Case Report

Apparent Provisional Diagnosis Validated by Histopathology: 2 Case Report that mimics TB Spine Conflict of interest: There is no Conflict of interest relevant to this paper to disclose

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Abstract:

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Received: 30 July, 2022 Accepted: 24 September, 2022 **Background:** The incidence of atypical clinic-radiological presentations of spinal TB is on the upsurge. Lesions that share similar features should be evaluated thoroughly. Tissue diagnosis remains the only foolproof investigation to confirm diagnosis before initiation of treatment.

Methods: We present 2 cases who were provisionally diagnosed as a case of Tubercular spondylodiscitis based on clinic-radiological findings. After failure of response from anti tubercular drugs, they underwent operative management for decompression of neural elements and histological confirmation of the provisional diagnosis.

Results: Clinical features like back pain, weight loss, gait abnormalities with radiological features like Magnetic resonance imaging and GeneXpert, CT guided FNAC helps in early detection and initiation of treatment of spinal TB. But in our case, 58year old female and 13 years old male presented with clinic-radiological features consistent with Spinal TB. Histopathology and immunohistochemistry confirm that first case is due to Aspergillus Spinal Epidural Abscess (ASEA) and second case due to round blue cell neoplasm consistent with Ewings Sarcoma.

Conclusion: This article highlights the importance of awareness of the different clinic-radiographic features of spinal lesions, which can mimic a Tubercular Spondylodiscitis. In order to avoid delayed diagnosis, clinicians must be aware of differential diagnosis from common to rare entity which may interfere with other clinical conditions.

Keywords: Aspergilus Spinal Epidural Abscess, ASEA, Mimicking Pott's Disease, Ewings Sarcoma, Blue cell tumor, Spine TB mimics,

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Introduction:

The clinical picture of spinal TB is extremely puzzling. Disease progress at a slow pace and it is insidious in onset¹. The diagnostic period, the onset of symptoms, may vary from a period of 2 weeks to several years. The manifestation of spinal TB depends on the severity and duration of the disease, the site of the disease, and the presence of complications such as abscess, sinuses, deformity, and neurological deficit ².

With the development of advanced imaging techniques and appropriate chemotherapy, most cases of spinal tuberculosis are swiftly diagnosed and are treated successfully. However, an atypical radiological presentation of spinal tuberculosis presents a challenge for an appropriate diagnosis and early treatment, due to the atypical clinical and radiographic features³. Several different features of atypical

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radiological presentation of tuberculosis have been described and reported⁴⁻⁶.

The differential diagnosis of spinal tuberculosis includes a variety of conditions which ranges from spinal trauma to primary or metastatic tumor of spine, pyogenic infections, sarcoidosis, other granulomatous infections like Candida, Aspergillus, Coccidioides imcites, Blastomyces, Actinomyces, Nocardia, atypical Mycobacterium, Brucella, non-venereal Treponema (yaws), Echinococcus (hydatid disease)⁷.

The most common presenting complaint in spinal tuberculosis is an insidious onset of back pain followed by limitation of motion and in the late phases, severe spinal deformity (gibbus) attributed to an acute kyphotic angulation. Systemic symptoms of weight loss, fever, and malaise may precede spinal involvement for several months. Neurological complications may be manifested as weakness and changes in bowel and bladder function. Paraplegia can occur in both the acute and late stages as a result of edema and vascular engorgement leading to compression of neural tissue or compromising its vascular supply^{7,8,9}.

Radiographic differentiation can be difficult but is sometimes reasonable. In pyogenic spine infection rapid loss of height in the disc, along with extensive sclerosis, the absence of gibbus deformities, and the absence or minimal presence of calcified paravertebral masses are usually present. In tubercular spondylodiscitis, there is the presence of a large adjacent soft tissue component, rim-enhancing abscesses, and bone fragments which usually compress neural elements¹⁰.

These clinic - radiological features are not typical for tubercular spondylodiscitis, rather in various reported articles, these features are consistent with other lesions mimicking Pott's disease¹¹⁻¹⁵.

The symptoms or signs of spinal tubercular spondylodiscitis are typically underreported from TB-endemic countries. A detailed assessment, including the patient history, clinical examination, laboratory and imaging examinations along with evidence of granulomatous inflammation in an invasive procedure like Fine needle aspiration cytology (FNAC) or tissue diagnosis by histopathology or immunohistochemistry is necessary to gather the information relevant to the condition to develop an accurate differential diagnosis and prompt treatment¹⁵.

We have presented two stimulating cases where although clinical and radiological images suggesting Tubercular spondylodiscitis, even in one case, FNAC was positive for the granulomatous disease, with the aid of histopathology it was confirmed that neither of the cases was Pott's disease rather other differentials should be included before initiation of antitubercular therapy.

Case Report:

Case 1:

58 years old female, hailing from Dhaka, Bangladesh housewife, normotensive, non asthmatic diabetic patient presented with the complaints of gradually increasing low back pain for 5 years which has aggravated for last 1 year. The pain was dull aching, nonradiating increases after movement and relieved by taking rest or analgesics. For last 5 months pain gradually increased in intensity started to radiate down to anterior aspect of left lower limb associated with decrease in walking distance. She also gave history of fever in the initial days mostly evening rise of temperature which later resolved with medication. She also gave H/O weight loss and lost 7-8 kg weight in the last 4 months which is significant.

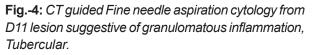
Physical examination at time of admission revealed spastic paraparesis. Both the legs were weak, with a motor power ranging from 4- in all muscle group of lower limbs as per Medical Research Council grade. Her sensation and reflexes were within normal limits. She had normal rectal tone. Complete blood count was negative for leukocytosis or anemia. Erythrocyte sedimentation rate was elevated at 90. Tuberculin test was positive (18mm). Emergent MRI was indicative of D11-D12 epidural abscess, discitis and osteomyelitis (Fig: 1,2,3).

The patient was admitted and started on empirical treatment with antibiotics (Meropenam, Linezolid and Metronidazole) for what was thought to be a bacterial spinal epidural abscess, Later on, cytopathology of the CT guided, per cutaneously drained fluid from the epidural collection was positive for granulomatous inflammation, mostly Tubercular. Smear showed adequate cellular material containing plenty of degenerative polymorphs, lymphocytes and histiocytes. A small number of epithelioid cell granulomas are seen in the background which represent mostly tubercular origin. As the patient lacked any neurological deficits or any signs of cauda



Fig.-1,2,3: Sagital, coronal and axial image of MRI T2WI showing D11-D12 epidural abscess with discitis





equine syndrome, spinal decompressive surgery was not indicated that time. Antitubercular therapy was initiated with rifampicin, pyrazinamide, ethambutol and isoniazide and pyridoxine was added along with anti TB drugs. Patient was discharged to complete the planned therapy. But after 1 month of initiation of anti tubercular therapy, patient pain condition did not improve rather it was increased in intensity with radiation to left lower limb. Her weakness in left lower limb also increased and motor power became 4 on the left side and 4- on the right side. Repeat MRI showed paravertebral soft tissue intensity in the D11-12 with liquefaction in the center consistent with spinal epidural abscess and there was significant cord compression with vertebral body osteomyelitis.

The patient underwent operative management by partial laminectomy of D11, D12 and subtotal removal of granulation tissue and pus by posterior midline approach (Fig 5,6). Tissue was sent for histopathology where bacteriological examination was negative for Gram Stein and ZN stein but histopathology reveals within necrotic debris colonies of Aspergillus spp are seen.

Medical management with long term oral voriconazole was pursued along with Anti tubercular therapy, and



Fig.-5,6: Per operative findings was granulation tissue with pus which was evacuated by posterior mid line approach

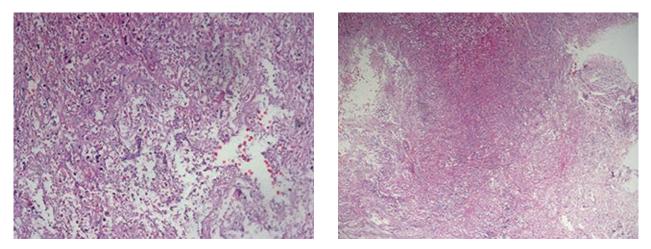


Fig.-7,8: Colour micro-photograph of histological slide showed necrotic debris along with Aspergillus spp.

patient was discharged to a skilled nursing facility to complete the planned 3-month course of anti fungal therapy. Physical and occupational therapy noted the patient to progress well, returning well, returning very near baseline upon discharge and at 3 months follow up period.

Case 2:

A 13 years old male, hailing from Dhaka, Bangladesh, student, normotensive, non asthmatic non diabetic patient presented with the complaints of intermittent low back pain for 2 months which has aggravated for last 15 days. The pain was dull aching, non radiating, more intense at night, increases after movement and relieved by taking rest. He also complaints about weakness of both lower limbs which he noticed 15 days after the back pain symptom was started. Initially he could walk with difficulties but later on he needed assistance for walking. He also gave H/O low grade

fever and progressive weight loss for last 2 months and loose 5 kg body weight within 1.5 months.

Physical examination at time of admission revealed spastic paraparesis. Both the legs were weak, with a motor power ranging from 3/5 on right side and 4-/5 on left side as per Medical Research Council grade. Knee and ankle jerk were diminished on the left side and intact on the right side. Planter was equivocal on the left side and flexor on right side. There was tenderness over right knee joint, but left knee joint was normal. His sensation and reflexes were within normal limits. He had normal rectal tone. Complete blood count was negative for leukocytosis or anemia. Erythrocyte sedimentation rate was elevated at 88. Gait was antalgic. Emergent MRI was indicative of L2-3, L3-4 Extradural Spinal space occupying lesion (SOL)with significant thecal compression and epidural abscess, however screening film of MRI of Brain was normal(Fig: 9,10,11).

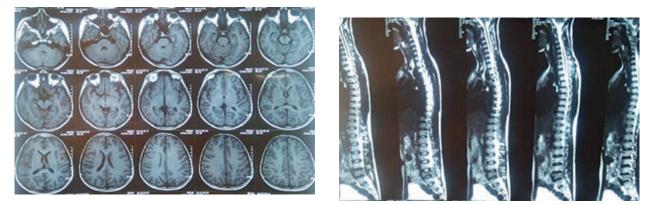


Fig.-9,10 : Screening film of MRI is normal but Whole spine showed partial collapse of L4 vertebral body with thecal compression

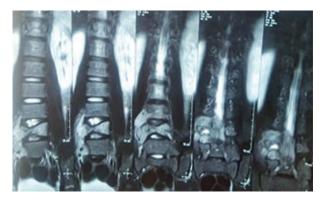


Fig.-11: Coronal section of Lumbo sacral spine showed partial collapse of L4 vertebral body with epidural abscess extending from L3-L5 level without involvement of disc space.

As patient had right sided knee joint pain, he had consulted with orthopedic surgeon earlier where he was diagnosed as a case of Juvenile Idiopathic Arthritis of Right knee joint. He was under conservative management with analgesic and disease modifying agents like methotrexate for a period of one month. But after failure of improvement for knee pain he was transferred to neurosurgical center. After extensive clinic - radiological evaluation, patient attendance was counseled regarding operative intervention for definitive tissue diagnosis and decompression of neural elements at the same time. So, patient underwent decompression of neural elements by hemilaminectomy of L4 with subtotal removal of pus and granulation tissue (Figure 12,13). Tissue was sent for histopathology where bacteriological examination was negative for Gram Stein and ZN stein but histopathology reveals malignant neoplasm composed of uniform, small and round cells with hyperchromatic nuclei and scanty cytoplasm. Cells are arranged in clusters with interspersed collagenous tissue, degenerative changes were present. This feature was consistent with small round blue cell tumor (Figure 14,15). Immunohistochemistry examination reveals Vimentin was positive in tumor cells. CD 99 was positive in tumor cells with moderate intensity, FLI-1 was also positive but it was negative for S-100 protein, LCA, Synaptophysin and CD 34. So, immunohistochemistry result was compatible with Ewing's Sarcoma.

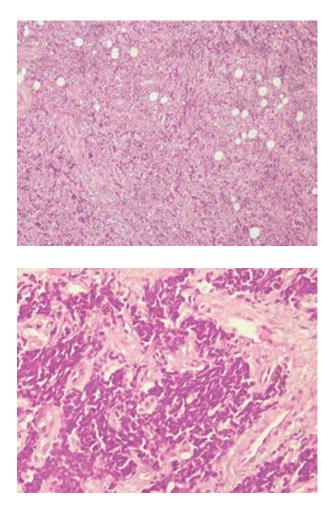




Fig.-12,13: Per operative image showing Pus with necrosed tissue which was excised and removed as piece meal fashion in first image, right sided decompression of thecal sac by hemi laminectomy and nerve root with thecal sac is completely decompressed in second image.

Fig.-14,15: *Histopathology reveals small round blue cell tumor where malignant neoplasm composed of uniform, small and round cells with hyperchromatic nuclei and scanty cytoplasm. Cells are arranged in clusters with interspersed collagenous tissue, degenerative changes were present.*

Physical and occupational therapy noted the patient to progress well (Muscle power improved to 4+ bilaterally), returning well, returning very near baseline upon discharge. Patient was discharged to a skilled nursing facility to consult with oncologist for further management of Ewing's Sarcoma and underwent chemotherapy.

Discussion:

The incidence of extrapulmonary TB (EPTB) is 3% when compared to pulmonary TB (PTB). Among extra pulmonary TB, skeletal TB (STB) contributes to around 10%, and spinal TB has been the most common site of STB. Thoracolumbar junction remains to be the most affected region of the spinal column followed by lumbar spine and the cervical spine [¹⁶].

As per the World Health Organization (WHO) in 2016, there was an estimated incidence of 10.4 million new TB cases. While European region contributed only 3%, the South East Asian Region alone had 46.5% of the global TB burden. Bangladesh is one of the high TB burden countries with 4% of the world's total TB cases reported in 2019 ^[17]. Consistent efforts are being taken by the WHO, and the WHO End TB Strategy for 2030 has been adopted by its member nations, which aims at 80% reduction of TB incidence rate and 90% reduction of TB deaths ^[18].

Despite the presence of distinguishing clinical features, definitive MRI findings indicative of spinal TB, there can still be significant overlap with other diagnoses and so a biopsy may be necessary to establish a confident diagnosis. Kumaran etal.^[19] present an intriguing single-center retrospective experience of etiologies that may mimic spinal tuberculosis and lay stress on numerous features that can help a physician to distinguish or at least identify a red flag based on their presentation. Some of these are of serious concern such as pyogenic spondylitis, spinal cord metastasis, and lymphomatous spread to the spinal cord. Breast, prostate, and lung cancer are the most common malignancies metastasizing to the spinal cord. Non-Hodgkin's lymphoma and Hodgkin's Lymphoma can rarely lead to spinal cord compression ^[20]. Usually these lesion involve the vertebral body and epidural compartment. Authors also discussed another common group of disorders like degenerative, traumatic, or metabolic in nature, like, old spinal cord trauma, degenerative disk disease, and osteoporotic involvement. They also discussed some cases, inflammatory in nature, like ankylosing

spondylitis and rheumatoid arthritis which showed similar characteristics.

Clinically, both tuberculous and malignant spinal cord diseases present with similar subacute myelopathy with backache, except the patients with spinal tuberculosis much younger than that of metastatic spine. This point always needs to be kept in mind while considering this differential diagnosis ^[21].

Although MRI is the imaging modality of choice to differentiate and establish provisional diagnosis, unfortunately, none of the available imaging modalities are reliable enough to clearly distinguish between spinal tuberculosis and spinal metastasis. As a result, histopathological evaluation is mandatory to confirm the diagnosis. CT-guided needle biopsy is an effective and safe procedure for diagnosing spinal lesions. Patel J et al ^[22] evaluated the diagnostic Efficacy, Sensitivity and Specificity of Xpert MTB/RIF assay for Spinal Tuberculosis. It is widely available modality for rapid identification of Mycobacterium tuberculosis in aspirated pus or biopsied material. The major limitation with this test is that in more than 50% of cases results are negative. Thus, it may be unspoken that the ultimate gold standard in decisively labeling a patient with spinal tuberculosis is the histopathology specimen demonstrating Mycobacterium tuberculosis; all of the other reminders just point toward the possibility of tuberculosis as an etiology ^[23,24].

In our first case, We describe a patient with a history of chronic low back pain treated with antibiotic, antitubercular and antifungal therapy along with surgerydecompression by posterior approach to a patient diagnosed with ASEA. She responded well with the surgery and antifungal therapy (Voriconazole) and there was significant improvement of neurological status in early post operative period. Aspergillus Spinal Epidural Abscess (ASEA) is a rare cause of compressive myelopathy. It closely mimics with tubercular spine disease and shares common clinical features. The most common is low back pain with or without fever. After an epidural abscess forms, symptoms of spinal cord compression and even paraplegia may occur. Men are affected more frequently than women and most infections involve the thoracic spine followed by lumbar spine and cervical spine ^[25]. In our case female was affected and thoracic spine was involved.

Differential diagnosis between spinal aspergillosis and tuberculosis is very doubtful on clinical and radiological

grounds alone. However, the peculiarity between the two is important, as delay in diagnosis and treatment may account for the continuing high morbidity and mortality of invasive aspergillosis. Radiologically, it is difficult to differentiate aspergillus and tuberculous spondylitis. Spinal tuberculosis, however, usually begins in the anterior inferior portion of the vertebral body, then spreads beneath the anterior longitudinal ligament to involve the adjacent vertebral body with secondary narrowing of the disc space ^[26]. In invasive aspergillosis, the lesion extends circumferentially and destroys all the surrounding spinal structures, i.e .vertebral bodies, discs, and neural arches, as wel1 as al1the contiguous structures, e.g., ribs, thoracic wal1, lungs, etc., as seen in our case and other reported cases. This feature, as seen on MRI (Figs. 1,2,3)may help in correct diagnosis.

In our second case, young man presented to us with gradually increasing low back pain, gait difficulties, weight loss with history of right knee joint pain. Initially he was diagnosed as a case of Juvenile idiopathic arthritis and started conservative management. But as the symptom progresses, it warranted our attention. Rare entities are not only difficult to predict but difficult to recognize, diagnose, and treat. Often the dilemma is to, investigate thoroughly saving time but financially burdening the patientand hospital, or, to investigate in gradual increments taking more time and effort while neurological deficit continued which causes irreversible damage to neural elements ^[13].

Sharma et al.^[27] reported that preservation of the intervertebral discarchitecture and lack of destruction of thevertebra are the imaging points in favor of aparaspinal Ewing's sarcoma as compared to aparaspinal tubercular abscess. But in our case, there was involvement of vertebra and lateral disc space along with formation of abscess. To save the undeniable neural elements, we performed decompression of neural elements by hemilaminectomy and obtain tissue for histopathological examination. The histological results were suggestive of small-round-cell malignancy, most probably Ewing's sarcoma.

The Extra skeletal Ewing's Sarcoma being a rare entity^[26-28], differs from the skeletal form but our case is consistent with the first large series (39 cases) of extraosseous Ewing's sarcoma (EOES) which waspublished by Angervall and Enzinger ^[29] in 1975, of which 12 patients had the tumor in the paravertebral

region mainly at the lumbar and sacral level. In our case there was extensive involvement of lumber region particularly from L3-L5 with paraspinal involvement.

This case further reminds us of the importance of the differential diagnosis of Ewing's sarcoma and compression fractures. For compression fractures of the spine, we must evaluate the cause with thorough local soft-tissue examination before the surgery and pay attention to eliminate the possibility of a tumor. In this case, we rule out all the possibilities of compression fracture by local examination and available imaging facilities but the possibility of tumor could not be ruled out as tumor marker were negative (Serum Ferritin level was within normal limits). Histologically there was small round blue cell tumor were malignant neoplasm composed of uniform, small and round cells with hyperchromatic nuclei and scanty cytoplasm. Cells were arranged in clusters with interspersed collagenous tissue, degenerative changes were present. The term round cell tumor defines a group of highly aggressive malignant tumors composed of relatively small and monotonous undifferentiated cells with increased nuclearcytoplasmic ratio. There are so many differentials among round cell tumor entity. The ubiquitous distribution and diverse histology of different round cell tumors pose a challenge in their diagnosis. The diagnostic aids like the use of special stain, cytometric immunocytochemistry, flow immunophenotyping, and reverse-transcriptase polymerase chain reaction help to differentiate and diagnose these group of tumors^[30]. So went for immunohistochemistry where Vimentin was positive in tumor cells. CD 99 was positive in tumor cells with moderate intensity, FLI-1 was also positive but it was negative for S-100 protein, LCA, Synaptophysin and CD 34. Immunohistochemistry result was compatible with Ewing's Sarcoma.

Conclusion:

In spite of the advancements made in rapid diagnosis and effective management, spinal TB continues to haunt medical professionals especially in South East Asia. Spinal TB is the most common entity but sometimes challenging to start empirical anti tubercular therapy without confirming the disease. Our aim of this article was to focus on differentials of tubercular spondylodiscitis which could not be denied even clinico-radiological mimics as spine TB. Appropriate and early histological diagnosis with immunohistochemistry confirmation is essential to plan appropriate management.

Compliance with ethical standards

Conflict of interest: The author declare that they have no conflict of interest.

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