



# Calvarial osteomyelitis in secondary syphilis: evaluation by MRI and CT, including cinematic rendering



Valentina Petroulia<sup>a,\*</sup>, Bernard Surial<sup>b,1</sup>, Rajeev Kumar Verma<sup>a</sup>, Christoph Hauser<sup>b</sup>, Arsany Hakim<sup>a</sup>

<sup>a</sup> University Institute of Diagnostic and Interventional Neuroradiology, Inselspital, Bern University Hospital, University of Bern, Switzerland

<sup>b</sup> Department of Infectious Diseases, Inselspital, Bern University Hospital, University of Bern, Switzerland

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## ABSTRACT

This is a case of a 22-year-old, HIV-negative, male patient with asymptomatic syphilitic osteomyelitis of the skull in the context of secondary syphilis. The diagnosis was made based on serology as well as CT and MRI scans. CT volumetric data was post-processed with cinematic rendering, which is a novel algorithm that allows for a photorealistic visualization of the lesions. Imaging and follow-up scans after treatment confirmed the diagnosis without the need to perform invasive procedures such as a biopsy.

## 1. Introduction

Syphilis is a systemic sexual transmitted infection caused by *Treponema pallidum* subspecies pallidum, belonging to the wide order of Spirochaetales, the spiral-shaped bacteria. *Treponema pallidum* has a high affinity for osseous structures. Bone involvement is usually associated with congenital or tertiary syphilis and is preferentially localized in the tibia, skull, sternum and clavicles. Although infrequent, these lesions can also develop in secondary syphilis [1] with long bones of extremities and skull being the most frequent sites of bony involvement. The pathophysiology of bony involvement in syphilis begins with the hematogenous dissemination and depositions of the bacteria after the primary infection in the periosteum of the bones, in the Haversian canals and medulla of the bones. Osteolytic lesions are less frequent and often seen in skull and clavicles with the classical appearance in conventional Radiographs and CT of worm-eaten bone and adjacent

sclerosis, mostly affecting the outer table and diploe. In MRI we may see signal changes of the bone marrow, enhancement of the adjacent periosteum and dura as well as adjacent soft tissue inflammation. At last osseous involvement can also present with a combination of periostitis and osteolytic lesions.

Since the lowest number of reported cases in 2000, there has been a worldwide increase in the incidence of syphilis in North America, Europe and China with the highest rates among men who have sex with men (MSM) and patients with concomitant HIV-Infection [2].

This current case is an atypical presentation of osteomyelitis of the skull in an asymptomatic young patient with secondary syphilis. Imaging played an important role in the diagnosis, and the treatment response upon follow-up studies confirmed the diagnosis without the need for biopsy.

\* Corresponding author.

E-mail address: [valentina.petroulia@insel.ch](mailto:valentina.petroulia@insel.ch) (V. Petroulia).

<sup>1</sup> These Authors contributed equally to this work.

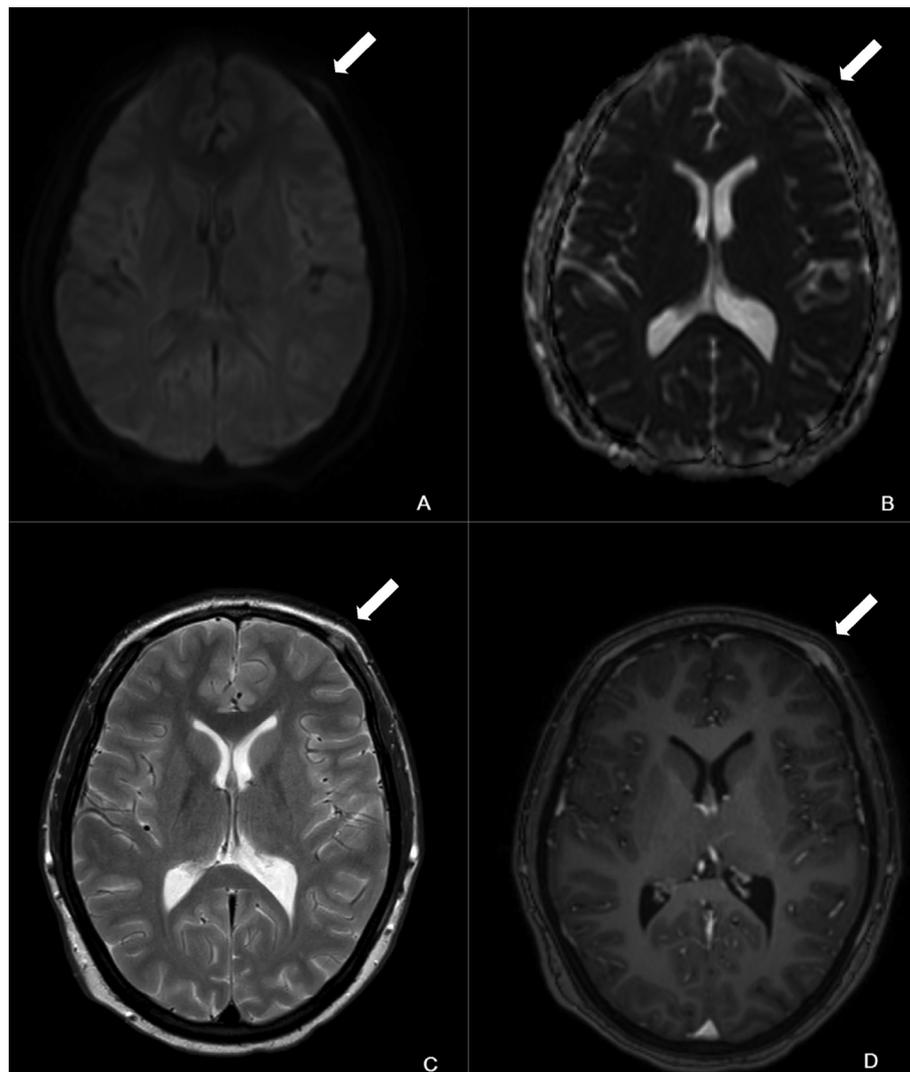
## 2. Case report

A 22-year-old male patient who was recently diagnosed with schizophrenia and positive serology for syphilis underwent a brain MRI to rule out organic etiologies of psychosis or neurosyphilis. Imaging showed no signs of neurosyphilis or other organic causes of psychosis; however, multiple skull lesions were identified in both frontal bones with a high T2 signal and soft tissue formation with contrast enhancement (Figures 1 and 2). A non-enhanced CT was performed to better characterize the lesions, following which at least 20 osteolytic lesions were identified ranging from 2 to 8 mm with irregular borders involving the outer table and diploe in both frontal and parietal bones with adjacent soft tissue swelling (Figure 3). These lesions were newly discovered when compared with a previous CT exam, which was performed a year earlier to exclude traumatic brain injuries. The presence of lytic lesions in a patient with a history of syphilis is suggestive of syphilitic osteomyelitis.

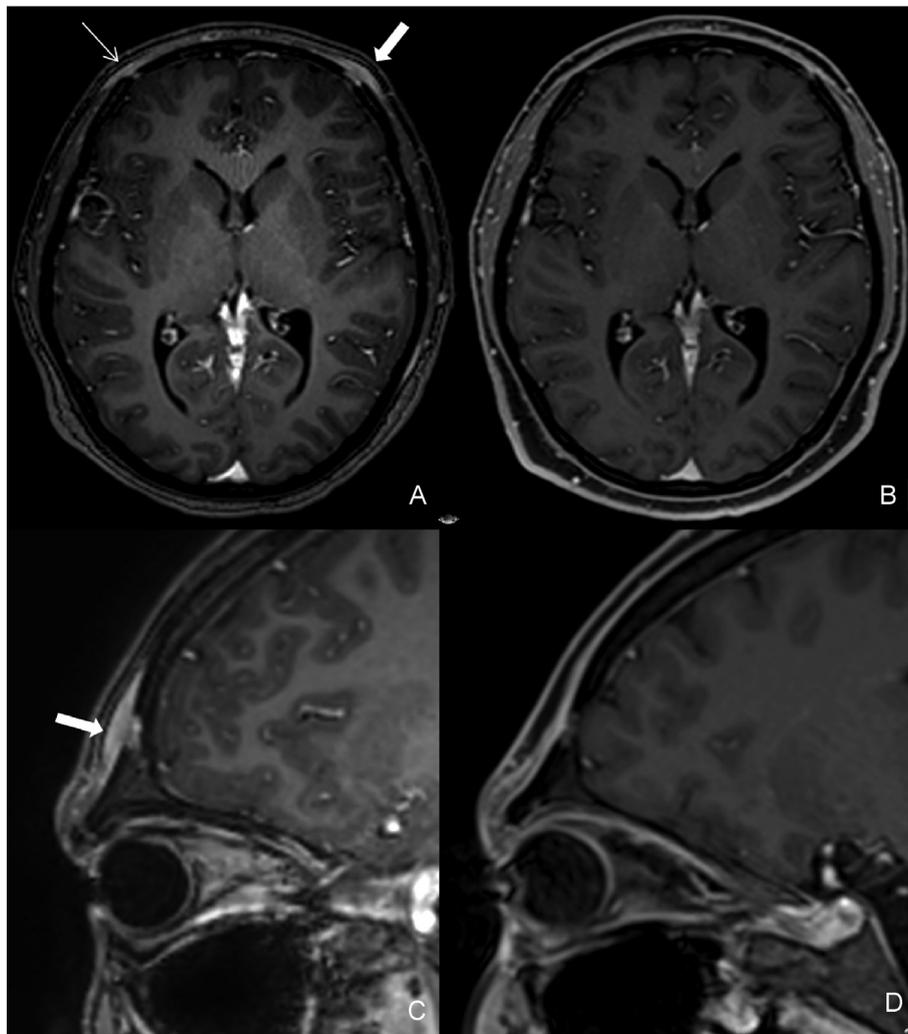
Consequently, the patient was referred to the infectious disease clinic for further evaluation, including a detailed medical history, clinical exam and further laboratory studies. The patient reported having had unprotected anal intercourse with anonymous male partners. He had never experienced symptoms suggestive of syphilis or been diagnosed with syphilis in the past. The patient denied experiencing fevers or other

systemic symptoms but experienced a rash and myalgia around the time of presentation.

Clinical exam showed a maculopapular rash of the trunk including violaceous nodules on the palms and soles, and an indolent cervical lymphadenopathy. The neurological examination was normal. Laboratory studies showed an elevated C-reactive protein of 146 mg/L, while the blood count as well as liver and renal function tests were within normal ranges. Screening tests for HIV, Hepatitis B and C as well as pooled swabs (oral, rectal and urethral) for *Gonorrhea* and *Chlamydia trachomatis* were negative. *Treponema*-specific antibodies (*T. pallidum* hemagglutination assay, TPHA) were significantly increased (1: 81,920) and the venereal disease research laboratory test (VDRL) indicated a positive result (1:8). The cerebrospinal fluid showed a normal cell count and a negative liquor/serum index for TPHA. Based on patient history, physical examination and serology, a diagnosis of secondary syphilis was concluded and three doses of 2.4 Mio IE of penicillin G benzathine were administered at one-week intervals. At six months, the VDRL titers normalized to 1:< 2. A follow-up MRI three months after the initial imaging revealed a diminution of the intra-/extraosseous soft tissue process as well as the contrast enhancement (Figure 2). Follow-up imaging and lab analysis confirmed response to the treatment for the postulated diagnosis of osteomyelitis in secondary syphilis.



**Figure 1.** Axial DWI/ADC Map (A,B), T2-spin echo (C) and 3D gadolinium enhanced fat saturated T1 MRI in axial plane (MPRAGE) showing a diffusion restricted skull lesion and adjacent soft tissue in the left frontal bone left (arrow) with T2 – hyperintense Signal of the skull lesion and T2 – hyperintense soft tissue and with correlated enhancing soft tissue.



**Figure 2.** Axial (A) and sagittal (C) 3D gadolinium enhanced fat saturated T1 MRI (MPRAGE) showing an ill-defined skull lesion in the left frontal bone (thick arrow) with enhancing soft tissue process. A similar smaller lesion (thin arrow) is present in the right frontal bone. A significant decrease of both lesions was seen in the follow-up MRI (B and D) three months after the onset of therapy.

### 3. Discussion

Syphilis infection is divided into four clinical stages: primary, secondary, latent and tertiary. The bone involvement in syphilis infection usually affects the superficial bones, e.g. tibia, skull, sternum and clavicles and manifests as periostitis, with syphilitic osteomyelitis and osteitis being rather a well-known finding in tertiary and congenital syphilis, but is atypical in secondary syphilis [1, 3]. It is typically discovered due to related symptoms such as pain or headache [4]. The high affinity of *T. pallidum* for osseous structures underlines the crucial role of imaging in the diagnosis of bone involvement in syphilis infection, especially in patients with vague or no bone symptoms at all.

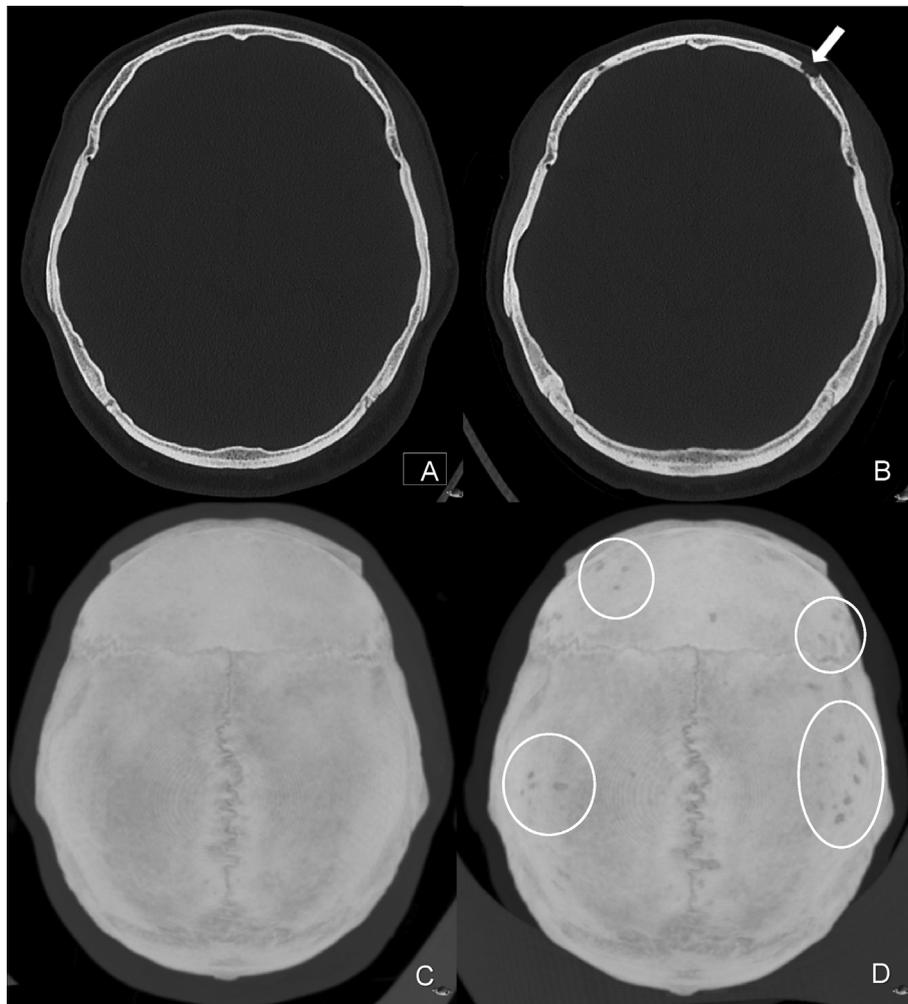
Hematogenous dissemination leads to bacterial depositions in the periosteum and the medulla of the bones, leading to a perivascular inflammation with the production of cellular infiltrates consisting of lymphocytes, plasma cells and monocytes. Therefore, this frequently manifests as periostitis. While osteolytic lesions in syphilis are less frequent, a multifocal pattern of osseous involvement is quite common and periostitis and osteolytic lesions can coexist [1, 5]. Gummata are the result of a granulomatous reaction and are usually associated with tertiary disease, but may also be present in secondary syphilis [6].

A retrospective case series reported a prevalence of bone lesions in 0.15–0.23% of all patients with early syphilis [1, 3]. A systematic review of the literature between 1964 and 2013 identified and

characterized 37 cases with bone involvement in secondary syphilis. Most patients were male (76%) with a median age of 32. A large proportion (30%) were HIV positive with a median CD4 cell count of 343 cells/mm<sup>3</sup>. Most frequently, the long bones were affected (n = 22), followed by the skull (n = 21). Other manifestations occurred in the ribs, clavicle, spine and sternum.

In contrast to the patient in the presented case, diagnosis of osseous syphilis was frequently made because of symptoms such as headaches indicating skull involvement, local tenderness of affected sites as well as nocturnal pain in long bones or joints that resolved after appropriate antimicrobial therapy [4, 7].

Conventional radiographs often provide insufficient information and can only detect advanced disease states. Therefore, high-resolution imaging techniques are crucial to detect bone involvement in syphilis, especially in regions with complex anatomy such as the facial skeleton and skull base. Modern CT scanners are capable of generating thin slices with increased sensitivity for small lesions, as well as the ability of acquiring 3D data volume with reconstruction. Different post-processing techniques allow radiologists and clinicians to better understand the topography and the extent of any lesions present. Maximum intensity projection (MIP) of the CT volumetric data is helpful in delineating osteolytic lesions in contrast to dense bony matrices, which could be missed due to the anatomical complexity (Figure 3). Post-processing of the CT volume with cinematic rendering (Figure 4) generates



**Figure 3.** Axial images of head CT in bone window (A) and MIP reconstruction (C), which was performed a year prior to the current presentation, with no evidence of skull lesions. The present CT (B) shows an osteolytic lesion (arrow) in the left frontal bone. The MIP reconstruction (D) shows multiple osteolytic lesions in frontal and parietal bones bilaterally (lesions marked in circles).

photorealistic images to create a clearer image for patient recognition as well as for clinicians addressing special concerns [8, 9].

The classical appearance of calvarial syphilis in conventional radiographs and CT is worm-eaten bone with adjacent sclerosis, mostly affecting the outer table and diploe of the skull. MRI detects signal changes in the bone marrow, enhancement of the adjacent periosteum and can indicate soft tissue inflammation. Furthermore, it can delineate the extent of soft tissue involvement of the underlying dura in skull lesions, and evaluate whether the central nervous system is involved.

Syphilis is known as the “*great imitator*” as it may resemble other diseases [10, 11]. Osteolytic lesions due to syphilis also have a broad differential diagnosis. Other causes for osteolytic lesions with or without adjacent soft tissue involvement in the skull include bone metastases, pyogenic osteomyelitis, multiple myeloma, lymphoma, sarcoma secondary to Paget’s disease, tuberculosis, as well as leukemia and Langerhans’ cell Histiocytosis in children [12]. Therefore, patient medical history and lab work are crucial to reach the correct diagnosis.

Antibiotic treatment alone seems to be effective in resolving bone lesions. Intramuscular or intravenous penicillin was the most commonly administered antibiotic for a median duration of three weeks (ranging from six days – five months). Symptoms such as fever and pain decrease rapidly with therapy, but complete resolution of the symptoms seems to

take several weeks or even months [4]. Treatment success is judged using VDRL follow-up to indicate a fourfold decrease within 12–24 months.

Since medical history, signs, symptoms and serology were all consistent with secondary syphilis in a calvarial manifestation, no biopsy of the lesions was needed in our patient who underwent treatment with three weekly doses of 2.4 Mio IE of benzathine-penicillin intramuscularly – similar to the treatment of late latent syphilis. VDRL-titers decreased to 1:< 2 within six months after the last injection, and a follow-up MRI of the brain showed a marked decrease in size and enhancement of the intra-/extra osseous soft tissue process, confirming the diagnosis of osteomyelitis in secondary syphilis.

#### 4. Conclusion

To conclude, the re-emergence of syphilis worldwide has re-introduced it into the daily routine of radiologists and physicians are frequently challenged with uncommon manifestations of this “*great imitator*”. Although rare, bone involvement can be found in the context of secondary syphilis – even in asymptomatic patients. Therefore syphilitic osteomyelitis should be on the list of differential diagnoses of osteolytic lesions. The bone lesions in CT scan and the soft tissue reaction depicted in MR scan in combination with the post-processing techniques



**Figure 4.** Post-processing of the initial head CT using cinematic rendering depicting the multiple osteolytic lesions of the skull. The image provides a realistic impression of the lesions.

are very helpful for the diagnosis and can preclude the performance of an invasive biopsy in the appropriate clinical setting.

#### Declarations

##### Author contribution statement

Valentina Petroulia: Conceived and designed the experiments; Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Bernard Surial: Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Rajeev Kumar Verma: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Christoph Hauser: Analyzed and interpreted the data. Wrote the paper.

Arsany Hakim: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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##### Competing interest statement

The authors declare no conflict of interest.

##### Additional information

No additional information is available for this paper.

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