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Case Report

Neuroborreliosis in an immunosuppressed patient

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ABSTRACT

Neuroborreliosis is a rare but significant manifestation of Lyme disease, particularly in immunosuppressed individuals. We present the case of a 43-year-old patient with a history of follicular lymphoma in remission, currently undergoing maintenance therapy with Rituximab, who presented with progressive neurological symptoms including peripheral facial paralysis, headache, tremors, and lower back pain. Initial cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis, but serological and PCR tests for *Borrelia burgdorferi* were negative. Given the epidemiological context and clinical presentation, a probable diagnosis of neuroborreliosis was made, with the seronegative results attributed to immunosuppression. The patient responded well to intravenous ceftriaxone with significant clinical improvement. This case highlights the diagnostic challenges of neuroborreliosis in immunosuppressed patients and emphasizes the importance of clinical judgment in the absence of confirmatory laboratory findings.

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Neuroborreliosis en un paciente inmunosuprimido

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RESUMEN

La neuroborreliosis es una manifestación rara pero significativa de la enfermedad de Lyme, particularmente en individuos inmunodeprimidos. Presentamos el caso de un paciente de 43 años con antecedentes de linfoma folicular en remisión, actualmente en terapia de mantenimiento con Rituximab, quien presentó síntomas neurológicos progresivos que incluían parálisis facial periférica, cefalea, temblores y dolor lumbar. El análisis inicial del líquido cefalorraquídeo (LCR) mostró pleocitosis linfocítica, pero las pruebas serológicas y de PCR para *Borrelia burgdorferi* fueron negativas. Dado el contexto epidemiológico y la presentación clínica, se realizó un diagnóstico probable de neuroborreliosis, atribuyéndose los resultados seronegativos a la inmunodepresión. El paciente respondió bien a la ceftriaxona intravenosa con una mejoría clínica significativa. Este caso resalta los desafíos diagnósticos de la neuroborreliosis en pacientes inmunodeprimidos y enfatiza la importancia del juicio clínico en ausencia de hallazgos de laboratorio confirmatorios.

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1. INTRODUCTION

Lyme disease, caused by *Borrelia burgdorferi*, is a multisystem infectious disease transmitted by ticks of the *Ixodes* genus [1]. Neuroborreliosis, a neurological manifestation of Lyme disease, typically presents with lymphocytic meningitis, cranial neuropathies, and radiculitis [2]. Diagnosis is generally confirmed through serological testing and CSF analysis. However, patients receiving B-cell depleting therapies, such as Rituximab, may not develop detectable antibody responses, complicating the diagnostic process. We present a case of probable neuroborreliosis in an immunosuppressed patient with negative serological tests, highlighting the need for a high index of clinical suspicion in such cases.

2. CASE REPORT

A 43-year-old man with a history of follicular lymphoma diagnosed in 2023, treated with R-CHOP chemotherapy followed by maintenance with Rituximab, visited his primary care physician in June 2024 due to cough, cold-like symptoms, and general malaise. He was treated symptomatically for a possible viral infection. One month later, he returned due to bilateral lower back pain, non-radiating, unresponsive to analgesics and anti-inflammatories, and lacking mechanical features. Four days later, the patient developed a headache and elevated blood pressure, prompting evaluation at an urgent care center and subsequent referral to the hospital emergency department for persistent headache despite analgesic treatment. Blood tests and brain CT scan were normal.

Following the ER visit, his primary care physician reviewed ambulatory blood pressure monitoring (ABPM) data, initiated antihypertensive treatment, and the headache resolved. Three days later, the patient returned complaining of worsening back pain preventing sleep, a progressively worsening tremor over the past week, and sudden onset of left-sided peripheral facial paralysis. Physical examination revealed, in addition to facial paralysis, horizontal saccades in both eyes, right eye tics, an unsteady tandem gait, mild dysmetria in the right hand during the finger-to-nose test, asynchronous intention tremor mainly in the upper limbs and head, and negative meningeal signs. The patient also recalled a tick bite about six weeks prior, which produced an erythematous lesion consistent with erythema migrans. Given these findings, he was again referred to the hospital emergency department, where hospitalization for further evaluation was decided.

Upon admission, the patient was afebrile with stable vital signs, except for elevated blood pressure. Laboratory analysis showed a normal blood count, a mild increase in creatine kinase 587 U/L [50-200 U/L], and positive IgM for Epstein-Barr virus (EBV). From the extensive laboratory workup performed to investigate a possible source of facial paralysis and headache taking into account patient's history of follicular lymphoma and ongoing Rituximab therapy, only EBV IgM was detected; since this finding was not

consistent with the patient's clinical presentation, a lumbar puncture was subsequently performed. We also highlighted that the positive EBV IgM was considered incidental, as PCR for EBV was negative in both plasma and CSF. Cerebrospinal fluid (CSF) analysis revealed 783 /µl [> 50/µl], mononuclear cells, mildly elevated proteins 242 mg/dL [> 50 mg/dL], and normal glucose levels. PCR testing for common viral and bacterial pathogens, including *Borrelia burgdorferi*, was negative. Brain MRI showed mild enhancement of the right trigeminal nerve without other abnormalities (Figure 1).

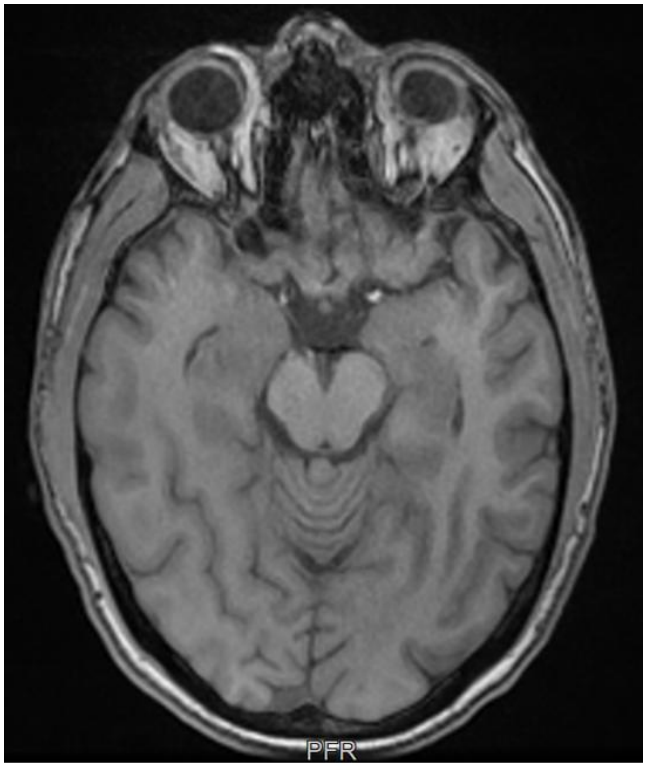

Figure 1*: Brain MRI showed mild enhancement of the right trigeminal nerve without other abnormalities.*

Given the clinical presentation and epidemiological context, a presumptive diagnosis of neuroborreliosis was made. Rituximab-induced immunosuppression was considered responsible for the lack of antibody response in serum and CSF. Empirical treatment with intravenous ceftriaxone (2 g/day) was initiated, with marked clinical improvement. The patient was discharged to complete a 14-day antibiotic course through a home hospitalization program. Follow-up revealed significant improvement in neurological symptoms, although facial paralysis persisted for a month before resolving. Microbiology testing detected PCR bands compatible with *B. burgdorferi* s.l. infection, targeting fragments of the flaB gene (specific to Lyme group borreliae) and the 5S-23S rRNA intergenic spacer. Nucleotide sequences showed 100% similarity (452 bp and 182 bp, respectively) with those of flaB and 5S-23S rRNA from *Borrelia garinii*.

3. DISCUSSION

This case illustrates the diagnostic challenges of neuroborreliosis in immunocompromised patients. Rituximab, an anti-CD20 monoclonal antibody, depletes B cells, affecting the humoral immune response and potentially causing false-negative serologic results [3]. Studies suggest that Lyme disease serology may be unreliable in these cases; requiring clinical diagnosis based on epidemiological exposure, symptoms, and CSF findings. Empirical antibiotic treatment should be considered when clinical suspicion is high [4].

The differential diagnosis included viral meningoencephalitis, lymphomatous infiltration, and other infectious or autoimmune causes. Positive EBV IgM was considered incidental, as EBV PCR was negative in both plasma and CSF [5]. MRI findings suggested possible involvement of the trigeminal nerve, though no definitive evidence of alternative causes was found.

This case underscores the importance of recognizing Lyme disease in immunosuppressed individuals and highlights the limitations of standard serologic tests. Similar diagnostic challenges have been recently described in immunocompromised patients receiving Rituximab [6], highlighting the role of PCR and CSF biomarkers such as CXCL13. Clinicians should maintain a high index of suspicion for neuroborreliosis in patients with compatible symptoms and epidemiological exposure, even in the absence of confirmatory laboratory findings [7].

4. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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