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Diagnostic delay in ankle and foot tuberculosis resulting in tuberculoma and tuberculous meningitis in a middle-aged female: A case report

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Abstract

A middle-aged woman presents with chronic foot arthritis which progressed to a non-healing ulcer, which was unresponsive to conventional antibiotics and debridement. She then developed cerebral manifestations and was empirically treated with antitubercular medications which led to healing of the ulcer. Unfortunately, delays in initiating treatment resulted in development of other extrapulmonary tuberculosis complications such as cerebral tuberculoma with tuberculous meningitis. She was subsequently diagnosed with neurocysticercosis which continued to worsen during her hospital stay. She eventually succumbed to her illness due to the complications and a possible nosocomial infection. This case highlights the challenges with diagnosis of uncommon presentations of common diseases in an endemic area, leading to diagnostic delays and development of serious complications.

Keywords

Extrapulmonary tuberculosis, tuberculoma, ankle and foot tuberculosis, tuberculous meningitis

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Introduction

Tuberculosis (TB) is an endemic disease, particularly in developing countries. Patients typically present with pulmonary symptoms and are diagnosed with routine investigations and initiated appropriate treatment with antitubercular medications (ATT). In some patients, TB can occur outside of the lung, usually after spreading via hematogenous route. In such patients, the typical symptoms of cough, fever, and weight loss are not often seen clinically.[1] Ankle and foot TB (AFTB) is an uncommon presentation of extrapulmonary TB and coupled with a lack of awareness among non-specialists and the similarity to other common diseases in clinical presentation, it can lead to diagnostic and treatment delays.[2,3] Delays in initiating ATT can lead to further dissemination of TB to other extrapulmonary sites such as the brain and cause cerebral tuberculoma and tuberculous meningitis (TBM). Furthermore, the diagnosis of cerebral tuberculoma can be challenging owing to its similarity in clinical presentation and imaging characteristics to other intracerebral pathologies

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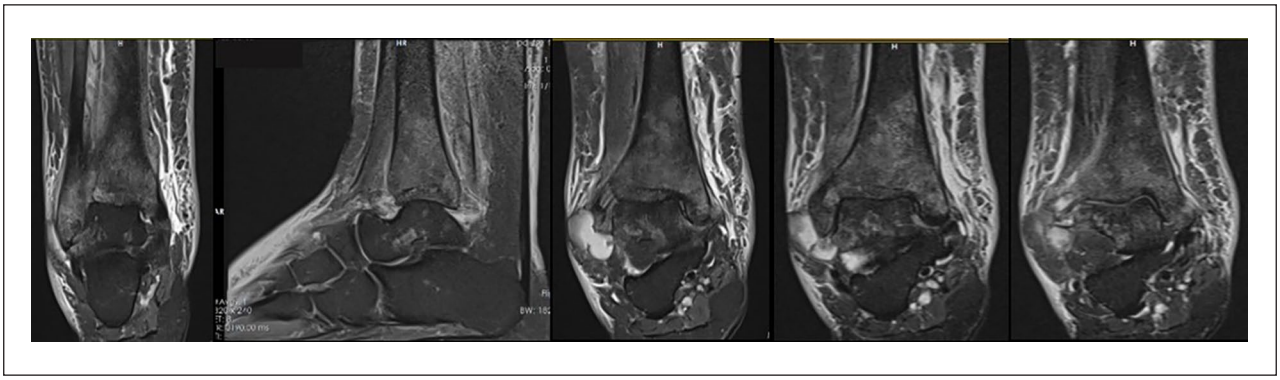

Figure 1. MRI of the right lower extremities showed thick fluid collection with heterogeneous signal intensities (complex collection) in subtalar joint and signal changes in most hind foot bones and some midfoot. There was narrowing of the tibiotalar joint space and destruction of the tibial subchondral bone (at the tibia talar dome), talus bone, and the fibular lateral malleolus. Tibial, fibular, talus, and mild calcaneus bone marrow edema surrounding the tibial lesions was seen with edematous infiltration of the per malleolar soft tissues with skin discontinuation suggesting an ulcer. There was diffuse marrow infiltration in the distal tibial (epiphysial-metaphyseal region), talus and distal epiphysis of fibula.
MRI: magnetic resonance imaging.

such as neurocysticercosis.[4] We present a case of a middle-aged woman with AFTB in whom delays in diagnosis and treatment led to cerebral complications.

Case presentation

A businesswoman in her 40s presented to the orthopedic outpatient clinic with an 8-month history of a painful and swollen right ankle without fever or weight loss. Examination of the ankle was indicative of a joint effusion with tenderness to palpation around the ankle joint. She had a limited range of motion at the ankle joint, mostly due to pain but an intact neurovascular exam in the right foot. Magnetic resonance imaging (MRI) of the ankle was done which showed narrowing of the tibiotalar joint space, with thick fluid collection and destruction of the cartilage tibial subchondral bone (at the tibial talar dome), talus bone and the fibular lateral malleolus (Figure 1(a) and (b)). A diagnosis of septic arthritis was made. Incision and drainage were done at the clinic and the patient was discharged home to follow up in a few days.

Five days later, the swelling and pain worsened. Debridement was done at another hospital under spinal anesthesia. The fluid discharge from the ankle was described as a yellowish cheese-like material.(Figure 2). She continued using antibiotics and wound dressing was done regularly but with no healing of the ulcer.

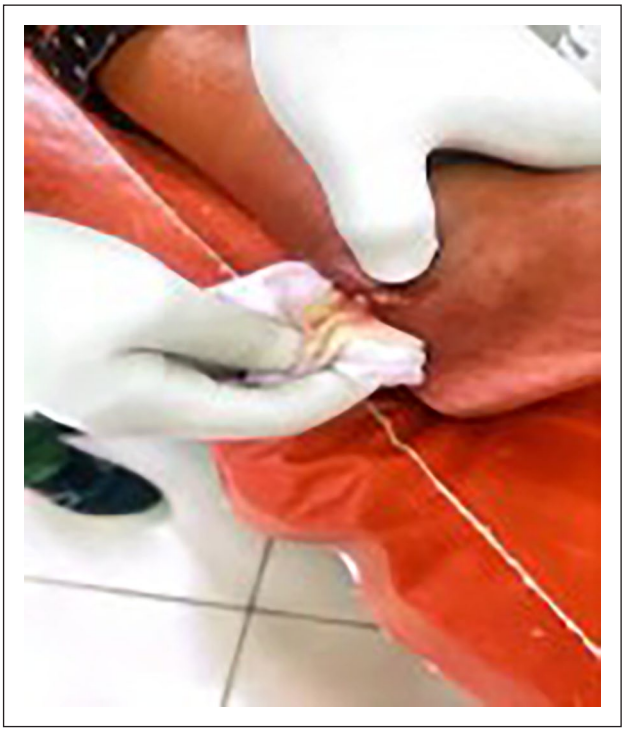

Figure 2. Yellowish cheese-like discharge seen after debridement of the ankle ulcer.

Three weeks after the debridement, she developed severe headaches, altered mental status, back pain and mouth deviation. She was admitted to the intensive care unit (ICU) with a diagnosis of sepsis and encephalopathy from the infected wound in the ankle. She was treated with ceftriaxone. metronidazole and dexamethasone initially. Later, the antibiotics were changed to meropenem and vancomycin owing to the lack of response to the initial therapy. She was also given empiric fluconazole and acyclovir. However, none of these treatments seemed to improve her general condition.

An MRI of the brain during her admission to the ICU was done and showed ring-enhancing lesions (Figure 3). The radiological diagnosis was tuberculoma or central nervous system (CNS) toxoplasmosis. Serological tests for Toxoplasma IgM, Cytomegalovirus IgM and HIV infection were negative. Blood cultures did not reveal any bacterial

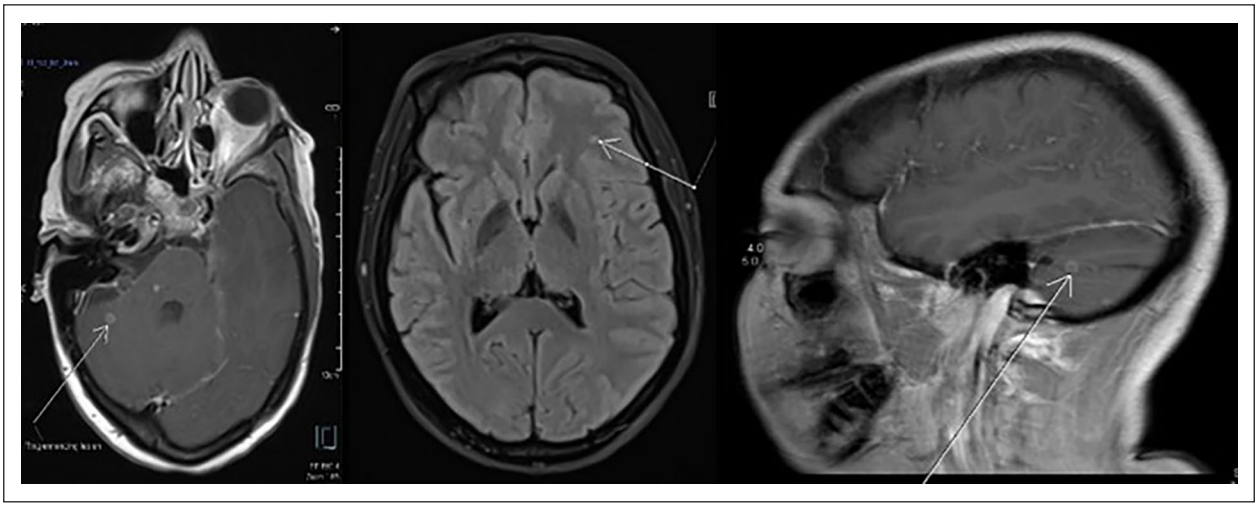

Figure 3. MRI brain showing few punctate focal lesions involving the cerebral hemispheres, brainstem, and cerebellum. The lesions were isointense on T1 and had high signals on T2/FLAIR. There was a lesion in the right cerebellum showing low T2/FLAIR intensity center with peripheral hyperintensity and mild surrounding edema which showed ring enhancement after contrast administration (white arrow). There was no significant mass effect.
MRI: magnetic resonance imaging.

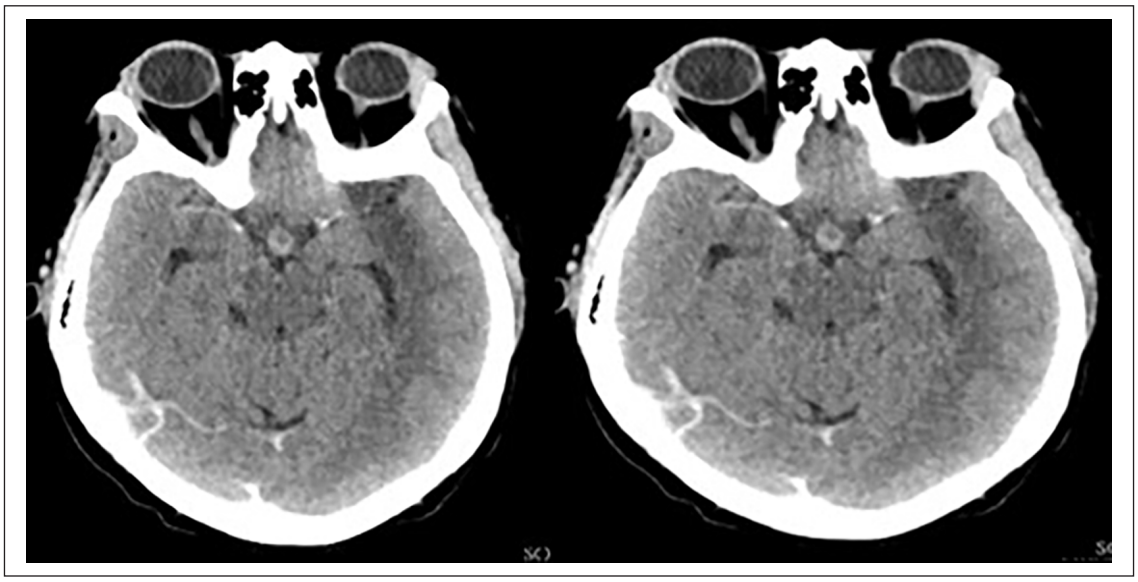

Figure 4. Non-contrast brain CT showing effacement of cerebral sulci and basal cisterns consistent with brain edema. There was leptomeningeal enhancement marked in the right occipital lobe and the cerebellum.
CT: computed tomography.

growth. Serum adenosine deaminase (ADA) was 9.1 U/L (normal level: 0–30 IU/L).

Based on the lack of response to antibiotics and radiological images, it was decided to initiate ATT. She remained admitted for another month while on ATT during which time her fever subsided and her mental status improved. A brain computed tomography (CT) scan done before discharge revealed features suggestive of meningitis, which was attributed to TB (Figure 4). She continued using ATT at home and noted that the ulcer in the right ankle healed within a few days after discharge.

Two weeks after discharge from the hospital, her mental status deteriorated again and she once again presented with severe headaches and fever. Brain MRI showed features of meningitis with communicating hydrocephalus (Figure 5). Brain MRI also revealed features suggestive of neurocysticercosis (Figure 6). She was initiated on albendazole 400 mg daily in addition to dexamethasone and carbamazepine.

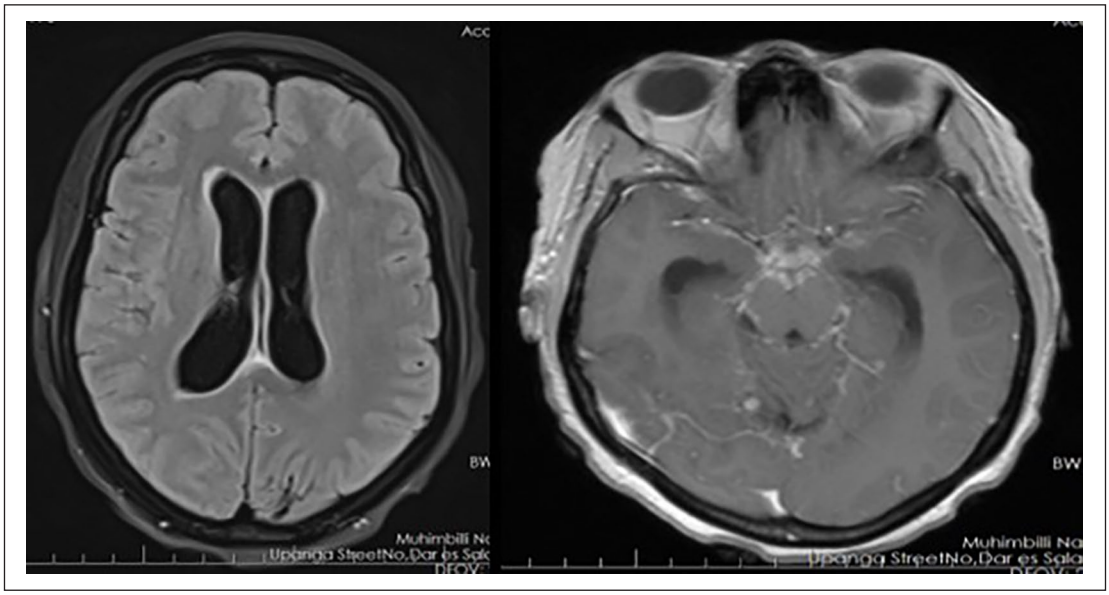

Figure 5. Brain MRI revealed dilatation of the ventricular system with widening of the temporal horns, due to communicating hydrocephalus. Post-contrast images demonstrated thick nodular leptomeningeal enhancement predominantly in the basal cisterns.
MRI: magnetic resonance imaging.

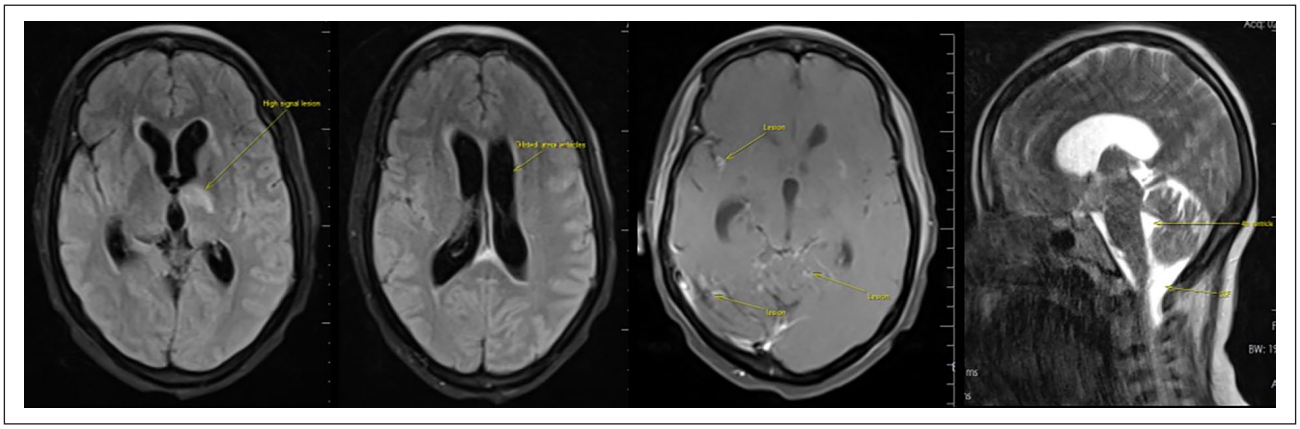

Figure 6. Brain MRI revealing left caudate hematoma, ventriculomegaly, prominent cerebrospinal fluid (CSF) at the fourth ventricle extending inferiorly to posterior of foramen magnum. There were multifocal intracranial hypodense lesions with associated multifocal calcifications—most likely neurocysticercosis.
MRI: magnetic resonance imaging.

During her hospital stay, she also developed intestinal obstruction which was managed conservatively with nasogastric tube decompression and manual removal of feces.

A lumbar puncture revealed low opening pressure and a turbid CSF. CSF analysis showed red blood cells (RBC) 2/mm^3, white blood cells (WBC) 1/mm^3. There were no polymorphs or lymphocytes and scanty epithelial cells. No bacteria was grown on culture. The CSF ADA was 176.2 U/L. She later developed an acute onset of dyspnea, which was confirmed to be due to pulmonary embolism by CT-pulmonary angiography (Figure 7). She was initiated on low-molecular weight heparin and later switched to rivaroxaban.

After a few days, she developed a new fever in the hospital while being on the above treatment. Unfortunately, the cause of the new fever could not be determined and she succumbed to her illness a few days later.

Discussion

Isolated involvement of the bone in TB is uncommon, and the variable clinical and radiological features may mimic pyogenic osteomyelitis, bone tumor, or other inflammatory and neoplastic processes of the synovium.[5] There are no clear guidelines for joint TB, whose treatment is still referred to

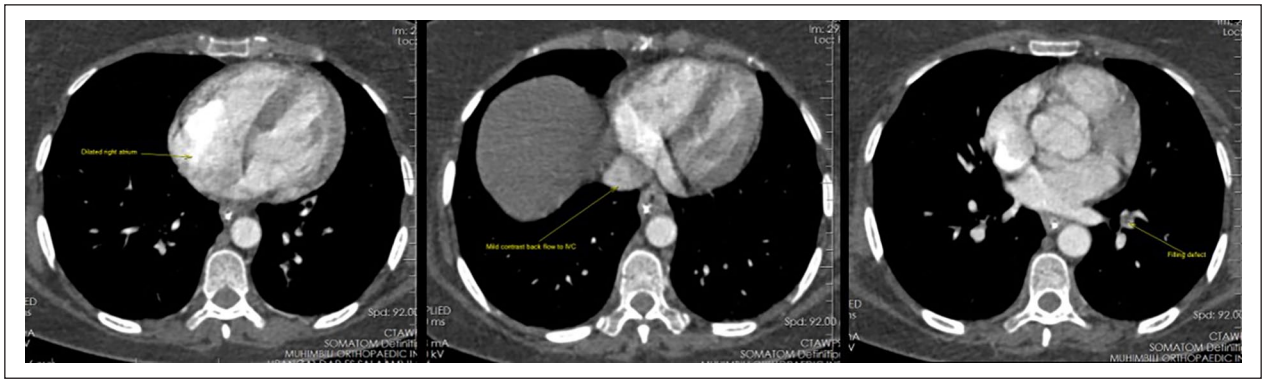

Figure 7. CT-pulmonary angiography revealed pulmonary embolism with dilated right atrium and mild contrast backflow to inferior venacava (IVC), consistent with signs of pulmonary hypertension.
CT: computed tomography.

guidelines for pulmonary TB.[6] Due to its atypical symptoms, joint TB is often neglected and misdiagnosed.[7–9]

AFTB is a rare presentation of TB, even in endemic areas. TB should be considered in the differential diagnosis for a patient presenting with a localized, painful swelling and a persistent draining sinus of the foot and ankle. Biopsy should be taken in all cases to identify the underlying etiology.[5] Unfortunately, biopsy was not done in this patient on initial presentation leading to a delay in diagnosis and further dissemination of TB to the brain. Diagnosis is often delayed due to lack of clinical suspicion and non-confirmatory biopsy reports.[10] In a study done by Duan and Yang, 15 patients with chronic synovitis of the ankle and suspicious cause of early-stage ankle TB underwent arthroscopic treatment. These cases all failed to confirm diagnosis of TB by ankle arthrocentesis. The diagnosis was confirmed by pathologic examination and culture.[11]

The diagnosis of AFTB was reached after the wound was noted to be healing within 1 month of ATT initiation. Early diagnosis and initiation of ATT is vital in all cases of AFTB to prevent further joint involvement and other complications.[10]

Cerebral tuberculomas are a rare but well-recognized complication of TB and most cases have associated TBM.[12] It is hypothesized that following an initial TB infection resulting in bacteremia, a foci of granulomatous inflammation may coalesce into a caseous tuberculoma.[13] In our patient's scenario, debridement of the ankle wound might have resulted in bacteremia and spread of mycobacteria to the brain, although this cannot be said with complete certainty as the cerebral manifestations may have also been a result of further dissemination of TB from the primary source.[14]

AFTB has been described previously in a 34-year-old female who developed it as a complication of her pulmonary TB while on treatment. It leads to tissue and joint destruction, similar to our patient. Fortunately, the patient responded well to treatment and was further treated with tibiotalocalcaneal arthrodesis to improve her joint function.

Paradoxical response to ATT, defined as the clinical or radiological worsening of pre-existing tuberculous lesions or the development of new lesions during appropriate treatment, creates a diagnostic difficulty. Paradoxical deterioration in the CNS clinically presents with headache, mental confusion, focal seizure, cranial nerve palsy and cortical signs such as hemiparesis, paraparesis, and hemianesthesia, as a result of enlargement or development of intracranial tuberculoma and hydrocephalus.[15,16] Our patient's clinical condition worsened a month after starting ATT but on repeat MRI there were no new lesions of tuberculoma except there were features of TB meningitis and hydrocephalus. Attention should be paid to paradoxical reactions in patients with TBM, and these patients should be kept under observation even after completion of ATT.[17]

The coexistence of neurocysticercosis and other lesions may be an incidental observation. It appears unlikely that neurocysticercosis is a risk factor for other intracerebral pathology. The location of neurocysticercosis lesions and whether or not there is surrounding perilesional edema does not appear to affect the location or severity of coexisting lesions.[18] Likewise, it is unlikely that cerebral tuberculoma predisposes the patient to neurocysticercosis. Human cysticercosis and TB are endemic diseases in developing countries. Both these diseases have certain common factors of origin.[19]

Differentiating between cerebral tuberculoma and neurocysticercosis can be challenging because of similarities in their clinical presentation and routine imaging.[20,21]

Unfortunately, the patient developed complications from her TBM and coexisting neurocysticercosis. Furthermore, her repeated and prolonged hospital stays may have predisposed her to a nosocomial infection which could have been the reason for the new onset fever that occurred a few days before she passed.

Conclusion

TB continues to be a burden in developing countries and a high index of suspicion is required for diagnosing TB in less common extrapulmonary sites such as the ankle and foot.

Appropriate and timely investigations are necessary to avoid diagnostic delays and enable early treatment to prevent further dissemination of TB and associated complications.

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Author contributions

H.F.S. was the primary attending physician and wrote the initial draft of the manuscript. S.M.M. was a major contributor to writing the manuscript. S.N.B. interpreted all the radiology images. All authors were involved in the care of this patient. All authors read and approved the final manuscript.

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Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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Data availability

The data used to support this case report are included within the article

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