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Borreliosis presenting as autonomic nervous dysfunction, phrenic nerve palsy with respiratory failure and myocardial dysfunction – a case report

Case Report

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Abstract: Unrecognized and untreated Borrelia infection can progress from localized inflammation (erythema migrans) to early or late generalized stage within weeks to months. Meningoradiculitis, arthritis, multiple erythemas, myositis, and myocarditis of the early generalized stage have a good prognosis after antibiotic treatment, but late manifestations can progress to chronic disease. Phrenic nerve palsy, autonomic nervous system dysfunction and carditis with acute heart failure are among rare manifestations as well as late generalised stage with myelitis. We present a case of a patient with meningoradiculitis, autonomic nervous dysfunction, respiratory failure due to phrenic nerve palsy and acute heart failure with systolic myocardial dysfunction. The diagnosis of Borrelia infection was confirmed by positive serological testing, appropriate response to antibiotic therapy and exclusion of other diseases. Our case suggests that in unexplained respiratory failure and acute systolic myocardial dysfunction, particularly associated with signs of meningoradiculitis, Borrelia infection should be included in the differential diagnosis.

Keywords: *Borrelia Burgdorferi spp • Autonomic dysfunction • Respiratory failure • Phrenic nerve palsy • Myocardial dysfunction*

1. Introduction

Lyme disease or Lyme borreliosis is the consequence of systemic infection and the immune response to Borrelia Burgdorferi sensu lato – a spirochaete transmitted to humans by a tick bite of Ixodes ricinus [1].

In Europe, Lyme disease is the most frequent tick-borne disease with the incidence of more than 300 cases per 100.000 inhabitants [2,3]. Lyme disease can manifest in three stages. Stage I, also called early localized inflammation, appears within the first few weeks after the tick bite, and manifests itself as erythema migrans around the tick-bite site. Early generalized stage or stage II begins weeks to six months after the tick bite, and is manifested as meningoradiculitis, arthritis, multiple erythemas, myositis, and myocarditis. In late generalised stage or stage III, appearing more than six months after the inoculation of Borrelia by the tick bite, encephalomyelitis, dermatitis chronica atrophicans, arthritis, and cerebral arteritis are the main manifestations [4].

Neuroborreliosis is the term used for neurologic manifestations of Borrelia infection similar to painful polyradiculitis, but with the tick bite history, prior erythema migrans, and or serological confirmation of Borrelia infection [4,5]. It is most often caused by Borrelia garinii. It is noted in 10-20% of symptomatic patients. The majority of patients presenting with an early systemic disease and less than 5% of patients presenting with a late systemic disease which can progress to chronic disease, have a good prognosis after antibiotic treatment [2,4,6,7].

For all manifestations of Lyme disease laboratory confirmation is essential for diagnosis, except for erythema migrans. Specific laboratory testing is a direct or indirect detection of Borrelial infection. Direct detection of the antigens is provided by a culture of Borrelia Burgdorferi spp. or by nucleic acid amplification techniques. Most often indirect tests are used - serological testings, detecting IgM and IgG antibodies against Borrelia Burgdorferi spp. in peripheral blood and cerebrospinal liquor simultaneously [3,5].

In case of systemic, neurological or cardiac manifestation parenteral antibiotics are recommended such as

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ceftriaxone, or oral doxycyline in milder cases. Two to four weeks of antibiotic treatment in properly diagnosed cases make an uneventful recovery [3,8,9].

Clinical symptoms and signs of neuroborreliosis are nonspecific, mimicking several neurological entities such as polyradiculitis, multiple sclerosis, polyneuropathy, and systemic diseases such as autoimmune diseases, fibromyalgia, etc. We present a case of a patient with late manifestation of Borreliosis, presenting as acute abdominal pain and obstipation due to autonomic dysfunction and respiratory failure due to phrenic nerve palsy in addition to transient acute heart failure with global systolic dysfunction.

2. Case report

A 66-year old male with well-balanced and treated arterial hypertension was admitted to the hospital with symptoms and signs of left lumboischialgia. He was operated due to a herniated disc at the lumbar vertebra II, III, IV three years ago. In hospital, his lumboischialgic pain resolved within a few days after opioid analgesia and resting. However, the patient became obstipated with nonspecific abdominal discomfort and in the next three days unbearable pain on the left side of the abdominal and lower anterior thoracic wall with sensations of tingling in the same area developing and spreading to the right anterior side of the thorax. This “new” pain was resistant to opioids and non-steroidal anti-inflammatory drugs.

The patient also developed some problems with urination but without significant urine retention. Abdominal ultrasound was performed, revealing a steatotic liver, meteoristic colon, and enlarged prostate. Several abdominal roentgenograms followed to exclude mechanical ileus. Finally, obstipation due to autonomic nervous dysfunction was diagnosed. In spite of medical treatment by bisacodil and lactulose, obstipation persisted. Magnetic resonance imaging of the thoracic and lumbar spine could not detect any major disease of thoracic spine. Only a minor left-sided herniated disc of the third and fourth lumbar vertebra was confirmed.

Electromyogram of the lower limbs confirmed a left-sided chronic polyradicular damage between the third lumbar and first sacral nerve root.

After diagnostic evaluations of the spine were completed approximately two weeks after admission, progressive dyspnea with acute respiratory failure was noted (paO_2/FiO_2 = 178.5) as arterial blood gas analysis on inspired air showed pH 7.401, bicarbonate 29 mmol/l, paO_2 5 kPa, $paCO_2$ 7.1 kPa, HbO2 77%. Arterial hypoxia improved after 4 L/min of oxygen via a binasal catheter (paO_2 8 kPa, $paCO_2$ 6 kPa, HbO_2 91%) and paO_2/FiO_2 increased to 240. A chest roentgenogram revealed bilateral lung consolidation of the lower segments without pulmonary congestion. Pulmonary embolisms were excluded by a CT angiography but a totally collapsed lower left lung lobe and elevated left diaphragm were found.

As soon as acute respiratory failure was diagnosed, the patient was admitted to medical intensive care unit. On admission he was oriented, afebrile, with blood pressure 147/70 mmHg and pulse 72/min. He was breathing spontaneously with respiratory rate of 25/min, using accessory respiratory muscles; over both lungs breathing sounds were weakened basally. On auscultation, the status of the heart was normal. The whole abdomen was painful on palpation, no resistances were palpable, and peristalsis was barely audible. The status of the extremities was normal.

In medical intensive care unit, i.v. and urine catheters were inserted, blood pressure was measured noninvasively every hour in the first 24 hours (later at least 6-times daily), continuous ECG and pulse oximetry were started. Blood samples were drawn for laboratory testing, including arterial blood gases. Arterial pH was 7.394, bicarbonate 30.5 mmol/l, paO_2 9.93 kPa, $paCO_2$ 6.85 kPa, $SatO_2$ 94.8 %, while receiving 40% of inspired oxygen. PaO_2/FiO_2 was 186, confirming pronounced respiratory failure of unexplained origin.

Chest roentgenogram was repeated, confirming again bilateral lung consolidation of the lower segments with elevation of the left diaphragm and this time with pulmonary congestion.

As there were signs of pulmonary congestion echocardiography was performed, showing normal heart valves, normal dimensions of atria and ventricles, reduced ejection fraction to 35% (normal over 55%), and hypokinetic septum and posterior wall. Acute myocardial infarction was excluded by a series of normal troponin I levels.

In intensive care unit opioids were replaced by a non-opioid analgesic metamizol as opioids were suspected to eventually cause obstipation. In addition, iv. neostigmine was administered. At the same time he received furosemide, ramipril, and amlodipine for treatment of arterial hypertension and heart failure, dalteparin for prevention of deep vein thrombosis and doxazosin for enlarged prostate.

In the intensive care unit the neurologist confirmed bilateral hypesthesia caudal to the 5th thoracic vertebra and mild spastic paraparesis of both lower limbs, suggesting thoracic myelopathy. Lumbar puncture was performed and liquor tested for neurotropic viruses, Ebstein-Barr and cytomegalovirus. Biochemical liquor examination was suspicious for serous meningitis due to pleocytosis with a leucocyte concentration well bel-

low 1000/ml (in our patient 228/ml) with lymphocyte predominance (205/ml). The tests for viruses in the liquor were negative. Polymerase chain reaction for Borrelia did not confirm Borrelial DNA in the liquor.

Liquor and serum were also tested for Borrelia Burgdorferi antibodies. IgG antibodies for Borrelia Burgdorferi in liquor (titer 1:1.024) and serum (titer 1:1.024) were positive, whereas IgM antibodies were negative.

The patient's history was re-evaluated. He remembered a tick-bite approximately 1,5 months prior to admission and erythema migrans a few days after that. Finally, Borreliosis was diagnosed by positive immunological tests of the serum and liquor in addition to polyradiculoneuritis of the lower limbs and autonomic dysfunction.

Phrenic nerve palsy was suspected by permanent elevation of the left diaphragm on several chest roentgenograms, performed during intensive care unit stay, thoracic CT scan and ultrasound, but was linked to Borrelia infection after positive serological testing.

Borrelial origin of systolic myocardial dysfunction was considered as well, but no myocardial biopsy was performed.

Antibiotic treatment with ceftriaxone 2 g iv. per day was started for the next 21 days. The patient's complaints improved gradually within the next few days. After 14 days of medical intensive care unit stay it was possible to transfer him to the Department of infectious diseases. He was oriented, afebrile, without any pain, with blood pressure 165/105 mmHg, pulse 78/min, breathing spontaneously with respiratory rate of 16/min; over both lungs breathing sounds were weak basally. PaO_2/FiO_2 was 284 (paO_2 was 11.7 kPa, FiO_2 31%). He was mildly dyspneic at rest and at minor exertion. Dyspnea was attributed predominantly to respiratory failure since bilateral lung consolidation of the lower segments and elevation of the left diaphragm was noted on chest roentgenogram, but without pulmonary congestion at that time.

At the Department of infectious disease the patient experienced asymptomatic paroxysm of atrial fibrillation with tachycardia that converted to sinus rhythm after iv. infusion of amiodarone. Treatment by furosemide, ramipril, and amlodipine was continued.

After a total 44 days of in-hospital stay he was finally discharged home. On discharge he was without any pain; blood pressure was 130/88 mmHg, pulse 92/min. He was breathing spontaneously with respiratory rate of 14/min, his respiratory failure resolved totally as no additional oxygen was needed to reach $SatO_2$ of 95%. However, on auscultation breathing sounds were still weakened basally over both lungs; chest roentgenogram revealed minor bilateral lung consolidation of the lower segments and elevation of the diaphragm. On discharge treatment consisted of dutasteride and tamsulosin for enlarged prostate, losartan for arterial hypertension, theophylline for dyspnea, oral amiodarone for prevention of paroxysms of atrial fibrillation and of acetylsalicylic acid.

During the next months his respiratory function improved further. However, exertional dyspnea during moderate exercise and during supine position at night still persisted. He performed spirometry, which revealed a heavy restrictive lung disease with normal CO transfer factor.

Three months after discharge increased intrathecal production of IgG antibodies for Borrelia was confirmed by indirect immunofluorescence method with increased index of Borrelian antibodies IgG in liquor and serum (1.63).

A year after discharge electromyogram of the diaphragm demonstrated severe axonal injury of both phrenic nerves, but three years later nerve conduction studies of both phrenic nerves still confirmed residual axonal injury.

Echocardiography after three years showed improvement of ejection fraction to 55-60% with minor apicoseptal hypokinesia and persistence of minor diastolic dysfunction. Three years after discharge exercise stress testing at workload of 6,5 MET could not record any ischaemic ECG signs. At that time he was receiving dutasteride and tamsulosin for enlarged prostate, ramipril, carvedilol, torasemide and acetylsalicylic acid for treatment of arterial hypertension, prevention of paroxysmal atrial fibrillation and heart failure and allopurinol for newly diagnosed gout.

3. Discussion

Our case suggests that stage II Borreliosis in adults may demonstrate itself as neurological and even as myocardial dysfunction.

The polyradiculoneuritis of the lower limb of our patient was attributed at the beginning to herniated lumbar disc. Later on, when thoracic myelopathy with bilateral hypesthesia caudal to the 5th thoracic vertebra and mild spastic paraparesis of both lower limbs were discovered, IgG antibodies for Borrelia Burgdorferi in liquor and serum were positive and in particular improvement of neurological complaints after appropriate antibiotic therapy, neuroborreliosis was diagnosed.

Phrenic nerve palsy and autonomic dysfunction, being the leading complaints in our patient, are very rare manifestations of stage II borreliosis, in contrast to cranial nerve palsy that was already frequently observed, most commonly affecting facial nerve uni- or bilaterally [2]. In Lyme disease there are only few case reports of phrenic nerve palsy and of autonomic dys-

function such as intestinal pseudo-obstruction, reflex sympathetic dystrophy and severe orthostatic hypotension [10-16]. Duray et al. report about lymphoplasmocellular infiltrates in the autonomic ganglia of patients with Lyme disease [17].

In our patient, there were problems with urination, but we assume that they were the consequence of the enlarged prostate. However, it is possible that they were worsened by Borrelia infection.

Obstipation in our patient was the leading sign of autonomic dysfunction, most probably due to Borrelia infection and to minor extent to opioid treatment as cessation of opioids did not improve obstipation satisfactory. Antibiotic treatment most effectively resumed bowel peristalsis.

Phrenic nerve palsy, responsible for worsening of respiratory failure and for admission to intensive care unit, was diagnosed gradually. The suspicion was raised by permanent elevations of the left diaphragm as confirmed by several chest roentgenograms, thoracic CT scan and ultrasound. Not until immunological tests of the serum and liquor were positive for Borrelia infection phrenic nerve palsy was linked to Borrelia infection. However, the first electromyogram study of the diaphragm demonstrated severe axonal injury of both phrenic nerves, and the electromyogram performed one year after discharge confirmed phrenic nerve injury. In addition, the phrenic nerve conduction study 3 years later still found some residual axonal injury. Residual axonal phrenic nerve injury after years pointed to transition to more chronic Borrelia infection - stage III neuroborreliosis, in which irreversible and progressive neurological damage is present in spite of parenteral antibiotic therapy that was started as soon as Borrelia infection was confirmed by positive serological tests [2].

Echocardiography in our patient demonstrated decreased ejection fraction of the left ventricle with hypokinesis of the left ventricle. In addition to Borrelia infection our patient had arterial hypertension that could participate in the observed decrease of ejection fraction. Echocardiographic changes improved after antibiotic therapy and treatment by antihypertensive agents, including inhibition of angiotensin converting enzyme by ramipril. During treatment we observed a paroxysm of atrial fibrillation. This finding is not specific for Borrelia carditis or even not described in this entity so far, but it occurs most often secondary to heart failure. The hallmarks of Borrelia carditis are atrioventricular blocks and myocarditis. Borrelia carditis is otherwise rare - with the incidence of 1% in all Lyme disease cases [18]. Unrecognized hypertensive heart disease with decreased ejection fraction was considered as a possible reason of echocardiographic findings and resulting paroxisms of atrial fibrillation. However, improvement after antibiotic therapy in particular of ejection fraction and of clinical signs pointed to Borrelial origin of heart failure.

Microbiological proof by direct microscopic examination in tissue specimens or detection of borrelial nucleic acids with PCR – polymerase chain reaction in body fluids and/or cultivation of bacteria or positive serological testing are crucial to confirm the presence of Lyme disease. In our case only serological testing of liquor and serum were positive for Borrelia Burgdorferi IgG antibodies, confirming the infection.

Myocardial biopsy was not performed to confirm Borrelia carditis.

We conclude that in cases with autonomic dysfunction and acute respiratory failure, in particular if they are observed together with unknown origin of acute heart failure with decreased ejection fraction, Borrelia infection should be included in differential diagnosis in order to start appropriate antibiotic therapy as soon as possible. In this way severe symptoms and signs of Borrelia infection can be mastered in time to prevent transition to stage III neuroboreliosis, when irreversible consequences are possible.

References

[1] Rizzoli A., Hauffe H.C., Carpi G., Vourc'h G.I., Neteler M., Rosa R., Lyme borreliosis in Europe. Euro. Surveill., 2011, http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19906

[2] Satz N., Klinik der Lyme-Borreliose, 2nd Edition., Verlag Hans Huber, Bern, 2002

[3] Stanek G., Wormser G.P., Gray J., Strle F., Lyme borreliosis, Lancet 2012, 379, 461-473

[4] Halperin J.J., Nervous system Lyme disease, Infect. Dis. Clin. N. Am., 2008, 22, 261-274

[5] Stanek G., Strle F., Lyme borreliosis: a European perspective on diagnosis and clinical management, Curr. Opin. Infect. Dis., 2009, 22, 450-454

[6] Steere A.C., Borrelia burgdorferi (Lymedisease, Lymeborreliosis), In: Mandell G.L., Bennet J.E., Dolin R. (Eds.), Principles and practice of infectious diseases, 5th Edition, Churchill Livingstone, Philadelphia, 2000

[7] Nau R., Christen H.J., Eiffert H., Lyme disease – Current state of knowledge, Dtsch. Artzebl. Int., 2009, 106, 72–82

[8] Wormser G.P., Dattwyler R.J., Shapiro E.D., Halperin J.J., Steere A.C., Klempner M.S., et al., The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America, Clin. Inf. Dis., 2006, 43, 1089–1134

[9] Gray J., European Concerted Action on Lyme Borreliosis 2012, http://meduni09.edis.at/eucalb/cms_15/

[10] Faul J.L., Ruoss S., Doyle R.L., Kao P.N., Diaphragmatic paralysis due to Lyme disease, Eur. Respir. J., 1999, 13, 700-702

[11] Silva M.T., Sophar M., Howard R.S., Spencer G.T., Neuroborreliosis as a cause of respiratory failure, J. Neurol., 1995, 242, 604-607

[12] Ishaq S., Quinet R., Saba J., Phrenic nerve paralysis secondary to Lyme neuroborreliosis, Neurology, 2002, 59, 1810-1811

[13] Winterholler M., Erbguth F.J., Tick bite induced respiratory failure. Diaphragm palsy in Lyme disease, Intensive Care Med., 2001, 27, 1095

[14] Chatila R., Kapadia C.R., Intestinal pseudoobstruction in acute Lyme disease: a case report, Am. J. Gastro., 1998, 93, 1179–1180

[15] Gila L., Guerrero A., Astarloa R., Martí P., Gutiérrez J.M., Reflex sympathetic dystrophy. A new manifestation of Lyme disease?, Enferm. Infec. Microbiol. Clin., 1990, 8, 32–35

[16] Burman M., Nguyen H.L., Murthy V., Sen Gupta P., Davies C., Wragg A., et al., Severe orthostatic hypotension in a diabetic patient may not be due to diabetic autonomic neuropathy, Clin. Med., 2011, 11, 290-291

[17] Duray P.H., Histopathology of clinical phases of human Lyme disease, Rheum. Dis. Clin. North. Am., 1989, 15, 691–710

[18] Huppertz H.I., Böhme M., Standaert S.M., Karch H., Plotkin S.A. Incidence of Lyme borreliosis in the Würzburg region of Germany, Eur. J. Clin. Microbiol. Infect. Dis., 1999, 18, 697–703