dyskinesia. Analytically, leucocytes 35,4x109/L, creatinine (Cr) 1.61mg/dL, Creatine Kinase (CK) 4549U/L, Troponin (TnT) 32ng/L, hypernatremia and hypokalaemia. SARS-CoV-2 RT-PCR test was negative. Being diagnosed with hypernatremic dehydration and prerenal AKI owing to a heatstroke with rhabdomyolysis, an aggressive fluid therapy was inducted.

RESULTS

The next day, despite the good clinical evolution and the resolution of dyskinesias, the patient was still proposed for hospitalization due to persisting critical blood test results. On the 2nd day of hospitalization, in spite of the surveillance and the aggressive fluid therapy support, there was an abrupt clinical and analytical worsening (Cr 3.89mg/dL; Urea 125mg/dL; CK>200000U/L; TnT 823ng/L; Lactate Dehydrogenase 7712U/L; elevated transaminases; having developed cardiogenic and disruptive shock there was the need for invasive ventilation, and the progressive worsening of the AKI demanded continuous venovenous hemodialysis. The patient was transferred to the intensive care unit, where he still is 15 days after admission.

CONCLUSIONS

This clinical case illustrates the importance of an accurate and prompt response from the Clinical Pathology Laboratory when facing extremely high values which require successive dilutions. The accuracy of these results is essential for the patient's follow up. As Pathologists, our role is to keep updated and adapt to the needs of the patients and clinicians even in the most difficult situations.
DISCLOSURE: No conflicts of interest.

Case report

M223

NEWLY DIAGNOSED CHRONIC LYMPHOCYTIC LEUKEMIA DURING SYMPTOMATIC COVID-19. CASE REPORT

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BACKGROUND-AIM

Patients with malignant diseases have high risk of severe or critical forms of COVID-19. Chronic lymphocytic leukemia (CLL) can dysregulate both the adaptive and innate immune response. There are CLL-related immune dysfunctions including T- and B cells, the phagocytic cells and the complement system. SARS-CoV-2 infection also affects the function of immune system, it causes mainly depletion of CD4+ and CD8+ T cells. When these diseases meet, the weakening of the immune system could help to avoid the fatal overreaction of the immune and inflammatory response.

METHODS

Presentation of two hematological cases

RESULTS

In our cases CLL manifested during a severe COVID-19 pneumonia. A 43-year-old man with IDDM went to hospital in February with bilateral COVID pneumonia. He was sent to hematology because of a malignant-looking vertebra CT. He had 17.2 G/L WBC, 62.9% lymphocyte, 33% pathological B cells. The diagnose is CD38+ B-CLL with two subclones. He has no paraproteinaemia but has high level IgM and IgG type antibody against SARS-CoV-2 S protein. The other case is a 53-year-old man who was hospitalized in March with severe COVID pneumonia. The signs of B-CLL arised in his blood (WBC 123G/L, lymphocyte 91%, hemoglobin 107g/L). The flow cytometric assay has shown 82% pathological B cells with the diagnosis of CD38- B-CLL. The IgH gene rearrangement was positive. He has 1,2g/L IgG kappa type monoclonal paraprotein. These two patients being in Rai 0-1 stage recovered after COVID pneumonia without going critical state in intensive care unit.

CONCLUSIONS

The long term follow-up of patients having CLL manifested during symptomatic COVID-19 could further improve our knowledge about the immune system being attacked from several sides.

Case report

M224

INTERFERENCE IN HBA1C DUE TO POSSIBLE HEMOGLOBIN PORTO ALEGRE IN THREE CASES

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BACKGROUND-AIM

Hemoglobin Pôrto Alegre (PA) is an abnormal human hemoglobin resulting from a missense mutation in the ninth residue of the beta chain hemoglobin; described in HGVS as NM_000518.4:c.29C>G; p.Ser10Cys.
It was first described by Tondo et al. In 1963 a Brazilian family of a Portuguese Caucasian descent. The mutation has a "silent" phenotype because of the fact that polymerization by intermolecular disulphide bonds would not occur in vivo, probably because of a compensatory synthesis of glutathione reductase. This mutation has also been found in a person with an unstable variant hemoglobin so this leads to no clinical problems (because it can coexist with abnormal variants).

METHODS

We present three cases of patients in whom HbA1c was determined for glycaemic control and hemoglobinopathy study. Samples were processed by capillary electrophoresis (CE) (Capillarys 3, SEBIA®, France), HPLC (ADAMS A1c HA-8180V; A. Menarini Diagnostics®, Italy) and immunoturbidimetry (Tina-quant Hemoglobin A1c Gen.3, Cobas 6000; Roche Diagnostics®, Switzerland).

RESULTS

In all cases it was observed a haemoglobin variant by CE. Due to their percentage and migration position, could be a beta chain variant called "Hemoglobin Pôrto Alegre". It was observed interference in the HbA1c analysis by CE with falsely high HbA1c value.

CONCLUSIONS

The variant, designed in dbSNP as rs33918131 is described in ClinVar as "Likely benign" by multiple submitters with no conflicts.
Hemoglobin PA has a low frequency in the general population, a found allele of 251216 (0.000003981) in a Southern European male (gnomAD). It has also been documented in a few patients from Brazil, Portugal, Argentina, Cuba, Puerto Rican and the Canary Islands, somebody descent.
The percentages of HbA1C are falsely elevated by CE; the non-glycated form of the variant comigrates with fetal hemoglobin and it is integrated with HbA0 when determining HbA1c, because of the elevated baseline.
Immunoturbidimetry uses a specific antibody against the last four aminoacids of the N-terminal end of the β chain, so HbA1c results will only be affected by variants that modify some of these 4 amino acids. Accordingly, immunochemical methods (methods based on structure difference) show less interference from hemoglobin variants than those based on charge differences such as HPLC or CE, however they do not have the ability to detect these variants.
In all three cases, it was recommended to perform genotyping to confirm variant, as well as request the determination of HbA1c by immunological methods for future occasions, avoiding interference in its determination.
The notable increase in the prevalence of hemoglobinopathies in our environment, due to globalization, forces clinical laboratories to have different tools suitable for both the determination of HbA1c and for the diagnosis of hemoglobinopathies.
Since most clinical laboratories use HPLC for the diabetes control, and PA variant may not be detected, it is possible that the frequency is being underestimated as it does not present with clinical symptoms, especially in Southern countries.

Poster Abstracts – EuroMedLab Munich 2021 – Munich, April 10–14, 2022 • DOI 10.1515/cclm-2021-5013
Clin Chem Lab Med 2021; 59, Special Suppl, pp S94 – S998, Nov/Dec 2021 • Copyright © by Walter de Gruyter • Berlin • Boston

Case report

M225

GREEN INCLUSIONS IN NEUTROPHILS IN PATIENTS AFTER LIVER TRANSPLANT SURGERY AS A MORPHOLOGICAL PREDICTOR BIOMARKER OF ACUTE LIVER REJECTION

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BACKGROUND-AIM

Green neutrophilic inclusions (GI) have been identified in different clinical conditions associated with acute liver injure and high mortality rate. Its nature has been related with hepatic lipofuscin phagocyted by neutrophils. We report three patients after liver transplant surgery in which these GI were detected in peripheral blood (PB).

METHODS

We included three male patients (64, 58 and 41 years old), which received a liver transplant due to the following: Wilson disease, hepatocarcinoma and fulminant hepatitis, respectively. Blood counts were analysed in Advia®2120i and digital images were acquired in CellaVision®DM96 using PB smears stained with May Grünwald-Giemsa. Liver biopsy samples were processed and stained with haematoxylin-eosin for histological analysis.

RESULTS

After 1-2 days of the liver transplant surgery, low values of haemoglobin (80, 83 and 70 g/L, respectively) and platelets (21, 32 and 37 x 109/L, respectively) were found in all three patients. The PB film revision revealed green inclusions within neutrophils in all of them. In addition, biochemical parameters indicating impaired liver function were increased, especially in patient 3 with the following values: AST: 28,173 U/L; NV: 5-40 U/L, ALT: 9,313 U/L; NV: 5-40 U/L, GGT: 107 U/L; NV: 5-40 U/L, LDH: 27,640 U/L; NV: <234 U/L. Moreover, lactate showed high values in all three patients (1.25, 13.76 and 4.15 mmol/L; NV: 0.5-2.2 mmol/L). Higher value of total bilirubin was found in patient 1 (6.5 mg/dL). Hepatic biopsy was performed in all three cases, showing the presence of ischemic areas and lipofuscin accumulation in 3/3. The diagnosis of acute rejection was stablished. Two of the three patients died (patients 2 and 3).

CONCLUSIONS

GI detected in neutrophils in PB correlated with liver ischemia finding in histological samples after transplant surgery. To our knowledge, this is the first report that demonstrates the relevance of GI finding as an acute rejection biomarker in patients undergoing liver transplant.

Case report

M226

THE IMPACT OF THE PREANALYTICAL ERROR ON HEMOGLOBIN CONCENTRATION RESULT OBTAINED IN POCT – THE CASE STUDY

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BACKGROUND-AIM

Decreased blood hemoglobin (Hb) concentration is an immediate life-threatening condition. Quick determination of Hb level is possible owing to point of care testing (POCT) – blood gas analysis. However, the preanalytical errors can be more frequent in POCT affecting the reliability of the results.
We present the case of Hb determination in patient with COVID-19 using POCT that illustrates the importance of preanalytical phase in POCT analysis and the need for continuous education of clinical staff involved in POCT.

METHODS

The 73-year-old patient was admitted to the Cardiac Surgery Clinic of the University Clinical Centre in Gdańsk (Poland) at the end of January 2021. On February 7, Real Time Polymerase Chain Reaction for COVID infection was performed, with a positive test result. The patient was transferred to the COVID Department, where he had arterial blood gas analysis several times a day on the ABL 835 Analyzer (Radiometer) due to respiratory failure.

RESULTS

On February 17, the patient underwent gasometry tests 4 times and following Hb (and hematocrit) values were obtained: at 2:42 a.m. - 10.0 g/dl (31.1%); at 8:26 a.m. - 22.0 g/dl (67.0%); at 10:08 a.m. - 10.1 g/dl (31.2%); at 11:16 p.m. - 9.2 g/dl (28.6%). For no other parameter such extreme differences were observed that day.
After making a call to the COVID Department, it turned out that when the arterial blood was collected around 8:00 a.m. to perform a blood gas analysis, the two-point calibration planned for this analyzer had just started. The syringe with patient's blood was put next to the device and the analysis was performed 20 minutes later, but the physician did not mix the blood just before the inserting the syringe into the device. The blood cells fell to one side of the syringe, causing them to condense, and the needle of the analyzer took blood from this place for testing. As a consequence, a falsely elevated Hb concentration and hematocrit have been obtained.

CONCLUSIONS

The example of this patient shows the importance of preanalytical phase and errors in obtaining the reliable results using POCT. The continuous training for the medical staff can significantly affect the quality of the obtained POCT results and reduce the number of errors in the preanalytical phase.

Case report

M227

THE IMPORTANCE OF IMMUNOPHENOTYPING IN DIFFERENTIAL DIAGNOSIS OF RICHTER'S SYNDROME: A CASE REPORT

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BACKGROUND-AIM

Richter's syndrome (RS) is a transformation of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) into high-grade lymphoma. It occurs in 2-10% of all CLL/SLL patients. In the most cases, normally indolent CLL transforms into a secondary diffuse large B-cell lymphoma (DLBCL). This transformation has an ominous prognosis and short survival time, so rapid diagnosis is of the essence. Flow cytometry immunophenotyping (FCI) can contribute to a faster diagnosis of RS.

METHODS

64-year-old man was hospitalized in the Clinical Hematology Department at the University Hospital Osijek for suspected lymphoproliferative disorder. For the last few months he felt weakness and noticed a growth on the skin and swollen lymph node on his neck. A broad spectrum of laboratory blood analysis with cytomorphological examination and FCI analysis of bone marrow and lymph node were requested.

RESULTS

Cytomorphological analysis of lymph node found numerous medium and large-sized lymphocytes,reffering to lymphoproliferative disorder-NHL. Cytomorphological analysis of bone marrow found multiplied small and large lymphocytes, reffering to lymphoproliferative disorder-CLL or possible Richter's syndrome transformation. Lymph node FCI analysis showed monoclonal population of large B-cells with immunophenotype: CD19+CD20+FMC7+CD43+CD5+sIg-lambda. Bone marrow FCI analysis found two monoclonal B-cell populations; a small population with B-CLL immunophenotype: CD19+CD20+CD23+CD43+CD5+sIg-lambda+, and a large population with identical immunophenotype as lymph node B-cells. Immunophenotype of large B-cells in bone marrow and lymph node are atypical for primary DLBCL (usually CD5-, CD10+), but characteristic for RS cells; DLBCL arising from CLL/SLL tends to retain a CLL/SLL immunophenotype (CD5+, CD10-). The only immunophenotype difference between two cell populations was expression of FMC7 on surface of large cells compared to expression of CD23 marker on surface of small cells. Patient was introduced in rituximab therapy, but unfortunately too late; he died two months later.

CONCLUSIONS

RS is considered to be very aggressive transormation from an indolent entity. It usually requires time-consuming multidisciplinary approach. From this case we can conclude that FCI is useful tool for prompt diagnosis and appropriate therapy application.

Case report

M228

ACITRETIN: COULD IT BE A TRIGGER IN AN ANTI-SYNTHETASE (ANTI PL7) ANTIBODY SYNDROME?

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BACKGROUND-AIM

Idiopathic inflammatory myositis are muscular diseases that can be differentiated into Polymyositis, Sporadic inclusion body myositis, Dermatomyositis, Immune-mediated necrotizing myopathy, Overlapping syndromes with myositis. New diagnostic biomarkers and autoantibodies have been identified, they are subdivided into myositis specific antibodies and myositis associated antibodies. The first group is rapresented by anti-synthetase antibodies, directed against aminoacyl-transfer-RNA synthetases, they include Jo-1, PL-7, PL-12, OJ, EJ, KS, Zo, Ha. The most frequently encountered clinical manifestations are myositis, pulmonary interstitial disease, arthritis with rigidity, fever, Raynaud's phenomenon. We describe the clinical case of a patient diagnosed with anti-PL7 positive antibody syndrome, probably induced by Acitretin, taken for the treatment of pustular psoriasis. The 67-year-old patient presents a polydistrict erythematous maculosus rash following triamcinolone administration. At the cutaneous biopsy, "alterations compatible with pustular dermatitis" are highlighted and this support the clinical diagnosis of pustular psoriasis. The patient accuses, after taking Acitretin, the onset of myalgia in the upper limbs, and contextual rigidity.

METHODS

Myoglobin and hsTnT were measured with the electrochemiluminescence method (ECLIA) (Cobas e-801, Roches), CK with the immunometric method (Dimension Vista, Siemens). The antinuclear antibody (ANA) were evaluated with the indirect immunofluorescence method (GEMINI COMBO, Alifax), the Immunoblot that detects antibodies to antigens associated with myositis was performed with the immunoblotting method (Dr. DOT, Alifax).

RESULTS

Laboratory tests show elevated values of CK (1669 IU), Myoglobin (1219 μg/L), hsTnT (171 pg/mL), ANA in IF on HEp-2000 positive with titer 1:160 and cytoplasmic pattern (AC -19). The fluoroscope picture is suggestive for auto antibodies to PL-7 and/or PL-12. The panel for anti-myositis antibodies (WB) detected the positivity anti-PL7 allowing to confirm the diagnosis of the syndrome from anti-synthetase antibodies.

CONCLUSIONS

The etiology of autoimmune myositis is not fully known, but viral infections, exposure to environmental factors or smoking may favor the onset of this syndrome, in which autoantibodies to tRNA synthetase play a pathogenetic role. In the literature there is a reported case of anti-PL7 syndrome arising in a patient with chronic HCV hepatitis under treatment with IFN-α. Our patient reports a symptomatology similar to that presented after taking Acitretin, years earlier, but attributable to statin treatment. The cause-effect relationship, the onset autoimmune myopathy after taking statin is widely demonstrated. Few cases are reported in the literature, to explain how Acitretin may be a possible trigger of autoimmune myopathy, probably on the basis of, in vivo, the resterification of Acitretin in Etretinate, which causes muscle damage. The patient, followed at our institution, presents after about 1 year positivity for anti-PL7 autoantibodies with the diagnosis of pulmonary interstitial disease in anti-synthase antibody syndrome. Our patient, currently, is treated with Rituximab.

Case report

M229

HYPERAMMONEMIA IN A 20 MONTHS OLD BOY WITH PARTIAL ORNITHINE TRANSCARBAMYLASE DEFICIENCY DUE TO A NOVEL MISSENSE HEMYZIGOUS VARIANT IN OTC GENE

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BACKGROUND-AIM

Ornithine transcarbamylase (OTC) deficiency is the urea cycle disorder that causes ammonia accumulation in the blood, it is acquired as X-linked trait or a new mutation. OTC deficiency can occur as a severe neonatal-onset disease in males and as a post-neonatal-onset (partial deficiency) disease in males and females. Hemizygous males and heterozygous females with partial OTC deficiency can present from infancy to later childhood, adolescence, or adulthood. OTC deficiency in male hemizygous are caused by point mutations that result in lower enzymatic activity, a destabilized protein or decreased affinity for the substrate. We present patient with post-neonatal OTC deficiency caused by OTC gene variant not reported so far.

METHODS

Our patient is 20 months old boy, the son of two healthy unrelated Caucasian, who was admitted to the hospital for drowsiness and vomiting. On arrival his laboratory findings showed compensatory metabolic acidosis with normal pH, low partial pressure of carbon dioxide and base excess of the extracellular fluid, elevated liver enzymes, ketonuria and ammonia level 183 μmol/L. Cobalamin, folic acid and homocysteine value were within the reference values.

RESULTS

After generous glucose-electrolyte solution was introduced, the ammonia value returned to normal within 18 hours. After stabilization of ammonia level, a normal diet was introduced which lead to its re-increase to 162μmol/L. Urine sample was collected and that time in order to determine organic acids and amino acids. Increased excretion of orotic acid and of uracil was found. Several amino acid concentrations were also increased. Based on the clinical presentation and laboratory findings, it was suspected that patient has OTC deficiency so the analysis of the OTC gene was requested and the child was introduced to low-protein diet.

CONCLUSIONS

NGS analysis revealed the missense variant c.798A>G p.(Ile266Met) in exon 8 of the OTC gene in a hemizygous state which so far has not been reported. This variant results in the substitution of an amino acid on protein level predicted to be diseases causing and has not been found in the genomAD database. For confirmation maternal sample was also analyzed and the mother was confirmed to have heterozygous family variant c.798A>G p.(Ille266Met).

Case report

M230

AN UNUSUAL CASE OF MONOCLONAL GAMMOPATHY IN A 12-YEAR-OLD MALE

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BACKGROUND-AIM

Plasmablastic Lymphoma (PBL) is a rare and aggressive haematological malignancy usually associated with Human Immunodeficiency Virus (HIV) infection or other immunodeficiencies. There is currently no available data on its prevalence as PBL only recently (2008) received formal WHO classification. It is immunophenotypically related to Multiple Myeloma. PBL has a male predominance (75%) with a peak incidence between the fourth and fifth decades. It is rare in paediatric patients with only a few cases been described. We present a 12-year-old newly diagnosed HIV-positive male on treatment, who presented at a tertiary hospital with a pathological fracture of the distal one-third of the left femur. On physical examination, the patient was found to have a soft tissue tumour on the chin. The patient was subsequently referred to paediatric oncology for workup.

METHODS

The positive findings were investigated with the use of computed tomography techniques, serum protein electrophoresis (SPE), immunofixation, EBV-encoded RNA (EBER) in-situ hybridization (ISH) and immunohistochemistry (IHC) for the biopsied lesions. Routine chemistry and haematological analysers were also employed for the workup of the patient.

RESULTS

Laboratory investigations showed microcytic hypochromic anaemia with a haemoglobin of 9.6 (reference range 10.3 -15.5 g/dL), β-2 microglobulin of 4 (reference range 1.1- 2.5 mg/L) and raised inflammatory markers. An SPE and immunofixation showed an unquantifiable monoclonal band that was typed as IgA Lambda. A BMAT revealed depleted iron stores and 8 % plasma cells that appeared dysplastic and reactive. Radiological investigations demonstrated the presence of a right proximal tibial and femoral mass located where the pathological fracture occurred. Histology of the biopsies taken of the lesions demonstrated large cells, most of which had a plasmacytoid appearance with multiple prominent basophilic nucleoli and eccentric nuclei, prominent apoptotic bodies, and brisk mitotic activity, features consistent with PBL. The tumour cells were positive for CD138, MUM1 and CD56 by immunohistochemistry. The proliferation marker (Ki-67) approached 100%. The CD20, CD79a, Bcl2 and Bcl6 proved negative. EBER-ISH (Epstein-Barr virus-encoded RNA in situ hybridisation) yielded a positive result.

CONCLUSIONS

Plasmablastic lymphoma should be suspected in any paediatric patient with pathological fractures in the background of an immunocompromised state. At present, evidence of a monoclonal band is not part of the diagnostic criteria for PBL. This study has demonstrated the potential value of SPE and immunofixation in children who present with pathological fractures.

Case report

M231

RECURRENT URINARY TRACT INFECTIONS IN A YOUNG FEMALE

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BACKGROUND-AIM

Type1 primary oxaluria is a rare inborn error of metabolism characterized by excessive urinary oxalate excretion and predisposition towards the formation of urine oxalate caliculi. Hyperoxaluria can also be secondary, due to excessive intake of oxalate or excessive intake of its precursor hydroxyproline. Primary hyperoxaluria is a rare condition reported to affect 1 in 58000 individuals and type 1 accounts for about 80% of all cases of primary hyperoxaluria, making it the most prevalent form. Genetic investigation plays a major role in confirming this diagnosis.
We present a 25-year-old female presented with a history of recurrent urinary tract infections, worsening chronic bilateral flank pain, dysuria, haematuria, and lower limb swelling. Urine dipstick revealed a 2+ haematuria, nitrates, and 3+ proteinuria. Vital signs were within normal limits.

METHODS

Patient workup and diagnosis were with the point of care testing and laboratory testing. Routine chemistry was performed on the Abbott analyzer and all biopsies were performed in the anatomical pathology department. The calculi were analysed by Fourier transform infrared spectroscopy (FT-IR) on an Agilent instrument and genetic testing was performed. and genetic testing was performed from DNA extracted from blood, followed by polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) analysis.

RESULTS

Laboratory investigations revealed stage 5 chronic kidney disease with an elevated urea 31. 4 mmol/L, (reference interval (RI) Urea 2.1 − 7.1 mmol/l), creatinine of 1116 μmol/L (RI, 49 − 90 μmol/L) with an estimated glomerular filtration rate (eGFR MDRD formula) of 4 ml/min/1.73 m2 (normal eGFR >60). Imaging of the kidneys revealed right and left non-functioning kidneys with bilateral staghorn calculi. Urinalysis revealed hyperoxaluria with urine oxalate levels of 300 μmol/l and an oxalate: creatinine ratio of 150 μmol/mmol creatinine (normal value < 40 μmol/mmol). A renal stone passed in the urine was found to be composed of calcium oxalate (chemical composition (%): calcium oxalate monohydrate (50%) and calcium oxalate dihydrate (50%). Genetic testing revealed the presence of a homozygous c.335C>A (p. A112D) mutation in the alanine glyoxylate aminotransferase (AGXT) gene which confirmed the diagnosis of primary oxaluria Type 1.

CONCLUSIONS

Early diagnosis of primary oxaluria can help in the prevention of ESRD. Intervention in the form of a liver transplant combined with a kidney transplant, which is the definitive treatment that may be required.

Case report

M232

A RARE CASE OF ESSENTIAL THROMBOCYTHEMIA WITH SECONDARY MYELOFIBROSIS AND FAST BLASTIC TRANSFORMATION

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BACKGROUND-AIM

BACKGROUND: Essential Thrombocythemia (ET) is a Ph negative myeloproliferative neoplasm (MPN), featured by maintained thrombocytosis (>450x109/L PLT) and increased large to giant megakaryocytes dispersed in the bone marrow (BM). Incidence of 0.2-2.3 cases/100,000 inhabitants, mostly in women 50-60 years old. Thrombotic and/or hemorrhagic complications can occur. Progression to blast phase (BP), Acute Myeloid Leukemia (AML), and Myelofibrosis (MF) is 2.1 and 9.3% at 15 years, respectively. Evolution to AML is unpredictable and frequently fatal, 2-7 months survival. Mostly with a transition phase (accelerated phase (AP)), with lower blasts percentage (10-19%). No evidence that Hydroxyurea (HU), ET most often used drug, increases AML incidence. AML treated patients, response rate is 71%, with 16 months overall survival. ET therapy aims symptomatic relief and complications prevention. Studies document delayed evolution to MF. Currently, absence of effective therapies to change unfavorable BP outcome, vary from supportive measures with low intensity therapy (eg. Azathioprine (AZT)), to more intensive ones, including induction chemotherapy (CT), and allogeneic hematopoietic stem cell transplant (HSCT), with the best survival rate, 47% at 2 years.

METHODS

CLINICAL CASE: 56-year-old Caucasian man, past smoking habits, diagnosed Parkinson's disease (2012) and MPN-ET (2000). At diagnosis JAK2V617F negative, splenomegaly and PLT 1,250,000. Started (2000) Busulfan, good response, suspended in 2003 due to hematological toxicity. Started HU, 17 years with response and no toxicity. February/19 cytopenias evidence: leukopenia 1.7x109/L, 0.870x109/L neutrophils (N), mild anemia (Hb 12.9g/L) normocytic and thrombocytosis (457x109/L), peripheral blood smear (PBS)- anisopoikilocytosis, teardrop cells, elliptocytes and N hypersegmentation, no blasts. Elevated LDH, vit B12 and folic acid deficiency; started supplementation. October/19 cytopenias improvement: leukocytes 2.37x109/L, 1,000x109/L N, Hb:13.3g/dl, maintained thrombocytosis (575x109/L). June/20 worsening: Hb 9.4g/dL, leukopenia 1.5x109/L, 0.819 x109/L N, PLT 459x109/L. Started HU. July/20 new worsening: Hb 7.3g/dL, leukopenia 1.0x109/L and severe neutropenia 0.468 x109/L, no thrombocytosis (346x109/L). BM aspirate: 6% myeloblasts. BM biopsy: reticulinic fibrosis of stroma (grade 2) secondary to ET and 20-30% of CD34+ blasts. Treated with AZT, good evolution and cytopenias improvement, but progressive thrombocytosis after 4 cycles, requiring HU reintroduction. BM biopsy (Nov/20): “MPN with intense fibrosis (grade 3) and some dispersed blasts, difficult to quantify (>5%?)”. Suspended AZT, maintained HU with normal blood count. Jan/21: ER with severe anemia, 5.9g/dL, transfused. After clinical reassessment, began new AZT cycle.

RESULTS

Report of an ET patient, who developed secondary MF and AML progression, rare in ET, almost simultaneously, 19 years after diagnosis. BP, AML, of abrupt installation, without AP, usual in MPN evolution. Although he had HU for 17 years, there is no consistent evidence of increasing incidence of AML.

CONCLUSIONS

CONCLUSIONS: Important to emphasize the need for frequent monitoring and attentive assessment of cytopenias, PBS observation and BM study. Aspirate and BM biopsy blasts number discrepancy may be due to effect of severe fibrosis. Due to clinics and co-morbidities, no eligibility for transplantation, treatment option was AZT, since intensive CT without subsequent HSCT does not offer greater survival. Early diagnosis and treatment are essential to quality of life and survival improvement.

Case report

M233

DISCORDANT PREGNANCY TEST RESULTS IN A PATIENT WITH ADVANCED PANCREATIC ADENOCARCINOMA

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BACKGROUND-AIM

A 53-year-old woman diagnosed with metastatic pancreatic adenocarcinoma was enrolled in a clinical trial as a third-line treatment after Nab-paclitaxel combined with gemcitabine progression. As part of her follow-up, the Oncologist requested a complete blood test, as well as a urine pregnancy test, which was positive.

METHODS

The qualitative urine pregnancy test used in the EL (Emergency laboratory) was the Menarini Clip Test Plus hCG Strip Foil. The test uses a mixture of monoclonal and polyclonal antibodies, and shows positive when hCG is >10 U/L. For serum samples, the assay used in the EL was the Siemens Dimension hCG, that quantifies only intact hCG using a sandwich method with a first antibody that binds to the α-subunit and a second one that binds to the β-subunit. The established cut-off point for gestation by the manufacturer is 5 U/L.
In the CORE laboratory (CL), where different methods were implemented for hCG hormone measurement, the urine pregnancy test used was the Dedicio hCG Pregnancy Test >25U/L, which uses a polyclonal anti-hCG (intact) antibody. The quantitative serum test used was the Siemens Advia Centaur XP Total hCG method, which uses antibodies directed to both intact hCG and free β-hCG subunit.
Finally, free β-hCG in serum was carried out using the IMMULITE FBC assay, which uses a sandwich-type method with a free monoclonal anti-β-hCG antibody and a free anti-β-hCG polyclonal antibody. This test has a cut-off point of 2 U/L to discard gestation

RESULTS

The patient denied the possibility of pregnancy. She had irregular menstrual cycle for the last few years and has not been sexually active for months, so a week later a second urine pregnancy test was requested to the EL. Again, the result was positive. ß-hCG was then analysed in a serum sample to confirm these results, but the result was <1 U/L.
“Hook” effect was ruled out by serial dilutions, so the urine pregnancy test was informed with a comment warning of a possible interference.
At the CL, the urine result was negative and the Total HCG was positive (164 U/L), as opposed to the EL. Finally, FBC was 108 U/L.

CONCLUSIONS

After a comprehensive review of the methods, it was clear that the patient only had free beta subunit in serum, showing an undetectable intact hCG on the EL Dimension and the pregnancy test of the CL. Elevation of FBC in hepatic cancer has already been broadly described on the literature, but it has to be considered too in positive pregnancy tests from oncology patients to discard possible errors that could emotionally harm the patient and/or delay a treatment.

Case report

M234

A CASE REPORT: HEMOPHAGOCYTIC SYNDROME

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BACKGROUND-AIM

Hemophagocytic lymphohistiocytosis, also known as hemophagocytic syndrome, is characterized by a non-malignant and uncontrolled activation and proliferation of macrophages and T lymphocytes, associated with a hyperproduction of cytokines, causing the main biological signs of the syndrome. This syndrome can be primary or genetic or secondary to different diseases, such as autoimmune, viral, oncologic, metabolic and treatment with immunomodulators. There are different clinical and laboratory criteria, according to the latest protocol in force since 2004, of which at least 5 of 8 must be met. The criteria are: 1. fever ≥ 38.5 ºC, 2. splenomegaly, 3. cytopenias (hemoglobin < 9 g/dL and/or platelets < 100. 000/mm3 and/or neutrophils <1000/mm3), 4. Hypertriglyceridemia >265 mg/dL and/or fibrinogen < 150 mg/dL, 5. Ferritin > 500 ng/mL, 6. CD25 ≥ 2400 U/mL, 7. Decreased or absent NK cytotoxic activity, and 8. Hemophagocytosis in bone marrow, cerebrospinal fluid, or lymph nodes.
Other clinical or laboratory findings consistent with the diagnosis are cerebromeningeal symptoms, lymphadenopathy, jaundice, edema, rash, altered liver enzymes, hyponatremia, hypoproteinemia, high VLDL and low HDL.

METHODS

A 43-year-old woman with severe psychomotor retardation secondary to neonatal cerebral hemorrhage came to the emergency department with fever of one week's evolution, with nocturnal predominance, shivering crises and profuse sweating.

RESULTS

In the analytical control, marked elevation of cytolytic enzymes LDH 3516 U/L, GPT 167 U/L, GGT 471 U/L, elevation of triglycerides 5820 mg/L and ferritin 16040 ng/mL. In addition pancytopenia (hemoglobin 6.5 g/dL, leukocytes 1.9x109/L, platelets 55x109/L) and increased fibrinogen 1150 mg/dL. The autoimmune study together with blood cultures and serologies were negative. Computed axial tomography showed splenomegaly.
During admission, worsening of the clinical situation, with icteric coloration after liver failure and greater alteration of coagulation and hemogram. Ferritin levels were 34120 ng/mL.
Given the high suspicion of hematologic pathology, bone marrow aspirate and biopsy were performed. The result was a hypocellular marrow with erythroid hyperplasia and images suggestive of hemophagocytic syndrome. Immunophenotyping with reduced NK cell activity was also performed. These findings were compatible with hemophagocytic syndrome.
High dose corticosteroids together with etoposide were started after confirming the diagnosis. Due to the poor evolution the patient finally died and genetic cause or secondary causes could not be ruled out.

CONCLUSIONS

Hemophagocytic syndrome is in most cases secondary to viral infections, mainly Epstein-Barr virus, but we should not rule out other pathologies, such as oncologic diseases, as it is an aggressive syndrome with multiorgan involvement in which early diagnosis and treatment are vital. It is important to study possible triggers through early evaluation of symptoms, bone marrow failure and liver and coagulation disorders. Very high ferritin levels > 10,000 ng/mL, accompanied by clinical LLH, are highly sensitive and specific.

Case report

M235

DOUBLE CHROMOSOMIC ANOMALY IN QUANTITATIVE FLUORESCENCE POLYMERASE CHAIN REACTION

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BACKGROUND-AIM

Trisomy 21, also known as Down syndrome (DS), is caused by a nondisjunction phenomenon in which approximately 95% of cases result in a regular trisomy 21 (three copies of chromosome 21), and approximately 5% have a copy of chromosome 21 that is translocated with another acrocentric chromosome from groups D (13-15) or G (21-22); that is, a chromosome 21 is joined to either of the chromosomes from groups D or G. This is known as a robertsonian translocation.
The X chromosome is one of the longest chromosomes and contains hundreds of genes, most of which do not influence sex determination. Normally females have two X chromosomes. However, 0.001% have three X chromosomes in their cells, known as triple X syndrome.

METHODS

We present the case of a 41-year-old pregnant woman (12+2 weeks) with two previous children. She has no medical history of interest. She came to the gynecology office for ultrasound and first trimester screening.

RESULTS

The ultrasound showed fetal growth restriction and the biochemical screening showed a high risk (1/4) for trisomy 21. After these findings and due to the age of the patient, following the protocol of our hospital, an invasive technique was necessary to confirm the results, proceeding to perform a chorionic villus biopsy.
First a molecular study of DNA extracted from the uncultured chorionic villus was performed to rule out the three most frequent aneuploidies (13, 18, 21) together with the study of the sex chromosomes (X and Y). In parallel, the same study was performed with DNA extracted from the mother's lymphocytes to rule out maternal contamination in the results. The result of this study, by Quantitave Fluorescence PCR (QF-PCR) showed us a female fetus with a triploid dose for chromosome 21 and X.
The cell culture showed a uniform cell population of 47 female chromosomes, with three chromosomes 21 and three chromosomes X. Two of these three chromosomes 21 and three chromosomes X were observed. Two of these three chromosomes 21 were linked together forming a derivative chromosome by robertsonian translocation. Chromosome formula: 47,XXX,+21,der(21;21)(q10;q10). The karyotype of the parents was normal.
The patient finally signed the consent for voluntary termination of pregnancy.

CONCLUSIONS

This is a case of DS due to a robertsonian translocation of chromosome 21 in a fetus, which in turn has a trisomy of the X chromosome, both originating de novo. The role of the laboratory is crucial to detect this type of structural and numerical chromosomal anomalies, performing molecular (QF-PCR) and cytogenetic (karyotyping) tests in order to offer genetic counseling in case of any alteration.

Case report

M236

ADVANTAGES OF CAPILLARY ELECTROPHORESIS IN HEMOGLOBIN D DETECTION, A CASE REPORT

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BACKGROUND-AIM

Hemoglobin D (HbD) is the fourth most occurring hemoglobin (Hb) variant, consisting in the replacement of glutamic acid with glutamine at 121 position on β chain. HbD gains clinical significance in association with either β thalassemia or HbS. Detection of HbD is a diagnostic challenge because HbD migrates at the same position with HbS in Alkaline Gel Electrophoresis (AGE), which is the method used in many clinical laboratories.
Our aim is to acknowledge the importance of Capillary Electrophoresis (CE) in the correct diagnosis of sickle cell anemia due to HbD presence, especially in countries like Albania that have few and unclear reports about HbD but are endemic for HbS in some regions.

METHODS

CE for Hb was performed on MINICAP Flex Piercing-Sebia, a fully automated system that uses the principle of liquid-flow CE in free solution.

RESULTS

Case Report: A 17 years old male patient was admitted in Hemoglobinopathies Department in Mother Theresa University Hospital, after an unclear diagnostic approach in 15 years (HbS-beta thalassemia, Sickle cell anemia). His first symptom was arthralgia at 2 years old and had blood transfusions periodically. The patient has been under iron chelating therapy. Laboratory tests during the current presentation were: Hb 8.4 g/dL, RBC 2.71 million/μL, MCV 97.9 fL, Ferritin 876 ng/mL, Total Bilirubin 3.69 mg/dL, Direct Bilirubin 0.51 mg/dL, LDH 1086 U/L, Reticulocyte count 5.6%. Retrospectively, AGE on Sebia Hydrasis showed 21.9% HbF, 1.2% HbA2, 70.4% HbS and 6.5% HbA. His mother's electrophoresis showed Heterozygous HbS, while the paternal examination was not possible. HPLC in 2020 showed 2.3% HbA2, 11.2% HbF, 37.5% HbS and an unidentifiable Hb variant of 44%.
Hb electrophoresis on CE performed at the last visit revealed 45.4% HbD, 38% HbS, 13.8% HbF and 2.8% HbA2. Acid gel electrophoresis confirmed the presence of two different bands HbS and HbD. The presence of HbD and HbS was also confirmed by molecular analysis of β-globin chains. Hemoglobin SD disease diagnosis was established.

CONCLUSIONS

CE is more sensitive than gel electrophoresis in detecting Hb fractions and provides good discrimination of HbD from HbS. CE offers the possibility to correctly diagnose Hemoglobin SD disease.

Case report

M237

USEFULNESS OF AUTOANTIBODIES IN THE DIAGNOSIS OF MYASTHENIA GRAVIS ASSOCIATED WITH THYMOMA: A CASE REPORT

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BACKGROUND-AIM

Myasthenia gravis (MG) is an autoimmune neuromuscular disease characterized by fluctuating muscle weakness and fatigue. The origin of the autoimmune response is unknown, but alterations of the thymus and genetic predisposition seem to play a key role.

METHODS

A case report: a 50-year-old woman with progressive general weakness for a month. It began with vision distortion until it became diplopia with subsequent drooping of the left eyelid. Fifteen days after debut, she associated jaw claudication and difficulty speaking and swallowing solids. These symptoms fluctuate over the days and are accompanied by fatigue. The grandmother, a maternal uncle, and a maternal second cousin are all diagnosed with MG.

RESULTS

Examination: fatigue with the Cogan manoeuvre at 33 seconds with increased ptosis until it covered the upper pupillary edge and with the appearance of diplopia. Scapular weakness 4/5 with fatigue after 15 claps. Without baseline pelvic girdle weakness but fatigued after 10 squats 4/5.
Complementary tests: the cranial magnetic resonance shows small high-signal FLAIR-T2 images in the subcortical white matter suggestive of areas of vasculo-degenerative gliosis (FAZEKAS 1). Non-contrast computed tomography shows a localized mass in the prevascular mediastinum suggestive of thymoma. Laboratory tests: anti-acetylcholine receptor antibodies (anti-AchR Ab) 21 nmol/L (levels above 0.50 nmol/L are indicative of MG), negative muscle-specific anti-tyrosine phosphokinase receptor antibodies (anti-MuSK Ab), positive anti-Titin antibodies (anti-Titin Ab) by immunoblotting.

CONCLUSIONS

MG is an infrequent disease with a prevalence between 27-400 cases per million inhabitants, more frequent in women between the second and third decade. 85% of patients have anti-AchR Ab (MG seropositive); 40% of seronegative cases have anti-MuSK Ab. Only 10-15% of patients with MG have an associated thymoma, being easy to suspect with an immunoblotting test that detects anti-striated muscle antibodies such as anti-Titin Ab, present in 75-85% of patients with MG associated with thymoma. We present the case of a patient with MG in which the origin of the condition is a thymoma but it has a clear family component that will have to be studied.

Case report

M238

HYPOPHOSPHATASIA. SERUM ALKALINE PHOSPHATASE AND PYRIDOXAL-5'-PHOSPHATE LEVELS. REPORT OF THREE CASES FROM ONE FAMILY

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BACKGROUND-AIM

Hypophosphatasia is a very rare bone metabolism disorder caused by a deficiency in tissue-nonspecific alkaline phosphatase (TNSALP) activity, due to mutations in the ALPL gene.
TNSALP hydrolyzes extracellular inorganic pyrophosphate (PPi) and pyridoxal-5'-phosphate (PLP). The symptoms ranging from severely impaired mineralization at birth, life-threatening to musculoskeletal pain in adulthood.
High PLP levels reflect defective PLP hydrolysis by TNSALP and decreased availability of pyridoxal (PL) to cross the blood-brain . PLP plays the role as a cofactor for the enzymes implicated in the metabolism of several neurotransmitters, such as gamma-aminobutyric acid (GABA) or serotonin.
The diagnosis is based on laboratory and molecular genetic testing of the ALPL gene to detect associated mutations with hypophosphatasia. Serum alkaline phosphatase (ALPL) activity is markedly reduced while 5'pyridoxal phosphate (PLP) are elevated.

METHODS

We report a 46-year-old patient with spondyloarthropathy who presents extreme and progressive muscle weakness of 15 years of evolution reaching wheelchair travel.
Assessed by endocrinology, low (TNSALP) values are detected repeatedly with no significant findings on muscle biopsy. No rickets in childhood or early loss of teeth.
The patient has two children aged 13 and 15 years, both are asymptomatic and we proceeded to the analysis of the serum levels of Alp and PLP for all of them.

RESULTS

Low values of TNSALP were detected repeatedly (<10 U/L; RV: 45-117) for the mother as well as a PLP elevation (165mmol/L; RV: 55±28). A genetic study was performed with the detection of the following heterozygous variant ALPL(NM_000478.6):c.1135C>A(p.His379Asn), considered patogenics for Adult Hypophosphatasia.
The serum ALPL and PLP values for the 13 and 15 years old children were respectively, of (55 U/L and 290 mmol/L; 42 U/L and 365 mmo/L). The same variant was detected in both cases.

CONCLUSIONS

Adult hypophosphatasia can be inherited in an autosomal recessive or autosomal dominant manner, depending on the specific effect of the genetic mutation on TNSALP activity. The highly variable expressivity of hypophosphatasia makes it difficult to carry out genetic counseling due to the clinical heterogeneity of the disease. The genetic may help us to manage this patients.

Case report

M239

CLINICAL CASE OF CYSTINURIA. THE IMPORTANT ROLE OF THE EMERGENCY LABORATORY

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BACKGROUND-AIM

Cystinuria is an inherited metabolic disorder characterized by excessive amounts of undissolved cystine in the urine. People with cystinuria cannot properly reabsorb cystine into their bloodstream, so the amino acid accumulates in their urine. As urine becomes more concentrated in the kidneys, the excess cystine forms crystals. Larger crystals become stones that may lodge in the kidneys or in the bladder. This condition is inherited in an autosomal recessive pattern and it caused by mutations in the SLC3A1 and SLC7A9 genes. The initial symptom is usually renal colic, hematuria, obstruction and/or infections of the urinary tract. Frequent recurrences ultimately may lead to kidney damage. Cystine stones represent only 1-2% of urinary stones.

METHODS

Importance of urine sediment examination

RESULTS

Female patient, 48 years of age, without family history of interest presented left iliac fossa fixed and non-irradiated pain lasting three days and fever. She had a long medical kidney stone history but she was never properly diagnosed. She visited an emergency department. The urine analysis reveals proteinuria, leukocytosis and the urine sediment examination shows abundant flat and hexagonal crystals, typical of cystine. Despite this the patient was sent home and she was told to take pain medication and antibiotic. Laboratory staff contacted the patient's primary care physician to recommend an appropriate study of the patient. Confirmatory diagnosis of cystinuria should be include urine amino acid determination, analysis of calculi by X-ray crystallography, 24-h determination of cystine in urine and a genetic study to characterize genetic mutations.

CONCLUSIONS

Patients with these rare disorders have recurrent stone formation that can lead to chronic kidney disease. There is often significant delay in the diagnosis of these disorders which can have a significant impact on their quality of life. Given the severity and chronicity of these conditions and the associated risk of progressive renal injury, the importance of early diagnosis and appropriate management cannot be overemphasized. This case report reveals the important role of urine sediment testing for the correct interpretation and classification of crystals and its use as a fast and cheap diagnostic tool in the clinical laboratory.

Case report

M240

PANICULITIS, PANCREATITIS AND POLYARTHRITIS SYNDROME. HOW USEFUL IS THE LABORATORY?

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BACKGROUND-AIM

The pancreatitis, panniculitis and polyarthritis syndrome (PPP) is produced mainly by the systemic release of pancreatic enzymes, which fundamentally causes involvement of the subcutaneous cellular tissue (primary panniculitis) and the periarticular space (arthritis), with less frequent involvement of the bone marrow.

METHODS

A 14-year-old boy who during his stay in the pediatric ICU presented symptoms suggestive of septic shock with a possible abdominal focus, severe renal failure and edema in both upper limbs.

RESULTS

Echo Doppler confirmed suppurative pyomyositis of the subscapularis in right upper limb. In the following days, he developed fluctuating bilateral polyarthritis, predominantly in the right elbows, knees, wrists and ankles, extra-articular collections and splenic abscess with negative cultures and pretibial skin lesions. In control blood tests, an increase in serum lipase (1043 U/L) was observed. Due to the symptoms presented by the patient, the diagnosis of PPP Syndrome was suggested. A bone marrow biopsy was performed, which reported compatibility with reactive myeloid hyperplasia. Magnetic resonance imaging showed no associated bone lesions. The pediatric ICU Service contacted the Pathological Anatomy Service to inquire about the possibility of confirming the presence of fat in a sample of synovial fluid. Faced with the refusal of said consultation, they went to the Laboratory Service to probe if said proposal was possible. They were offered the possibility of staining with the Sudan III technique. The result obtained was positive, observing in optical microscopy the presence of moderate drops of fat. To confirm the definitive diagnosis, a sample of pretibial skin lesions was sent to pathology, which confirmed presence of panniculitis with enzymatic digestion of fat. Finally, the diagnosis of PPP syndrome was confirmed.

CONCLUSIONS

PPP syndrome is a rare clinical triad, more common in middle-aged men, and rare in childhood. Only 30% present abdominal symptoms, 2-3% of pancreatic panniculitis cases while polyarthritis has been recorded in up to 54-88% of patients. Our case stands out for occurring in a young patient in whom the clinical triad concurs. The role of the laboratory was essential to confirm the definitive diagnosis.

Case report

M241

LITHIUM-INDUCED NEPHROGENETIC DIABETES INSIPIDA. ABOUT A CASE

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BACKGROUND-AIM

Diabetes insipidus (DI) is a rare disease that causes polyuria due to the elimination of a high volume of diluted urine. This polyuria may be due to the absolute or relative lack of secretion of vasopressin or antidiuretic hormone ADH ("central diabetes insipidus, CDI"), to its lack of action ("nephrogenic diabetes
insipidus, NDI"), or to hypotonic urine output secondary to excess fluid intake with inhibition of ADH (“primary or psychogenic polydipsia”).
From the laboratory point of view, DIN is characterized by low urinary osmolarity, hypernatremia, and
increased serum osmolarity due to an alteration in the concentrating capacity of the kidney, translated into a picture of dehydration due to volume depletion that can become deadly.
In the course of lithium treatment, intoxication by it, although rare, is a serious situation that we must prevent. It can be caused "voluntarily" (by premeditated or involuntary overdose by the patient), although in most cases it is accidental, and may be triggered by intercurrent kidney disease, decreased salt intake,
excessive sweating, diarrhoea, vomiting, dehydration and/or interaction with drugs, all of which are
circumstances that lead to an increase in lithemia. Long-term administration of lithium can induce an
alteration in renal function, affecting concentration capacity with the subsequent appearance of NDI.

METHODS

We present the case of a patient with bipolar disorder treated with lithium as a mood stabilizer, who debuted with a DIN due to intoxication with this drug, and where the laboratory played a fundamental role at the time of diagnosis and initiation of treatment.

RESULTS

Presentation of the case. A 68-year-old patient with long-standing bipolar disorder under treatment with
lithium salts for 20 years, who was admitted to the Internal Medicine ward due to neurological symptoms
with progressive confusional syndrome, extrapyramidal rigidity and dysarthria. The last week refers
excessive intake of water, polyuria, tremor at rest and hyperthermia. In this context, a biochemical study was requested, obtaining the following results: Urea 84 mg/dL (13–43); Creatinine 1.81 mg/dL (0.7–1.3);
Potassium 4.3 mEq/L (3.5–5.1); Sodium 164 mEq/L (136–145); Chlorine 111.2 mEq/L (95–110); serum
osmolarity 354 mOsmol/Kg (275–295); urinary osmolarity 320 mOsmol/Kg (150–1400); litemia 1.8 mmol/L (0.6–1.2). Rest of parameters within normal limits. After the biochemical results obtained, the patient is diagnosed with DIN secondary to lithium treatment, suspending treatment with it and increasing hydration. Treatment with amiloride and carbamazepine was started due to its renal antidiuretic effect, observing a progressive improvement.

CONCLUSIONS

A major complication of long term lithium therapy is DIN. Lithium is a mon g the three main causes of NDI in adults, antagonizing the effect of ADH and thus achieving a decrease of it in the collecting tubule cells by inhibiting the hydroosmotic action of ADH.

Case report

M242

SEVERE SUBACUTE GENERALIZED MYASTHENIA GRAVIS WITH BULBAR INVOLVEMENT

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BACKGROUND-AIM

Introduction: Myasthenia gravis (MG) is an autoimmune disease in which anti acetylcholine receptor antibodies (RACH) are synthesized that block or destroy postsynaptic receptors at the n euromuscular junction. With an incidence of 3 4 cases per million inhabitants per year and two times higher in women than in men, it shows a bimodal pattern, with an early peak between 20 40 years (predominantly female) and a late peak in the eighth decade (male predominance). The thymus is proposed as the origin of the antigens that cause this autoimmune pathology, with MG seropositive patients presenting abnormalities in this organ (thymoma or Clinically, we observe fluctuating muscle weakn ess as the main symptom (pathognomonic), with ocular symptoms also being characteristic (presentation form in half of the patients is in the way of diplopia or ptosis), dysphagia, jaw claudication, facial weakness and even respiratory failure.
The diagnosis should be suspected after a compatible clinical history and neurological examination. A series of complementary tests must also be carried out, such as the response to anticholinesterase drugs (Tensilon test), neurophysiological studies and isolated fib er electromyography.
From the laboratory point of view, RACHs, positive in 90% of patients with moderate to severe generalized MG, have an approximate sensitivity of 80% and a specificity close to 100%. False positives have been described, at low incidenc e, in Lupus, autoimmune hepatitis or in patients with amyotrophic lateral sclerosis (ALS). Anti MuSK (muscle specific tyrosine kinase) antibodies appear in 30 40% of seronegative forms, anti LPR4 antibodies being less frequent in the usual study of the disease.

METHODS

Presentation of the case. An 85 years old patient admitted for mixed and progressive oropharyngeal dysphagia of 2-3 months of evolution that prevents oral tolerance. In the anamnesis, he refers coughing attack with ingestion as well as voice changes (twangy) throughout the day and that are accentuated at night. On examination, he presented fatigue in the shoulder girdle after 20 repetitions and weakness in the neck flexors. Rest of physical examination within normal limits.
Suspecting MG, an autoimmunity study was requested from the Laboratory, obtaining the following results: RACH: 10907.09 nmol/L (0 1); Ac. Anti MuSK: 0 U/mL (0 0.4); Ac. Anti Nuclear (Hep 2, IFI): negative; Vitamin B12: 700 pg/mL (186 1054); Rheumatoid Factor: 41 U/mL (2.4 1 4), TSH: 1.669 µUl/mL (0.551-4.781). Rest of biochemical and immunological parameters within normal limits. An electromyography was performed, observing findings compatible with post synaptic neuromuscular transmission alteration (compatible with MG).

RESULTS

With these results and based on the symptoms presented, the patient is diagnosed with severe subacute generalized MG with bulbar involvement (phonatory and swallowing), and treatment with pyridostigmine, corticosteroids, and immunosuppressants is started.

CONCLUSIONS

Discussion. Neuromotor dysphagia is a very common symptom in the elderly population and, in turn, a rare form of MG presentation, so that clinical suspicion and the role of the laboratory are essential for its diagnosis, treatment and improvement in the pa tient's quality of life.

Case report

M243

MULTIPLE MYELOMA IN A YOUNG PATIENT. A CASE REPORT.

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BACKGROUND-AIM

Monoclonal gammopathies are a group of heterogeneous clonal plasma cell proliferative disorders. Plasma cell proliferative diseases have different presentations, treatments, and outcomes. Pre-malignant disorders include monoclonal gammopathies of undetermined significance (MGUS) and smoldering multiple myeloma (SMM). The diagnosis requires the absence of end-organ damage attributable to the clonal plasma cell disorder. Both SMM and MGUS are considered precursors to multiple myeloma (MM) with a 10% and 1% risk of progression per year respectively. Multiple myeloma is the second most common form of haematological malignancy after non-Hodking lymphoma and accounts for aroun 1% of all cancer.
Symptoms of multiple myeloma can include anemia, bone pain, renal failure, weakness, hypercalcemia and/or weight loss attributable to the underlying clonal plasma cell disorder. Multiple myeloma is a disease of older people with the median age at diagnosis being 69 years. Over 60% of diagnoses are made in those greater than 65, and less than 15% of diagnoses are made in those under 55years. Due to these data, several scientific societies recommend that serum protein electrophoresis (SPE) should not be determined in people under 50 years old without clinical suspicion of monoclonal gammopathy. However, the lack of clinical information in the laboratory request is a common deficiency. The aim of this case report is to warn of the presentation of the disease in patients under the usual age of diagnosis and how laboratory algorithms can help detect these cases.

METHODS

A 40-year-old patient studied for allergic rhinitis for whom a general laboratory test was requested. Despite the fact that the patient had previously consulted his doctor for dorsal-lumbar pain of 4-5 months of evolution, the patient had no results of serum protein electrophoresis or serum total proteins study in the last year.

RESULTS

Laboratory results showed the following: anaemia (hemoglobin 10.2 g/dl), normal values of calcium and creatinine and very high serum total protein value (12.8 g/dl). Therefore, a serum protein electrophoresis study was extended by a laboratory algorithm. The SPE revealed a M-spike (5.30 g/dl) in beta-2 region. Immunotyping by capillary electrophoresis confirmed the presence of a monoclonal protein and determine the isotype IgG kappa. Free kappa light chains (151.84 mg/l), free lambda light chains (5.73 mg/l), ratio K/L (26.50), IgG (5707 mg/dl), IgA (27 mg/dl), IgM (8mg/dl), LDH 181 U/l and β2-microglobulin (4.4 mg/l) were added to complete the stratification and prognosis study. Finally, the patient was diagnosed with Multiple Myeloma IgG kappa ISS2.

CONCLUSIONS

Despite the low incidence of MM in people under 50 years, the laboratory must have tools and algorithms to detect patients with laboratory data suggestive of monoclonal gammapathy. Mainly, in laboratory requests which complete clinical information had not been provided. The clinical laboratory plays an essential role in the diagnosis, follow-up, stratification and prognosis of the monoclonal gammopathies diseases, being laboratory data the cornerstone of the International Myeloma Working Group criteria.

Case report

M244

ANALYSIS OF DELETIONS IN BMPR1A AND PTEN GENES IN PATIENT WITH BREAST CANCER AND A HISTORY OF PRENATAL ENCEPHALOPATHY AND COLON ADENOCARCINOMA

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BACKGROUND-AIM

Patient with clinical judgment that includes prenatal encephalopathy with secondary epilepsy; colon adenocarcinoma and infiltrating ductal carcinoma of the right breast, stage IA, luminal B. Presents oncological history of interest: sister with ovarian cancer at 46 years and brother with larynx cancer at 52

METHODS

An analysis was performed on the patient's sample by massive sequencing using the Illumina NextSeq™ 550 System sequencer of all the genes of the hereditary cancer panel present in Imegen's Hereditary OncoKitDx.
The analysis carried out includes a study of CNVs (variation in number of copies for detection of duplications and deletions) of the previously indicated genes.
The variants detected have been described according to the reference sequence of the professional HGMD database, contrasted with different databases and in silico prediction programs and classified according to the potential pathological effect that they may produce on the gene they affect. Variants have been considered changes with a number of readings > 50X and with a frequency greater than 25%

RESULTS

We highlight the following CNVs that could be associated with the patient's phenotype:
One of them is the deletion in the chromosomal region 10q23.2 of the BMPR1A gene that would result in a loss in the number of copies of the genomic region that includes exons 3 to 13.
The other deletion is located in the PTEN gene on chromosomal region 10q23.31 that would result in a loss in copy number of the genomic region spanning exons 1 through 7.

CONCLUSIONS

It is likely that it is the same deletion, although, since it is a panel of genes and not the entire exome, we cannot conveniently delimit the variant. That is why they must be confirmed by another technique such as Multiplex-ligation dependent probe amplification (MLPA) or CGH Array.
The BMPR1A gene is related to hereditary mixed polyposis syndrome and juvenile intestinal polyposis, while the PTEN gene is related to Cowden syndrome and macrocephaly/autism syndrome. Both phenotypes related to our patient.

Poster Abstracts – EuroMedLab Munich 2021 – Munich, April 10–14, 2022 • DOI 10.1515/cclm-2021-5013
Clin Chem Lab Med 2021; 59, Special Suppl, pp S94 – S998, Nov/Dec 2021 • Copyright © by Walter de Gruyter • Berlin • Boston

Case report

M245

"ANTI-M2, SP-100 AND PML POSITIVE ANTIBODIES IN PATIENT WITH HYPERTRANSAMINASEMIA: A CASE REPORT"

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BACKGROUND-AIM

Autoimmune hepatitis (AIH) is a hepatic necroinflammatory disease considered to be of autoimmune origin. It has a low prevalence and, although it predominates in females, it can affect children or adults of both sexes. The diagnosis of AIH requires the exclusion of other causes of liver damage and is based on a combination of criteria established by the International Autoimmune Hepatitis Group. Clinical manifestations are highly variable, ranging from asymptomatic to fulminant liver failure.
Primary biliary cholangitis (PBC) is an autoimmune disease characterized by progressive destruction of the intrahepatic bile canaliculi, which produces cholestasis and more or less severe liver damage. The prevalence is low and mainly affects women in the fifth decade of life.
The overlap syndrome manifests itself when analytical and/or histological manifestations of the two autoimmune diseases (AIH and PBC) coexist in the disease. The frequency of these overlap syndromes is unclear, although it is considered that up to 10% of adult patients with autoimmune liver disease may have an overlap of this type.

METHODS

Case presentation:
A 75-year-old patient who, during a routine check-up by his medical center, observed an increase in liver enzymes with no apparent cause. The patient has no personal or family clinical history of interest (no diabetes mellitus, no high blood pressure, no alcoholism): she only had a tonsillectomy when she was 5 years old. She is without hepatotoxic drugs treatments.

RESULTS

The patient, asymptomatic, undergoes routine control tests, where a marked and isolated hypertransaminasemia is observed with values of: GOT 185* (1-32 U/L), GPT 246* (0-55U/L), GGT 71* (9-36 U/L). The patient also presents a slight elevation of LDH 249* (125-220 U/L). A month later, an analysis was performed again, where the values of transaminases and LDH were confirmed (and even increased). A serological study against hepatitis A, B and C is also performed, which is negative.
The patient is finally referred to the Digestive Service to complete the study:
- Biochemistry: GOT 341*, GPT 386*, LDH 320*
- Specific proteins: IgA 279 (69-517 mg/dL), IgM 552* (33-293 mg/dL), IgG 1737* (552-1631 mg/dL), Ceruloplasmin 32 (20-60 mg/dL), Alpha1-antitrypsin 216* (90-200 mg/dL).
- Alpha-fetoprotein: normal
- Proteinogram: normal, polyclonal increase of gamma globulins.
-Anemia study: normal.
- TSH: normal.
- Autoinmunity Study: Antinuclear anti-body (ANA) positive, with AC-6 pattern (multiple nuclear dots), titer 1/80; and AC-21 pattern (AMA like), at high titer.
ENAs sreening and ENA EUROIMMUN Blot: negative.
Antimitochondrial antibody (AMA) positive at a titer of 1/320.
EUROIMMUN Liver Blot: hepatic anti-anticytosol antibody (negative), anti-LKM (negative), anti-gp 210 (negative), anti-sp100 (positive), anti-PML (positive), anti-SLA (negative).
- Abdominal ultrasound: no assessable pathological findings in the examination performed.
After this results, the patient is referred to the hepatology clinic for control and treatment. She finally underwent a liver biopsy to support the autoimmune diagnosis, which was not concluded due to an insufficient sample for diagnosis.

CONCLUSIONS

After the exhaustive study, based on autoimmunity tests, an autoimmune liver disease with possible overlap syndrome is diagnosed. The patient is under typical corticosteroid treatment for autoimmune hepatitis, waiting for a control analysis to support the diagnosis.
This overlapping clinical process is characterized by presenting antibodies related to AIH and AMA. In this disease it is also characteristic to have increased IgG and IgM in the serum.
Early diagnosis of autoimmune liver diseases possible thanks to the autoimmunity laboratory. In addition, rapid diagnosis is very important to avoid liver tissue deterioration and progression to cirrhosis, an irreversible process that currently requires liver transplantation with certain complications.

Case report

M246

PEDIATRIC CASE WITH ISOLATED ALKALINE PHOSPHATASE ELEVATION

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BACKGROUND-AIM

Alkaline phosphatase (ALP) is an enzyme that can be found in almost all tissues in the body. Values that increase up to 2-10 times the reference range in infants and early childhood can be detected incidentally. If it cannot be associated with any other pathology, this case is called childhood benign transient hyperphosphatasia. ALP levels return to normal in about 1 month. In this paper, a 7-year-old female patient who presented with unilateral leg pain and ALP level of 1332 U/L is reported. The aim of this study is to keep in mind the phenomenon of transient benign hyperphosphatasia before in-depth investigations in patients with isolated ALP elevation.

METHODS

The patient's biochemistry tests were performed on Beckmann Coulter AU2700 and AU5800 analyzers. Thermostability method was used to investigate ALP isoenzymes

RESULTS

The only symptom of the patient, whose biochemical tests were within normal limits, except for ALP, was leg pain. According to the thermostability method, the ALP result was found to be 800 U/L (60%) after the sample was kept at 56oC in a bain-marie container for 10 minutes. This result showed that increased ALP isoenzyme was not of bone origin. After 4 days, it was learned that the ALP level decreased to 716 U/L according to the laboratory tests performed in another center. That clinical condition is defined as childhood benign transient hyperphosphatasia. As can be understood from its name, it is a benign phenomenon and covers the cases of ALP elevation which are usually encountered incidentally in samples taken for other reasons or in routine controls. The underlying pathology is usually not found, and it is observed that the ALP level decreases within 4 months in the cases that are followed up.

CONCLUSIONS

Examination results are of great importance in making clinical diagnoses today. Increasing reporting day by day necessitates taking new steps on laboratory quality and requirements. With the awareness that the reported results will change the diagnosis, treatment and follow-up of the patients, it is closely related to the laboratory specialists to reduce unnecessary medical requests and to ensure more effective use of health services.

Case report

M247

NMDA AUTOIMMUNE ENCEPHALITIS IN A PSYCHIATRIC PATIENT: CASE REPORT.

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BACKGROUND-AIM

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is an autoimmune disease that develops as a multistage syndrome with a broad differential diagnosis. NMDAR are located on the surface of neuronal cells and play an important role in neural plasticity and synaptic signal transduction. Therefore, a reduction of exposure of those receptors provokes an imbalance in NMDA signaling pathways and, consequently, a cortical hyperexcitability.
Since these antigens are involved in normal brain functions, patients exhibit high rates of neuropsychiatric symptoms, paranoia, mania, epileptic seizures, etc. These neuropsychiatric symptoms appear in 70% of the patients at the beginning of the disease and can cause confusion in differential diagnosis between encephalitis and psychiatric disorders.
The syndrome is more frequent in young women and almost half of the cases are associated with neoplasia, in particular with ovarian teratomas.

METHODS

A 25-year-old woman followed up by the Psychiatric department for depression and anxiety with drugs addiction, was referred to the emergency service for presenting acute psychiatric symptoms such as disinhibited behavior, psychosis, mutism and instability. Brain magnetic resonance image (MRI) was not altered. Abdominal/pelvis computerized tomography and echography were performed suggesting ovarian malignant pathology (teratoma or germ cell tumor). Lumbar puncture was made and showed normal red and white blood cell count.
Serological tests for neural viruses were negative.

RESULTS

Autoimmune test revealed strong positive NMDAR antibodies in serum (titer 1/100), and cerebrospinal fluid (CSF) as well. NMDAR antibodies were detected by indirect immunofluorescence assay using a human recombinant cell line (Sprinter XL, Euroimmun®).
Despite of negative MRI and non-pathological CSF, the patient was diagnosed with NMDA autoimmune encephalitis and started treatment with immunoglobulins. Teratoma was removed successfully and the neurological status was favorable after the surgery.

CONCLUSIONS

Our case reinforces the idea that we should consider autoimmune pathology under some psychiatric symptoms, in order to make a correct differential diagnosis. An early treatment in these cases is important to prevent neural damage.

Case report

M248

DIAGNOSIS OF MULTIPLE MITOCHONDRIAL DYSFUNCTION SYNDROME: A CASE REPORT

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BACKGROUND-AIM

Case presentation of Multiple Mitochondrial Dysfunction Syndrome (MMDS) associated with NFU1.

METHODS

Multiple mitochondrial dysfunction syndrome (MMDS) is a group of inborn errors of energy metabolism with poor prognosis resulting from the malfunction of several metabolic pathways. It usually begins during infancy and is characterised by growth retardation, neurological involvement, respiratory failure, lactic acidosis and premature death.

RESULTS

A 4-month-old infant was admitted due to respiratory failure, hypotonia, refusal of feeding and irritability. Laboratory tests showed lactate: 25.8 mg/dl (4.5-19.8), AST: 48 U/l (< 32), ALT: 65 U/l (< 55) and LDH: 383 U/l (125-220). Brain magnetic resonance imaging showed white matter alteration and delayed myelination. In view of the suspicion of metabolic disease, amino acids, organic acids and acylcarnitines were requested in blood and urine, as well as a clinical exome to screen for metabolic disorders. The metabolic study revealed hyperglycinemia and hyperglycinuria, as well as elevated urinary excretion of 2-ketoglutaric and 2-ketoadipic acids. The genetic study revealed the presence in homozygosis of the c.622G>T (p.Gly208Cys) mutation in the NFU1 gene, classified as pathogenic, by producing the change of a highly conserved glycine for a cysteine at position 208 of the protein, close to the binding motif of the Fe-S group. A segregation study was then performed in the parents, who turned out to be asymptomatic carriers.

CONCLUSIONS

The MMDS comprises a series of autosomal recessively inherited diseases caused by defects in the biosynthesis of the iron-sulphur (Fe/S) cluster, which induce the abnormal function of lipoic acid-dependent enzymes, such as the 2-oxoacid dehydrogenase complex, alpha-ketoglutarate dehydrogenase, branched-chain ketoacid dehydrogenase and protein H of the glycine degradation system. This cofactor is synthesised in the mitochondria in a reaction catalysed by the enzyme lipoic acid synthetase, which in turn requires an Fe-S centre as a cofactor, the assembly of which involves several proteins, including NFU1, so that mutations in the gene encoding this protein are the cause of NFU1-associated multiple mitochondrial dysfunction syndrome, as in the present case.
Therefore, the role of the clinical laboratory in the biochemical and molecular diagnosis of this group of clinical entities is crucial for the differential diagnosis with other pathologies with overlapping clinical phenotypes.

Case report

M249

BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM WITHOUT SKIN INVOLMENT: A CASEREPORT

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BACKGROUND-AIM

Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive hematologic neoplasm that originates from plasmacytoid dendritic cell precursors.). Most patients initially present with cutaneous manifestations, typically asymptomatic violaceous and purpuric patches, that mimic ecchymoses, cutaneous T-cell lymphomas, and leukemia cutis. A minority of patients will present with systemic involvement without skin lesions. The diagnosis requires Bone Marrow or skin biopsy demonstrating blast cells with plasmacytoid morphology and positive expression of CD123, CD4, and CD56. An accurate diagnosis of BPDCN is essential in order to provide treatment promptly, especially considering that the initial clinical presentation is often indolent and the prognosis is generally poor

METHODS

Our case is a 38-year-old woman from the Dominican Republic arrived at our emergency room from another center with suspected acute leukemia. The complete blood cell count (CBC) performed with the instrument Sysmex XN revealed anemia with hemoglobin of 89 g/L (referent interval [RI] 120-160), mild neutropenia ($1{,}43x10^9$/L ; RI 2,00-9,00), thrombocytopenia ($42x10^9$L; RI 150-400) and presence of nucleated red blood cells (NRBC). The instrumental morphological flags indicate the possible presence of atypical lymphocytes (Abn_Lympho?), erythroblasts (NRBC present), and immature granulocytes (IG_Present)The WDF scattergram showed the presence of a cluster of highly fluorescent cells which is colored half with the color code of monocytes and half with the one of immature granulocytes. This abnormality could indicate the presence of blasts.

RESULTS

The peripheral blood smear review by optical microscopy showed immature granulocytes (3,2%), NRBC and blast (4%) with a typical morphology: they are medium-size cells with irregular nuclei, fine chromomatic and small nucleoli, the cytoplasm is grey-blue and sometimes with vacuoles or with pseudopod-like cytoplasmic projections.The bone marrow examination revealed the presence of a monomorphic neoplastic population positive for CD45, CD15, CD68 and CD56 but negative for TdT, CD354, CD4, CD117, CD123 and myeloperossidase.Peripheral blood flow cytometry revealed 45% CD45dim cells within the blast gate, positive for CD4, CD33,CD14, CD64, CD56 and CD123.The molecular biology test showed NPM1 mutation, while there were no mutation for FLT3 gene and MLL-PTD mutation.

CONCLUSIONS

Based on these results, the diagnosis of blastic plasmacytoid dendritic cell neoplasm was made, according to the World Health Organization classification.