

# Multiple intracranial and spinal cord syphilitic gummas in a human immunodeficiency virus-negative man with untreated syphilis

## A case report

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### Abstract

**Rationale:** Multiple syphilitic gummas involving both the brain and spinal cord are quite rare. Central nervous system (CNS) syphilitic gummas are commonly misdiagnosed as CNS tumors, and clinical suspicion and diagnosis of a syphilitic gumma by physicians are vital to avoiding unnecessary surgeries. Our case emphasizes the importance of routine serologic syphilis tests and standard therapy with penicillin in patients with a CNS mass.

**Patient concerns:** A 22-year-old previously healthy man presented with a 9-day history of progressive right lower limb weakness.

**Diagnosis:** The diagnosis of gummatous neurosyphilis was based on positive serological, cerebrospinal fluid tests for syphilis and magnetic resonance imaging (MRI) findings, which revealed the presence of multiple dural-based enhancing masses with marked edema.

**Interventions:** Therapy consisting of intravenous penicillin G at 24 million units daily divided into 6 doses were given for a total of 21 days, along with 3 weekly intramuscular injections of benzathine penicillin G (2.4 million units) to ensure that the syphilitic lesions in the CNS were adequately treated.

**Outcomes:** Complete resolution of the lesions was observed on MRI over a 3-month period.

**Lessons:** The importance of routine serologic syphilis tests and standard therapy with penicillin in patients with central CNS mass lesions is noted to avoiding unnecessary surgeries.

**Abbreviations:** BPG = benzathine penicillin G, CNS = central nervous system, CSF = cerebrospinal fluid, HIV = human immunodeficiency virus, MRI = magnetic resonance imaging, RPR = rapid plasma regain, TPPA = *Treponema pallidum* particle agglutination assay, TRUST = toluidine red unheated serum test, VDRL = Venereal Disease Research Laboratory.

**Keywords:** gumma, gummatous neurosyphilis, multiple, neurosyphilis, spinal cord

## 1. Introduction

Neurosyphilis is an infectious disease caused by involvement of the central nervous system (CNS) by *Treponema pallidum*. It is

usually classified into 5 syndromes: asymptomatic neurosyphilis, syphilitic meningitis, meningovascular syphilis, parenchymatous neurosyphilis (general paresis and tabes dorsalis), and gummatous neurosyphilis. Studies show that gummatous

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SS and RY contributed equally to this paper and should be considered co-first authors.

This study was approved by the ethics committee of the third hospital of Mianyang. Informed written consent was obtained from the patient for publication of this case report and accompanying images.

The authors have not published or submitted this manuscript or its accompanying data elsewhere.

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neurosyphilis is the rarest form of the various types.<sup>[1,2]</sup> And a literature search from 1980 to 2017 revealed the majority of CNS syphilitic gummas to be single,<sup>[3–8]</sup> with a minority consisting of multiple lesions.<sup>[9,10]</sup> Multiple syphilitic gummas involving both the brain and spinal cord are quite rare. Very few cases of intracranial and spinal cord syphilitic gummas have been reported.<sup>[9]</sup>

CNS syphilitic gummas are commonly misdiagnosed as brain tumors, resulting in surgery.<sup>[3–8]</sup> Standard penicillin therapy accompanied by magnetic resonance imaging (MRI) findings of a decrease in mass size is useful for the diagnosis of CNS syphilitic gummas in cases where neurosyphilis can be diagnosed based on cerebrospinal fluid (CSF) examination, thereby avoiding unnecessary surgeries.

Here, we describe a rare case of multiple intracranial and spinal cord syphilitic gummas in an immunocompetent man with untreated syphilis. Our report emphasizes the importance of routine serologic syphilis tests and standard penicillin therapy in patients with CNS mass lesions.

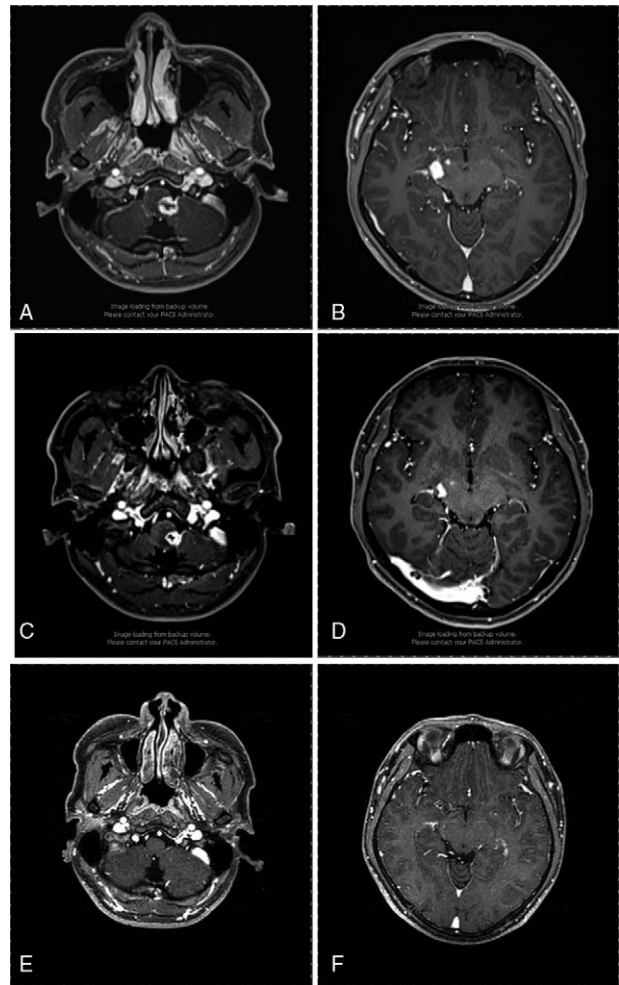
## 2. Case report

### 2.1. History and examination

A 22-year-old previously healthy man presented with a 9-day history of progressive right lower limb weakness. Five days before admission, he had become bedridden and developed a tremor in his right lower limb. He also reported a 20-day history of headaches, cough and nasal congestion without treatment. He had a 10-year history of generalized headaches. He denied any previous skin or mucous lesions or painless genital ulcers. The patient worked in a bar and had many sexual partners since he was 16 years old. A review of his systems yielded no other findings. A neurological examination showed that the strength in the right lower limb was reduced, with grade 3/5 muscle strength, and revealed tendon hyper-reflexia in the right lower limb and positive pathologic reflexes bilaterally. The Romberg test could not be assessed due to leg weakness. The remaining neurological examination results were unremarkable.

A complete blood count, urea, electrolytes, liver function tests, and other routine test results were normal. Autoimmune, paraneoplastic autoimmune, and vasculitic lab tests were negative. The patient was negative for human immunodeficiency virus (HIV). Serologic testing for syphilis revealed a positive *T pallidum* particle agglutination assay (TPPA), and a toluidine red unheated serum test (TRUST) revealed a titer of 1:4. CSF analysis revealed 84 white blood cells/ml, a total protein level of 2.08 g/l, and a glucose level of 2.95 mmol/l. Analysis of the CSF resulted in a positive TRUST (1:4). CSF cultures were negative for bacteria, mycobacteria, and fungi. Pathological analysis of the CSF revealed no malignant cells.

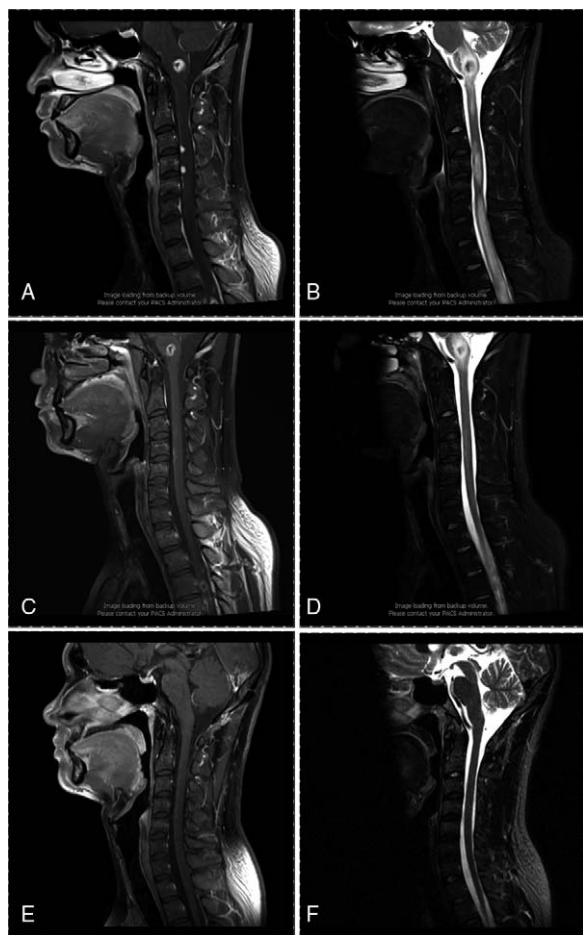
MRI of the brain and spinal cord revealed the presence of multiple dural-based enhancing masses. One irregular ring-enhancing lesion with a central hypointense area and extensive surrounding edema was observed in the medulla (Fig. 1A). Two small homogeneously enhanced nodules were found in the right hypothalamus and right cerebral peduncle (Fig. 1B). Six additional homogeneous-enhancing or ring-enhancing lesions were found in the spinal cord at the C3 (Fig. 2A and B), C4 (Fig. 2A and B), T3 (Fig. 3A and B), T4 (Fig. 3A and B), T5 (Fig. 3A and B), and S1 (Fig. 3A and B) levels.



**Figure 1.** Brain MRI with contrast at different stages of treatment (A–F). (A, B) Pretreatment, 1 irregular ring-enhancing lesion with a central hypointense area in the medulla and 2 small homogeneously enhanced nodules in the right hypothalamus and right cerebral peduncle. (C, D) The lesions were smaller 1 week after treatment. (E, F) No lesions were found 3 months after treatment. MRI = magnetic resonance imaging.

### 2.2. Therapy and follow up

Intracranial and spinal cord syphilitic gummas were suspected based on serologic syphilis testing, CSF analysis, and MRI findings. Therapy consisting of intravenous penicillin G at 24 million units daily divided into 6 doses was given for a total of 21 days, along with 3 weekly intramuscular injections of benzathine penicillin G (BPG, 2.4 million units) to ensure that the syphilitic lesions in the CNS were adequately treated. Oral prednisolone (40 mg) was also prescribed 24 hours before the start of penicillin and was continued for 3 days. Three days after initiating treatment, the patient began to show a dramatic improvement with increased motor strength in the right lower limb. Repeat MRI performed 1 week later showed significant improvement in all enhancing abnormalities (Fig. 1C and D and Fig. 2C and D). Complete resolution of all symptoms was observed within 3 weeks of treatment. Follow-up MRI 3 months later showed no enhancing intracranial and spinal cord lesions (Fig. 1E and F and Fig. 2E and F), which confirmed the diagnosis of syphilitic gummas. The patient is healthy and recovering well.



**Figure 2.** Cervical cord MRI of the patient at different stages of treatment (A–F). T1-weighted post gadolinium images (A, C, E) and T2-weighted images (B, D, F) showing significant resolution of the lesions pretreatment (A, B), at 1 week after treatment (C, D) and at 3 months after treatment (E, F). MRI = magnetic resonance imaging.

### 3. Discussion

We describe a rare case of multiple intracranial and spinal cord syphilitic gummas in an immunocompetent man with untreated syphilis.

Syphilis is mainly transmitted through sexual intercourse. Although the incidence of syphilis decreased dramatically after the introduction of penicillin in the early 1940s, the incidence of syphilis has begun to significantly increase worldwide in the HIV era. Syphilis disproportionately occurs among men who have sex with men, and a high proportion of patients are coinfecting with HIV. Additional populations with a higher prevalence of syphilis include young adult men (ages 20–29 years old), sex workers, and people living on the margins of society such as those in poverty.<sup>[11]</sup> Approximately one-third of people with untreated syphilis have been reported to have further clinical manifestations, including gummatous neurosyphilis or cardiovascular syphilis.<sup>[12]</sup> In our study, the patient was 22 years old and had many sexual partners since he was 16 years old. He denied previous skin or mucous lesions or painless genital ulcers and did not receive any therapy for early syphilis. The patient was in the high-risk group for syphilis; thus, serologic testing for syphilis was performed, and gummatous neurosyphilis was suspected

according to positive serologic tests and MRI findings. Here, we emphasize the importance of an accurate and detailed patient history, especially a sexual history, and routine serologic syphilis testing when encountering high-risk patients with CNS gummas.

Two types of serologic tests are necessary to establish a diagnosis of syphilis. Nonspecific lipoidal tests (rapid plasma regain [RPR], TRUST and Venereal Disease Research Laboratory [VDRL]) are usually performed as screening tests. Treponemal-specific tests (microhemagglutination assay for *T pallidum* antibodies, TPPA, or fluorescent treponemal antibody-absorbed tests) are chosen as confirmatory tests. Of the 3 types of nonspecific lipoidal tests, the TRUST has been widely used in China. Studies have shown that the TRUST is comparable to the RPR and VDRL tests.<sup>[13–15]</sup> Although CSF tests (CSF pleocytosis, CSF protein, CSF lipoidal, and treponemal-specific tests) are helpful to confirm the diagnosis of gummatous neurosyphilis in patients with mass lesions in the CNS, negative CSF tests may not exclude the presence of gummatous neurosyphilis.<sup>[1,4,8]</sup> In such cases, standard therapy with penicillin is useful to confirm the diagnosis.

CNS syphilitic gummas commonly develop from the dura and pia mater. Single or multiple masses attached to the dura or pia mater can invade the brain and spinal cord parenchyma. T1-weighted MRI usually shows a hypointense or isointense lesion. T2-weighted MRI; however, can reveal a hyperintense, isointense, or hypointense lesion. Enhanced T1-weighted images include homogeneous enhancement with surrounding edema or ring-enhancement with a central hypointense area that represents necrotic changes. These MRI findings may be suggestive of a high-grade primary brain tumor such as glioblastoma multiforme with tumor necrosis or a metastatic neoplasm. Thus, CNS syphilitic gummas are always misdiagnosed as CNS tumors. Since syphilitic gummas commonly develop from the dura and pia mater, perilesional meningeal enhancement and thickening are useful to differentiate gummas from tumors. In our case, the MRI findings were typical. Most masses were dural-based, and 1 irregular ring-enhancing lesion with a central hypointense area and extensive surrounding edema was observed in the medulla.

A clinical suspicion and diagnosis of a syphilitic gumma by physicians are vital. A differential diagnosis should be performed between CNS syphilitic gummas and other CNS diseases including meningioma, glioblastoma, lymphoma, metastatic neoplasm, toxoplasmosis, and bacterial and fungal infections. CNS syphilitic gummas are commonly misdiagnosed as brain tumors, resulting in surgery. High-dose penicillin therapy accompanied by MRI findings of a decrease in mass size is useful for the diagnosis of CNS syphilitic gummas, thereby avoiding unnecessary surgeries. In our case, CNS syphilitic gummas were suspected based on serologic syphilis testing, CSF analysis, and MRI findings, and the diagnosis was confirmed by complete resolution of the MRI lesions after high-dose penicillin therapy.

The standard treatment for neurosyphilis, including gummatous neurosyphilis, is high-dose intravenous penicillin therapy. The recommended treatment regimen is aqueous crystalline penicillin G at 18 to 24 million units per day administered as 3 to 4 million units intravenously every 4 hours for 10 to 14 days. An alternative regimen is 2.4 million units of procaine penicillin G administered intramuscularly daily in addition to 500 mg of probenecid administered orally 4 times daily for 10 to 14 days. Another alternative regimen is 2 g Ceftriaxone administered intramuscularly or intravenously for 10 to 14 days.<sup>[16]</sup> However,



**Figure 3.** Thoracic cord MRI with contrast pre-treatment (A, B). T1-weighted post gadolinium image (A) and T2-weighted image (B) showing lesions at the T3 level, T4 level, T5 level, and S1 level pretreatment. MRI = magnetic resonance imaging.

recommended treatments may fail. Ariñez Barahona et al reported the treatment of a patient with gummatous neurosyphilis with 2.4 million units of intramuscular benzathine penicillin for 5 weeks. Six months later, the patient developed a new cerebral gumma lesion.<sup>[3]</sup> A follow-up lumbar puncture should be performed every 6 months until the CSF cell count is normal. CSF VDRL and protein levels can also be monitored, although these levels tend to normalize at a slower rate than the cell count. If CSF pleocytosis does not improve after 6 months, retreatment should be considered.<sup>[16]</sup> In our case, we intravenously administered 24 million units of penicillin G daily for a total of 21 days, followed by 3 weekly intramuscular injections of BPG (2.4 million units), to ensure that the CNS syphilitic gummas were adequately treated.

#### 4. Conclusions

In conclusion, we describe a rare case of multiple intracranial and spinal cord syphilitic gummas in an immunocompetent man with untreated syphilis. This case emphasizes the importance of an accurate and detailed patient history, especially a sexual history, routine serologic syphilis testing in the high-risk group, and standard intravenous penicillin therapy when patients with CNS gummas are encountered. Partial or complete resolution of MRI lesions after penicillin therapy can be useful to confirm the diagnosis.

#### Author contributions

**Data curation:** Sisi Shen, Ruiyi Yang, Liwei Tang.

**Formal analysis:** Sisi Shen, Libo Wang, Liwei Tang.

**Investigation:** Sisi Shen, Ruiyi Yang, Libo Wang, Liwei Tang.

**Methodology:** Sisi Shen, Ruiyi Yang, Libo Wang.

**Supervision:** Bo Liu.

**Writing – original draft:** Sisi Shen.

**Writing – review and editing:** Ruiyi Yang.

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