Case Report

Neurosyphilis presenting with characteristic MRI findings of diplopia and stroke

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Abstract: The incidence of neurosyphilis is currently rising due to an up-spike in sexual transmission of the causative pathogen *Treponema pallidum*. Neurosyphilis is difficult to diagnose due to its broad array of nonspecific clinical manifestations and lack of defining characteristics on magnetic resonance imaging (MRI). We report a case of neurosyphilis presenting with characteristic MRI findings of diplopia and subacute stroke syndrome, and review the literature to assist in differential diagnosis. A 37-year-old heterosexual Chinese male presented with a 2-month history of headache. Firstly, he was diagnosed with “tension-type headache” because of normal brain MRI. The patient developed vertical diplopia and slight numbness in the right partial body for the second administration to our institute. Personal history revealed a primary syphilis infection 11 months previously, which was treated with intramuscular bicillin. Subsequent brain MRI demonstrated an infarction in the left thalamus, a marked thickening and enhancement of the left oculomotor nerve, and focal meningeal enhancement. Magnetic resonance angiography (MRA) of the head showed no abnormalities. The patient received treatment with intravenous penicillin G and steroids. 3 months after discharge, brain MRI demonstrated complete resolution of the left oculomotor nerve and focal meningeal enhancement. Our case emphasizes the importance of early diagnosis and complete cure of syphilis to prevent progression and ensuing neurological damage. Standard follow-up is necessary for confirmation of adequate treatment response.

Keywords: Syphilis, neurosyphilis, oculomotor nerve palsy, stroke, magnetic resonance imaging

Introduction

Neurosyphilis is not uncommon in clinical practice and incidence is rising in parallel with the recent increase in syphilis infection [1]. Further, diagnosis is challenging due to broad array of nonspecific clinical manifestations and lack of defining characteristics on magnetic resonance imaging (MRI). Neurosyphilis is always misdiagnoses of epilepsy [2], cerebral vascular disease [3], intracranial space occupying lesions [4] and Alzheimer's disease [5]. Here, we report a case of neurosyphilis presenting with imaging features of diplopia and subacute stroke syndrome.

Case presentation

A 37-year-old heterosexual Chinese male presented with a 2-month history of headache. Two weeks before admission he had consulted a local hospital for continuous moderate headache. No abnormal signs were documented in the medical records and brain MRI revealed no obvious abnormalities. He was diagnosed with “tension-type headache” and treated conservatively with oral analgesics. He was without symptoms until two days before admission to our institute when he developed vertical diplopia and slight numbness in the right partial body. He had no history of diabetes mellitus or hypertension. Personal history revealed a primary syphilis infection 11 months previously, which was treated with intramuscular bicillin (2.4 million units/week for 3 weeks). The patient reported that his serological evaluation for syphilis 3 months later was negative but no documentation was provided.

Neurological examination revealed slight palsy of the left inferior rectus and impairment of light touch sensation in the right partial body. No signs of meningeal irritation were found. Routine full blood cell count, inflammatory
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markers, serum electrolytes, and vitamin B12 levels were normal. Serum rapid plasma reagin (RPR) (1:128) and *Treponema pallidum* particle agglutination (TPPA) (1:20480) were strongly and repeatedly positive. Human immunodeficiency virus (HIV) testing was negative. Cerebrospinal fluid (CSF) examination showed normal opening pressure on lumbar puncture, an elevated white blood cell (WBC) count of 180/μl (66% lymphocytes) and an elevated protein level of 1.29 g/l. Both CSF RPR (1:16) and TPPA were positive, confirming neurosyphilis based on the diagnostic criteria set forth by the Centers for Disease Control and Prevention (CDC). Brain MRI after admission demonstrated an infarction in the left thalamus, a marked thickening and enhancement of the left oculomotor nerve, and focal meningeal enhancement (Figure 1A-G). Magnetic resonance angiography (MRA) of the head showed no abnormalities (Figure 1H) and computed tomography-angiography (CTA) of the aorta was normal.

The patient received treatment with intravenous penicillin G (6.4 million units every 8 hours for 15 days) and steroids (prednisone 10 mg everyday for the first three days to prevent the Jarisch-Herxheimer reaction). By treatment day 10, vertical diplopia was improved significantly. After 2 weeks of therapy, repeat CSF examination showed a protein level of 0.97 g/l with normal WBC count (2/μl) and normal opening pressure. Both the CSF RPR (1:16) and TPPA were still positive. After discharge from our hospital, the patient received follow-up treatment with intramuscular bicillin (2.4 million units weekly) for 3 weeks in a local hospit-
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3 months later, the follow-up MRI demonstrated complete resolution of the left oculomotor nerve and focal meningeal enhancement. Figure 2.

Neurosyphilis can occur at any stage of the infectious course [1, 6]. There are five syndromes in the clinical spectrum of neurosyphilis: asymptomatic neurosyphilis, syphilitic meningitis, syphilitic meningovascularitis, dementia paralytica (or general paresis of the insane), and tabes dorsalis. Acute syphilitic meningitis usually occurs within the first 2 years of infection and presents with headache, meningeal irritation, and confusion. Syphilitic meningovascularitis may manifests as a subacute stroke syndrome due to small vessel arteritis. Cranial nerve palsies are common in the period of syphilitic basilar meningitis or meningovascularitis, and abnormalities of the optic, oculomotor, trochlear, abducens, facial, and vestibulocochlear nerves have been reported [6]. MRI can reveal thickening and contrast enhancement of cranial nerves [1].

Discussion

The natural history of syphilis has three stages. Primary syphilis manifests as a chancre or painless ulceration at the site of transmission and regional lymphadenopathy. Secondary syphilis is characterized by the presence of a macular rash. Tertiary syphilis is detected as damage to the central nervous system, cardiovascular system, bones, or joints, skin, and mucous membranes [7, 8]. Lymphocyte infiltration extending along the cranial nerve at the base of the brain may underlie cranial nerve enhancement.

Our patient presented with partial left oculomotor nerve palsy and a subacute stroke syndrome. MRI findings of oculomotor nerve lesion, cerebral infarction, and focal meningeal enhancement suggested the presence of syphilitic meningovascularitis. The complete resolution of left oculomotor nerve palsy and focal meningeal enhancement on follow-up MRI after treatment confirmed the diagnosis of syphilitic meningovascularitis.

Seeley reported a case of neurosyphilis resembling ours, with an MRI finding of oculomotor nerve lesion [8]. The patient had a history of syphilis treatment 25 years previously. The lesion was considered an oculomotor nerve gumma, and was completely resolved with penicillin treatment. An extraordinarily uncommon manifestation of neurosyphilis associated with meningitis, cerebral gumma is a space-occupying mass of granulation tissue contiguous with the dura and pia mater characterized by infiltration of lymphocytes and plasma cells along the brain and meninges [6]. The lesion becomes irreversible when the inflammatory cells are replaced by fibrous tissue and necrosis. However, the diagnosis of syphilitic gumma for both our patient and that reported by Seeley was not confirmed without pathological evidence.

Omer TA and his college [10] reported a case of neurosyphilis presented with acute collapse against a background of memory difficulties over six months. MRI of brain revealed abnormal in the right frontal area and bilateral mesial temporal areas. Blood and cerebrospinal fluid analysis revealed an active syphilis infection. This report highlights the importance of considering neurosyphilis in the differential diagnosis when mesiotemporal changes are seen on magnetic resonance imaging.

And many cases of confirmed neurosyphilis have no abnormal neuroimaging findings [11, 12]. The major implication of our case is the possible combination of oculomotor nerve lesion, cerebral infarction, and focal meningeal enhancement in neurosyphilis. Compared to other possible causes of these signs, such as neurosarcoidosis and lymphoma, neurosyphilis is more readily curable if diagnosed and treated in time. Therefore, it is important to consider the possibility of neurosyphilis as a possible cause of cranial nerve palsy complicated with cerebral infarction, especially in sexually active young adults. Contrast-enhanced MRI is necessary to identify associated brain lesions.

Our case emphasizes the importance of early diagnosis and complete cure of neurosyphilis. Standard follow-up is necessary to confirm treatment efficacy. For confirmed neurosyphilis cases, CSF examination should be repeated every 6 months in the first 2 years or until the results are normal [6, 9]. Serum RPR should be performed every 3 months in the first 2 years [9]. A fourfold or greater reduction in RPR titer (both serum and CSF) is the mark of effective treatment. If these parameters do not fall in the first 2 years or increase due to a relapse, treatment should be reinitiated.
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Disclosure of conflict of interest

None.

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