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SCHIZOAFFECTIVE DISORDER, BIPOLAR TYPE: ASSOCIATION WITH CRONIC LYME DISEASE

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INTRODUCTION

Lyme disease (LD) is a tick-borne infectectious disease caused by spirochete Borrelia burgdorferi (Bb). Bb infection usually develops in three stages. Several days following intradermal inoculation, erythema migrans (EM) rash may be evident (stage 1.). After a month Bb invades the blood stream causing fever, malaise, chills, headache, muscle pain, arthralgiae, joint pain and swelling of lymph nodes. A few weeks to few months after infection non-specific symptoms usually disappear and the disease evolves (stage 2), which usually corresponds with rheumatic, neurologic or cardiac disturbances (headache, dizzines, facial palsy, shooting pain, numbness, tingling, arthralgia, bone pain, arrhytmia, shortness of breath, Spirochete can invade the central nervous system (CNS) resulting in lyme neuroborreliosis (LNB) in 10% to 15% of patients with untreated or undertreated Bb infection (Halperin 2015), (Zajkowska et al.2007). Patients with LNB frequently experience peripheral nervous systems inflammation with cranial nerve palsy, multifocal inflammatory changes, myositis, and rarely inflammatory changes in the central nervous system (CNS) causing meningitis, encephalitis, transverse myelitis. As many systemic infectious and inflammatory diseases, many months or years after the initial infection, different late-onset neuropsychiatric manifestations may occur (stage 3); psychiatric symptoms, seizures, cognitive impairment and encephalopathy (Wright et al, 2012, Markeljević et al, 2011). Lyme neuroborreliosis can manifest with different psychiatric conditions, mood disturbances, psychosis with hallucinations, delusions, paranoia, and also cognitive impairment with memory and concentration problems. However, these symptoms do not necessarily indicate CNS infection and alone are not diagnostic feature of LNB, because many things can affect behavior in the absence of damage of the CNS. Furthermore, LNB may develop even after antibiotic therapy, suggesting that Bb infection may cause lyme-induced neurodegenerative changes (Mattingley et a., marker of the tissue hypoxia and disease severity as well as the predictor of the outcome at seriously diseased patients. 2015). Antimicrobial therapy cures about 95% of LNB cases, and usually required prolonged parenteral and oral antibiotic treatment in those rare patients with parenchymal CNS involvement (Halperin et al 2015)

Herein, we describe one patient with untreated chronic LNB presented with bipolar disorder. Emphasis is placed on the atypical onset of clinical symptoms, difficulties encountered in establishing diagnosis and successful treatment.

CASE DESCRIPTION

A 45-year-old men admitted to the outpatient unit of the Department of Neurology, Clinical Hospital Centre Zagreb, Croatia due to persistent neuropsychiatric disturbances including dizzines, muscle weakness, exertion intolerance, chronic fatigue, sleep disturbance, psychotic symptoms, mood symptoms and cognitive impairment, which had progressed significantly over the past six months. At addmission he manifested psychotic symptoms; delusion, auditory hallucinations, disorganized behavior, rapid speech and thinking. There were also mood symptoms including agitation, dysphoria and affective distance. He was on olanzapine and aripiprazole at the time of addmission and had an outpatient psychiatrist.

Medical history reveals that the patient's initial symptoms appeared in May 2019; dizziness, tinitus, nausea, malaise, arthralgia, muscle pain and muscle weakness, for which he was examined in the emergency department. Unit. He was recommended additional internal and neurological examination, which he refused. His symptoms soon worsened, and he developed an action tremor in his hands, lost his apetite and lost body weight. The patient's first psychiatric addmission was in Decemeber 2019 due to manic symptoms; disinhibition, restlessness, excess energy, irritability, agitation, aggressiveness,

excessive and rapid speech, He had trouble concentrating and sleeping. Cognitive functions were impaired by attention and concentration disorders. The patient met DSM-V criteria for schizoaffective disorder, bipolar type I, with a typical intermittent curse, of the disease, in which psychotic symptoms and symptoms of manic behavior alternated. He has been started on haloperidol, fluphenazine, olanzapine and diazepam, but without significant effect. Meanwhile, his mental state progressed in the sense of insane fixations, somatic delusions and confusion. On the behavioral level he manifested aggressive tendencies. The patient became completely inpendent on the supervision and care of another person. He was then put on olanzapine and ariprirazole, which was discontinued after a few months by the patient due to a poor effect and adverse effects. Since 2020, he has been examined several times in the emergency unit due to polymorphic complaints; myalgia, arthralgia, nausea, vomiting, weight loss, muscle weaknes, but again refused further diagnostic evaluation. In April 2023, extensive medical work up was performed. Brain MRI showed no abnormalities. Thyroid-stimulating hormone (TSH), T3 and T4 were within normal range. Electromyoneurography findings showed a radicular lesion without signs of myopathy and polyneuropathy. Immunoserology including Hu, Yo, Ri, ANA, ENA, RF, CCP, ANCA autoantibodies to intracellular neuronal antigens and autoantibodies against extracellular neuronal antigenes (NMDAR, AMPAR1/R2, DPPX, CASPR2, LGI1, GABAR B1/B2 were all negative. On that occasion, he remembered that he had a tick bite in 2013, but he did not notice a bull's eye EM rash, so he did not seek medical help or was treated with antibiotics. A lyme antibody enzyme immunoassay was positive for IgG, while an indirect immunofluorescence assay for lyme IgM was negative. Cerebrospinal fluid (CSF) analysis showed total protein 1.1 g/l, pleocytosis (330/3) and Bb-specific antibiodies IgG produced intrathecally. The diagnosis of lyme neuroborreliosis (LNB) was established according to the established criteria (Mygland et al. 2010). It was determined that anmicrobial treatment was necessary as he has not been treated with antibiotics 10 years prior and there were clear signs of active Bb infection. The patient was started on intravenous ceftriaxon 2 g/daily during 35 days followed by doxycycline 100 mg (twice daily) eight weeks. We evaluated psychiatric symptoms and physical symptoms using clinical rating scales for symptomatology. Three weeks after the start of therapy, his psychotic symptoms began to improve. After completion of treatment, he had completely recovered from psychotic symptoms, but some mood symptoms remained, racing thoughts, poor concentration and decreased need for sleep. The neurological examination revealed mild postural tremor, CSF analysis showed improvement of pleocytosis (14/3). An enzyme immunoassay showed significantly lower titer of lyme antibody. On the combination of clonazepam in the morning and olanzapine 5 mg at bedtime, the patient showed improvement, with recurring fatigue, malaise, muscle aches, and cognitive difficulties that persisted for more than 6 months after treatment, which reflects symptoms of chronic LD.

DISCUSSION

This case emphasizes the clinical course, workup findings and management of chronic LNB, in a patient whose leading symptom is schizoaffective disorder of bipolar type I. This case is unique in that it demonstrates schizoaffective disorder, bipolar type I as a consequences of unrecognized and untreated chronic LNB, with a good therapeutic response to antibiotic therapy even years after tick bite anf bb infection.

It has been reported that LNB can manifest with a wide range od psychotic and mood symptoms (Fallon et al. 1994) Although the schizoaffective disorder is a rare complication of Bb infection, it is crucial to recognize them and start management early. Patients are more likely to recover completelly if Bb infection is detected and treated early as possible after tick bite, in the acute stage within the first 30 days of exposure. Because Bb infection is frequently missed or misdiagnosed, and up to 30% of patients did not rembember experiencing EM rash, 5-20% of patients may develop chronic LD. The risks of chronic LD increases the longer a Bb infection stays untreaed or undertreated, but some people experience persistant symptoms, even after treatment. Chronic LD is usually marked by symptoms of fatigue, fevers, malaise and muscle aches. The treatment failure rate for chronic LD was estimated 16-39% for early LD. Up to 15-40% late-stage lyme patients develop neurological disorders. It is unclear why some individuals experience chronic symptoms, even after treatment. Few cases have shown that patients can develop neuropsychiatric complications even after antibiotic therapy (Bär et al. 2005, Mattingley and Koola 2015). Iti is believed that Bb infection may trigger an autoimmune response and prolonged inflammation as a result of interactions between damaged neurons and hyperactive microglia. This uncontrolled inflammatory mediated neurodegenerative damage can manifests in the chronic symptoms of LD secondary to Bb infection (Bransfield et al. 2012).

As a part of investigation of clinical spectrum of LD, this patient manifested chronic LD with physical, cognitive and emotional symptoms. Psychiatric symptoms in our patient developed several years after the tick bite and Bb infection, and the patient has not been consequently treated with antibiotics. Psychiatric symptoms improved significantly after prolonged antibiotic therapy, which indicates that the psychiatric symptoms in our patient could be a consequence of the direct Bb invasion, and to a lesser extent the result of inflammation-mediated neurological damage. After the ceftriaxon and doxycycline treatment the CSF findings improved, but not completely normalised. It is still unclear whether different symptoms of chronic LD are attributable to active infection or inflammatory process. However, effective and sufficient treatment with antibiotics is crucial, not only in the acute but also in the chronic phase of the disease, especially in previously untreated patients, since the majority of symptoms improved until the terminal stage of the disease with encephalopathy associated with permanenet cognitive impairment. Contrary, presence of specific Bb-immunoglobulins in serum and CSF, in the absence of

specific clinical symptoms that would indicate CNS involvement, routine antimicrobial treatment in already treated patients is not indicated. The need for therapy is assessed according to neuropsychiatric symptoms, not just CSF finding, since serum findings and intratecal synthesis of antibodies may persist for years in LNB, and their further evaluation is sometimes indicated. Serological tests of LD should include simultaneous detection of specific antibodies in the serum and CSF as assesment of antibodies index.

CONCLUSION

We have described here an unusual case of chronic untreated LD in a patient with bipolar disorder. Despite the fact that antimicorbial treatment was started at a late stage of the disease, it led to a complete recovery of bipolar disorder, while the LD progressed to the stage of chronic LD with symptoms of fatigue, malaise and cognitive disturbances. The emphasis is on the antimicrobial treatment of chronic LNB because recovery can be significant despite the fact that the treatment was started at a late stage of the LD. Literature in regards to bipolar disorders in the setting of Bb infection is scarce. Future studies are needed to elucidate the effectiveness of antibiotic therapy in the treatment of bipolar disorder in untreated chronic LNB.

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None to declare.

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Iva Šarac: conception, writing the first draft, manuscript preparation, execution.
Helena Šarac: conception, organization, manuscript preparation, analysis, design.
Fran Borovečki: organization, review and critique.
Neven Henigsberg: analysis, review and critique.
Hanna Pašić: design, analysis
Ivan Jurak: organization, analysis.

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