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Case Series

Microbiology Section

Unusual and Uncommon Presentations of Extrapulmonary Tuberculosis: A Case Series

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ABSTRACT

Tuberculosis (TB) is primarily a disease of the lungs; however, Extrapulmonary TB (EPTB) mainly affects the lymph nodes, pleural cavity and spine. Other sites are considered rare and uncommon. Authors present five interesting cases of EPTB from different sites. The first case involved thyroid TB that had spread to the neck. The Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) test was positive. The patient was started on antitubercular treatment and was discharged after undergoing incision and drainage. The second case is of an immunocompetent patient with disseminated TB, which spread from the lungs to the pleura, muscles, subcutaneous tissue and skin, resulting in fistula formation. The CBNAAT was positive, and the Line Probe Assay (LPA) indicated that the strains were sensitive to rifampicin and isoniazid. The third case details a female patient with genital TB who was unable to conceive. An ultrasound examination revealed issues in the adnexa. The CBNAAT was positive (with low levels of *Mycobacterium tuberculosis* detected, and rifampicin was found to be sensitive), but her sputum sample was negative. The fourth case describes disseminated TB in a seropositive female, where her synovial fluid tested positive and her Computed Tomography (CT) chest findings were suggestive of TB. The fifth case is of abdominal TB in a patient with a history of previous abdominal surgery. Her CBNAAT was positive and she recovered following treatment. In present study, all the cases presented unusual manifestations and the diagnosis was made based on radiological findings combined with microbiological laboratory investigations. Therefore, clinically suspecting these cases and confirming the diagnosis through microbiological tests is critically important.

Keywords: Abdominal, Cartridge-based nucleic acid amplification test, Disseminated, Menstrual, Thyroid

INTRODUCTION

TB is a common granulomatous disease caused by *Mycobacterium tuberculosis*, primarily affecting the lungs in about 80% of cases worldwide [1]. India contributes almost a quarter of the global TB burden [2] and is the second most common cause of death among infectious diseases [3]. EPTB is rarely smear-positive and is generally considered non contagious [4]. Research indicates that the percentage of patients with EPTB is higher in tertiary care centres in India, ranging from 30-53% [5]. Recent studies suggest that EPTB sites may vary based on geographic location, population groups and a wide range of host factors [6-8]. In India, extrapulmonary manifestations mainly affect lymphatics (35%), the pleural cavity (20%), the spinal region (10%) and the genitourinary tract (9%) [9]. Present series is of five different cases of EPTB which were diagnosed mainly based on clinical suspicion.

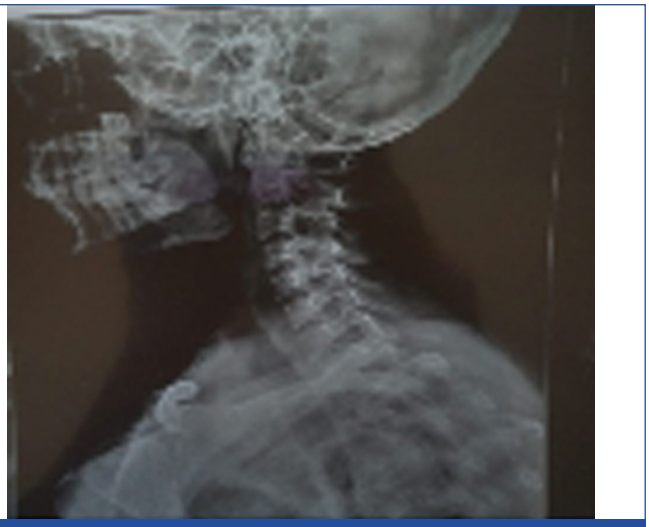
CASE SERIES

Case 1 (Thyroid TB that has Spread to the Posterior Triangle of the Neck)

A 30-year-old female engineer presented with complaints of a swelling measuring 5×5 cm on the left side of her neck [Table/Fig-1], which had been present for the last two months. The ulcerative lesion had shown purulent discharge for the last 3-4 days. There was no history of fever, cough, haemoptysis, weight loss, or loss of appetite. Additionally, there was no past history of TB in her family or herself. An ultrasound examination of her neck revealed a hypoechoic lesion with peripheral vascularity in the right lobe of the thyroid gland and a heteroechoic lesion was observed in the VB region of the lower posterior triangle. Pus discharge from the lesion was sent for CBNAAT, which detected *Mycobacterium tuberculosis* with rifampicin sensitivity. Acid-fast staining did not reveal any Acid Fast Bacilli (AFB). Incision and drainage were performed [Table/Fig-2]. This case illustrates EPTB of the thyroid gland that had spread to the neck. A follow-up taken six months later showed that she continued her treatment regularly, which consisted of isoniazid (H), rifampicin (R), ethambutol (E), and pyrazinamide (Z) in the intensive phase, followed by isoniazid, rifampicin and ethambutol in the continuation phase (i.e., 4HRZE/2HRE). Complete healing was observed on X-ray [Table/Fig-3].

[Table/Fig-1]: Swelling on left neck.

[Table/Fig-2]: Picture of neck after incision and drainage.



[Table/Fig-3]: X-ray of neck indicating healed lesion.

Case 2 (Disseminated TB from Lungs to Pleura to Muscles and then to Skin)

A 26-year-old male presented with complaints of swelling over the right chest wall for the past 20 days. He reported a history of fever lasting eight days but denied any cough, haemoptysis, weight loss, or loss of appetite. There was no noted history of TB in his family or personal history of the disease.

On examination, the swelling was found to be well-organised and non cystic. An Ultrasound (USG) was advised. On the 20th day, the USG revealed a spindle-shaped lesion, measuring approximately 5.6 cm×2 cm×5 cm, located 0.9 cm deep to the skin. There was no internal vascularity observed, and the volume of the lesion was approximately 30 cc. A calcified focus measuring 0.4 cm was also noted. This organised collection on USG appeared to be extending from the intercostal space to the deep pleural space.

For further examination, the patient was advised to undergo a CT scan. The CT scan revealed three major findings:

1. A small well-defined enhancing area of consolidation in the inferior lingual lobe.
2. A well-defined, hypodense, peripherally enhancing lesion in the right anterior chest wall near the costo-chondral junction, extending from the T6-T9 vertebral levels and involving the skin, subcutaneous tissue, intercostal muscles, and the inferior rib surface, with no evidence of rib erosion or oedematous changes.
3. Centrilobular nodular opacities in the apical segments of the right upper lobe, anterior segment of the left upper lobe, inferior lingual lobe and posterior basal segments of both lobes.

An aspirated sample from the chest was sent for acid-fast staining and CBNAAT. On acid-fast staining, AFB was not detected, but the CBNAAT result showed the presence of *Mycobacterium tuberculosis*, with rifampicin sensitivity. His sample was also sent for a LPA, which revealed sensitivity to both isoniazid and rifampicin. He was started on treatment for drug-sensitive TB (4HRZE/2HRE), and the patient responded well. Incision and drainage were performed after 1.5 months. This case illustrates an immunocompetent patient with disseminated TB, progressing from the lungs to the pleura, muscles, subcutaneous tissue and skin. A follow-up after six months indicated that the patient had responded well.

Case 3 (Genital TB)

A 23-year-old female presented with complaints of abdominal pain and infertility. She had been married for three years but had been unable to conceive. She reported no history of fever, cough, or weight loss. Notably, her best friend had been diagnosed with TB five years prior, and the patient had been in contact with her. It is possible that the infection was present in a latent form and was diagnosed when the patient sought help for infertility.

The patient was advised to undergo USG, which revealed an adnexal mass in the ovary. An ovarian biopsy was sent for histopathological examination, which revealed fragments of ovarian parenchyma with stromal fragments containing thick-walled cystic fragments and cuboidal epithelial lining. There was no evidence of malignancy on histopathological examination.

A CT scan of the abdomen showed several findings in addition to the adnexal mass:

1. Adnexal masses putting pressure on the distal ureter, with mild hydronephrosis and proximal hydroureter.
2. A soft-tissue lesion measuring 6×6.2×5 cm (CC×TR×AP), with cystic components, involving the right adnexa, from which the right ovary was not separately identified. These findings suggested a complex ovarian mass, requiring correlation with USG/MRI of the pelvis.
3. A large cystic lesion measuring 4.4×3.5×3.9 cm (CC×TR×AP) involving the left adnexa, from which the left ovary was not separately identified, suggestive of a large ovarian cyst.
4. Thickened and irregular urinary bladder wall measuring 3.8 mm, suggestive of cystitis.

Her kidney function tests were normal. Based on the USG and CT scan findings, the gynaecologists suspected endometrial TB. A sample of her menstrual blood was sent for acid-fast staining and CBNAAT testing. The CBNAAT was positive (with *Mycobacterium tuberculosis* detected and rifampicin sensitivity). The acid-fast staining of the direct sample was negative, but concentrated samples showed positivity with scanty bacilli (2 bacilli per smear).

Later, the Mantoux test was also positive. Her sputum was negative for acid-fast staining and CBNAAT. This was a case of endometrial TB, which is one of the major causes of infertility. The patient was started on a regimen of isoniazid, rifampicin, ethambutol and pyrazinamide (4HRZE/2HRE). She was advised to attempt conception after one year and an ultrasound was scheduled to be repeated after six months. Upon follow-up after six months, the patient responded well to treatment.

Case 4 (Disseminated TB from Lungs to Synovial Fluid and Iliac Lymph Nodes)

A 40-year-old seropositive female patient presented with pain in her right knee, radiating towards the ankle and toes. She was on anti-retroviral treatment and did not exhibit any limping. Due to her seropositivity, a CT scan of the chest was performed, revealing multiple bronchio-centric nodules in the bilateral lung parenchyma, mild pleural effusion and subsegmental atelectasis. A CT scan of the abdomen showed an enlarged left external iliac lymph node with suspected necrosis and May-Thurner syndrome. This syndrome was diagnosed based on the CT scan findings combined with clinical features. The patient did not report any respiratory symptoms, fever, weight loss, or loss of appetite, nor did she have any history of TB. Synovial fluid was sent for bacteriological examination, which showed no growth. A venous Doppler of both lower limbs indicated subcutaneous oedema in the right lower limb. A bone marrow biopsy showed a granulomatous lesion. The patient's sample was sent for CBNAAT and acid-fast staining. The CBNAAT was positive (*Mycobacterium tuberculosis* detected at a very low level, and rifampicin was sensitive), while acid-fast staining was negative. She was admitted to the hospital for two months. Thus, this case was indicative of disseminated TB from the lungs to synovial fluid and iliac lymph nodes. She was started on intensive-phase treatment and was scheduled for a follow-up after six months.

Case 5 (Abdominal TB)

An 18-year-old female was brought to the casualty department with a complaint of discharge from her abdomen. She had experienced fever and abdominal pain for the past month. She had a history

of TB six months earlier and had taken antitubercular treatment for only two months. There were no respiratory complaints. An ultrasound revealed intestinal obstruction, and she had a history of one abdominal surgery. The discharge was located two centimeters away from the suture line. Her discharge [Table/Fig-4] was sent for CBNAAT and acid-fast staining since she had only completed two months of treatment. Acid-fast staining revealed scanty bacilli. The CBNAAT result was positive (*Mycobacterium tuberculosis* detected at a low level and rifampicin was sensitive). The clinician was immediately informed of the results and she was started on antitubercular treatment (4HRZE/2HRE), and the fluid was drained. A month later, the patient's father reported that she had recovered and was continuing her treatment. Efforts to contact the patient telephonically after six months were unsuccessful.

[Table/Fig-4]: Catheter for drainage fluid inserted for abdominal TB.

DISCUSSION

In EPTB lymph node TB is the most common form. Disseminated TB primarily occurs due to haematogenous spread from the lungs, particularly in untreated patients, those who defaulted on treatment, or relapse cases. Diagnosis is challenging in these patients due to unusual presentations. Present case series includes five interesting cases with different sites of EPTB. The first case is TB of the thyroid gland; the second involves a serious sinus formation from the lungs to the chest wall; the third case is menstrual TB; the fourth case involves TB of the knee; and the fifth case is abdominal TB. Only one patient was immunocompromised (the one with TB of the knee affecting the synovial fluid). The age group of the five cases was 30 years, 26 years, 23 years, 40 years, and 18 years, respectively. This indicates that no patient was found at the extremities of the age spectrum. In a study conducted on EPTB by Shrivastava AK et al., the highest number of positive cases for EPTB were observed in the 20-39 years age group [5].

The first case involves an immunocompetent patient with thyroid TB that has spread to the neck. Thyroid TB should be differentiated from all major diseases of the thyroid. Three interesting cases of thyroid TB were presented by Majid U and Islam N [10]. The diagnosis of all three cases was based on Technetium-99 thyroid scintigraphy, followed by Fine-Needle Aspiration Cytology (FNAC). In present study, suspicion was raised based on symptoms and radiological findings, which were subsequently confirmed by CBNAAT.

In the second case, a sinus formed due to the spread of TB from the lungs to the pleura, muscles, subcutaneous tissue and skin. Radiological examination revealed an organised collection that appeared to extend from the intercostal space to the deep pleural space. Some investigators believe that chest wall TB occurs due to the reactivation of latent foci formed during haematogenous or lymphatic dissemination of primary TB, while others suggest it occurs via direct extension from contiguous lung or pleura [11-13]. In present case, it was a case of direct extension from the pleura. Due to the young age of the patient, the symptoms might have presented later in the disease course. The diagnosis was confirmed by CBNAAT.

The third case was that of menstrual TB diagnosed when the patient presented with complaints of infertility, accompanied by abdominal pain. According to Shahzad S, 40% of infertile females with genital TB do not present with other symptoms [14]. In these instances, USG is the mainstay for diagnosis. USG may show a heterogeneous and thin endometrium, endometrial fluid, calcification, or bands and intrauterine synechiae in endometrial TB. It can also demonstrate the presence of hydrosalpinges with cogwheel signs, inhomogeneous enlarged ovaries, free peritoneal fluid and fixed adnexal masses. In present case as well, the diagnosis was based on the presence of an adnexal mass. Very few cases of endometrial TB have been reported, and present case was confirmed by CBNAAT.

The fourth case was one of knee TB in a seropositive patient. The increase in the incidence of TB among HIV patients may be due to either the reactivation of latent infection or an increased susceptibility to *Mycobacterium tuberculosis* due to compromised immunity. Henderson MS and Fortin HJ of the Mayo Clinic reported on a large series of patients treated for knee TB [15]. Those cases were diagnosed radiologically. In present study, the main clue to TB was a granulomatous lesion identified on the bone marrow biopsy. Following the biopsy, CBNAAT and acid-fast staining were performed, confirming the diagnosis.

The fifth case was that of a TB defaulter from whom the disease later disseminated to the abdomen. Successful treatment of TB involves taking antitubercular drugs for at least six months. Poor adherence to treatment means that patients remain infectious for a longer period, are more likely to relapse or succumb to TB, and this can result in treatment failure as well as foster the emergence of drug-resistant TB or spread to other organs. In present case, patient had taken treatment for only two months. She had a history of abdominal surgery and exhibited suture marks on the abdomen. Discharge was observed two centimeters away from the suture marks. Clinical suspicion was raised immediately in this case because the patient was a treatment defaulter. The diagnosis was further confirmed by CBNAAT.

High clinical suspicion, consideration of differential diagnoses and drawing conclusions based on clinical and laboratory findings will help initiate treatment and save patients' lives. In present study, all cases had unusual presentations and the diagnosis was made based on radiological findings combined with microbiological laboratory investigations. Authors want to highlight the importance of CBNAAT and acid-fast staining, both crucial for confirming the diagnosis and initiating treatment. In all cases, the diagnosis was confirmed by CBNAAT, which is more sensitive and specific compared to acid-fast staining [16,17]. Therefore, confirmation should not rely solely on acid-fast staining.

CONCLUSION(S)

The EPTB is underreported due to its unusual presentations. These unusual presentations should be correlated with radiological or pathological findings and microbiological investigations such as acid-fast staining and CBNAAT should be employed for confirming the diagnosis and initiating treatment.

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