—Case Reports—

Neurosyphilis Mimicking Ramsay Hunt Syndrome

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A 36-year-old man presented with facial nerve palsy, hearing loss, vertigo and headache. He was initially diagnosed with Ramsay Hunt syndrome and treated with a systemic steroid and valaciclovir; however, his symptoms deteriorated. Serum rapid plasma reagin (RPR) and treponema pallidum hemagglutination tests were positive. Cerebrospinal fluid analysis revealed an elevated white blood cell count and positive RPR, confirming the diagnosis of neurosyphilis. Penicillin G (PCG) was administered, and his facial nerve function and headache improved. However, left-side hearing loss worsened temporarily, which was assumed to be a Jarisch-Herxheimer reaction. Betamethasone was administered along with PCG, and he recovered completely. (J Nippon Med Sch 2015; 82: 254–256)

Key words: neurosyphilis, Ramsay Hunt syndrome

Introduction

Syphilis is a sexually transmitted infection caused by *Treponema pallidum*. Although penicillin has reduced the incidence of syphilis over the past decades, it has been receiving attention again in recent years along with increased HIV infection[1,2].

Neurosyphilis can develop in patients with syphilis, but it is difficult to diagnose because of its variable time of onset and nonspecific clinical presentation. In immunocompetent individuals especially, the disease manifests insidiously with nonspecific symptoms, and establishing a diagnosis of neurosyphilis is sometimes very arduous. Neurosyphilis is considered to be one of the presentations of tertiary syphilis, but *Treponema pallidum* invades the central nervous system immediately after infection and neurosyphilis may present as acute meningitis with cranial nerve dysfunction[3].

Here, we report the clinical and magnetic resonance imaging (MRI) findings in a patient with secondary syphilis with neurosyphilis suffering from facial and vestibulocochlear nerve dysfunction[4]. Epidemiological data indicate a worldwide re-emergence of syphilis, and a high index of suspicion is needed to make a diagnosis of neurosyphilis[3].

Case

A 36-year-old healthy, heterosexual man presented with a two-day history of facial nerve palsy, hearing loss, vertigo and headache. Two weeks earlier, he had experienced exanthema on the left palm. He had had sexual intercourse at an adult-entertainment shop three months prior to presentation.

He had no fever or any other symptoms such as auricle pain. On physical examination, oral aphtha, left-side hearing loss, and weakness of the left orbicularis muscle, cheek muscle and masseter muscle were detected, although no auricular vesicles or signs of meningeal irritation were observed. Complete blood cell count and biochemical markers were unremarkable. Head magnetic resonance imaging (MRI) revealed findings similar to those seen in patients with Ramsay Hunt syndrome (**Fig. 1**). Ramsay Hunt syndrome was suspected on the basis of his clinical symptoms, and a systemic steroid and valaciclovir were administered. Although he was treated for Ramsay Hunt syndrome for ten days, the patient's symptoms deteriorated with time. A blood sample obtained at the time of presentation showed positive results in a rapid plasma reagin test and Treponema pallidum hemagglutination assay (RPR: 9.84 R.U./TPHA: 925.8

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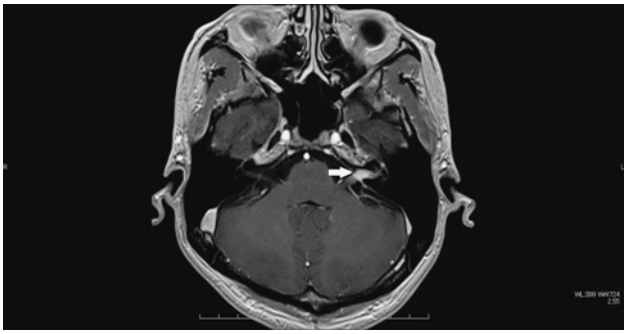

Fig. 1 Head MRI showed a high-intensity area (**arrow**) from the left cerebellopontine angle to the internal acoustic meatus. Ramsay Hunt syndrome was suspected from this finding.

T.U.). A test for human immunodeficiency virus antibodies was negative. At this time, we considered the possibility of neurosyphilis and obtained cerebrospinal fluid (CSF). CSF analysis revealed 228 leukocytes (monocytes: 188, polycytes: 40) per microliter, a low glucose level of 45 mg/dL (the blood glucose level was 90 mg/dL), an elevated protein level of 114 mg/dL (normal range: 10–40 mg/dL), and a positive RPR test (1.78 R.U.). CSF was negative for varicella-zoster virus (VZV) antibodies. The patient was diagnosed with neurosyphilis. He was admitted to our hospital, and Penicillin G (PCG) (4 million units every 4 hours) was administered intravenously for 14 days.

No fever or side effects were observed. The patient's facial nerve function and headache gradually improved after initiation of the treatment. However, six days later, he complained of increased left hearing loss (left-side hearing on hospitalization day 1: 30 dB, on day 6: below 105 dB), which was suspected as being part of the Jarisch-Herxheimer reaction.

The aggravated hearing loss led us to treat the patient with systemic betamethasone (10 mg per day), which was gradually tapered by the end of the PCG treatment. His hearing acuity promptly improved with the treatment (left-side hearing on hospitalization day 13: 75 dB, after leaving hospital [day 62]: 20 dB), and complete recovery of CSF pleocytosis as well as facial and vestibulocochlear nerve function was observed at the 5-month follow-up examination. The MRI lesion shown in the figure had also disappeared. The RPR score, used as an index of treatment evaluation, was also negative (0.00 R.U.) six months after the initiation of treatment.

Discussion

Although our patient was initially suspected of having Ramsay Hunt syndrome, the positive serology test for syphilis and CSF findings finally led to the diagnosis of neurosyphilis. With systemic PCG administration, complete and prompt clinical improvement was observed.

Since *Treponema pallidum* cannot be cultivated, diagnosis of syphilis is based on serologic tests for syphilis, or detection of the organism directly in microscopic tests such as the dark-field method. Generally, neurosyphilis is diagnosed on the basis of clinical findings, the presence of CSF pleocytosis, positivity on the CSF RPR test, and rapid response to intravenously administered PCG. Although the CSF RPR test has high specificity (94%), the sensitivity for diagnosis is only 27%[5]. The central nervous system may become involved during any stage of syphilis from several weeks to several years after the initial infection[6]. However, neurosyphilis tends to be overlooked in the early stages of syphilis as most patients are asymptomatic, and it is usually diagnosed in the tertiary stage. Furthermore, neurosyphilis is classified into early neurosyphilis, which mainly invades the meninges and cranial nerves, and late neurosyphilis, which mainly invades the brain and spine[3]. The present patient had experienced skin rash typical of secondary syphilis within three months of sexual exposure, and was diagnosed as having secondary syphilis complicated with neurosyphilis. He had a headache and cranial nerve disorders including facial nerve palsy, auditory disorder, and dizziness, all of which are characteristic of early neurosyphilis.

The Jarisch-Herxheimer reaction occurs in up to 95% of syphilis patients[7]. Although there is no strong evidence to support the combined use of steroids with PCG treatment[8], such treatment might prevent the Jarisch-Herxheimer reaction, which results from a hypersensitivity reaction to treponemal antigens produced by the destruction of large numbers of spirochetes by PCG. In fact, the patient's hearing loss temporarily worsened significantly under PCG treatment, and improved on steroid administration. An animal study showed that the vestibulocochlear nerve of guinea pigs contain unmyelinated nerve fibers, and that Schwann cells play an important role in the repair of peripheral nerves[9,10]. We speculate that the vestibulocochlear nerve, which contains unmyelinated nerve fibers, tends to receive more damage from the Jarich-Herxheimer reaction.

Syphilis tends to affect the central nerves, and one review study showed that this happens in 25–60% of syphilis patient[3]. Optic nerve and otosyphilis complications caused by neurosyphilis have also been reported[6,7].

Syphilis is a treatable disease; however, treatment

should be administered intravenously when the disease affects the central nervous system. When patients have cranial nerve disorders or neuropsychiatric complaints along with a history of a physical affair or erythema on the palm, physicians should consider the possibility of neurosyphilis to arrive at a proper diagnosis and provide adequate treatment.

Conflict of Interest: None.

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