



## Case report

## Calvarial lytic lesions in neurosyphilis with ocular involvement

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## ABSTRACT

We report a case of calvarial lytic lesions in neurosyphilis with ocular involvement. A 42-year-old woman with a past medical history of polysubstance abuse presented with recent bilateral vision loss. CT revealed numerous calvarial lytic lesions and multiple myeloma was initially suspected. Syphilis screening with RPR and confirmative CSF studies were positive for active infection. The patient was treated with Penicillin G and demonstrated clinical improvement. The objective of this study was to provide insight into a rare manifestation of syphilis with osseous involvement and encourage further discourse into establishment of standards of care for syphilitic osteomyelitis. There exist no evidence-based guidelines regarding optimal treatment route and duration, role of bone biopsy, determination of therapeutic impact, and threshold for surgical intervention in the management of syphilitic osteomyelitis.

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## Introduction

Syphilis is a venereal disease caused by the spirochete *Treponema pallidum* (*T. pallidum*), characterized by distinct stages of infection with an expansive constellation of symptoms [1]. Rates of syphilitic infections in the United States have increased annually since 2000, with 129,813 cases reported in 2019 [2]. Notably, cases of osseous involvement in syphilis have been documented in the literature [3–7], however, there exist no guidelines for management or therapeutic endpoints in the treatment of syphilitic osteomyelitis. We present a unique case of calvarial lytic lesions in neurosyphilis with ocular involvement with the goal of inviting further investigations into the management of syphilitic osteomyelitis.

## Case report

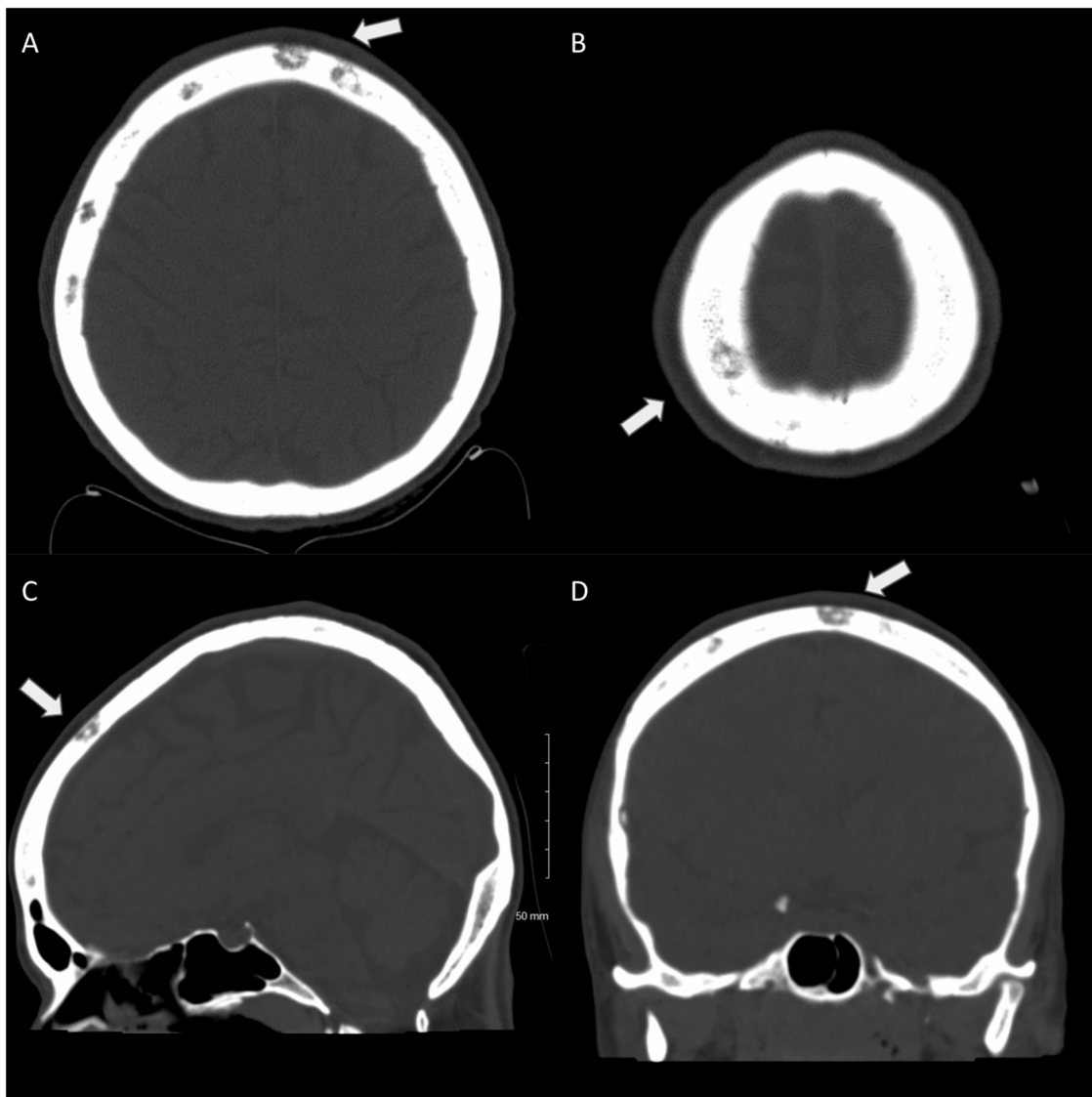
A 42-year-old woman presented to the ED for evaluation of bilateral vision loss with associated redness, pain, whitish discharge from both eyes, and occasional fever and chills. Onset of symptoms began one week prior to arrival, with unintentional weight loss of approximately fifteen pounds over two months. Patient endorsed a history of intravenous opioid use and unprotected sexual activity with a partner. Past medical history included hypothyroidism and anxiety managed with synthroid and sertraline.

Initial evaluation in the ED showed bilateral conjunctival injection with elevated intraocular pressures to 24 mmHg and 25 mmHg on the left and right sides, respectively, and corneal abrasions with areas of patchiness on the left eye. Painful perianal condyloma lata were present and perivaginal herpetic lesions were noted with white-yellow vaginal discharge. Patient had a single fever of 101.2 °F on the evening of admission with spontaneous resolution, but otherwise stable vital signs throughout the remainder of her hospital course. Head CT imaging was significant for numerous small scattered lytic lesions throughout the calvarium (Fig. 1). Laboratory values significant for elevated protein (9.2 g/dL), decreased albumin to globulin ratio (0.4), elevated ESR (> 120 mm/h), CRP (2.2 mg/dL), Beta-2-microglobulin (4.7 mg/dL), normocytic anemia (10.8 g/dL), mild thrombocytosis (510,000 platelets/mcL), unremarkable white blood count, and urine drug screen positive for cocaine, opiates, and amphetamines. The patient was given ceftriaxone, acyclovir, doxycycline, azithromycin, erythromycin eye drops, proparacaine eye drops, and admitted to the hospital.

Given RPR positivity with RPR ratio > 1:256 and ophthalmologic assessment suggestive of neurosyphilis as opposed to secondary syphilis, patient was started on Penicillin G 4 million units IV every 4 h for ocular syphilis with granulomatous uveitis, and suspected underlying neurosyphilis. Fluoroscopy guided lumbar puncture was performed with CSF studies positive for VDRL reactivity, quantitative titer with 1:2 ratio, elevated protein (96 mg/dL), and lymphocytic pleocytosis (52) with negative culture, confirming the diagnosis of neurosyphilis. Further confirmatory results including reactive TP-PA IgG and VDRL positivity returned, substantiating diagnosis of neurosyphilis. Additional infectious workup included negative

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**Fig. 1.** CT imaging of calvarial lytic lesions (arrows) A. Axial view of multiple lesions located within the frontal and right parietal bones (slice 43), B. Axial view of lytic lesions within right parietal bone (slice 53), C. Sagittal view of lytic lesions within frontal bone (slice 28) D. Coronal view of lytic lesions within frontal bone (slice 49).

Quantiferon gold, positive HSV 1,2 IgG, active HCV RNA titers (333k IU/mL), negative HIV testing, wet mount with clue cells and trichomonas, negative blood cultures, and negative urine cultures. Additional lytic lesions workup included normal PTH/Calcium/Alkaline Phosphatase/ACE, unremarkable CXR, SPEP with polyclonal gammopathy and immunofixation negative for monoclonal protein, and UPEP with polyclonal kappa proteins with no definite monoclonal protein identified.

Ocular syphilis with bilateral granulomatous uveitis was managed with prednisolone acetate and cyclopentolate eye drops with gradual improvement of vision in the right eye and minimal improvement of vision in the left eye. Additionally, she completed a course of acyclovir for suspected herpetic lesions and metronidazole for bacterial vaginosis and trichomonas. Patient tolerated the antibiotic regimen well, however, only completed 8 out of 10 days of planned Penicillin G therapy prior to leaving the hospital against medical advice and was lost to follow-up.

## Discussion

Various degrees of osseous involvement in syphilis have been documented in the literature [3–8], with one of the earliest studies

suggesting bone involvement as an uncommon sequela of infection [9]. Calvarial lytic lesions in secondary and tertiary syphilis have been identified in a minority of cases [3–7] with diverse clinical presentations ranging from asymptomatic infection to a skull mass with chronic headaches [5,7,8]. Given the rarity of cases, no large scale studies have been performed to generate guidelines for management of syphilitic osteomyelitis. Treatment with parenteral Penicillin has resulted in clinical improvement in several cases of syphilitic osteomyelitis [3–8], however, there is no consensus in favor of a particular route of administration or duration of treatment.

The role of bone biopsy also remains unclear when syphilis is the primary diagnosis as a positive result is unlikely to significantly alter antibiotic management. Invasive bone biopsies were performed in two studies [10,11] to confirm growth of *T. pallidum* within lytic lesions found on imaging, and treatment with parenteral Penicillin was completed in both cases with clinical improvement. Furthermore, due to the challenge of culturing *T. pallidum* with only recent breakthroughs in obtaining in-vitro *T. pallidum* cultures [12], there currently exists no standardized microbiological means to determine impact of treatment apart from indirect measures such as resolution of CSF values and serum RPR titers [13]. More studies should be conducted to clarify the utility of biopsies in syphilitic osteomyelitis.

Additionally there is conflicting evidence regarding the utility of post-treatment imaging in determining therapeutic impact as certain studies have demonstrated improvement of bone lesions after antibiotic therapy [4,5,7,8], while others witnessed delayed to no significant changes in lesions [3,9,14]. Determination of the most efficacious imaging modality for evaluating syphilitic lesions post-treatment requires further investigation, as CT and PET imaging both appear to be reasonable choices for evaluating therapeutic impact [15]. Lastly, surgical management of syphilitic bony lesions remains an option [11], however there is limited literature available to identify the threshold for intervention.

To the best of our knowledge, this is the first documented case of calvarial lytic lesions in neurosyphilis with ocular involvement. Maintaining clinical suspicion for syphilis in the setting of lytic lesions is essential, as early treatment can prevent irreversible complications. In this case study, expedited treatment with intravenous Penicillin G was implemented for treatment of underlying neurosyphilis, resulting in clinical improvement of the primary complaint of vision loss. Duration of treatment of 10 days was selected primarily for treatment of underlying neurosyphilis, as there is limited data on length of treatment for syphilitic osteomyelitis. We urge further investigation into ideal treatment route and duration, role of bone biopsy, determination of therapeutic impact, and threshold for surgical intervention.

#### CRedit authorship contribution statement

**Michael F. Chan:** Conceptualization, Investigation, Writing – original draft. **Fekadesilassie Moges:** Investigation, Writing – review & editing. **Dawit Major:** Investigation, Writing – review & editing. **Radek Buss:** Investigation, Writing – review & editing. **Ankoor Biswas:** Supervision, Investigation, Writing – review & editing.

#### Ethical approval

Not applicable.

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#### Conflict of interest

All authors have no conflicts of interest to declare.

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#### Consent

Not applicable.

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