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LETTER TO THE EDITOR

Concomitant neurosyphilis and herpes simplex encephalitis in an immunocompetent patient: a case report

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Dear editor: Neurosyphilis (NS) has increased in incidence over the last few decades, particularly during the acquired immunodeficiency syndrome (AIDS) era [1]. Since NS is highly treatable, early diagnosis and management is essential. However, as one of the "great imitators", NS can present with atypical neurological manifestations besides the classical "tabes dorsalis" and dementia [1], which contribute to delays in treatment. Here, we present a challenging case of dual infection with NS and herpes encephalitis (HSE).

A 51-year-old male was brought to our hospital after he was found unconscious in his home. Three months prior to admission, his family had noted social isolation and behavioral changes and the patient complained of visual and auditory hallucinations. Two weeks before his admission, he was referred to psychiatry after he developed agitation and behaved aggressively. He had no other relevant history. The psychiatric work-up included a negative brain magnetic resonance imaging scan (MRI, Fig. 1) and a normal biochemical work-up. He was diagnosed as having a psychotic episode and received haloperidol and lorazepam with some control of his symptoms.

Upon arrival to the emergency department, he was found to be unresponsive, tachycardic and in respiratory acidosis. He had a generalized tonic-clonic seizure that responded to diazepam. He was afebrile and there were no localizing findings on neurological examination. Standard biochemical tests were normal (complete blood count, blood chemistry, liver function tests, and autoimmune work-up). He was intubated and admitted to the intensive care unit, where he was treated with sodium valproate. After 5 days, he was weaned off the ventilator and transferred to the neurology service. He remained inattentive and his neurologic exam revealed universal hyperreflexia and frontal release signs. An electroencephalogram showed diffuse generalized slowing and bi-frontal irritative activity. An MRI showed T2 hyperintensities with restricted diffusion in the fronto-temporal white matter (Fig. 1). MR angiography was normal. Cerebrospinal fluid (CSF) showed ten lymphocytes, discreetly elevated protein (71 mg/dL) and normal glucose. He tested negative for human immunodeficiency virus serology, but had a positive serum venereal disease research laboratory (VDRL) (1:16 dilution). CSF VDRL was positive (1:4 dilution), and NS was confirmed by a positive fluorescent treponemal antibody-absorption test. CSF polymerase chain reaction was positive for herpes simplex virus 1 (HSV-1).

The patient was stated on IV penicillin (24,000,000 UI/day) and acyclovir (10 mg/kg TID) and continued sodium valproate. After 2 weeks, the patient was alert and cooperative; he could follow complex commands and had no memory alterations, although he remained temporally disoriented. At 1 month follow-up, the patient had resumed his normal daily activities.

Despite the difficulty in associating a specific imaging pattern with NS, there are two classical findings: cerebral gummas (dural-based lesions mimicking meningiomas) and mesial temporal lobe abnormalities [1]. The latter are particularly relevant for a differential diagnosis with HSE. Indeed, there are several reports of NS mimicking HSE in the literature. In one case, a 50-year-old man presented with a 3-month history of neuropsychiatric symptoms [2]. His MRI showed T2 hyperintensities with restricted diffusion in both mesial

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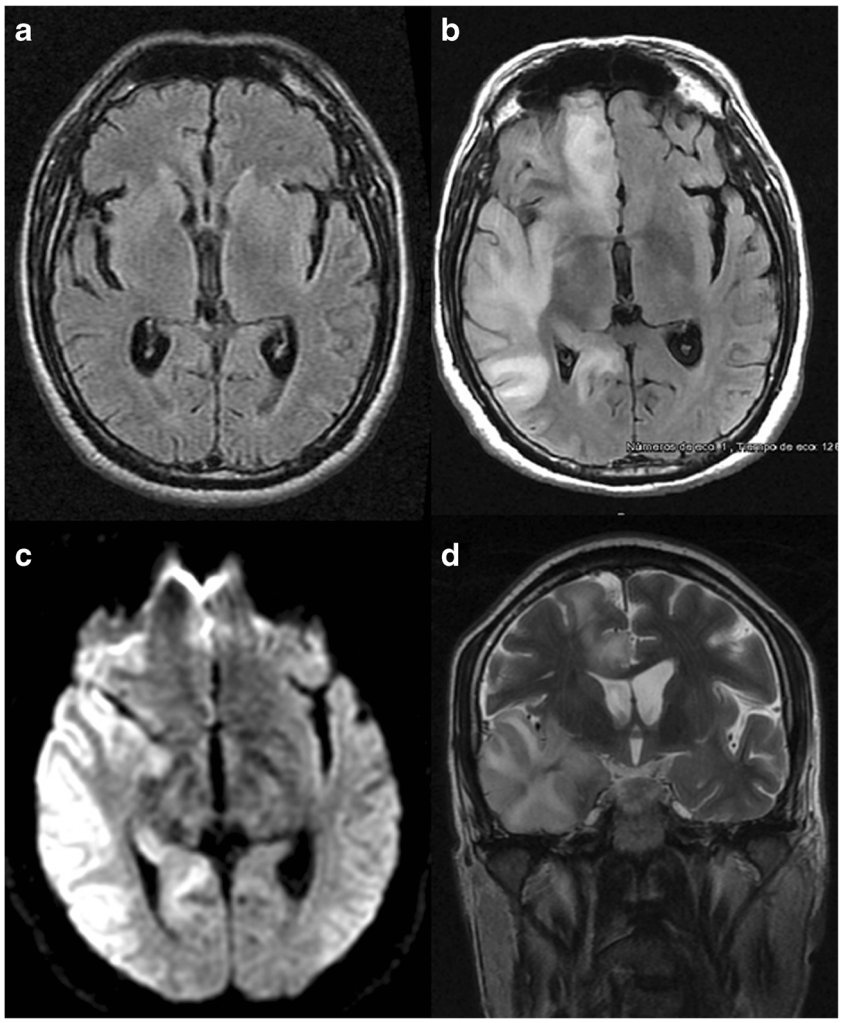

Fig. 1 MRI findings. Normal MRI, 2 weeks before his admission (**a**). An MRI during his hospitalization revealed right sided fronto-temporal white matter hyperintensities and restricted diffusion (**b**, **c**), predominantly involving the temporal lobe (**d**)

temporal lobes—classic findings in HSE. However, molecular testing for HSV was negative and he was found to have positive titers for syphilis. A recent literature review found at least 24 cases worldwide where there were mesial temporal lobe changes on MRI concurrent with a diagnosis of NS [3]. Our patient had more extensive lesions, involving both the right temporal and bi-frontal lobes.

Of course, mesial temporal lobe abnormalities on MRI are not exclusively found in HSE. Acute hemorrhagic leukoencephalitis (Hurst's disease), gliomatosis cerebri, systemic lupus erythematosus, primary CNS lymphoma, and autoimmune encephalitis (particularly limbic encephalitis) can all have similar findings. In our case, the diagnosis of HSE was confirmed by serological and molecular testing. Additionally, gyral enhancement, hemorrhage, and areas of restricted diffusion are frequently seen in HSE but rarely in NS [3]. However, the recent increase in NS incidence has been followed by an increase in atypical presentations such as the meningovascular form, often associated with infarcts, hemorrhages, and meningeal-gyral enhancement [4].

Our case is only the second documented case of co-infection with NS and HSE. Simultaneous infection with Treponema pallidum and herpes simplex virus in general is not uncommon, as both are sexually transmitted and share similar risk factors, but they usually present with cutaneous manifestations. However, there are reported cases of HSE with other concomitant central nervous system infections. One case describes a patient with AIDS and a subacute presentation of seizures, confusion and headaches, who was documented to have HSE, *Cryptococcus* meningitis and NS [5]. Our case is especially interesting because our patient was immunocompetent and never received any immunomodulators or immune suppressants, whereas all the previous cases involved patients with some form of immunodeficiency.

Classical medical teaching of diagnostic parsimony (Occam's razor) emphasizes that a single pathologic process should be sought when confronting a difficult case and that atypical presentations of a common disease are more likely that typical presentations of an uncommon disease. Conversely, Hickam's dictum states that more than one

pathology is always possible and should not be excluded solely to satisfy Occam's razor, while dual pathology is probably underdiagnosed in immunocompromised patients but is likely extremely rare in immunocompetent individuals. We believe that, in our patient, the first subacute phase of neuropsychiatric disease was due to NS and the later development of seizures and altered mental status was due to HSE. This challenging case demonstrates the need to keep the differential diagnosis broad and relevant possibilities need to be properly investigated and ruled out by confirmatory testing.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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