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Original Article

Cerebral syphilitic gumma mimicking malignant brain tumor in a human immunodeficiency virus-negative patient

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Abstract: Cerebral syphilitic gumma is considered an uncommon involvement of the brain during tertiary syphilis and the differentiation from a brain mass in HIV-negative patients with syphilis is still challengeable to clinicians. We report an unusual case of cerebral syphilitic gumma mimicking malignant brain tumor in a human immunodeficiency virus-negative patient. A 41-year old man complaining of headache was found to have a brain mass on his CT scans and MRI. A rapid plasma reagin screening and the treponema pallidum hemagglutination assay was reactive in serum but Venereal Disease Research Laboratory results were negative in cerebrospinal fluid. Suspecting a brain tumor, the mass was completely surgically resected through supraorbital keyhole approach. The pathological examination demonstrated a syphilitic gumma. water-soluble penicillin G was intravenously administered for 10 days from postoperative day. 2 weeks and Three months postoperatively, the follow-up MRI scans showed that the enhancing mass in the right frontal region had disappeared; edema around the enhancing mass had also disappeared.

Keywords: Cerebral gumma, neurosyphilis, syphilis, brain tumor

Introduction

The incidence of neurosyphilis has decreased dramatically over the past 50 years, but cases still linger within the general population and are seen from time to time, particularly in those immunocompromised by human immunodeficiency virus (HIV) or other causes [1, 2]. Cerebral syphilitic gumma is considered an uncommon involvement of the brain during tertiary syphilis and the differentiation from a brain mass in HIV-negative patients with syphilis is still challengeable to clinicians [3, 4]. Here, we report an unusual case of cerebral syphilitic gumma mimicking malignant brain tumor in a human immunodeficiency virus-negative patient.

Case report

The patient is a 41-year-old right-handed man with no significant past medical history, who presented with a 10-day history of headache. He had no past history of diabetes mellitus or hypertension, but had a clear extramarital sexual history. He denied any history suggestive of syphilis and had no past surgical or family history.

Vital signs at admission were stable. He was mentally alert and did not have any cognitive or memory disturbance. He also did not show any evidence of language impairment. Both pupils showed normal light reflex. The result of the examination of cranial nerves was normal, and there were no other neurological deficits. There were no rash on the body and no superficial lymphadenopathy.

The results of the following investigations were normal: complete blood count, serum electrolytes, liver function test, blood urine nitrogen, and serum creatinine. Serum rapid plasma reagin screening (RPR) was positive, the treponema pallidum hemagglutination assay (also called TPHA test) was also positive. Human Immunodeficiency Virus (HIV) testing was negative. Cerebrospinal fluid (CSF) examination revealed a protein level of 37 mg/mL, glucose 42 mg/mL and a differential cell count includ-

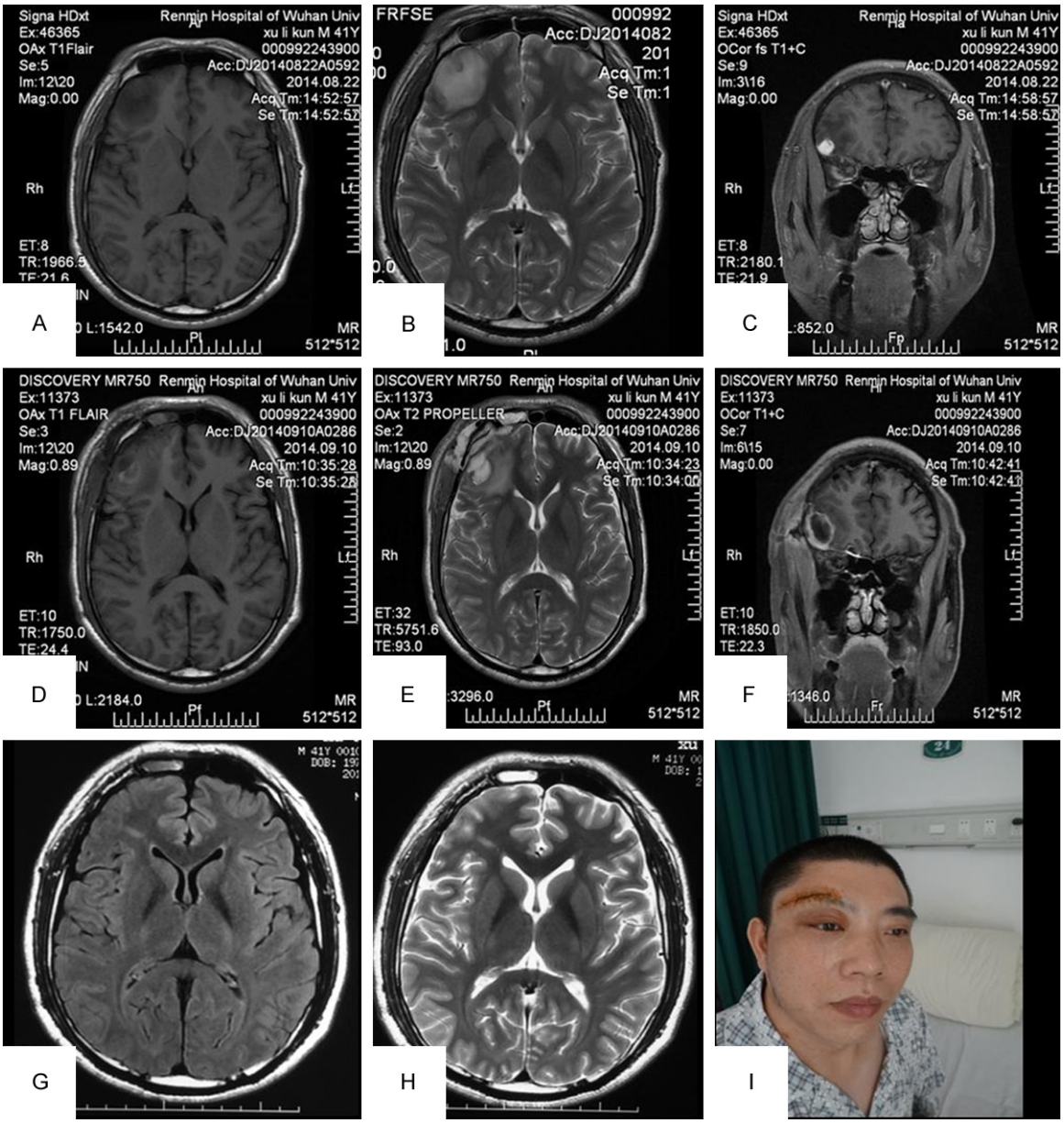

Figure 1. Brain magnetic resonance imaging (MRI) scans of the patient. A: Non-contrast-enhanced, T1-weighted image showed a round mass-like lesion with hypointensity in the right frontal lobe. B: T2-weighted images demonstrated severe cerebral edema around the enhancing mass. C: Contrast-enhanced T1-weighted coronal image revealed a mass adjacent to the enhanced durra over the cerebral convexity. D-F: 2 weeks after operation, the postoperative MRI scans showed that the enhancing mass in the right frontal region had disappeared. G, H: Three months after operation, the postoperative MRI scans showed that edema around the enhancing mass had also disappeared. I: The incision of supraorbital keyhole approach.

ing polymorphonuclear cells (2 cells/mm^3), lymphocytes (5 cells/mm^3). CSF RPR and TPHA were negative. Additional CSF studies obtained included culture for mycobacterium tuberculosis, a cryptococcal latex agglutination test and fungal culture, which were all negative.

Computed tomography (CT) scanning of the brain revealed a low-density lesion in the right frontal lobe. Brain magnetic resonance imaging (MRI) revealed a round enhancing mass that measured 1.2×1.6×1.4 cm in size (**Figure 1A**). There was severe cerebral edema around the

enhancing mass (**Figure 1B**). The mass was adjacent to the enhanced dura in the right frontal lobe (**Figure 1C**).

Management

Malignant brain tumors including primary CNS lymphoma, glioblastoma or metastatic brain tumor were suspected. The mass was completely surgically resected through supraorbital keyhole approach since the margin of the mass was well defined. On intraoperative findings, the mass was found to be yellowish in color and hard in texture, and was attached to the dura of the basal frontal lobe. On histopathological examination, the specimen revealed the typical features of granulomatous inflammation including necrosis, fibrosis, and infiltration of a large number of lymphocytes and plasma cells.

The patient was finally diagnosed with brain gumma according to history, clinical manifestations, laboratory and histopathology examination. So, water-soluble penicillin G was intravenously administered at a daily dose of 24×10^6 U for 10 days from postoperative day. Thereafter, the headache disappeared, and there were no other neurological deficits. He was discharged from the hospital 11 days after operation. 2 weeks and Three months postoperatively, the follow-up MRI scans showed that the enhancing mass in the right frontal region had disappeared, edema around the enhancing mass had also disappeared (**Figure 1**).

Discussion

The clinical course of syphilis is classically divided into the following phases: primary syphilis, secondary syphilis, latent syphilis, and tertiary syphilis [5]. With the advent of penicillin in the early 1940s the incidence of syphilis decreased dramatically [5]. Cerebral syphilitic gumma is rare manifestations of tertiary syphilis, which account for less than 0.5% of all intracranial lesions [6]. Syphilitic gumma is classic examples of granulomatous inflammation. They may affect any organ and can reach sizes of up to 10 cm in diameter [4]. The gumma classically consists of a dense inflammatory infiltrate consisting of large numbers of lymphocytes and plasma cells, with occasional polymorphonuclear lymphocytes, surrounding a central, caseous necrotic core. Multinucleated giant cells, fibroblast proliferation, and collagen production may also be present. Vascular proliferation, endarteritis with intimal thickening, and perivascular inflammation are characteristic; the latter criterion is particularly useful in distinguishing this lesion from the tuberculoma [7].

Infection with human immunodeficiency virus (HIV) is a known predisposing factor for development of neurosyphilis and probably accelerates its course [8]. Therefore, cerebral gumma is nowadays increasingly reported in HIV-positive patients [9]. The natural course of syphilis has 4 well-defined stages. These stages may become less defined in the presence of coinfection with HIV [9]. Some early or late syphilis without adequate penicillin treatment, and some latency syphilis treated with antibiotics, can lead to clinical features of neurosyphilis and classic course changes, resulting in an increasing number of “atypical neurosyphilis”.

Syphilitic gumma can occur anywhere within the brain. The majority of reported cases were in the cerebrum, with some cases in other locations, including corpus callosum, third ventricle, basal ganglia, thalamus, hypothalamus, pituitary, brainstem, cerebellopontine angle, et al. [7]. Among convexity lesions, most were located in the frontal lobe, followed by the region of the parietal lobe. Most reported cases were single lesion, multiple elisions was also reported [10]. The symptoms of brain gumma are similar to those of other tumors arising from brain parenchyma and are often accompanied by a seizure. So, it is obvious that these lesions can present with a wide array of signs and symptoms and do not demonstrate any finding unique to gummatous lesions.

Despite modern advances in imaging studies, the diagnosis of neurosyphilis and intracerebral mass lesions remains elusive. On CT scans, gumma most common appear as hypodense or heterogeneous lesions that enhance vigorously with contrast [7]. On MRI, gummatous lesions usually show hypo-intensity on T1-weighted images, hyper-intensity on T2 and enhancement with gadolinium. Occasionally, these lesions appear isointense on T1 and isointense or hypointense on T2-weighted imaging [9]. The neuro-imaging findings of cerebral gumma, including enhancement patterns, may be nonspecific or may mimic intracranial neoplasms.

Serologic testing that includes nontreponemal tests and treponemal tests are considered the standard detection method for tertiary syphilis.

Nontreponemal tests are initially used to test or screen patients for syphilis and include the Venereal Disease Research Laboratory (VDRL) and the Rapid Plasma Reagin (RPR) tests. Due to the rate of false-positive results from nontreponemal tests, all positive results should be confirmed with a treponemal-specific test such as the T. pallidum particle agglutination or the fluorescent treponemal antibody absorption test [5]. In addition to the tests mentioned, the diagnosis of neurosyphilis is based on clinical symptoms and CSF analysis. However, the diagnosis of neurosyphilis is frequently plagued by the large proportion of false-negative CSF tests, as was seen in our patient. In fact, CSF VDRL tests may be negative in as many as 70% of patients with neurosyphilis [7]. Of the CSF tests, the VDRL test was positive in 62%, the fluorescent treponemal antibody absorption test was positive in 60%, and the T. pallidum hemagglutination assay was positive in 83% [7]. It is evident, therefore, that physicians continue to consider a gummatous lesion in the differential diagnosis for a brain lesion in those with a positive serum test, even in light of a negative CSF assay.

Although the standard treatment for neurosyphilis including CNS gumma is high dose intravenous Penicillin therapy, at least 4 patients with cerebral syphilitic gumma were misdiagnosed as glioma and underwent surgical treatment [3, 4, 12, 13]. In our patient the clinical presentations with increased intracranial pressure and the radiological appearance of a single irregularly enhancing lesion with extensive surrounding edema was highly suggestive of a malignant brain tumor. Surgery could have been avoided if the diagnosis had been made preoperatively.

Disclosure of conflict of interest

None.

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