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Leiomyosarcoma of inferior vena cava complicated by Budd-Chiari syndrome and disseminated intravascular coagulation – case report

Case Report

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Abstract: Leiomyosarcoma of inferior vena cava is a rare malignant mesenchymal tumor of the venous system that typically occurs in adulthood. Correct and early recognition of leiomyosarcoma is very important, because a complete resection of the tumor (with occasionally chemio- or radiotherapy) can lead to prolonged survival. We report a case of a 54-year-old man suffering from the leiomyosarcoma of inferior vena cava with infiltration of retroperitoneum and right adrenal gland.

Keywords: *Leiomyosarcoma • Inferior vena cava • Mesenchymal tumor • Budd-Chiari syndrome*

1. Introduction

Leiomyosarcoma of the inferior vena cava (IVC) is a rare (only around 400 cases worldwide have been reported) malignant mesenchymal tumor (derived from medial smooth muscle cells) of the venous system [1-3]. It appears more often in women, between the 5thand 6th decade of life [4]. Clinical symptoms of the disease are not characteristic and can appear several years before diagnosis [5]. Here we present a case of a patient with leiomyosarcoma of the inferior vena cava complicated by Budd-Chiari syndrome and disseminated intravascular coagulation (DIC).

2. Case report

A 54-year-old male was admitted to the hospital with complaints of right-upper- quadrant abdominal pain lasting 1 month, weight loss (5 kg for 1 month), night sweats, legs pain and edema. Past medical history included arterial hypertension and varicose veins with an episode of superficial thrombophlebitis (one month before admission to the hospital). Physical examination was unremarkable apart from the mild right-upper-quadrant abdominal tenderness. Laboratory test revealed elevated concentration of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), D-dimer, fibrinogen, INR and aPTT, decreased albumin concentration

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and low platelet number (Tab.1). Abdominal ultrasound showed hypoechogenic structure alongside head of pancreas. Because of ultrasound findings, computer tomography of the abdomen was performed (Fig.1).CT scans revealed widened, partially occluded inferior vena cava in upper part (diameter 38 mm), loss of contrast in left renal vein, distal part of right renal vein and left testicular vein, suggesting possible massive thrombus. In addition, there were identified masses adjacent to the probably enlarged lymph nodes and widen vessels in the right renal space.

Altogether, abdominal CT scan suggested neoplasm of unknown origin. To rule out neoplasm of the digestive tract gastroscopy and colonoscopy were performed and results were negative. Level of carcinoembryonic antigen (CEA), cancer antigen 19-9 (Ca19-9), alpha-fetoprotein (AFP) and prostate-specific antigen (PSA) were normal. Chest CT scan revealed enlargement of paratracheal and subcarinal lymph nodes. Peripheral lymph nodes were not palpable, bone marrow biopsy was normal. Elevated inflammatory markers of unknown origin lead to the administration of empiric ally chosen antibiotic (cephalosporin). Patient was discharged from the hospital with the diagnosis of IVC thrombosis. Therapeutic doses of heparin were recommended.

Table 1. Laboratory test results of the patient during 1st and 2nd hospitalization.

	First hospitalization	Second hospitalization	Normal range
CRP	161,6	263,6	<10 mg/l
ESR	84/88	116/>125mm	<12 mm
WBC	7,5	2,9	4,0-10,0 G/l
RBC	4,31	2,9	4,5-5,9 T/L
HGB	14,1	8,5	13,5-17,5 g/dl
HCT	40,5	25,6	40,0-51,0%
PLT	123	86; 35	150-400 tys/ml
AST	24	2495	0-35 U/l
ALT	32	1312	0-45 U/l
ALP	79	449	42-98 U/l
GGTP	33	165	0-38 U/l
Bilirubin	22,3	32,0	0,0-20,0 uM/l
LDH	464	2461	< 450 U/l
BUN	6,8	25,3	3,2-7,1 mmol/l
Creatynin	91	243	71-133 umol/l
TP	70,6	55,4	64-83 g/l
Albumin	31	20,4	35,0- 52,0 g/l
INR	1,63	7,08	0,85-1,15
aPTT	44,0	58,3	25-33,5 sec
D-dimer	4967,68	>10000	<500 ng/ml
Fibrinogen	9,0	1,3	1,8-3,5 g/l

Four weeks later the patient appeared in the Emergency Department with complaints of sustained abdominal pain, fatigue, nausea and vomiting, diarrhea, fever and night sweats. In comparison to previous laboratory tests, present results were much more alarming consisting of anemia, leukopenia, low platelet numbers, markedly elevated CRP and ERS, decreased albumin concentration, renal insufficiency and liver damage (Tab.1). On ultrasonography (USG) liver and spleen were both enlarged, and free fluid in peritoneal cavity was present. Doppler US exhibited absence of venous flow within the IVC. CT of abdomen (Fig.2) showed heterogeneous mass within the IVC extending to the right atrium with only peripheral blood flow. In addition, loss of contrast in left renal vein, distal part of right renal vein and left testicular vein was observed together with hepatosplenomegaly, diffuse heterogeneity of the liver, suggesting hepatic venous congestion, ascites and free fluid in pleural cavity.

Progression of thrombosis was accompanied by changes in laboratory tests suggesting DIC: low platelet level, prolonged INR and aPTT, low fibrinogen and elevated D-dimer. Treatment with broad-spectrum antibiotics, heparin and methyloprednisolon were initiated. In spite of this treatment condition, the patient rapidly deteriorated and died due to multi organ failure on the 5th hospital day.

On autopsy, leiomyosarcoma of the inferior vena cava with infiltration of retroperitoneum and adrenal

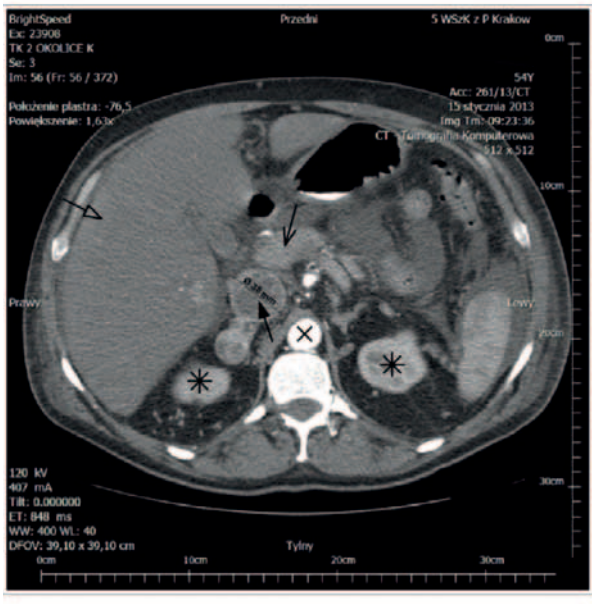

Figure 1. CT scan of abdomen done during first hospitalization. It shows widened (diameter 38 mm), partially occluded inferior vena cava with masses that suggested thrombosis (marked by ⟶). Surrounded organs are marked as followed: liver ⟶, pancreas ⟶, kidneys ✳, aorta ✕.

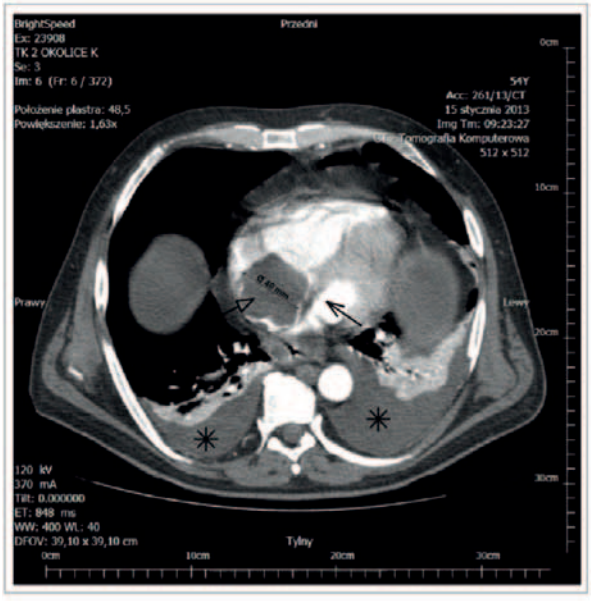

Figure 2. CT scan done during second hospitalization. The image of heart revealed masses in right atrium (marked by ⇨), extended from inferior vena cava. Left atrium is marked by → . In addition the free fluid in both pleural cavities is presented (✳).

Figure 3. Gross apearrance of the tumor on autopsy (total size 17 x 5 cm).

gland was diagnosed (Fig.3). In French Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC) scheme, which is widely used for grading of soft tissue sarcomas and is based on a score obtained by evaluating three parameters: tumor differentiation, mitotic rate and amount of tumor necrosis, the tumor was classified as G3 (2+3+1). Staging on the basis of TNM system was appraised as aT2bN0M0. Additionally thrombosis of vena cava inferior, common iliac veins, renal veins, hepatic veins and right atrium were found, and as a consequence Budd-Chiari syndrome and massive liver necrosis. Further histological examination revealed leiomyosarcoma composed of spindle cells

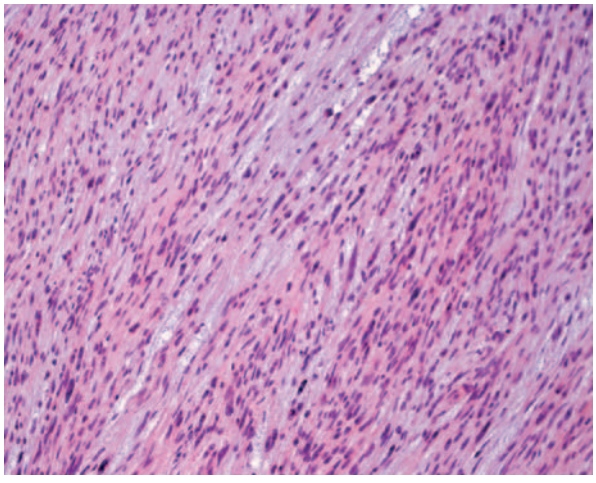

Figure 4. Photomicrograph of the tumor. The tumor is composed of spindle cells (hematoxylin and eosin, x 200)

(Fig.4) with positive immunohistochemistry staining for

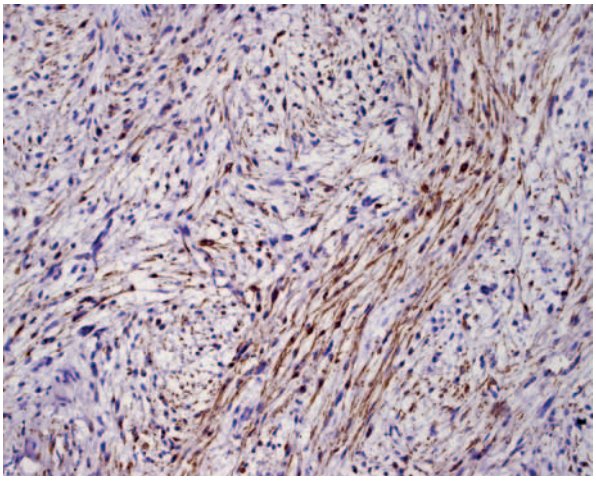

Figure 5. Tumor cells with positive immunohistochemistry staining for desmin (zoom x 200).

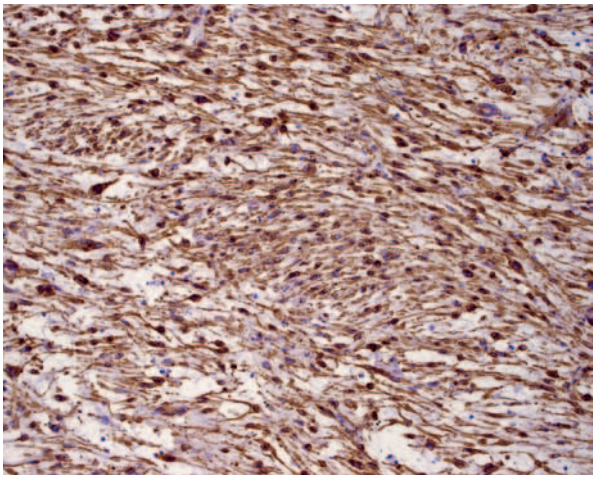

Figure 6. Tumor cells with positive immunohistochemistry staining for SMA (zoom x 200).

desmin and smooth muscle actin (SMA) (Fig.5, 6).

3. Discussion

The leiomyosarcoma of inferior vena cava is a rare malignant mesenchymal tumor (derived from medial smooth muscle cells) of venous system [1,2]. Leiomyosarcomas arising in the IVC are most frequently seen in the sixth decade of life (median age 56), with a female predominance (68%) [3,6]. They are slow-growing progressive tumors with an extremely poor prognosis [7,8]. Symptoms are nonspecific (abdominal pain, distention, dyspnea, weight loss, back pain) and may precede the diagnosis by several years [9,10]. However, some tumors may also present with more distinct signs such as an abdominal mass, deep venous thrombosis due to IVC occlusion, or less commonly as an acute Budd-Chiari syndrome [11]. Symptoms can vary according to the level of IVC invasion: lower segment includes the area below the renal veins (34%), middle segment consists of the area between the renal and hepatic veins (42%) and upper segment that extends from the entry of the hepatic veins up to the right atrium (24%) [3,12]. Those tumors that arise in the lower segment cause right-lower quadrant abdominal pain, back pain and lower extremities edema [13]. Localization in the middle segment causes right-upper-quadrant abdominal pain and sometimes renovascular hypertension [13]. Budd-Chiari syndrome is a rare presentation of tumors that invade IVC above hepatic veins [13]. If the IVC tumor invades, right atrium arrhythmias, dyspnea, new heart murmurs and heart failure could be observed [3,5]. Intravascular leiomyosarcoma may also be accompanied by symptoms of venous thrombosis [14]. The tumor has 3 main growth patterns: 62% of cases demonstrate extraluminal, 5% intraluminal, and 33% extra- and intraluminal growth patterns [15]. Early diagnosis is very difficult. In some cases the first sign of the disease could present as distant metastases, located usually in liver, lung, brain, and lymphatic spread occurring later [3,11]. Abdominal ultrasound, CT scan and/or magnetic resonance imaging (MRI) are necessary to make a diagnosis. CT and MRI are also helpful in assessment of its spreading, localization among other organs and possible distant metastases [14]. Nowadays with the development of image techniques, such as positron emission tomography (PET), the diagnosis of retroperitoneal tumors as well as staging and treatment planning appear to be more accurate [5]. Despite all these advanced technologies, the histopatology is still crucial for diagnosis [5]. Histopathology of leiomyosarcoma reveals spindle tumor cells, which are positive for markers of smooth muscle activity including vimentin, muscle actin, alpha-smooth muscle actin and desmin [5]. Material could be obtained by USG or CT guided biopsy or intraoperatively [16]. However, because of nonspecific symptoms, delay in diagnosis is common – 33% leiomoysarcomas of IVC is diagnosed at autopsy [17].

Differential diagnosis should include other spindle-cell-shaped neoplasms such as tumors of nerves sheaths, myofibroblastic tumors, synovial sarcoma, fibrosarcoma [14]. Inferior vena cava could also be invaded by renal carcinomas, pheochromocytomas, hepatomas or testicular tumors [5,18-20].

Because of limited experience optimal management of IVC leiomyosarcoma is unknown [5]. Surgery alone or combined with chemio-radiotherapy are not curative, but give the only hope of prolonged survival [19]. For those patients diagnosed early, the optimal treatment, according to some authors, include total surgical resection of the tumor but prognosis is still poor [7]. Radical surgery is possible with tumors in middle and lower portion of IVC [3]. Leiomyosarcomas of the upper part and right atrium are usually unrespectable [3]. Invasion of the middle section of IVC brings also better prognosis, because symptoms occur earlier [21]. In contrast, tumors involving upper portion of the IVC, high-grade tumors, and those associated with Budd-Chiari syndrome or IVC occlusion have particularly bad prognosis [11,21]. Over 50% of patients who underwent radical resection develop tumor recurrence, and the 5-year survival rate ranges between 31 and 62% [7].

4. Abbreviations and acronyms

IVC- inferior vena cava, CRP- C-reactive protein, ESR- erythrocyte sedimentation rate, WBC–white blood cells, HGB–hemoglobin, HCT–hematocrit, PLT –platelets, AST–aspartate aminotransaminase, ALT–alanine aminotransferase, ALP–alkaline phosphatase, GGTP–gamma glutamyltranspeptidase, LDH–lactate dehydrogenase, BUN – blood urea nitrogen, TP – total protein, INR–international normalized ratio, aPTT–activated partial thromboplastintime,CT- computerized tomographic scan, CEA- carcinoembryonic antigen, Ca 19-9- cancer antigen 19-9, PSA- prostate-specific antigen, AFP–alpha-fetoprotein, USG–ultrasonography, DIC–disseminated intravascular coagulation, FNCLCC–French Federation Nationale des Centres de LutteContre le Cancer, TNM – neoplasm staging system describes tumor size, involvement of regional lymph nodes and distant metastases, SMA – smooth muscle

actin, MRI–magnetic resonance imaging, PET–positron emission tomography.

Conflict of interest statement

Authors state no conflict of interest.

References

[1] Beiles C.B., Jones R.M., Fell G., Recurrent leiomyosarcoma of the inferior vena cava, Aust. N. Z. J. Surg., 1997,67, 67-68

[2] Nasher M., Wasiewicz J., Murawa P., Nowakowski W., Primary leiomyosarcoma of the interior vena cava. A case report and review of the literature, Wspolczesna Onkol.,1999, 2, 55–56

[3] Bonura A., Saade C., Sharma P., Leiomyosarcoma of the inferior vena cava, Australas Radiol., 2006, 50, 395–399

[4] Lotze U., Reponova J.,Muth G., Oltmanns G., Reich H.C., Etzrodt G., Kaiser W.A., Mutschke O., Ortmann M., Stippel D.,Wahlers T., Leiomyosarcoma of the inferior vena cava extending into the right atrium. A rare differential diagnosis of a right atrial tumor with fatal outcome, Herz, 2012, 37,573–578

[5] Reddy V.P., Vanveldhuizen P.J., Muehlebach G.F., Dusing R.W., Birkbeck J.P., Williamson S.K., Krishnan L., Meyers D.G., Leiomyosarcoma of the inferior vena cava: a case report and review of the literature, Cases J., 2010, 23,3:71

[6] Hemant D., Krantikumar R., Amita J., Chawla A., Ranjeet N., Primary leiomyosarcoma of inferior vena cava, a rare entity: Imaging features. Australas Radiol., 2001,45(4), 448-451

[7] Hashimoto M., Kobayashi T., Tashiro H., Amano H., Oshita A., Tanimoto Y., Kuroda S., Tazawa H., Aikata H., Chayama K., Fujii M., Arihiro K., Ohdan H.,A huge metastatic liver tumor from leiomyosarcoma of the inferior vena cava: report of a case, Surg. Today, 2012, 42, 505–508

[8] Bailey R.V., Strimbling J., Weitzner S., Hardy J.D., Leiomyosarcoma of the inferior vena cava: report of a case and review of literature, Ann Surg., 1976, 184, 169-173

[9] Gowda R.M., Gowda M.R., Mehta N.J., Osborne R., Bixon R., Vasavada B.C., Sacchi T.J., Right atrial extension of primary venous leiomyosarcoma: pulmonary embolism and Budd-Chiari syndrome at presentation-a case report, Angiology, 2004 Mar-Apr,55(2), 213-6

[10] Terzic M., Aksam S., Bila J., Maricic S., Arsenovic N., Pelvic leiomyosarcoma obstructing vaginal opening — case report, Cent Eur J Med.,2012, 7, 245-248

[11] Abisi S., Morris-Stiff G.J., Scott-Coombes D., Williams I.M., Douglas-Jones A.G., Puntis M.C., Leiomyosarcoma of the inferior vena cava: clinical experience with four cases, World J SurgOncol.,2006, 4,4:1

[12] Alexander A., Rehders A., Raffel A., Poremba C., Knoefel W.T., Eisenberger C.F., Leiomyosarcoma of the inferior vena cava: Radical surgery and vascular reconstruction, World J Surg Oncol., 2009,7:56

[13] Griffin A.S., Sterchi J.M., Primary leiomyosarcoma of the inferior vena cava: a case report and review of the literature, J SurgOncol.,1987,34(1), 53-60

[14] Tilkorn D.J., Hauser J., Ring A., Goertz O., Stricker I., Steinau H.U., Kuhnen C., Leiomyosarcoma of intravascular origin–a rare tumor entity: clinical pathological study of twelve cases, World J Surg Oncol., 2010, 8:103

[15] Hartman D.S., Hayes W.S., Choyke P.L., Tibbets G.P., From the archives of the AFIP. Leiomyosarcoma of the retroperitoneum and inferior vena cava: radiologic-pathologic correlation, Radiographics, 1992, 12, 1203–1220

[16] Yadav R.,Kataria K., Mathur S.R., Seenu V., Leiomyosarcoma of inferior vena cava: A case series of four cases,I ndian J Pathol Microbiol., 2012, 55:83-5

[17] Delis S., Triantopoulou C., Bakoyiannis A., Tassopoulos N., Dervenis C., Leiomyosarcoma of the infrarenal portion of the inferior vena cava in a cirrhotic patient with hepatitis C, Abdom Imaging, 2008, 33,222–224

[18] Matsui Y., Fujikawa K., Oka H., Fukuzawa S., Takeuchi H., Adrenal leiomyosarcoma extending into the right atrium, Int J Urol.,2002, 9, 54–56

[19] Kieffer E., Alaoui M., Piette J.C., Cacoub P., Chiche L., Leiomyosarcoma of the inferior vena cava: experience in 22 cases, Ann Surg., 2006, 244(2), 289-95

[20] Wilmshurst P., Leiomyosarcoma in the right atrium and occluding the inferior vena cava, Br Heart J.,1995, 73, 236

[21] Shvarts O., Han K.R., Lam J.S., Belldegrun A.S., Primary leiomyosarcoma of the inferior vena cava presenting as a renal mass, Rev Urol., 2004,6(1), 39-42