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Case Report

Multiple cerebral syphilitic gummas mimicking brain tumor in a non-HIV-infected patient: A case report

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ABSTRACT

We present a unique case of symptomatic early neurosyphilis in a non-HIV-infected patient. A 47-year-old man with a history of diabetes mellitus presented with generalized seizures. He did not manifest any neurological deficits. At first, multiple brain tumors were suspected based on findings from magnetic resonance imaging of the brain. However, serological and cerebrospinal fluid tests for syphilis yielded positive results, and the masses were reduced using amoxicillin. Multiple cerebral syphilitic gummas were therefore diagnosed. High-dose penicillin therapy was initiated and syphilitic gummas disappeared after five months. *Treponema pallidum* could invade the central nervous system at an early phase, and sometimes may be difficult to distinguish from malignant brain tumor. If intracranial lesions are identified in a syphilis-infected patient, cerebral syphilitic gumma should be considered as a differential diagnosis.
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1. Introduction

Syphilis is caused by infection with *Treponema pallidum* and may present as multiple symptoms. When *T. pallidum* invades the central nervous system (CNS), patients may present with symptoms of neurosyphilis such as meningitis, vasculitis and syphilitic gumma. Neurosyphilis is typically thought to present as a tertiary syphilis, but rarely may invade the CNS several months after infection. Here, we present an uncommon case of multiple cerebral syphilitic gummas initially mimicking malignant brain tumor.

2. Case report

The patient was a 47-year-old man with a history of type 2 diabetes mellitus treated by oral hypoglycemic medications without complications. The *T. pallidum* hemagglutination assay (TPHA) and serum rapid plasma reagin screening (RPR) yielded negative results 6 months before this admission. He had engaged in sexual intercourse at brothels 4 months before the ictus and chancre appeared after 1 month, but he had been ignoring it. He presented with sudden onset of generalized tonic-clonic seizures and was admitted to the emergency department. On admission, level of consciousness was alert and no neurological deficits were observed. He displayed no signs of meningeal irritation. Syphilitic roseola was observed on the skin in the hypogastric region. Results of blood cell counts and biochemical analyses were normal, including for tumor markers and autoimmune antibodies. TPHA test and RPR yielded positive results, but results were negative for human immunodeficiency virus (HIV) on admission. Magnetic resonance imaging (MRI) of the brain revealed multiple mass lesions that were enhanced and adjacent to the dura in the left cerebral hemisphere (Fig. 1). Computed tomography (CT) of the thoracoabdominal region revealed no lesions such as syphilitic gummas. Cerebrospinal fluid (CSF) examination showed: cell count, 199/μL; glucose, 61 mg/dl; and protein, 116 mg/dl. Positive results were obtained for TPHA and fluorescent treponemal antibody absorbed (FTA-ABS) immunoglobulin G in CSF. CSF cultures were negative. No abnormalities were identified on CSF cytodiagnosis. Consequently, the patient was diagnosed with primary or secondary syphilis and amoxicillin was administered orally at 1500 mg/day. Initially, the intracranial lesions were considered as malignant brain tumors, such as high-grade glioma, metastatic brain tumor or primary CNS lymphoma, and were to be investigated. However, these lesions reduced in size with only 14 days of amoxicillin (Fig. 2), so the final diagnosis was multiple cerebral syphilitic gummas. He was hospitalized and penicillin G was administered intravenously at

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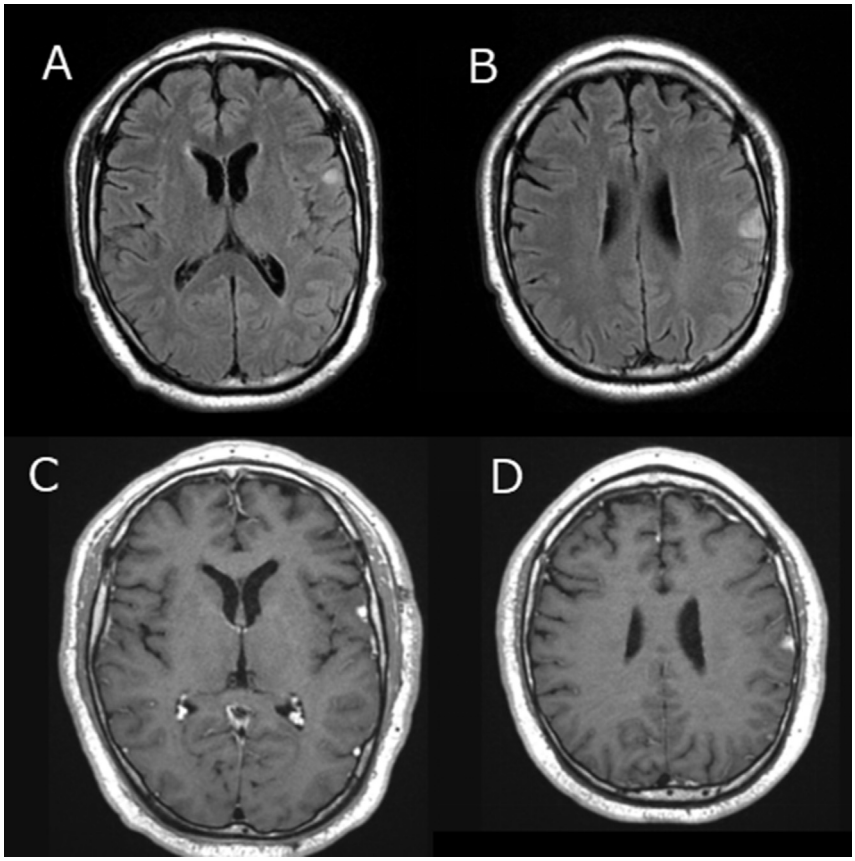

Fig. 1. Brain MRI findings on admission. **A, B)** Fluid-attenuated inversion recovery (FLAIR) images show hypertense lesions in the cortical areas of the left frontal and temporal lobes. **C, D)** Lesions show enhancement with gadolinium.

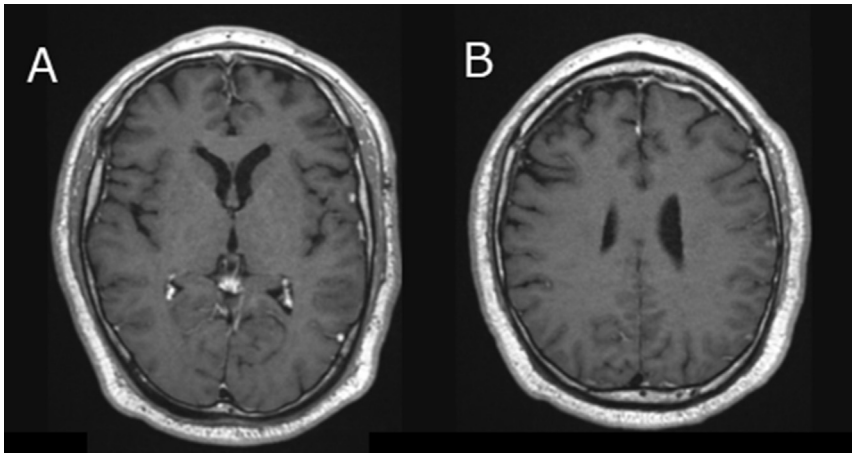

Fig. 2. Brain MRI after 14 days of treatment with low-dose amoxicillin. **A, B)** T1-weighted post-gadolinium images show reduction of enhancement.

24×10^6 U for 14 days, following CDC guidelines. The subsequent course of the patient was uneventful, with no neurological deficits (Fig. 3). Five months after starting administration, no intracranial lesions were identifiable on brain MRI (Fig. 4).

3. Discussion

Recently, incidents of syphilis infection have been re-appearing in developed countries [1]. In Japan, the number of patients infected with syphilis has been increasing since around 2010, and 4557 patients had syphilis infection in 2016. Various reasons have been proposed, including: 1) high risk sexual behavior among men who have sex with men; 2) illicit drug use; and 3) concomitant HIV infection [2,3]. The clinical manifestations are typically divided into several distinct stages: primary, secondary, latent and tertiary. Neurosyphilis can occur 1–30 years following syphilis infection [4,5]. Syphilitic gummas can present 3–12 years following infection as inflammatory fibrous nodules that are locally destructive [5]. These are typically seen in the tertiary stage in any organ, including in the CNS [6]. Cerebral

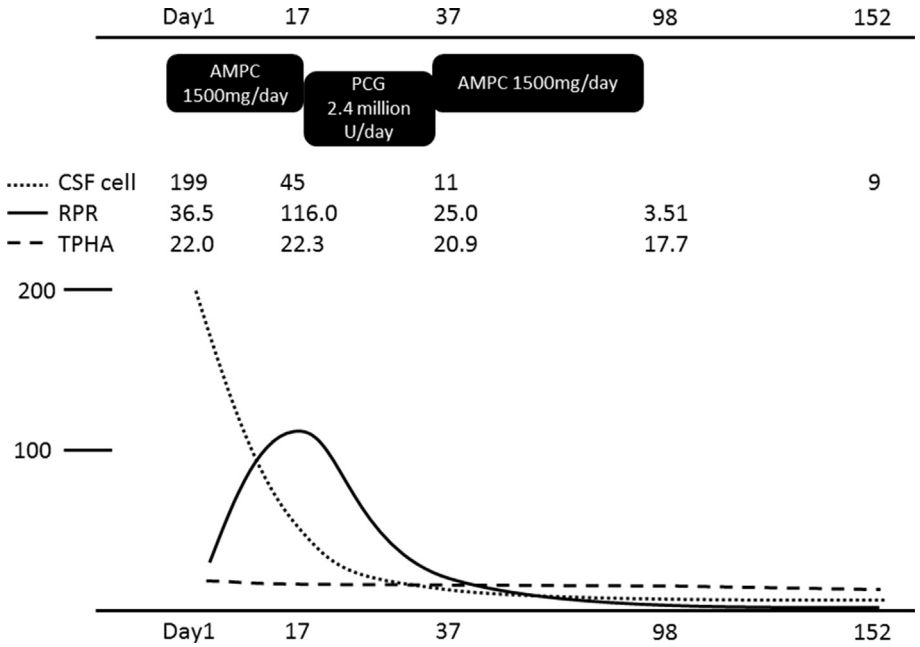

Fig. 3. Clinical course of our patient. After the treatment, CSF cytology was improved and the results of the RPR test was turned to negative. PCG: benzylpenicillin potassium, AMPC: amoxicillin, CSF: cerebrospinal fluid, RPR: rapid plasma regain, TPHA: *T. pallidum* hemagglutination assay.

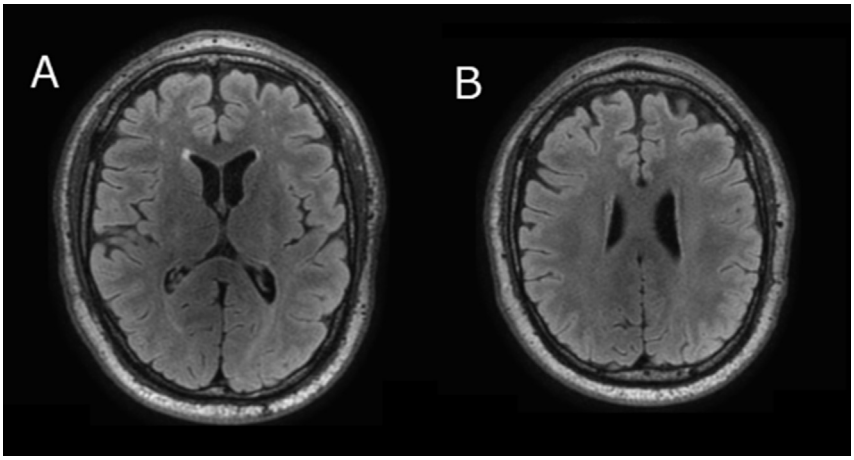

Fig. 4. Brain MRI after 5 months of treatment with high-dose penicillin. **A, B)** Fluid-attenuated inversion recovery (FLAIR) images show complete resolution of hypertense lesions.

syphilitic gumma is usually seen as a single lesion, but multiple lesions are reported on rare occasions [7].

The possibility must be considered that infection with HIV accelerate CNS infiltration of syphilis and increases the risk of neurological complications [8]. Although early neurosyphilis of patients without HIV infection has been reported, cerebral syphilitic gumma occurring early after syphilis infection is extremely rare, as in our case [9]. To the best of our knowledge, this represents the first report of multiple cerebral syphilitic gummas in early neurosyphilis in a non-HIV-infected patient. Accelerated CNS infiltration of syphilis has been presumed to be related to concomitant diabetes mellitus in addition to HIV infection [10]. However, the underlying mechanisms remain unclear.

The diagnosis of cerebral syphilitic gumma is based on clinical symptoms and CSF analysis [11]. Noticing that intracranial lesions reduce with the use of penicillins may also be diagnostically helpful [1]. The standard treatment for neurosyphilis and cerebral syphilitic gumma is high-dose penicillin therapy. Better outcomes are obtained with shorter intervals from diagnosis to treatment. Because cerebral syphilitic gummas reduced with low-dose amoxicillin in this case, early neurosyphilis may show good therapeutic response. *T. pallidum* seems to be rarely identified in cerebral syphilitic gumma, so craniotomy is not recommended [1]. When intracranial pressure shows acute increases or antibiotics do not elicit a response, surgery should be considered as an exception. However, sometimes patients are misdiagnosed with malignant brain tumor and undergo unnecessary surgical treatment [12]. If intracranial lesions are seen in a syphilis-infected patient, cerebral syphilitic gumma should be considered among the differential diagnoses.

Authorship statement

All authors meet the ICMJE authorship criteria.

Conflicts of interest disclosure

There are no conflicts of interest.

Informed patient consent

The patient/next of kin has consented to submission of this case report to the journal.

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