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Cerebral syphilitic gumma misdiagnosed as brain abscess: A case report

Mu LK *et al*. Cerebral syphilitic gumma

Li-Kun Mu, Li-Feng Cheng, Jing Ye, Meng-Yan Zhao, Jin-Long Wang

Abstract

BACKGROUND

Cerebral syphilitic gumma is a relatively rare clinical disease. Its clinical manifestations are non-specific, and the imaging manifestations are similar to other intracranial occupying lesions, often misdiagnosed as tumors or abscesses. There are few reports on this disease in the relevant literature. To our knowledge, we have reported the first case of Cerebral syphilitic gumma misdiagnosed as a brain abscess. We reported this case and provided useful information for clinical doctors on neurosyphilis diseases.

CASE SUMMARY

We report the case to explore the diagnostic essentials of cerebral syphilitic gumma and attempt to mitigate the rates of misdiagnosis and missed diagnosis by equipping physicians with knowledge of neurosyphilis characteristics. The clinical diagnosis and treatment of a patient with cerebral syphilitic gumma were reported. Clinical manifestations, classifications, and diagnostic points were retrospectively analyzed. Results The patient was admitted to hospital with fever and limb weakness. Brain magnetic resonance imaging showed multiple space-occupying lesions and a positive serum *Treponema pallidum* gelatin agglutination test. The patient was misdiagnosed as having a brain abscess and underwent craniotomy. A postoperative pathological diagnosis of syphilis gumma was made. The patient improved and was discharged after penicillin anti-syphilis treatment. Follow-up recovery was satisfactory. Conclusion Cerebral syphilitic gumma is rare in clinical practice, and clinical manifestations, imaging examination, and serological examination lack specificity. Thus, it is often

misdiagnosed and missed. Clinical diagnosis should be considered in combination with multiple examinations, such as clinical features of patients, positive serological tests for syphilis, elevated cerebrospinal fluid cell counts, protein quantification, imaging examinations, and postoperative pathologic examinations.

CONCLUSION

Cerebral syphiliticis rare in clinical practice, it is often misdiagnosed and missed. Clinical diagnosis should be considered in combination with multiple examinations.

Key Words: Neurosyphilis; Cerebral syphilitic gumma; Brain abscess; Misdiagnosis; Treatment; Case report

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Core Tip: Cerebral syphilitic gumma is a relatively rare clinical disease. Its clinical manifestations are non-specific, and the imaging manifestations are similar to other intracranial occupying lesions, often misdiagnosed as tumors or abscesses. There are few reports on this disease in the relevant literature. To our knowledge, we have reported the first case of Cerebral syphilitic gumma misdiagnosed as a brain abscess. We reported this case and provided useful information for clinical doctors on neurosyphilis diseases.

INTRODUCTION

Cerebral syphilitic gumma is a late form of syphilis caused by *Treponema pallidum* (*T. pallidum*), which invades the central nervous system and often develops 3-20 years after syphilis infection. Cerebral syphilis gummata is a rare type of neurosyphilis with an incidence of only 2%, and the affected population is mainly middle-aged and elderly men who are mostly newly diagnosed with intracranial masses[1]. With an insidious

onset, nonspecific clinical manifestations, and the imaging findings resembling other intracranial space-occupying ring enhancements, the condition poses challenges in differential diagnosis, making it susceptible to misdiagnosis and mistreatment. Surgical treatment, often mistaken for a tumor or abscess, necessitates pathological examination for accurate confirmation of the diagnosis[2]. The clinical data of a patient with cerebral syphilis gummata admitted to the Department of Neurosurgery at Shengli Oilfield Central Hospital are reported below to further deepen our understanding of this disease.

CASE PRESENTATION

Chief complaints

A 55-year-old female patient was admitted to the hospital owing to "intermittent fever with weakness of right limbs for half a month" on June 28, 2019.

History of present illness

Half a month ago, the patient experienced right limb weakness without obvious inducement, coinciding with two episodes of low-grade fever with diarrhea. After oral administration of cephalosporins at a local clinic (details unknown), the patient exhibited marked improvement in diarrhea and return to normal body temperature. However, the right-sided weakness persisted, and there the patient tended to lean towards the right rear while standing. Subsequently, she was referred to our neurology clinic, and brain magnetic resonance imaging (MRI) showed multiple intracranial space-occupying lesions with surrounding edema. Considering the possibility of a brain abscess, metastases were not excluded (Figure 1). On the same day, the patient was admitted to our department with a diagnosis of brain abscess from the neurology clinic. Since the onset of the disease, the patient had paroxysmal headache, dizziness, and blurred vision, without limb twitching or numbness.

History of past illness

The patient had a history of "liver abscess" for half a year and underwent puncture drainage of liver abscess and anti-infection treatment in the Department of Hepatobiliary Surgery of our hospital.

Personal and family history

The pus culture from the puncture revealed Klebsiella pneumoniae, and the remaining medical history was unremarkable.

Physical examination

Physical examination on admission revealed a temperature of 36.9 °C; heart rate, 86 beats/min; respiration, 18 breaths/min; and blood pressure, 131/75 mmHg, and physical examination of the heart, lungs, and abdomen showed no significant abnormalities.

Laboratory examinations

Laboratory tests indicated a white blood cell (WBC) count of 10.9 × 10^9/L; neutrophil percentage, 82.4%; and direct neutrophil count, 9 × 10^9/L; other blood biochemical parameters showed no significant abnormalities.

Imaging examinations

Neurological examination revealed clear consciousness, clear and fluent speech, normal orientation, intact calculation, and memory functions. Pupils were equal and round bilaterally, responding well to light sensitivity. Fundus examination identified bilateral papilledema. Eye movements were well-coordinated, and there were no abnormalities in the examination of other cranial nerves. Muscle strength was graded as V in the left limb and IV in the right limb, with normal muscle tone. Tendon reflexes were brisk (+-+-), while pathologic reflexes were absent (+ACY-minus+ADs-). Sensory and synkinesis examinations showed no abnormalities, and there was a normal sense of resistance in the neck.

MULTIDISCIPLINARY EXPERT CONSULTATION

Preliminary diagnosis included brain abscess and post-puncture drainage of the liver abscess. Abdominal ultrasound after admission showed a 14 mm × 9 mm heterogeneous echogenic area in the right liver; however, positron emission tomography and computed tomography revealed no evidence of malignancy. Considering the patient's medical history, a hematogenous brain abscess was suspected. The initial approach involved dehydration to reduce intracranial pressure, administration of meropenem for anti-infection, and fluid replacement. Lumbar puncture (July 1, 2019) revealed a cerebrospinal fluid pressure of 280 mm H_2O (1 mm H_2O = 0.0098 kPa). Routine examination indicated a WBC count of 49 × 10^9/L, while biochemical and cytological examinations showed no significant abnormality. After 1 wk of treatment, the symptoms of headache and blurred vision were slightly improved, but no significant improvement in the weakness of the right limb was noted. A repeated brain MRI (July 8, 2019) revealed multiple intracranial space-occupying lesions, with surrounding edema showing only slight reduction than in the previous examination (Figure 2).

FINAL DIAGNOSIS

The patient did not support the diagnosis of brain abscess during treatment; subsequently, a thorough inquiry into the medical history was conducted again. The patient reported a history of unprotected sexual activity following a divorce. A physical examination conducted 1 year prior had revealed a positive *T. pallidum* antibody in the blood, with no subsequent specialized treatment administered. Four preoperative examinations were performed in the hospital, revealing a *T. pallidum* antibody level of 15.77 S/CO and a positive *T. pallidum* particle agglutination test. Syphilis confirmatory tests indicated weak positivity for anti-P47 and anti-P15 antibodies and positivity for anti-P45, anti-P17, and anti-*T. pallidum* antibody IgG. According to the relevant data and the imaging characteristics of the patient, the possibility of cerebral syphilitic gumma

could not be ruled out, and pathological biopsy was recommended for some lesions. After obtaining consent from the patient and her family, a complete left occipital craniotomy brain lesion resection was performed on July 11, 2019 (Figure 3). The postoperative pathology was indicative of cerebral syphilitic gumma (Figure 4A).

TREATMENT

On July 12, a dermatology consultation was requested, and the recommended treatment plan included: (1) Conducting serological examinations for syphilis in sexual partners and close contacts; and (2) administering intravenous penicillin at 4 million U ivdrip q6h × 14 d, subsequently switched to intramuscular benzathine penicillin at 2.4 million U qw × 3 times.

OUTCOME AND FOLLOW-UP

The patient's symptoms resolved after treatment. Repeated brain MRI (July 25, 2019) showed that the multiple intracranial lesions and surrounding edema were significantly reduced compared to the previous imaging (Figure 4B). Brain MRI (March 1, 2020) indicated disappearance of multiple intracranial lesions (Figure 4C).

DISCUSSION

Cerebral syphilitic gumma occurs when *T. pallidum*, originating from a primary infection, spreads throughout the whole body, penetrates the blood-brain barrier, and induces chronic infectious diseases in the central nervous system. Its incidence has increased in recent years[3,4]. Cerebral syphilitic gumma is divided into: (1) Asymptomatic, (2) interstitial syphilis (meningovascular syphilis), (3) parenchymal syphilis (paralytic dementia, spinal phthisis), and (4) gummatous syphilis. Gumma is a late-onset neurosyphilis with a long incubation period that occurs 8-12 years after syphilis infection[5]. Gummatous lesions may appear anywhere in the brain tissue, such as the posterior fossa, pons, midbrain, cerebellopontine angle, corpus callosum, or cerebral convexity[6]. Imaging examinations showed lesions that were either single or

multiple. Computed tomography scans exhibited low or isodense areas, with possible ring enhancement. On MR T1WI, the lesions appeared as low or isointensity, while on T2WI, they showed high signal intensity. Post-enhancement, nodular or ring enhancement was observed. However, these imaging findings were similar to other intracranial space-occupying lesions, such as malignant meningioma, glioma, metastases, tuberculoma, cryptococcal tumor, sarcoma, and brain abscess, which were not characteristic of syphilis gumma, making differentiation challenging[7]. Hence, surgical resection or craniotomy biopsy has been easily misdiagnosed as neoplastic lesions[6]. This patient had multiple intracranial syphilis gumma located in the frontal lobe, occipital lobe, and paraventricular region, showing central necrosis, meningeal tail sign, significant edema around the lesion, and a mild mass effect. These findings are similar to those of brain abscesses and can easily lead to misdiagnosis.

Upon entering the central nervous system, *T. pallidum* adheres to hyaluronidase on the cell membrane of the vessel's inner wall, using its own mucopolysaccharide as a receptor. This interaction leads to the decomposition of the mucopolysaccharide of the vessel, resulting in vascular collapse and the development of obliterative arteritis or periarteritis. Because the body's inflammatory cells infiltrate and develop edema, granulomatous changes occur locally in the damaged area, with caseous necrosis in the center, mostly surrounded by a large area of the edema zone, and the adjacent meninges are often thickened owing to inflammatory reactions. Patients often present with symptoms of increased intracranial pressure, such as headache, vomiting, or blurred vision, which are similar to other lesions of the nervous system and are not characteristic of syphilis gumma; however, a history of unprotected sexual behavior significantly contributes to the diagnostic considerations for this disease and warrants careful attention.

The specimens examined included serum and cerebrospinal fluid, and *T. pallidum* nonspecific antibody tests rapid plasma reagin test (RPR) and toluidine red unheated serum test are commonly used for screening. Specific antibody tests such as the *T. pallidum* particle agglutination assay (TPPA), *T. pallidum* hemagglutination assay, and *T.*

pallidum antibody absorption test can be used to confirm the diagnosis of *T. pallidum* infection. Positive specific antibodies indicate syphilis infection but cannot distinguish whether the infection is short-term or long-term, whereas nonspecific antibodies can reflect the activity of syphilis infection, and the combination of the two can further confirm the diagnosis. Patients often exhibit abnormal changes in WBC counts and protein levels in the cerebrospinal fluid. Laboratory tests are crucial for the diagnosis and treatment of this disease; however, these results may be false-positive or false-negative. Therefore, based on a full understanding of the clinical history, a comprehensive analysis of imaging examinations and laboratory findings can facilitate a preoperative diagnosis of this disease. Nonetheless, postoperative pathological biopsy remains the gold standard for confirming the diagnosis.

After the diagnosis is confirmed, the patient must be actively treated with antibiotics against syphilis. Remission is often associated with the normalization of cerebrospinal fluid cell counts and reduction of protein levels, such as the reduction and conversion of cerebrospinal fluid RPR and TPPA, indicating good treatment results[8]. Postoperative follow-up showed that the main clinical symptoms of this patient significantly improved and disappeared, and re-examination of the brain MRI showed that the number of lesions was significantly reduced, indicating that the therapeutic effect was satisfactory. Currently, penicillin is still the recommended drug of choice for the treatment of neurosyphilis, as it can significantly improve the clinical symptoms of patients and reduce intracranial lesions. According to early, adequate, regular, and whole-course treatment principles, alternative drugs such as ceftriaxone, doxycycline, or erythromycin should be selected for patients allergic to penicillin.

Causes of misdiagnosis may include: (1) The patient's admission with symptoms resembling "intermittent fever", and a history of "liver abscess", often leading to misdiagnosis as bacterial infectious diseases; (2) cerebral syphilitic gumma's rarity in clinical practice, where patients often present to dermatology departments, and neurosurgeons may lack sufficient awareness of this disease; (3) inadequate attention to the patient's sexual history by medical staff and oversight of the syphilis serological

examination results upon admission, contributing to misdiagnosis; and (4) the lack of clear specificity in imaging findings for cerebral syphilitic gumma, further complicating the diagnostic process.

CONCLUSION

The clinical manifestations of neurosyphilis are complex and similar to those of many neurological and other systemic diseases. Because patients themselves and doctors often misdiagnose and miss the diagnosis owing to the abovementioned reasons, clinicians should enhance their understanding of neurosyphilis, heighten disease awareness during clinical processes, and consider neurosyphilis when facing unexplained central nervous system infections, cerebrovascular issues, parenchymal damage, or cases with inadequate therapeutic response, especially if there is uncertainty about the underlying cause. Routine syphilis serology and cerebrospinal fluid examinations are crucial in such scenarios to exclude the possibility of neurosyphilis. This proactive approach will aid in avoiding missed diagnoses and misdiagnoses, ensuring prompt identification and treatment of this manageable disease.

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Figure Legends

Figure 1 Enhanced magnetic resonance imaging images captured on June 28, 2019. A: T1 images; B: T2 images; C: FLAIR images; D: Diffusion-weighted imaging images.

Figure 2 Intraoperative image of left occipital lobe lesion.

Figure 3 Pathological section.

Figure 4 Magnetic resonance imaging images. A: Enhanced magnetic resonance imaging (MRI) image captured on July 8, 2019; B: Enhanced MRI image captured on July 25, 2019; C: Enhanced MRI image captured on March 1, 2020.

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