

LYME NEUROBORRELIOSIS ASSOCIATED WITH THROMBOPHILIA – THE QUANDARY OF THE PARTICIPATION OF THESE TWO DISORDERS IN VISUAL ALTERATIONS: A CASE REPORT

VICTORIA BÎRLUȚIU¹, RAREȘ MIRCEA BÎRLUȚIU²

^{1,2}“Lucian Blaga” University of Sibiu, ²“Foișor” Clinical Hospital of Orthopedics, Traumatology and Osteoarticular Tuberculosis, Bucharest

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Abstract: Each year, more than 300 000 cases of Lyme disease are confirmed in the US and 85 000 cases in Europe, of which in 15%-20% cases, the central nervous system involvement is recorded. Chronic Lyme encephalopathy, rarely associated in North America, more commonly described in Europe, is hard to be diagnosed after a long period of time after the infection; no clinical or imagistic elements are evocative for neuroborreliosis. The presented case is of a patient with unidentified thrombophilia with borreliosis that causes brain thrombosis, unusual manifestations of reversible blindness and amputation of the vision field.

INTRODUCTION

Chronic Lyme disease is associated with hypercoagulability, with increasing fibrinogen, fibrin, coagulation factor II (prothrombin) and thrombin/antithrombin complexes. Pairing chronic Lyme disease with hereditary hyper-coagulability predisposes in addition to blood clotting. We present the case of a patient with thrombophilia and neuro- borreliosis, whose hypercoagulable state was diagnosed in the course of the chronic infection.

CASE REPORT

We present the case of a 45-year-old Caucasian woman, pharmacist assistant by profession, with a history of duodenal ulcer (1990) and a miscarriage, who at admission presented occipital headache and vision changes that were reported like bilateral amputation of lower visual field. Symptoms began 1 month prior to her presentation in the emergency room, where a cranial computerized tomography (CT) scan was performed in order to exclude an acute intracranial pathology.

The conclusions of the CT scan were: minimal maxillary sinus mucosal thickening and right sphenoid sinus retention cyst. The patient was evaluated by an otorhinolaryngologist, the association between the headache and an ear, nose, and throat condition being excluded. The patient continues to experience headaches, reports visual changes and image distortion, becomes agitated, being diagnosed with anxiety and is treated as an outpatient with anxiolytics. 30 days after the onset, vomiting occurs, the visual changes are emphasized, blindness is present and resolves spontaneously 24 hours later, symptoms for which she is admitted to the Infectious Diseases Department.

Neurologic examination and physical examination were unremarkable: afebrile, without signs of meningeal irritation, symmetrical light reaction pupils, without motor deficit, except for osteotendinous hyperreflexia and right Babinski reflex in flexion.

Laboratory examinations revealed the following

alterations: a thrombocytopenia of 116.000/mm³, alanine aminotransferase 78U/L (reference values 20 to 43), aspartate aminotransferase 44U/L (reference values 20 to 40), international normalized ratio (INR) of 1.64, Quick's time of 19.8 seconds; viral hepatitis B, C, HIV, herpes simplex virus type 1 and type 2, cytomegalovirus and the Epstein-Barr virus infections are excluded, as well as the collagen disease, the thyroid disease, syphilis, tuberculosis and toxoplasmosis. The cerebrospinal fluid (CSF) examination was associated with a low CSF pleocytosis of 54 leukocytes/mm³ with 99% lymphocytic pleocytosis and a protein of 0,429 g/l.

The cranial CT scan was performed again and revealed occipito-parietal lacunar and hypodense lesions with gyrus hyperdensity after intravenous contrast agent was injected, without other parenchymal injuries; the conclusion was: bilateral occipito-parietal subacute and chronic ischemia. A cranial magnetic resonance imaging (MRI) was performed and the findings were: bilaterally occipital hyperintensities FLAIR changes with temporal extension, affecting the white and gray matter, and marked peri-gyrus hypervascularization after i.v administration of contrast agent.

The conclusion of the MRI was: bilateral occipital encephalitis, with left temporal extension. The patient is investigated from a hematological point of view: a thrombophilia is confirmed (Factor V Leiden mutation, mutation of methylenetetrahydrofolate reductase (MTHFR) C677T – positive) and a treatment with anti-clotting medication was initiated with Low molecular weight heparin (LMWH), enoxaparin sodium. Because the patient reports a tick bite five years ago without erythema migrans, she is investigated also for borreliosis; immunoglobulin (Ig) G ELISA positive test, Immunoblot analyses for Lyme IgG being positive from both serum and CSF. Chemokine (C-X-C motif) ligand 3 (CXCL3) detection was not performed.

Her evolution was favourable under treatment with ceftriaxone 2g/day for 21 days, anti-clotting medication, with improved visual field that still remains decreased, at

¹Corresponding author: Victoria Bîrluțiu, B-dul. Corneliu Coposu, Nr. 2-4, Cod 550245, Sibiu, România, E-mail: victoriabirlutiu@yahoo.com, Phone: +40744 875751

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discharge a treatment with doxycycline is recommended 2x100mg/day for the next 60 days.

DISCUSSIONS

Lyme disease is attributed in North America to *Borrelia burgdorferi* sensu stricto. (1) In Europe, there are four species of *Borrelia* responsible for the disease: *B. burgdorferi*, *B. afzelii*, *B. garinii* and *B. spielmanii*. In addition, there are other species involved in the disease in certain geographical areas: *B. americana*, *B. andersons*, *B. bavariensis* (*B. garinii* OspA serotype 4), *B. bisettii* (2), *B. lonestari* (3), *B. valaisiana*, *B. kurtenbachii*, *B. miyamotoi*, phylogenetic similar (4,5) and *B. crocidurae* (6), isolated from patients with Lyme-like disease clinical picture.

Each year, more than 300 000 cases of Lyme disease are confirmed in the US (7), 85 000 cases in Europe, of which, in 15%-20% of cases, the central nervous system involvement is recorded. The nervous system involvement in Lyme disease is present in the second stage of evolution of the disease, the most commonly being cranial nerve palsy (especially the facial nerve is affected, in 1 of 3 cases the palsy is bilateral (8), radiculopathy associated with general symptoms like: arthralgia, myalgia and fatigue.

In Europe, most commonly found is the peripheral nervous system involvement as painful radiculitis with sensory, motor or mixed symptoms. Less frequently severe symptoms such as diffuse polyneuropathy that imitates Guillain-Barre syndrome are identified, axonal neuropathy, impaired CNS such as lymphocytic meningitis with low cellularity, a slight increase of proteins, and normal or slightly increased levels of CSF glucose. Chronic Lyme encephalopathy, rarely associated in North America, more commonly described in Europe, is hard to be diagnosed after a long period of time after the infection. No clinical or imagistic elements are evocative for neuroborreliosis - MRI aspects suggest either a brain stem injury or a cerebrovascular ischemia. It is associated with memory and attention impairment, emotional lability, sleep disorders in 15% of cases (9,10), psychosis (11), schizophrenia (12), hearing or visual hallucinations. (11,13) Meningo-vascular Lyme neuroborreliosis evolves with secondary cerebral infarcts (14), through inflammatory cell infiltration, adventitia fibrosis, intima proliferation in lumen and complete arterial obstruction by thrombus, brain stem infarction. A second form of chronic Lyme neuroborreliosis is chronic Lyme meningoencephalomyelitis/meningoencephalitis that can evolve as infiltrative or atrophic type. In the infiltrative type, from a pathogenic point of view, there is an important cellular immune response, perivascular lymphocytic infiltrate, microglial reaction and vasculitis; in some cases multiple periventricular demyelinating areas are described. The atrophic form is dominated by cognitive decline, dementia and subacute presenile dementia (15,16), predominantly frontotemporal cerebral atrophy evidenced by neuroimaging (17), neural destructions (15), and microglia and astrocyte proliferation. Other symptoms in the chronic stage are transverse myelitis and radiculoneuritis. After Lyme disease, cognitive and psychiatric symptoms may persist, without the possibility of establishing the presence of the infection in the CNS and without any benefits after applying the antibiotic treatment again. Through the symptomatic pleiomorphism (18), Lyme disease is suitable for the differential diagnosis with other chronic inflammatory diseases, degenerative diseases, autoimmune diseases, psychosomatic disorders (19), the difficulty of diagnosis being motivated both by not

knowing the moment of the tick bite and of the erythema migrans (in 30% of cases). The therapeutic response of late neurological manifestations forms is really good at oral therapy with doxycycline. (20)

CONCLUSIONS

The presented case is of a patient with unidentified thrombophilia (Factor V Leiden positive mutation, mutation of MTHFR C677T - positive) until now, the emergence of the neurological manifestations, with a miscarriage, for which she was not investigated in terms of a hematological disorder on that particular occasion. Heterozygous mutations of factor V Leiden are associated with a more increased risk of thrombosis held between 20-35 times higher than the general population.

Our patient's clinical picture is due to the combination of coagulation activation by *Borrelia* infection in a patient with a hereditary predisposition. The presence of hypoprothrombinemia, thrombocytopenia was most likely associated with antiprothrombin antibodies or antiphospholipid antibodies (aPL), which were tested later, explaining the presence of thrombosis. MTHFR 677 is more often associated with early heart disease and stroke. Pairing this hereditary predisposition with borreliosis causes brain thrombosis, unusual manifestations of reversible blindness and amputation of the vision field, rarely cited in the literature.

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