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A Report on Rare Cases of Isolated Organ Extrapulmonary Tuberculosis

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ABSTRACT

Only about 15% of all TB cases are extrapulmonary (EPTB) but isolated organ EPTB is relatively uncommon and can manifest as other diseases. Isolated EPTB is difficult to diagnose because it results from paucibacillary presentation. This study aimed to review the clinical, radiographic features, diagnostic work-up and clinical outcomes of 12 rare cases of EPTB affecting a single organ.

This was a retrospective, observational study of the medical records from January 2022 to December 2024 from a tertiary care centre in eastern India. Isolated EPTB patients in unusual anatomical sites were included and patients with a concurrent pulmonary or disseminated tuberculosis were excluded. Microbiological (e.g. GeneXpert) and histopathological diagnosis were used to confirm the diagnosis. The treatment of all patients was done according to the guidelines of NTEP for anti-tubercular therapy.

A total of 12 patients aged 46.16 years (mean age) and eight males were assessed. The clinical presentations included musculoskeletal tuberculosis (four cases), subcutaneous abscesses (two cases), Cutaneous scrofuloderma, laparoscopic port site infection, tubercular proctitis, tubercular tongue ulcer, thyroglossal cyst, and genitourinary tuberculosis (one case each). The duration of symptoms varied from 15 days to two years. In six cases, histopathological confirmation was obtained and in the other six cases microbiological confirmation was obtained. Anti-tubercular treatment (ATT) resulted in clinical resolution in all patients.

Isolated EPTB often encounters delays in diagnosis due to its subtle and non-specific clinical presentations. Clinicians should maintain a high index of suspicion for atypical single-organ sites. Timely imaging and targeted tissue sampling for microbiological and histopathological evaluation are essential for establishing a definitive diagnosis and ensuring effective management.

Categories: Pulmonary, Emergency Medicine, Preventive Medicine

Keywords*: extra-pulmonary tuberculosis, isolated organ tuberculosis, rare presentation, genexpert, anti-tubercular therapy.*

INTRODUCTION

Tuberculosis (TB) affects the lungs most commonly. However, it has the potential to affect any bodily tissue. Approximately 15% of TB cases are extrapulmonary tuberculosis (EPTB), which is commonly seen with TB infection of the pleura and lymph nodes [1-3]. In EPTB, the affected tissues include also the central nervous system, the meninges, gastrointestinal tract, genitourinary system, bones, joints and pericardium [4]. The most common form of disseminated involvement in mycobacteria is multifocal involvement of one or more organs which is usually the result of the haematogenous dissemination, while isolated organ EPTB is very rare and may mimic more common diseases. Isolated

organ EPTB is difficult to diagnose, especially due to the low numbers of bacilli seen and the complexity of obtaining an appropriate specimen for analysis. The advent of molecular techniques such as GeneXpert has notably enhanced diagnostic sensitivity in such contexts. Also, the imaging findings, though valuable, lack specificity and can mimic various other conditions, thus often requiring confirmatory biopsy. Here, we present a report on the rare types of single-organ EPTB cases we have encountered within our clinical purview over the last two years. The current study, containing 12 interesting cases, aimed to assess the presentation, clinical-radiological profile, mode of diagnosis, and response of those patients for further treatment in rare types of EPTB cases with single organ involvement.

CASE PRESENTATION

Study Design and Patient Selection

The current case series was a retrospective observational study conducted in the Department of Pulmonary Medicine at a tertiary care centre in Eastern India. Institutional records from January 2022 to December 2024 were reviewed. Patients attending the Directly Observed Treatment Short-course (DOTS) centre with a confirmed diagnosis of tuberculosis were screened for eligibility. Patients with pulmonary tuberculosis, disseminated tuberculosis, tuberculous lymphadenitis, pleural tuberculosis, and central nervous system tuberculosis were excluded. Only patients with isolated organ extrapulmonary tuberculosis involving uncommon anatomical sites, without evidence of concurrent pulmonary or disseminated disease, were included in the study. The diagnosis of tuberculosis was established either microbiologically (GeneXpert MTB/RIF assay, acid-fast bacilli smear microscopy, culture, or PCR-based tests) or histopathologically by demonstration of granulomatous inflammation with or without caseous necrosis. All the cases were clinically evaluated, detailed history, physical examination, laboratory investigations, and radiological assessment using ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), or other relevant imaging modalities according to the site were carried out individually, as per the retrospective records. Demographic characteristics, clinical presentation, duration of symptoms, radiological findings, microbiological and histopathological results, treatment record, and outcome details during the follow up were extracted retrospectively.

All patients received anti-tubercular therapy according to the National Tuberculosis Elimination Programme (NTEP) guidelines and were monitored for clinical response during follow-up visits. We assessed a total of 12 patients with a mean age of 46.16 years (8 males, 4 females). Eight of them were over 50 years old, and two were below 20 years. All the patients were immunocompetent except for comorbidities. None of the patients had pulmonary TB at presentation or in the past.

Case 1: Musculoskeletal TB (Left Wrist Joint)

A 60-year-old male presented with a painless swelling in the right hand, fever, and loss of weight (LOW) for 2 months. He had no known comorbidities. Examination revealed a soft, fluctuant, non-tender, fixed swelling over the radial side of the left wrist, measuring 5x5 cm (Figure 1A). An X-ray of the wrist showed soft tissue swelling on the radial side of the wrist joint involving the radial tubercle (Figure 1B). Pus aspirated from the swelling was acid-fast bacilli (AFB) positive and GeneXpert positive (Rifampicin sensitive). The patient achieved clinical resolution with 6 months of anti-tubercular therapy (ATT).

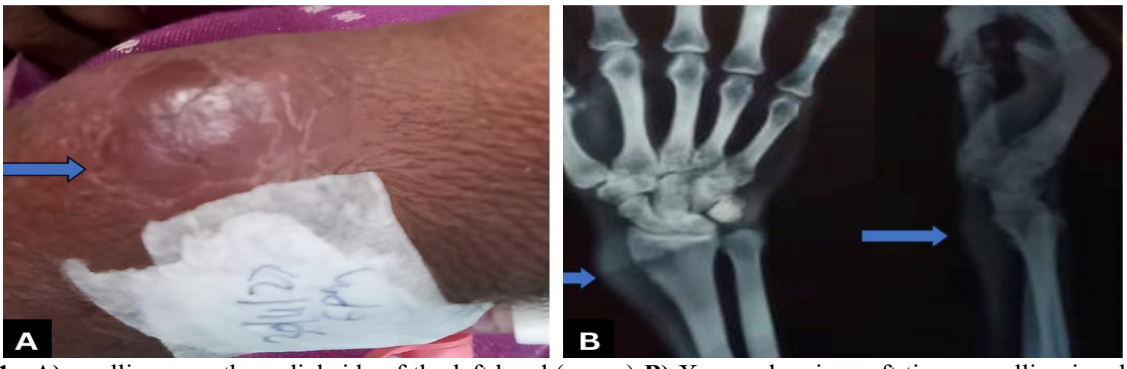


Figure 1: A) swelling over the radial side of the left hand (arrow) **B)** X-rays showing soft tissue swelling involving the radial tubercle (arrow)

Case 2: Tubercular Tenosynovitis and Arthritis

A 58-year-old female presented with swelling over the right forearm and fever for 2 months. She had a history of autoimmune disease (idiopathic inflammatory myositis) for 4 years and was taking Ayurvedic medicine. Examination showed a firm, tender swelling (4x5 cm) over the right distal forearm (Figure 2A). An X-ray of the right hand showed soft tissue swelling and osteolysis of the middle phalanx. MRI of the right wrist showed tenosynovitis of the flexor tendons, along with bony involvement of the index finger (Figure 2B). Pus aspiration from the swelling was Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) positive (R sensitive). The patient resolved clinically with 6 months of ATT.



Figure 2: A) swelling over the right hand. **B)** Tenosynovitis of the flexor tendons of the hand, along with bony involvement

Case 3: Tubercular Wrist Osteomyelitis

A 27-year-old male presented with swelling over the right wrist causing difficulty in movement following trauma, and a low-grade fever for 2 years. Examination revealed a tender swelling (5-6 cm) over the right wrist's ulnar surface with restricted movements. X-rays of the arm and hand showed subcutaneous swelling with underlying distal ulnar bone reactive changes. Pus aspirated was AFB and CBNAAT negative. However, a biopsy from the synovial tissue of the carpal bones showed caseating granulomatous inflammation (Figure 3) and was AFB positive. Clinical resolution occurred with 6 months of ATT.

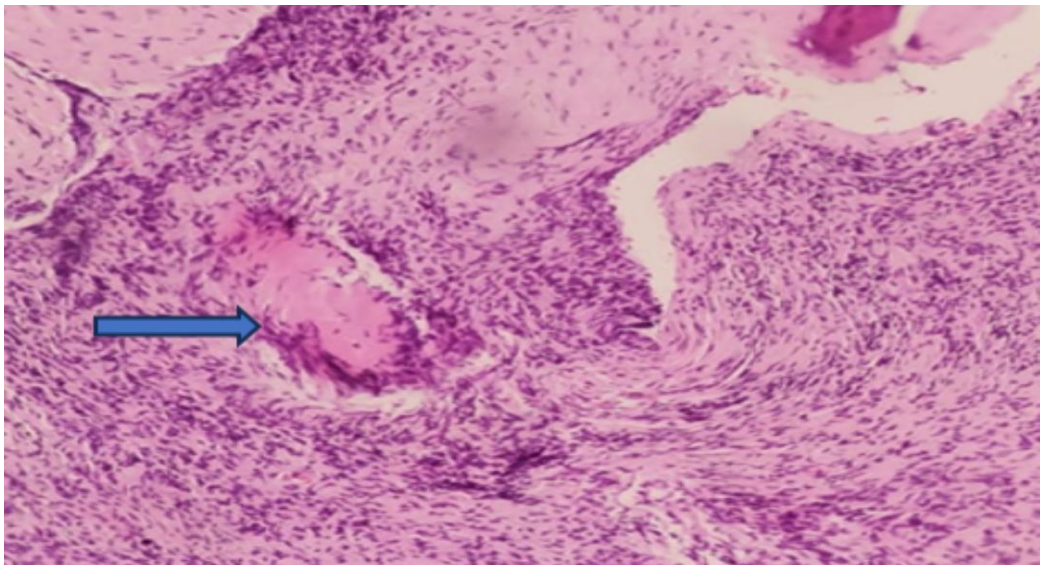


Figure 3: HPE (Haematoxylin and eosin (H&E) stain, ×100 magnification) represents synovial tissue of carpel bones: caseating granulomatous inflammation

Case 4: Musculoskeletal TB (Forearm and Hand)

A 32-year-old male presented with swelling over the back of the right hand and ulnar aspect of the forearm for 15 days, which had progressed to discharging pus. Examination showed a soft, fluctuant, erythematous swelling with a discharging

sinus. An X-ray of the hand and forearm (Figure 4) showed erosion of carpal bones with intercarpal joint space narrowing and reactive changes in the shaft of the ulna. Pus aspirate was AFB negative but CBNAAT positive (R sensitive). Clinical resolution was achieved with 6 months of ATT.



Figure 4: X-ray hand and forearm: erosion of carpal bones with intercarpal joint space narrowing and reactive changes in the shaft of the ulna with subcutaneous swelling

Case 5: Subcutaneous TB (Anterior Chest Wall Abscess)

A 16-year-old male presented with a swelling over the anterior chest wall, fever, and loss of appetite and weight for 1 year. Examination revealed a significant, well-defined, non-tender swelling over the anterior upper chest wall around the midline, measuring 10x10 cm (Figure 5A). USG Thorax noted a well-defined heterogeneously hypoechoic collection (11x11x1.5 cm) deep in the muscular plane. HRCT thorax confirmed a large cold abscess (Figure 5B). USG-guided pus aspiration was CBNAAT positive. The patient achieved clinical resolution with 6 months of ATT.

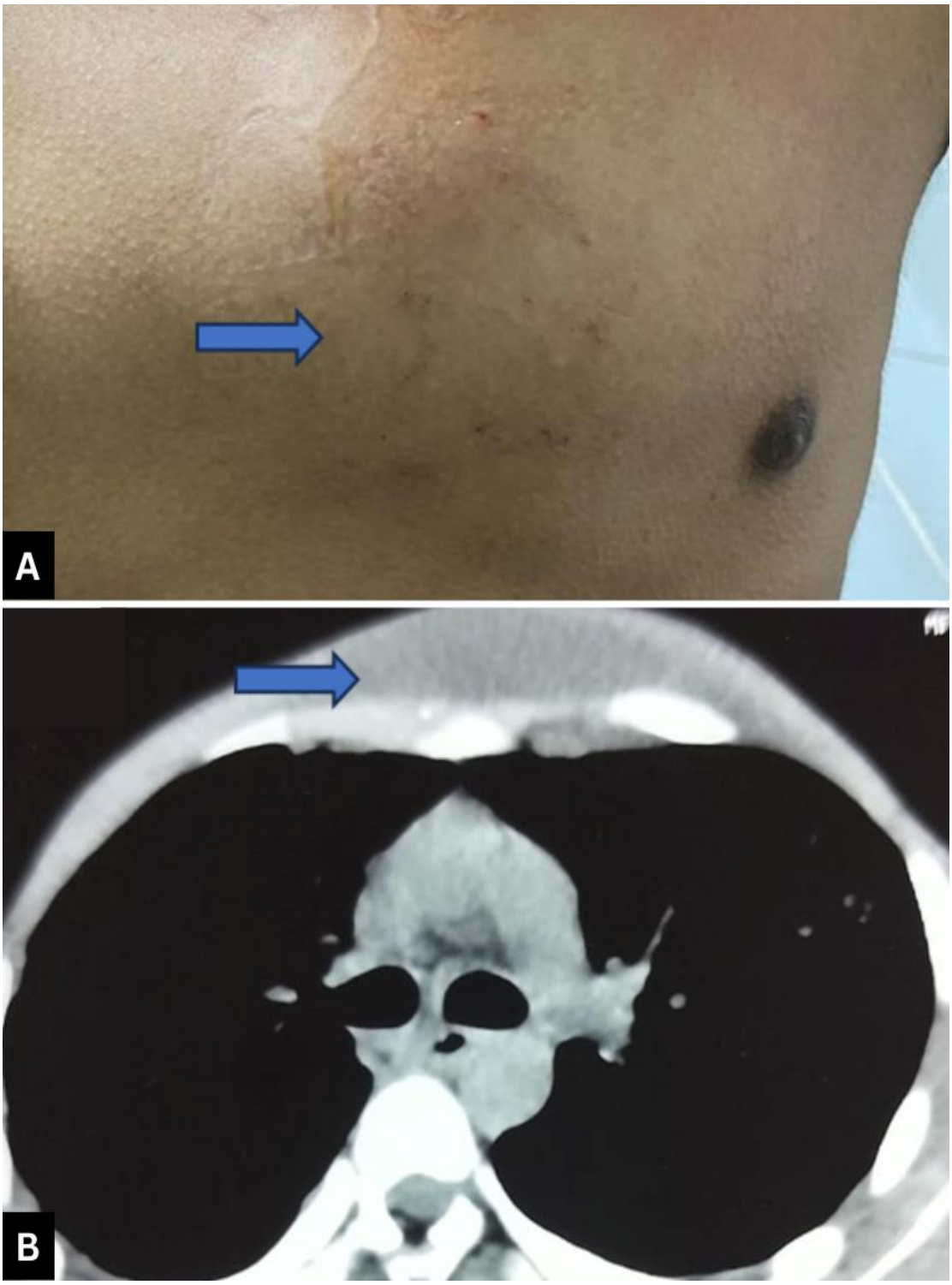


Figure 5: A) chest wall swelling. **B)** CT chest showing subcutaneous collection

Case 6: Subcutaneous TB (Multiple Abdominal Cold Abscesses)

A 63-year-old male presented with progressively increasing swelling over the right hypochondrium, fever, abdominal pain, and intermittent vomiting for 3 months. He had a history of a tubercular abscess over the left hypochondrium in 2020 (completed 6 months ATT). Examination showed a soft, fluctuant swelling (4.2x2.2 cm) with overlying erythema and a discharging sinus tract (Figure 6A). USG and CT of the abdomen showed thin-walled hypodense encysted collections bilaterally involving the muscle plane (Figure 6B). Pus aspiration detected Mycobacterium tuberculosis (MTB). Clinical resolution was achieved with 6 months of ATT.

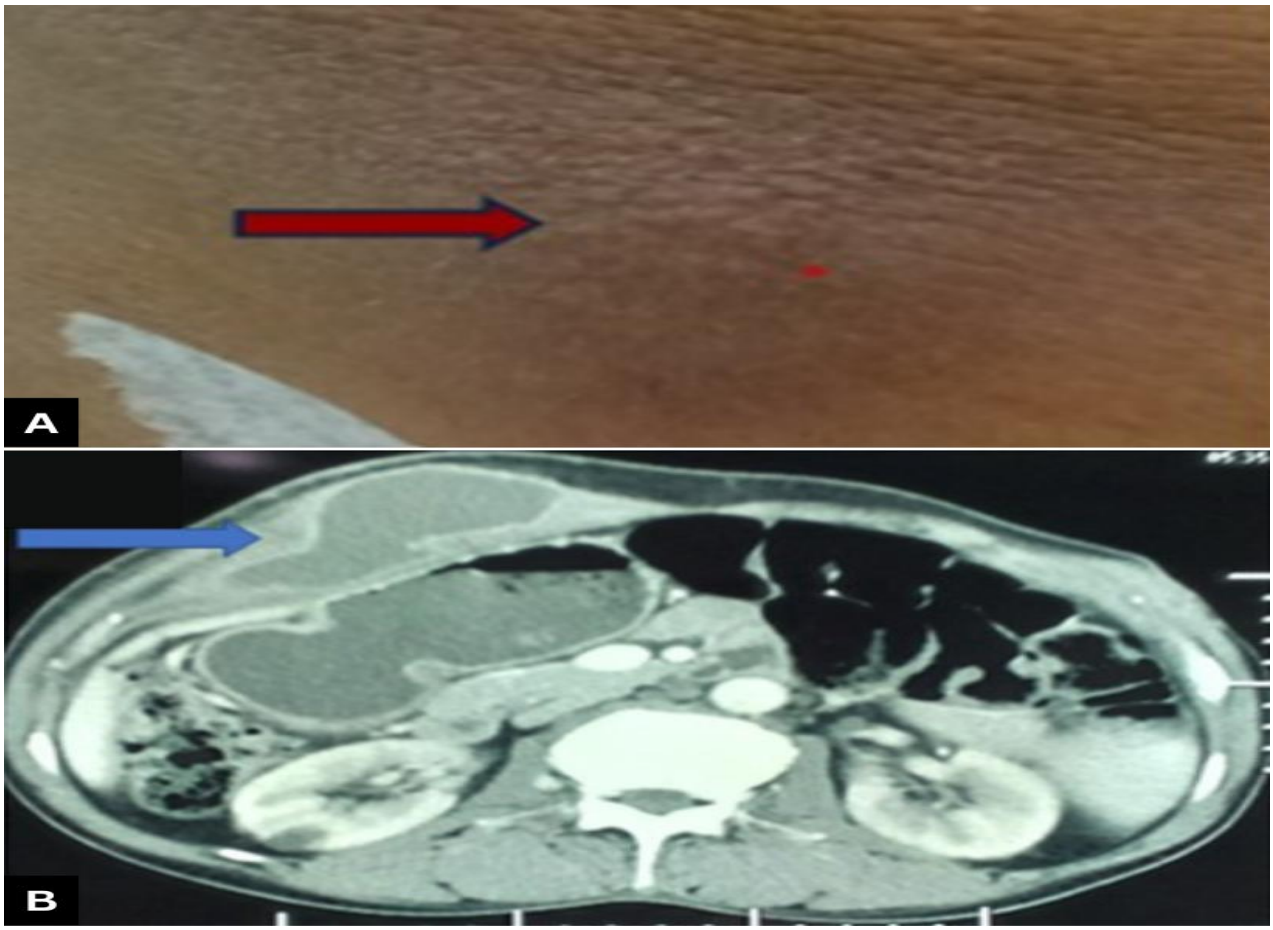


Figure 6: A) Abdominal swelling with sinus tract. **B)** CT showing subcutaneous collection

Case 7: Cutaneous TB (Scrofuloderma)

A 53-year-old male presented with painless, non-itchy skin lesions over the face, neck, and upper chest for 6 months, which had coalesced into hypertrophied scar-like lesions. Examination revealed three painless brown plaques (2-6 cm) over the neck and upper chest (Figure 7A). Skin biopsy from the border of a lesion showed tuberculoid granulomas with discrete central caseation in the upper dermis and a hyperkeratotic epidermis (Figure 7B). The patient showed clinical resolution with 6 months of ATT.

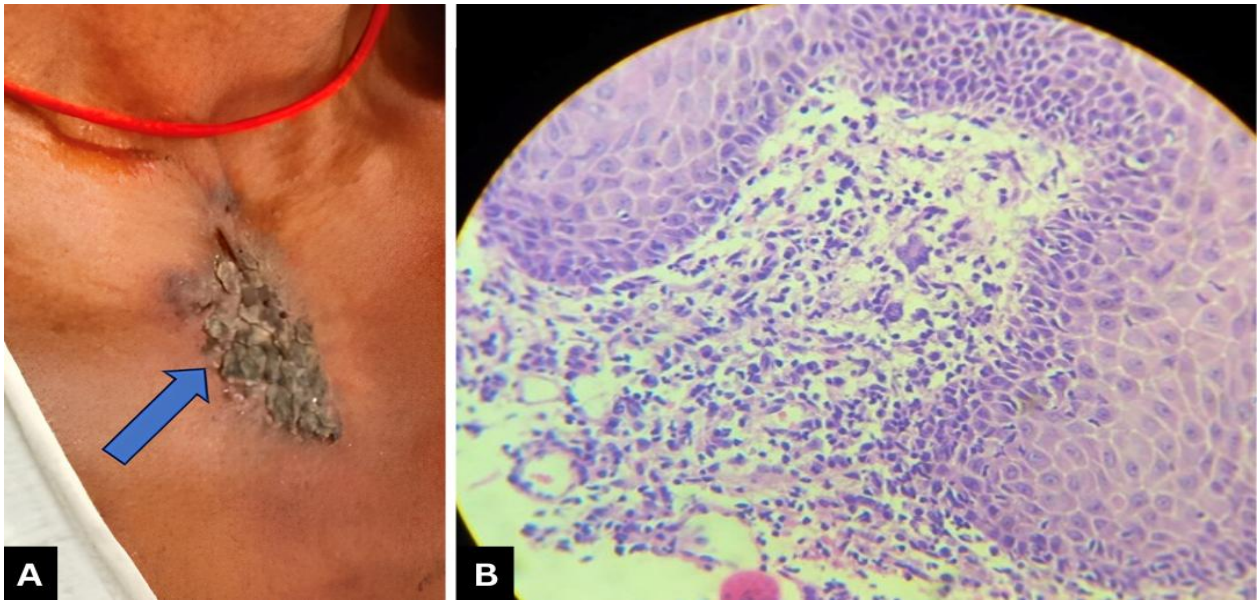


Figure 7: (A) Verrucous plaque over the anterior chest wall (arrow). (B) Histopathological (biopsy taken from the border of the lesion). section showing epithelioid cell granulomas with chronic inflammatory infiltrate, consistent with cutaneous tuberculosis. H&E stain, ×200 magnification.

Case 8: Laparoscopic Port Site TB

A 57-year-old female reported serous fluid discharge from an upper abdominal surgical wound 1 month after a laparoscopic cholecystectomy. Examination confirmed serous fluid discharge and erythema from port site wounds in the right hypochondrium and epigastrium (Figure 8A). CT of the abdomen revealed a branching sinus tract extending to the hepatic surface. Serous fluid CBNAAT detected MTB. Microscopic examination of the excised sinus tract demonstrated necrotizing epithelioid cell granulomas (Figure 8B). Treatment involved surgical excision and 6 months of ATT, yielding a full clinical response.

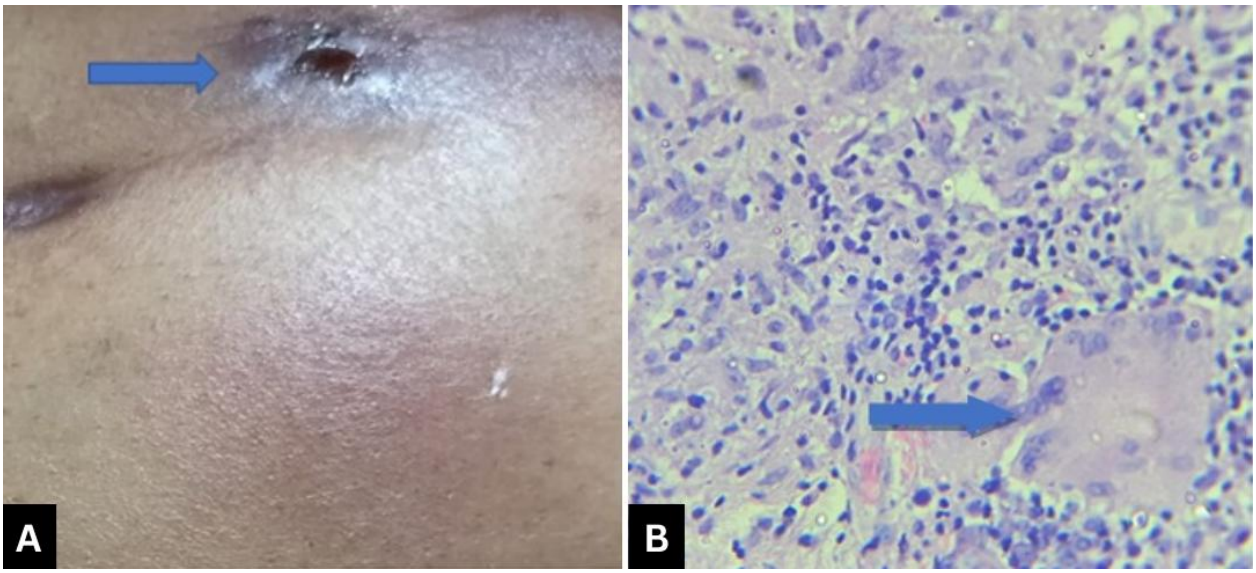


Figure 8: A) Infected laparoscopic port site. **B)** Microscopic examination of excised sinus tract demonstrating granulomatous inflammation with multinucleated giant cells (arrow), consistent with tuberculous involvement of the port site over the anterior abdominal wall. Hematoxylin and eosin (H&E) stain, ×200 magnification

Case 9: Tubercular Proctitis

A 55-year-old female complained of constipation with cramps and dull aching abdominal pain during straining for 1 year. A per-rectal examination elicited pain. CT of the abdomen showed circumferential rectal wall thickening with mesorectal and left external iliac lymph nodes. A colonoscopy revealed prolapsed hemorrhoids, rectal ulcers, and stenosis. A biopsy from the rectal stricture (Figure 9) showed granulomatous proctitis with caseous necrosis. Clinical resolution was achieved with 6 months of ATT.

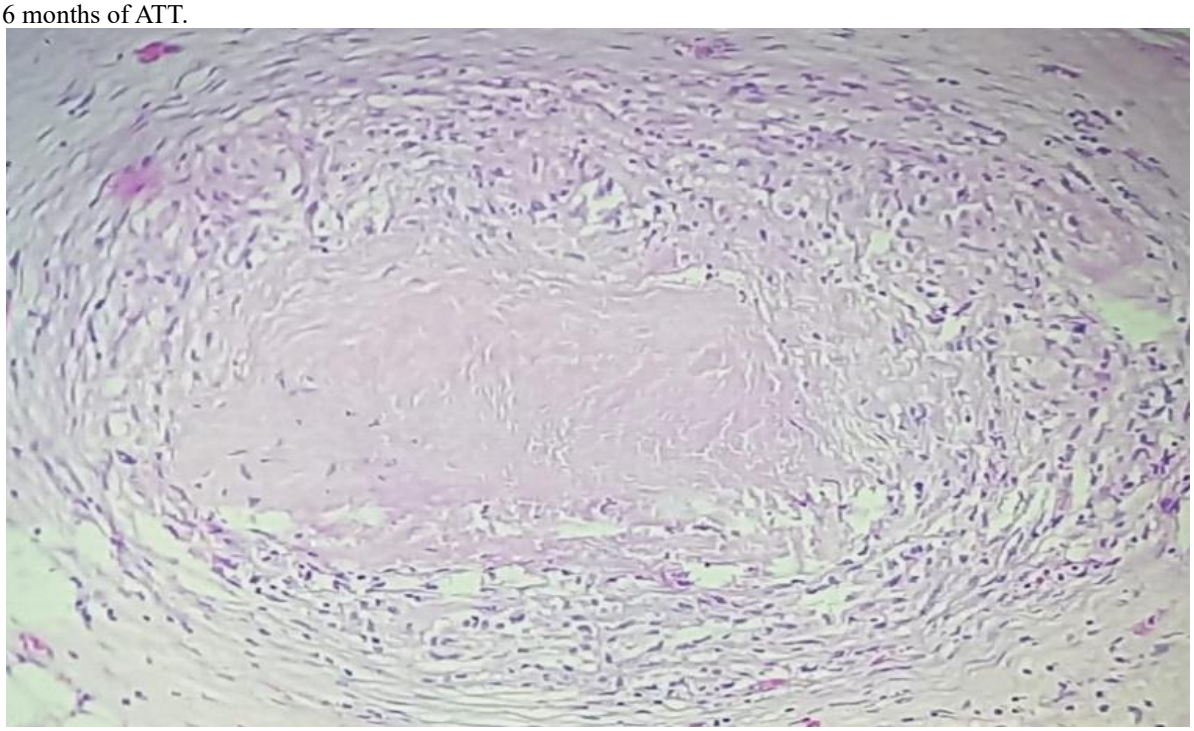


Figure -9: Histopathological section from the lesion showing an epithelioid cell granuloma with central caseous necrosis, consistent with tuberculous involvement. Hematoxylin and eosin (H&E) stain, ×200 magnification.

Case 10: Tubercular Oral Ulcer of the Tongue

A 65-year-old female with hypertension presented with a single painful oral lesion on the lateral aspect of her tongue for 2 months. Examination revealed a nodular, oval, tender, shallow swelling with erythema over the right lateral aspect of the tongue (Figure 10A). A biopsy from the ulcer showed chronic inflammation along with granulomas comprising epithelioid cells and large giant cells (Figure 10B). The patient exhibited significant healing and clinical resolution with 6 months of ATT (Figure 10C).

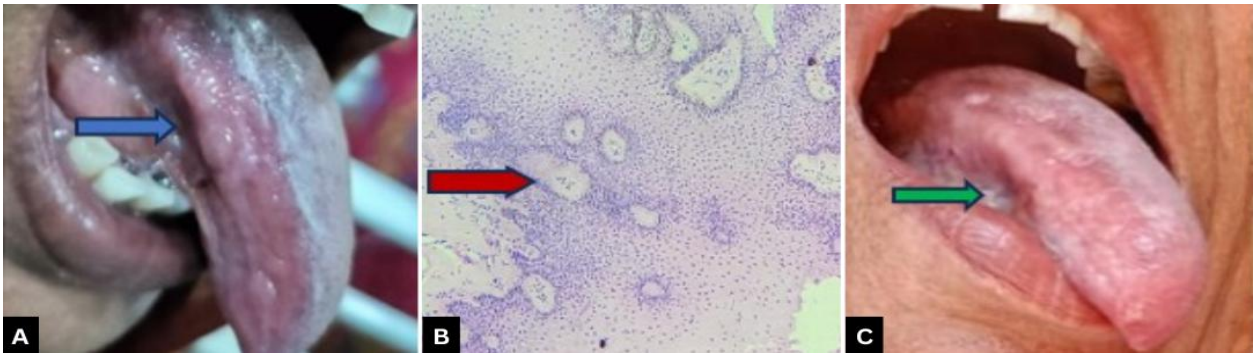


Figure 10: Tubercular ulcer of the tongue. (A) Ulcerative lesion on the lateral border of the tongue (blue arrow). (B) Histopathological section showing epithelioid cell granulomas with chronic inflammatory infiltrate, consistent with tuberculosis (red arrow). H&E stain, × 200 magnification. (C) Significant healing of the lesion following anti-tubercular treatment (green arrow).

Case 11: Tubercular Thyroglossal Cyst

A 9-year-old male presented with painful swelling over the right neck and fever for 15 days. He had a history of tubercular lymphadenitis 2 years prior. Examination showed a tender, non-erythematous right-sided neck swelling. CT of the neck showed a thin-walled, smooth, well-defined homogeneous fluid-density lesion in the anterior midline (Figures 11A and 11B). Excision of the thyroglossal cyst was performed. Histology showed chronic granulomas suggestive of TB (Figure 11C). The patient achieved clinical resolution with 6 months of ATT (Figure 11D).

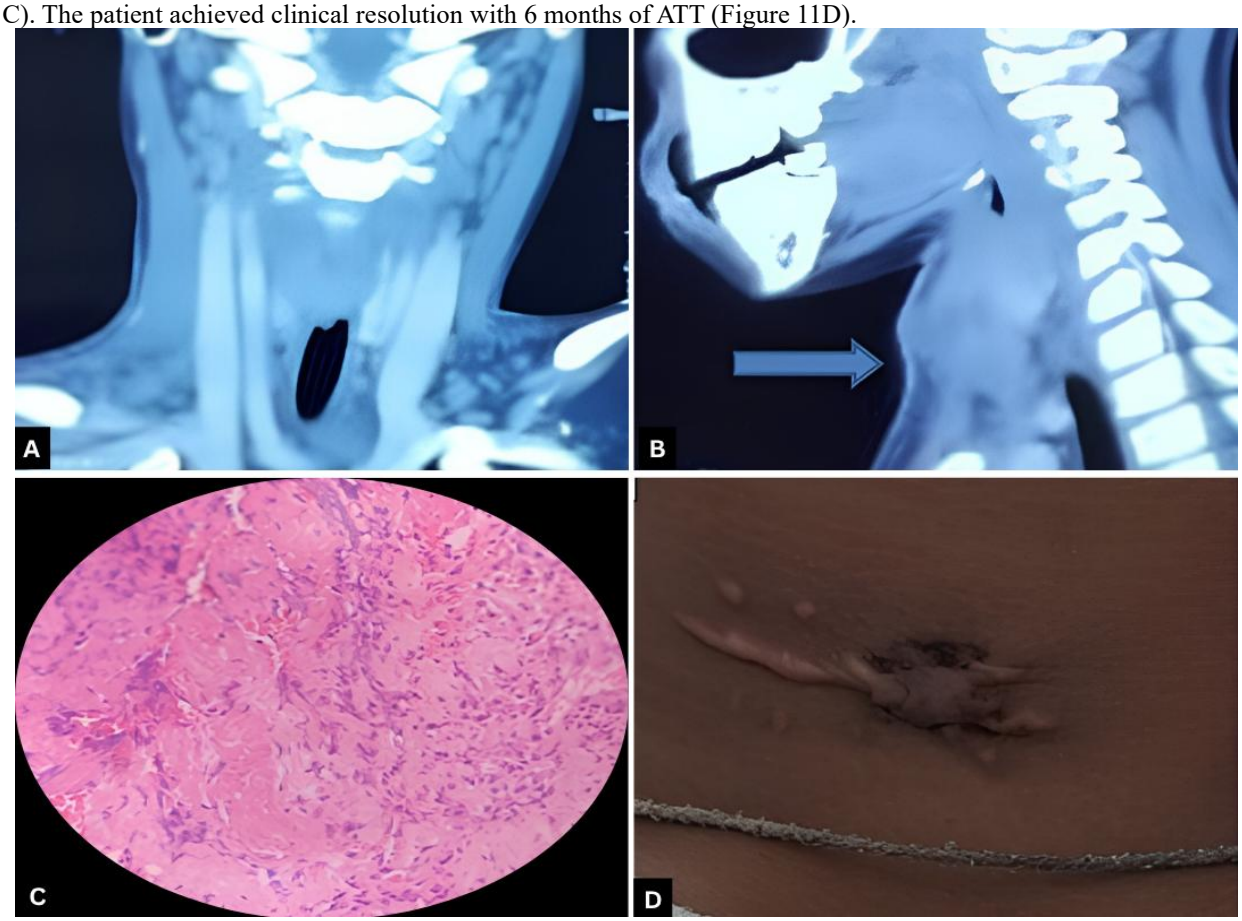


Figure 11(A-D): A-B) CT neck thin-walled, smooth, well-defined homogeneously fluid-density lesions with an anterior midline location. **C)** Histopathology (H&E stain, × 100 magnification) chronic granulomas suggestive of TB. **D)** Excision of thyroglossal cyst showing healing after 2 months of anti-tubercular treatment.

Case 12: Genitourinary TB

A 59-year-old male presented with left testicular swelling, fever, increased urinary frequency for 2 months, and weight loss. Examination showed a left-sided smooth, tender, fluctuant, and fixed scrotal swelling (3-4 cm) with overlying erythema. CT of the abdomen showed pyelitis with urethritis, solid cystic areas, and calcification replacing the scrotal sac (Figures 12A and 12B). Urine GeneXpert detected MTB (Rifampicin resistance not detected). Clinical resolution was achieved within 6 months of ATT.

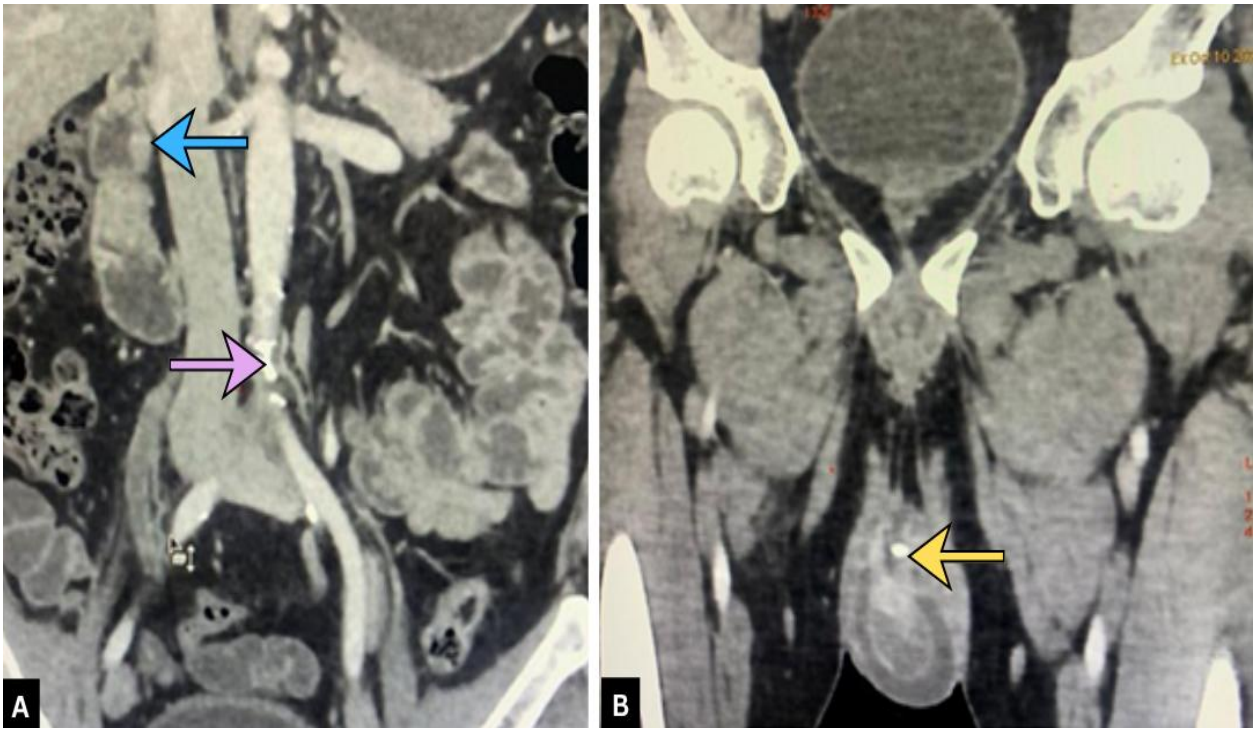


Figure 12: A-B CT abdomen - pyelitis with urethritis, solid cystic areas, areas of calcification replacing the scrotal sac.

DISCUSSION

EPTB, although comparatively less prevalent than its pulmonary counterpart, presents a complex and formidable challenge in clinical practice. Isolated EPTB cases account for 15-20% of all tuberculosis cases, with the most common sites being the lymph nodes (50%), pleura (18%), genitourinary system (13%), bones and joints (6%), gastrointestinal system (6%), central nervous system (3%), and spine (3%) [1-3].

The first 4 cases highlight musculoskeletal TB (Fig. 1-4), which typically results from the reactivation of dormant bacilli residing in pulmonary or extraosseous sites, facilitated by haematogenous, lymphatic or direct spread mechanisms. The disease initiation triggers an anti-inflammatory response within the synovium, leading to granulation tissue proliferation, effusion formation, and fibrin deposition. This process ultimately leads to bone demineralisation, cartilage destruction, and caseous necrosis, causing swelling over the bone and subcutaneous tissue [6,7]. Microbiological confirmation remains pivotal, with approximately 80% of cases testing positive.

This underscores the significance of accurate diagnostic techniques such as aspiration and biopsy to speed up therapeutic interventions and hence reduce long term morbidity [8]. We report 4 cases of musculoskeletal TB, each with an involvement of the upper limb. Tuberculosis of hand and wrist joints is a rare type of skeletal tuberculosis (1%) [9,10]. Usually, it involves pain and swelling of the wrist or hand joints, which may or may not be limited. Numerous small, pearly nodules, commonly known as "rice bodies" based on their appearance, are regarded as a strong indicator of tuberculous tenosynovitis by Woon et al [11]. Differential diagnosis includes: subacute or chronic suppurative arthritis, benign bone tumour, osteomyelitis, rheumatoid arthritis or Poncet's disease. There are three stages to tuberculous tenosynovitis: hygromatous (serous with normal tendon), serofibrinous (granulation tissue and rice bodies), and fungoid (caseation, abscesses, and tendon rupture) [12]. Systemic symptoms made a diagnosis of bone TB suspect of chronic osteomyelitis, as we experienced in our clinical practice. However, microbiological culture of the pus and biopsy confirmed the diagnosis of TB, highlighting the need for early diagnosis and treatment to avoid joint damage and loss of function.

Case 5 is a subcutaneous TB that manifested as an abscess on the chest wall while Case 6 had an abdominal abscess. Chest wall TB is uncommon and accounts for about 10% of all EPTB, with primary sternal TB only accounting for 0.3% [13]. The infection may be contiguous from pulmonary or pleural involvement, from chest wall adenitis, by direct transcutaneous inoculation or by haematogenous dissemination. All underlying anatomical structures may be involved in subcutaneous

TB. Skeletal muscle involvement in abdominal wall TB is rare and can be either contiguous spread from an adjacent site or haematogenous spread [14]. Subcutaneous TB presents itself usually as painless, cystic masses that do not show inflammatory signs in the skin, but rather are similar to a cold abscess or fluctuating solid tissue mass [15]. Diagnostic tools are key including ultrasonography and thoracic CT scans – in our case, geneXpert has become a rapid diagnostic tool that helps collect material for analysis with the help of a guided needle aspiration. The usual management includes antitubercular therapy (ATT) as well as surgical drainage, and surgical biopsy as an alternative diagnosis or treatment.

Case 7 is an exogenous and endogenously acquired case of Cutaneous TB which demonstrates a wide variety of clinical morphologies (Fig. 6). These lesions are difficult to diagnose because they can be confused with other dermatological problems and are frequently misdiagnosed. In the case of scrofuloderma, the endogenous TB generally occurs as an extension from an adjacent structure such as a lymph node, joint, or bone [16]. Commonly affected areas are the neck, axilla and groin; and the lesions are first noticed as firm subcutaneous nodules. As these nodules increase in size they ulcerate and form draining sinus tracts [17]. Scrofuloderma lesions are characterized by scarring. Initial lesions may heal spontaneously but keloid scars, retractions and atrophic sequelae may remain. Diagnosis includes skin biopsy for histopathology, AFB stains, CBNAAT and cultures.

Rare complications associated with laparoscopic surgery are also port site TB (as seen in case 8). There are two types of port site infections: early and late infections. It has been suggested that the infection of the port site at an early stage is due to skin commensals, and at a late stage to non-mycobacterial tuberculosis. A few reports of TB as port site infections have been reported. Sandeep et al presented a case series of 20 patients diagnosed after laparoscopic cholecystectomy (LC) with port site TB [18]. The infections are often related to failure of surgical instruments used in laparoscopy to be sterile during the procedure [19]. A thorough diagnostic procedure should be performed in cases where post-surgical sinuses do not resolve or recur after treatment, and TB should be considered as a possible cause.

Case 9 is a very uncommon form of gastrointestinal TB, which is manifested as a rectal stricture (Fig. 8). The most common symptom of gastrointestinal TB is ulceration, and less commonly hypertrophic, which is seen usually at the ileocecal junction and rarely in the colon or rectum. The six forms of ano-rectal TB include fistulae in ano (the most common), a short and annular stricture, multiple small mucosal ulcers, a lupoid form and a verrucous form and ulcers with undermined edge [20]. Rectal strictures caused by TB, like in our case, have not been reported very often[21]. Rectal TB usually presents with non-specific symptoms of bleeding per rectum and changes in bowel habits, making diagnosis difficult in the absence of other symptoms. The diagnosis of rectal TB requires a thorough evaluation of the endoscopy, radiological studies and examination of the biopsy specimens.

Case 10 shows a rare case of oral TB affecting the tongue (Fig. 10) which occurs in about 0.1% of cases [22]. Oral TB typically is secondary to pulmonary dissemination and/or hematogenous spread and is primarily seen in older patients, particularly the tongue, gingiva, and buccal mucosa. TB of the tongue is most common and can present in various forms like ulcers, nodules, plaque, fissures, or vesicles. These ulcers are typical of TB with the base containing a thick mucus substance and cause severe, unremitting and gradually aggravating pain [23]. A complete diagnostic process, including clinical history, physical examination and histopathological evaluation is essential. The diagnosis of confirmation usually involves the demonstration of caseating granulomatous lesions on biopsy to exclude other differentials. In our instance, the biopsy revealed characteristic lesions underscoring the significance of histopathology in the diagnosis.

Case 11 is a thyroglossal cyst (Fig. 11) which is a benign fibrous cyst formed by a persistent thyroglossal duct. It's usually found in the mid-line, from the base of the tongue to the suprasternal area. It begins at birth until 70 years of age, and thus is a frequent aetiology of midline masses [24]. In children, these cysts are painless swellings in the neck, but in adults, these cysts are infected and may have symptoms including painful tongue protrusion and dysphagia [25]. Imaging studies usually show clear lesions with rim enhancement (such as CT scan) [26]. While very uncommon, TB of the thyroid gland or thyroglossal cysts only accounts for a very small proportion of the histologically diagnosed cases and is estimated at 0.1-0.4% [27]. Due to the overlapping symptoms, TB might mimic other diseases such as subacute thyroiditis, thyroid abscess or malignancy. It may be hematogenous or directly from adjacent structures. The thyroid gland is relatively resistant to TB infection due to its rich blood supply, high concentration of iodine and natural bactericidal properties of the gland [28]. Histopathology is required to diagnose thyroid TB. The clinical presentation was compatible with thyroglossal cyst infection and the histopathological findings confirmed the diagnosis of TB in the present case.

Urogenital TB (30-40% of EPTB cases) (Case 12) results from hematogenous dissemination from chronic latent pulmonary TB [29]. Patients typically have a variety of symptoms, such as dysuria, haematuria, cloudy urine, fever, back pain and micturition. In males, the genital expression is mostly directed towards the epididymis, and can lead to scrotal swelling and infertility. However, tuberculosis of the urethra is a rare condition because the urethra is regularly exposed to mycobacterium tuberculosis infected urine. It comprises only 1.9% to 4.5% of urogenital tuberculosis cases and is almost never seen in isolation [30]. However, the insidious onset and nonspecific symptomatology may lead to diagnostic delays and irreversible organ damage. Diagnosis entails a meticulous approach integrating medical history, clinical examination,

radiological investigations, and urine microbiological analysis for AFB and GeneXpert. Urine analysis of sediment from a 24-hour specimen detects AFB in 80-90%of genitourinary TB. Urine culture, which requires 6-8 weeks for diagnosis, has a false-negative rate of 10-20% [31]. Our patient had scrotal involvement as well as pyelitis and urethritis. Thus, AFB was detected in the urine, thereby confirming the diagnosis.

CONCLUSION

The non-specific and often subtle clinical presentation, combined with a low index of suspicion, can result in delayed diagnosis of EPTB, particularly in rare single-organ cases without pulmonary or disseminated TB involvement. Therefore, clinicians should maintain a high level of suspicion for TB, even when the site of involvement is atypical, such as the subcutaneous abscess, osteomyelitis, surgical wound site infection, oral ulcers, etc., especially in India. Imaging is crucial in guiding the management approach and facilitating tissue sampling for biopsy and microbiological examination for definitive diagnosis. AFB and GeneXpert test performance should be considered a routine strategy for all extra-pulmonary samples in India.

Additional Informations

Author contributions All authors contributed to the study's conception and design. A. Kaur, M. Patro, and B. Satpathy performed material preparation, data collection, and analysis. L S Das, D S Bharani, B Kandwal, and S Mallik wrote the first draft of the manuscript. S Mallik and G Sahoo performed the final review and editing. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest: The authors declare that they have no competing interests.

Ethical statement: The ethical clearance was obtained from the Institutional Ethics Committee, IMS and SUM Hospital, Bhubaneswar.

Consent to participate and consent for publication

All patients provided written consent for using their data for scientific purposes and publishing it in a journal article.

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