Case Report

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Pathology Section

Cryptococcal Spondylitis Mimicking Tuberculous Spine in a Previously Treated Case of Spinal Tuberculosis: A Rare Case Report with Review of Literature

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ABSTRACT

Spinal tuberculosis is a common cause of vertebral infection in endemic regions such as India, where the burden of tuberculosis remains high. Conversely, specific fungal infections may manifest with clinical and radiological characteristics that closely resemble those of other conditions, thereby complicating the diagnostic process and potentially resulting in the administration of inappropriate therapies. The present case is of a 76-year-old male patient who experienced persistent lower back pain for a duration of six months and had a prior medical history of treated tuberculosis. Radiological assessment via Magnetic Resonance Imaging (MRI) revealed lytic destruction affecting the T10 vertebral body, pedicle, and right transverse process, as well as involvement of the adjacent vertebrae, specifically T9 and T11. Given the clinical suspicion of recurrent tuberculosis, a more comprehensive evaluation was subsequently performed. Histopathological examination of the lesion demonstrated granulomatous inflammation with the presence of fungal organisms. Special staining with Periodic Acid–Schiff (PAS) confirmed features consistent with cryptococcal infection. The patient was later managed with appropriate antifungal therapy. This case highlights the importance of considering fungal aetiologies in patients with spondylodiscitis who do not respond to anti-tubercular treatment. Early tissue diagnosis supported by special stains plays a crucial role in establishing the correct diagnosis and guiding timely management. Increased awareness of such atypical presentations is essential to avoid delays in treatment and to improve patient outcomes.

Keywords: Extra pulmonary tuberculosis, Fungal granuloma, Fungal infections, Histopathology, Spondylodiscitis

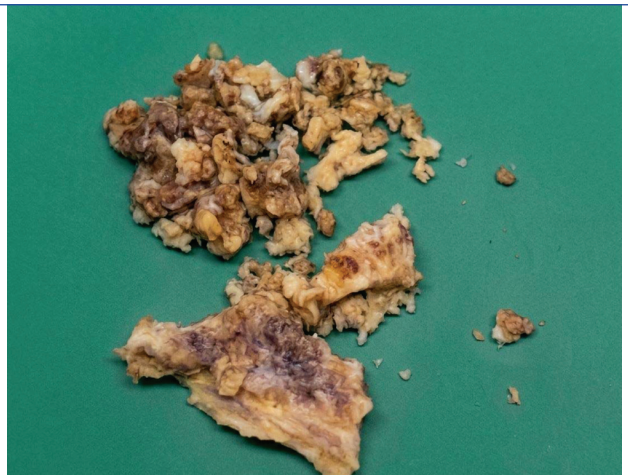
CASE REPORT

A 76-year-old man presented to the outpatient department of orthopaedics with complaints of persistent lower back pain for the past six months. The patient had a notable history of spinal tuberculosis and had completed a full course of anti-tubercular therapy two years before the present episode. On examination, a tender swelling measuring approximately 3.5×3×2 cm was observed over the spine. There was no local rise in temperature, redness, rash, draining sinus, or discolouration at the affected site.

There was no history of fever or evening rise of temperature. On systemic examination, no lymphadenopathy or hepatosplenomegaly was detected. The patient had no altered gait, paraesthesia, or neurological deficit. There was no history of HIV infection, steroid use, malignancy or diabetes mellitus in the patient. Routine investigations revealed a normal complete blood count. Liver, thyroid and renal function tests were within normal limits. Blood glucose levels were within normal limits and HbA1c was 5.2%. C-reactive protein was 30 mg/L.

MRI of the spine was performed to find the cause of his pain. Imaging demonstrated poorly defined lytic destruction affecting the T10 vertebral body, right pedicle, and transverse process. Additional discrete lytic lesions were identified in the posterior portion of the T9 vertebra and the anterior portion of the T11 vertebra. Considering the patient's clinical history and the radiological findings, the main clinical suspicion was a recurrence of spinal tuberculosis.

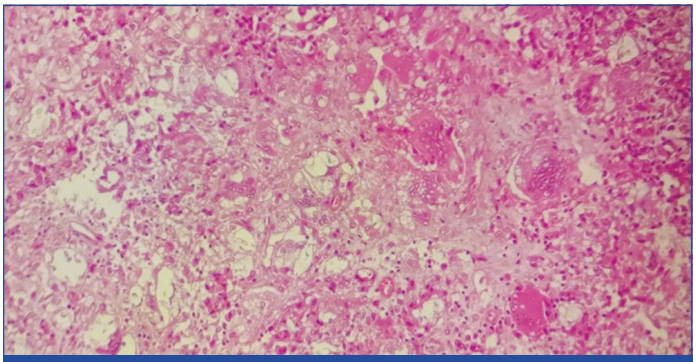
To confirm the diagnosis, a surgical excision of the lesion from the T10 vertebral body was performed, and the tissue was submitted for histopathological evaluation. On gross examination, the excised specimen consisted of multiple grey-brown to grey-white soft-tissue bits and bony fragments, altogether amounting to a volume of 15 mL [Table/Fig-1].



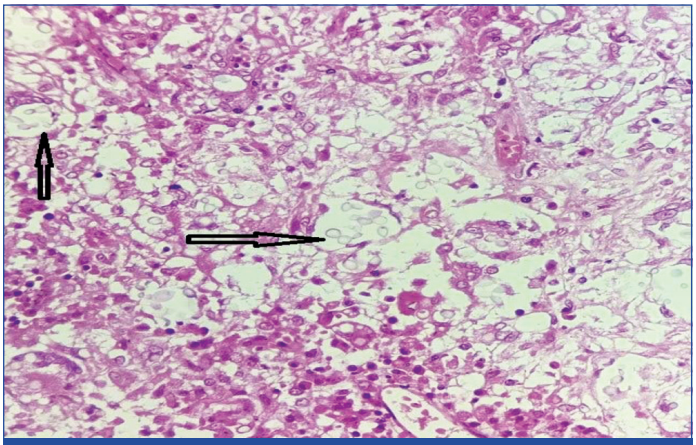
[Table/Fig-1]: Gross-multiple grey-brown to grey-white soft-tissue bits and bony fragments all together amounting to 15 cc.

Histological evaluation of the tissue sections showed bony trabeculae along with adjacent tissue exhibiting a pronounced granulomatous inflammatory response. The inflammatory infiltrate consisted of epithelioid cells along with lymphocytes, histiocytes and multinucleated giant cells, all within a fibrous connective tissue background [Table/Fig-2]. Multiple foci of necrosis were seen across the specimen. Acid fast stain for Mycobacterium tuberculosis was done and was found to be negative. On detailed microscopic evaluation, numerous round, encapsulated fungal organisms exhibiting budding were identified within the granulomatous areas, showing features characteristic of Cryptococcus [Table/Fig-3]. To confirm the presence of these fungal elements, a special PAS stain was performed. PAS staining clearly demonstrated the fungal organisms, thereby confirming the diagnosis of spinal cryptococcosis

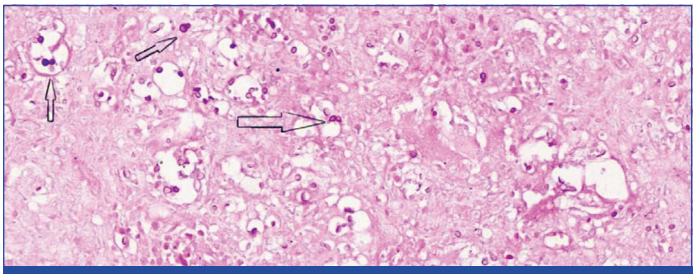
[Table/Fig-4]. The patient was started on intravenous antifungal therapy i.e., Amphotericin B and later on Fluconazole therapy as per standard protocol. The patient on follow-up showed significant symptomatic improvement with reduction of pain and size of the lesion. There was no progression reported.



[Table/Fig-2]: Section shows inflammatory cells comprising of epithelioid cells, histiocytes lymphocytes and occasional multinucleate giant cells. (Haematoxylin and Eosin, X100).



[Table/Fig-3]: Section shows round, encapsulated fungal organisms exhibiting budding were identified with features characteristic of Cryptococcus (Haematoxylin and Eosin, X200).



[Table/Fig-4]: Section shows round, encapsulated fungal organisms as shown by the arrow. {Periodic acid Schiff (PAS) stain X200}.

DISCUSSION

Differentiating spinal cryptococcosis from a tuberculosis relapse remains a profound diagnostic challenge due to identical clinical symptoms, overlapping radiological destruction, and deceptively similar histopathological features. In countries with a high burden of tuberculosis, clinicians rarely suspect skeletal cryptococcosis initially, creating a major diagnostic dilemma where patients are often started empirically on anti-tubercular therapy. In tuberculous endemic areas, spinal cryptococcosis closely resemble tuberculous spondylitis or metastatic disease, as has been reported in the earlier literature. Delay in diagnosis can cause serious consequences, including permanent neurological impairment. Gupta R et al., and Adsul N et al., described cases of vertebral cryptococcosis initially misdiagnosed and treated as spinal tuberculosis, highlighting the overlapping clinical manifestations of long-standing back pain, vertebral destruction, and paraspinal involvement [1,2]. Later on, the continued cord compression eventually resulted in complete paraplegia, making surgical decompression necessary [2].

Such misdiagnosis mainly occurs because cryptococcal osteomyelitis closely resembles tuberculous spondylitis in its clinical presentation. On histopathology, cryptococcus can elicit a granulomatous reaction characterised by epithelioid histiocytes, multinucleated giant cells, and areas of necrosis that may be either caseating or non-caseating features that closely resemble a typical tubercle. Similarly, Zhou Y et al., in their report, described about the destructive osteomyelitis of the spine with granulomatous inflammation closely resembling tuberculous pathology on histology [3]. In the present case, the same granulomatous pattern initially supported an erroneous suspicion of recurrent tuberculosis. Other clinical differentials that need to be considered in the present case include lymphoma, metastatic carcinoma, other fungal infections such as blastomycosis and histoplasmosis.

Disseminated cutaneous and skeletal cryptococcosis are responsible for 5-10% of cases, and commonly affect the vertebral column [2-4]. In addition to mimicking tuberculosis, cryptococcal lesions in bone can also resemble metastatic disease due to their destructive and expansile appearance. Mansoor CA and Koya J have pointed out that isolated lumbar lesions with cortical disruption may be mistaken for skeletal metastases, thereby further complicating the diagnostic process [4]. At imaging, studies by Wang C et al., have shown that spinal cryptococcosis is characterised by the presence of lytic lesions accompanied with cortical disruption, eccentric involvement, irregular sequestrum formation, and paraspinal soft-tissue extension. These features bring into differentials the more ominous malignant or neoplastic processes, adding to the diagnostic dilemma [5].

Skeletal cryptococcosis is not strictly confined to the spine; the ubiquitous fungus can disseminate to highly unusual bones, even in completely immunocompetent hosts. Singular localised infections have been documented in the facial skeleton, including an unprecedented case isolated entirely to the zygomatic bone [6]. It has also been reported in the diaphysis of the tibia [7], and as a solitary lytic lesion eroding the inner table of the skull in a patient with transient lymphopenia [8]. While usually presenting as a solitary bony focus, cryptococcus can occasionally present as a widely disseminated disease involving multiple bones (such as the ribs, sternum, and iliac bones) alongside asymptomatic pulmonary nodules [9].

The findings in the present study are similar to the existing literature on skeletal cryptococcosis, such as the presentation aslong standing back pain, lytic destructive nature of the vertebral lesions, presence of epithelioid granulomas and its close resemblance to tuberculosis at initial clinical presentation. Nevertheless, the occurrence in already treated case of spinal tuberculosis, complicated the diagnosis more so, as a mimicker of disease recurrence. In contrast to the disseminated cases in the published literature [9], the patient in the present study demonstrated evidence of localised vertebral involvement without systemic spread or immunocompromised status.

As the clinical and radiological parameters are insufficient for a definitive diagnosis, a tissue biopsy is mandatory. Under the microscope, Cryptococcus appears as spherical, variable-sized narrow-based budding yeast cells surrounded by a thick polysaccharide capsule. Special stains are indispensable for morphological confirmation. Gomori Methenamine Silver (GMS), PAS and Mucicarmine stains are highly valuable for highlighting the yeast wall and capsule respectively. In the present study; the PAS stain vividly highlighted the yeast spherules of cryptococcus.

In the present study, culture and the associated biochemical investigations like urease and phenoloxidase activity, and cryptococcal antigen test by latex agglutination was not performed as the sensitivity of the same on tissue sample is low. The diagnosis in the present case was established on the basis of histopathology and PAS stain, along with Mucicarmine and GMS stains, plays a key role in the histopathological confirmation of cryptococcal infection on tissue sections. A thorough pathological evaluation ultimately

clarified the diagnosis, shifting it from a presumed recurrence of tuberculosis to primary fungal osteomyelitis.

Although fungal infections, especially, Cryptococcus neoformans frequently affects immunocompromised individuals; nevertheless, immunocompetent individuals might also be affected, as noted in the present case [10].

CONCLUSION(S)

Fungal involvement of the spine, though rare, needs to be kept in mind when spondylitis does not improve with anti-tubercular therapy. Confirming the diagnosis early through tissue sampling, along with the use of special stains, plays an important role in identifying the organism and starting appropriate antifungal treatment without delay. Better awareness of these uncommon presentations can help in reducing avoidable complications and help in correct management.

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