Case Report

Cerebral syphilitic gumma presenting with intracranial gumma and pathologic vertebrae fractures

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A B S T R A C T

A 37-year-old female was admitted with worsening neurologic function. On arrival from an outside hospital, the patient was obtunded and intubated. Magnetic resonance imaging of the brain revealed nodular enhancement of the leptomeninges, intracranial osteolytic lesions, and diffuse vasogenic edema causing mass effect. Imaging of the thoracic spine revealed pathologic compression fractures of 4 thoracic vertebrae. On review of the patient’s electronic medical record, the patient had previously received treatment for secondary syphilis with intramuscular benzathine penicillin G. Surgical biopsies of the frontal bone and dura showed diffuse, chronic inflammation while a biopsy of the adjacent brain parenchyma revealed replicating spirochetes. The patient was subsequently prescribed dexamethasone and benzathine penicillin G. She regained neurologic function but later signed out against medical advice without completing her treatment regimen.

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Introduction

Syphilis, caused by Treponema pallidum, may present in distinctive stages throughout its disease course. Despite the presence of T. pallidum in cerebrospinal fluid (CSF) in a matter of hours after infection, symptomatic neurosyphilis is often described as a late manifestation [1,2]. Approximately 15%-40% of patients with untreated syphilis will develop tertiary syphilis [2]. Characteristic findings in tertiary syphilis are the formation of gumma or the presence of bony involvement or late neurological symptoms (namely tabes dorsalis and general paresis) [2]. Amongst those that develop tertiary syphilis, patients may acquire a rare disease of the central nervous system (CNS) called cerebral syphilitic gumma in which patients develop gumma of the brain parenchyma. These lesions are commonly misdiagnosed as an intracranial malignancy and require surgical pathology for confirmation [3]. Furthermore, due to abundant vasculature of the bone marrow and periosteum, these structures may act as a reservoir for hematogenous infections. As with the more commonly involved organisms, T. pallidum may cause osteomyelitis with perivascular...

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lymphocytic infiltration. Subsequently, the sequelae of an infectious process in bone may result in necrosis, sclerosis, osteoporosis, sequestrum formation, or spontaneous fracture [4–6]. We present a case of a patient who presented with cerebral syphilitic gumma and pathologic compression fractures of the thoracic vertebrae.

Case report

A 37-year-old immunocompetent, HIV-negative female with a history of polysubstance abuse, work as a commercial sex worker, and recently diagnosed seizure disorder presented to an outside hospital with a several month history of left-sided weakness, urinary incontinence, mild photophobia, ataxia, and headache. At the time of admission, the patient denied constitutional symptoms, nausea, vomiting, childhood seizure disorders, and changes in her vision. On history, approximately 4 months prior, the patient presented to a county clinic with an evolving, maculopapular rash on the soles of her feet. She had a rapid plasma reagin (RPR) of 1:32 and was subsequently diagnosed with presumed secondary syphilis. She received a single intravenous dose of benzathine penicillin G. Her RPR was retested on admission and was found to be 1:4 and confirmatory testing with T. pallidum antibodies was positive.

She subsequently received magnetic resonance imaging (MRI) which demonstrated extensive cerebral edema of the frontoparietal lobes. The edema was most predominant at the vertex within the brain parenchyma causing downward mass effect on the corpus callosum. There was nodular enhancement of the frontoparietal lobes and vertex along the path of the superior sagittal sinus measuring approximately 5 cm. There were also multiple nodular enhancements of the dura extending along the right interhemispheric fissure. No ventriculomegaly or hydrocephalus was noted. The patient was subsequently started on benzathine penicillin G but her illness acutely worsened. She was transferred to our hospital.

On arrival, the patient was intubated and sedated with propofol. She became bradycardic with her heart rate decreasing to 36 beats per minute. On physical exam, she was spontaneously moving her lower extremities, did not follow commands, and her pupils were constricted but equal and reactive to light bilaterally. Computed tomography (CT) of the head revealed large, bilateral areas of hypoattenuation within the supraventricular white matter consistent with diffuse vasogenic edema with accompanying effacement of sulci and the right lateral ventricle (Fig. 1A-C). There were 3 osteolytic lesions in the right frontal bone (Fig. 1D, E). MRI of the brain with contrast at our institution again showed nodular enhancement along the falx cerebri on T1-weighted fast field echo (Fig. 2A-C). Enhancement of the superior dura of the bilateral frontal lobes extended towards

![Image](https://via.placeholder.com/150)

**Fig. 1** – Axial CT images of the head on admission demonstrating diffuse cerebral edema with sulcal (A, B) and lateral ventricle (yellow arrow; C) effacement secondary to mass effect. There are large, bilateral hypodense regions (red asterisks; B) within the supraventricular white matter, consistent with diffuse cerebral vasogenic edema (B). The CT images of the head using bone algorithm demonstrate 2 osteolytic lesions within the frontal bone (blue arrows; D, E).
the brain parenchyma and resembled small, rim-enhancing lesions with dural tails (Fig. 2B). Sulcal and right lateral ventricle effacement (Fig. 2A) secondary to diffuse, bilateral vasogenic edema of the supraventricular white matter (Figure 2A-D) was once again demonstrated. Three mildly enhancing intraosseous lesions were seen in the calvarium measuring approximately 1.2 × 0.9 cm, 0.8 × 0.5 cm, and 1.1 × 0.6 cm in the posterior right frontal bone, anterior right frontal bone, and anteromedial left frontal bone, respectively (Fig. 2D-F). In addition, there was a punctate focus of restricted diffusion in the superomedial right frontal lobe, consistent with a punctate area of vascular infarction (Fig. 3). There was no evidence of an acute territorial infarct or midline shift. Given these findings, the differential diagnosis from neuroimaging was syphilitic meningitis with gummas, leptomeningeal tuberculosis, leptomeningeal malignancy, and neurosarcoidosis.

As part of the infectious workup, a CT with intravenous contrast of the spine was also ordered on day 7 of admission. Age-indeterminate superior endplate compression fractures with minimal loss of vertebral height were noted at the level of T3 through T6 (Fig. 4A-C). No evidence of osteoporosis or osteopenia was present. A follow-up MRI of the thoracic spine revealed similar findings. Short tau inversion recovery (STIR) sequence demonstrated mild STIR hyperintensity along the
superior endplates of T3 through T6 without evidence of ligamentous injury. Linear hypointensities on T1-weighted and hyperintensities on T2-weighted imaging and T1-weight fat-saturated were also seen, which were consistent with superior endplate compression fractures (Fig. 4E-G). No evidence of spinal cord stenosis or marrow edema was present.

The patient received benzathine penicillin G daily and dexamethasone every 6 hours. Neurosurgery was consulted for leptomeningeal biopsy. Areas biopsied included the right frontal bone, dura of the right frontal lobe, and right frontal lobe parenchyma. The biopsies revealed focal chronic dural inflammation and a reactive neocortex with chronic inflammation and rare spirochetes, which is consistent with syphilitic meningoencephalitis. The patient continued to improve on the general neurology service and was eventually transferred to the original outside hospital. The patient signed out against medical advice the following day and has been lost to follow-up despite several attempts to contact the patient.

Discussion

*Treponema pallidum* is a spirochete that causes syphilis via sexual transmission and vertical transmission during pregnancy. Clinical manifestations of syphilis are a result of a local inflammatory response to replicating spirochetes [7]. Infected individuals most commonly follow a disease course that is classically divided into 4 distinct stages: primary, secondary, latent, and tertiary syphilis.

Patients with primary syphilis present with a single, painless ulcer (chancre) or multiple lesions either on the genitals or on other parts of the body. Primary syphilis is usually associated with painless regional lymphadenopathy. Resolution of these lesions will typically be followed by secondary syphilis 6-8 weeks after the initial chancre. Secondary syphilis is characterized by fever, headache, and a maculopapular rash involving the trunk and extremities including the palm of the hands and soles of the feet [8]. As the symptoms and rash lessen, the patient will enter a latent phase which may last years. In the first 1-2 years of latent syphilis, patients are still considered to be infectious due to syphilis-like relapses [9]. Approximately 15%-40% of patients will develop tertiary syphilis, which is characterized by cardiac or neurologic destructive lesions, skin and visceral gumma, and bony involvement [2]. While the incidence of primary and secondary syphilis has steadily increased since its historic low in 2000 and 2001, the incidence of tertiary remains low due to proper treatment with antibiotics and relatively low rate of progression for untreated secondary syphilis [2,10,11].

Neurosyphilis, a syphilitic infection of the central nervous system, is a component of both early and late syphilitic stages. Early neurosyphilis (primary, secondary, and early latent syphilis) is defined by the presence of CSF abnormalities in neurologically asymptomatic patients with serologic evidence of an underlying syphilis infection. Late neurosyphilis (late latent and tertiary syphilis) manifests as severe symptoms, including chronic meningitis, meningovascular stroke-like syndromes, and neurological forms of tertiary syphilis (tabes dorsalis and general paresis). A rare manifestation of tertiary meningovascular syphilis is cerebral syphilitic gumma. Preoperative misdiagnosis of cerebral gumma is most commonly diagnosed as glioma due to its rare incidence, absence of a clear history, and unreliable imaging characteristics [12–14].

![Fig. 3 – Axial diffusion-weighted imaging (A) and corresponding apparent diffusion coefficient (B) on day 1 of admission demonstrating an area of restricted diffusion in the superomedial right frontal lobe (orange arrows), most likely representing a punctate vascular infarction.](image-url)
Fig. 4 – Sagittal (A) and coronal (B, C) CT of the thoracic spine with intravenous contrast on day 7 of admission demonstrating age-indeterminate superior endplate compression fractures of T3, T4, T5, and T6 (red arrows; A–C). Sagittal MRI with intravenous contrast on day 10 of admission. STIR (A), T2-weighted (B), T1-weighted (C), T1-weighted fat-saturated with intravenous contrast (D) MR imaging sequences demonstrate mild STIR hyperintensity along the superior endplates of T3, T4, T5, and T6 (red arrows; D), consistent with acute superior endplate compression deformities with minimal loss of height of T4, T5, and T6 vertebral bodies. Similar linear hyperintensities (red arrows; E, G) and hypointensities (red arrows; F) are seen on T1-weighted and T2-weighted imaging.

While imaging of cerebral syphilitic gumma is not diagnostic, it is frequently used to further correlate clinical characteristics of the disease. Gumma lesions can appear on CT as hypoattenuated or heterogeneously attenuated lesions due to underlying hemorrhage, necrosis, or calcification [14]. Contrast-enhanced MRI shows ring-enhancing nodularity within the cerebral cortex and subcortex with low or mixed signal foci within the center of the lesion containing caseous necrosis. These lesions are typically accompanied by large areas of edema, often with mass effect. Gadopentetic acid-enhanced scans reveal irregular annular enhancement, adjacent meninges intersecting at an obtuse angle, and thickening and enhancement of surrounding meninges and cranial nerves [13]. The findings of significantly enhanced nodules with surrounding vasogenic edema are not exclusive to cerebral syphilitic gumma and may also be seen in cases of metastatic lesions to the brain, malignant meningioma, and inflammatory granulomas. It appears that a distinguishing finding of cerebral syphilitic gumma is the obtuse angle of the intersecting meninges as these lesions are extracranial and are located outside of the cerebral parenchyma [13,15,16]. The central area of the nodular lesions is generally hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Dural enhancement along with a “dural tail” may be present [14,17]. It has been proposed that gumma lesions form a dural tail secondary to inflammatory granulomatous tissue
leading to reactive changes in adjacent connective tissue with hypervascularity [18].

Bony involvement of syphilis (secondary or tertiary stage) includes osteitis, osteomyelitis, osteoporosis, pathologic fractures, congenital skeletal malformations, destructive lesions, and intraosseous lesions [19–22]. Osteomyelitis may be divided further between gumma and syphilitic osteomyelitis. To differentiate, pathologic evaluation of gumma osteomyelitis will demonstrate necrosis and occasional giant cells. Pathology of both subtypes of osteomyelitis will reveal perivascular lymphocytic infiltration [6]. Syphilitic spinal column involvement is rare with only a few reported cases [23–27]. Compression fractures may occur in the setting of syphilitic vertebral involvement secondary to intraosseous gumma [28].

Our patient leaving against medical advice and not attending follow-up appoints is of concern. Besides the concern of transmission to other individuals, she also only received partial treatment. Moreover, patients with neuroinvasive syphilis require an even longer duration of treatment as benzathine penicillin has poor penetration of the blood-brain barrier [29]. Urgent treatment with benzathine penicillin G may drastically change the clinical course and avoid future morbidity and mortality. Thus, our patient is at risk for reoccurrence and/or progression of her disease.

In conclusion, tertiary syphilis, such as cerebral syphilitic gumma, should be on the differential with patients with a history of secondary syphilis who present with neurologic deficits. Imaging of cerebral syphilitic gumma is often nonspecific and may include differential diagnoses consistent with other granulomatous-causing etiologies. However, the diagnosis becomes more likely in high-risk patients and those with positive RPR or treponemal antibodies, history of primary or secondary syphilis, or rapid improvement following penicillin agents.

Conclusion

The incidence of tertiary syphilis and neurosyphilis is rare with the advent and widespread usage of effective antibiotics. We present a case of biopsy-confirmed cerebral syphilitic gumma disease, a form of neurosyphilis. We describe the neuroimaging of cerebral syphilitic gumma, including nodular enhancement of the leptomeninges, intracranial gumma lesions, and multi-level vertebral compression fractures. Patients drastically improve following prompt treatment with benzathine penicillin.

Generic written consent input

No consent obtained for this case report as this is a retrospective study with no patient identifiers. “Formal consents are not required for the use of entirely anonymized images from which the individual cannot be identified - for example, X-rays, ultrasound images, pathology slides or laparoscopic images, provided that these do not contain any identifying marks and are not accompanied by text that might identify the individual concerned.”

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