ORIGINAL RESEARCH

Rare Clinical Forms and Variants of Cutaneous Tuberculosis – A Case Series

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ABSTRACT

Introduction: The complex phenotypic nature of cutaneous tuberculosis sometimes makes it challenging to diagnose the rare forms and variants of this chronic and debilitating skin infection which is caused by Mycobacterium tuberculosis. **Materials and Methods**: The study was conducted at a tertiary care centre, in which medical records of patients suffering from rare or atypical features of cutaneous tuberculosis diagnosed by biopsy between 1st November, 2021 to 31st March 2024 were identified and evaluated. **Results:** We found five out of nine patients of age ranging from 10 to 63 years, from an endemic region and identified uncommon phenotypes such as ulcerative and annular lupus vulgaris, tuberculous chancre, gummatous tuberculosis, and disseminated tuberculosis with skin involvement. Along with cutaneous tuberculosis other body organs were also found to be affected with tuberculosis in two of our patients. **Discussion:**The rare or atypical morphological presentation in our series of cases indicated the wide variety of cutaneous tuberculosis which could cause diagnostic delays. It is also crucial to differentiate these rare forms from similar-looking skin diseases to prevent misdiagnosis, disfigurement, and potentially fatal outcomes. **Conclusion:**Successful diagnosis and treatment required a comprehensive approach involving dermatologists, chest physiciansandorthopedic surgeons.

Keywords: Rare cutaneous TB, Ulcerative skin TB, Gummatous TB

INTRODUCTION

Cutaneous tuberculosis (CTB), caused by *Mycobaterium tuberculosis*is uncommon, comprising of 1-2% of all the extrapulmonary tuberculosis worldwide[1,2]. In India theprevalence varies from 0.25 to 0.6%[2]. The probability of rarity further increases with rare or atypical presentation. There is also a high likelihood of misdiagnosis and incorrect treatment protocol when these rare or atypicalphenotypes of CTBsimulate other dermatological conditions. We attempt to describe these rare forms and differentiate them from other closely resembling skin diseases.

MATERIALS AND METHODS

The study was conducted at a tertiary care centre in North India in the Department of Dermatology, Venereology and Leprosy. Patients diagnosed with cutaneous tuberculosis by skin biopsy in the form of histopathological evaluation/culture for Mycobaterium tuberculosis/cartridge-based nucleic acid amplification test (CB-NAAT) between 1st November, 2021 to 31st March 2024 were evaluated. Rare or atypical clinical featuresin clinical images of cutaneous tuberculosis patients were searched and they were based on deviation from the common morphology and/or aberrant anatomical location of various subtypes of cutaneous tuberculosis according to its classification system[1]. The medical records consisted of investigation reports and pre-biopsy and post-treatment clinical imagestaken routinely along with written informed consents from each patient or their guardians accordingly. Detailed diagnostic evaluation of these patients included routine blood investigation (complete blood count, liver function test, renal function test, blood sugar, erythrocyte sedimentation rate), viral makers for hepatitis B and C viruses and human immunodeficiency virus, routine urine analysis, Mantoux test and cutaneous biopsy. Radiological investigations included chest x-rays, computed tomography scan thorax and abdominal ultrasonography as indicated.All patients received category 1 anti-tubercular treatment (ATT) from Directly Observed Therapy Shortcourse

(DOTS)centrerecommended by World Health Organization[1].

RESULTS

A total of nine patients suffering from cutaneous tuberculosis were found. Five out of nine patients showed rare or atypical features of cutaneous tuberculosis along with complete medical records. As a result, 5/9 patients,3 females and 2 males with age ranging from 10 to 63 years,were included in the study. The description of cases of rare or atypical features of cutaneous tuberculosis are given as follows:

CASE 1

A ten-year-old girl had a slowly progressive linear, erythematous, firm, non-tender 0.5X2cm ulcerated plaque with peripheral reddish-blue discoloration on the right chest for six months [Figure 1a]. She experienced weight loss, malaise, and intermittent moderate fever in the evening for past three months. The patient's grandmother had died from an unknown complication related to pulmonary tuberculosiswhileundergoingtreatment. Local physicians were unable to help patient. Respiratory symptoms and lymphadenopathy wereabsent. Haematological, biochemical blood tests and viral-markers were normal, except for a positive Mantoux test. The plaque was diagnosed as ulcerative lupus vulgaris through histopathology[Figure 1b]. The patient was referred to the respiratory medicine department which ruled out pulmonary tuberculosis (TB). After six months of category I anti-tubercular treatment, a linear residual atrophic scar was left behind along with a papule in the centre[1]. Thus, the duration of ATT was further increased by three months which led to complete resolution without any recurrence so far [Figure 1c].

CASE 2

An 18-year-old female had a progressive hyperkeratotic, annular, firm, non-tender plaque on left lower cheek [3cmX 7cm] for 2 years [Figure 2a]. There was no history of cough, fever, malaise or weight loss. Her mother had untreated pulmonary tuberculosis and passed away from the illness. Therefore, the patient was informed about the contagious nature and seriousness of the disease and sought opinion from the respiratory medicine department. Routine tests, viral markers, sputum for acid-fast bacilli (AFB) and chest X-ray were normal. The Mantoux test was positive. Histopathological evaluation showed ill-defined epithelioid cell granulomas in the dermis [Figure 2b]. Treatment with Category 1 ATT led to complete resolution of the annular plaque-type lupus vulgaris after six monthsand no recurrence seen one year post-treatment[Figure 2c].

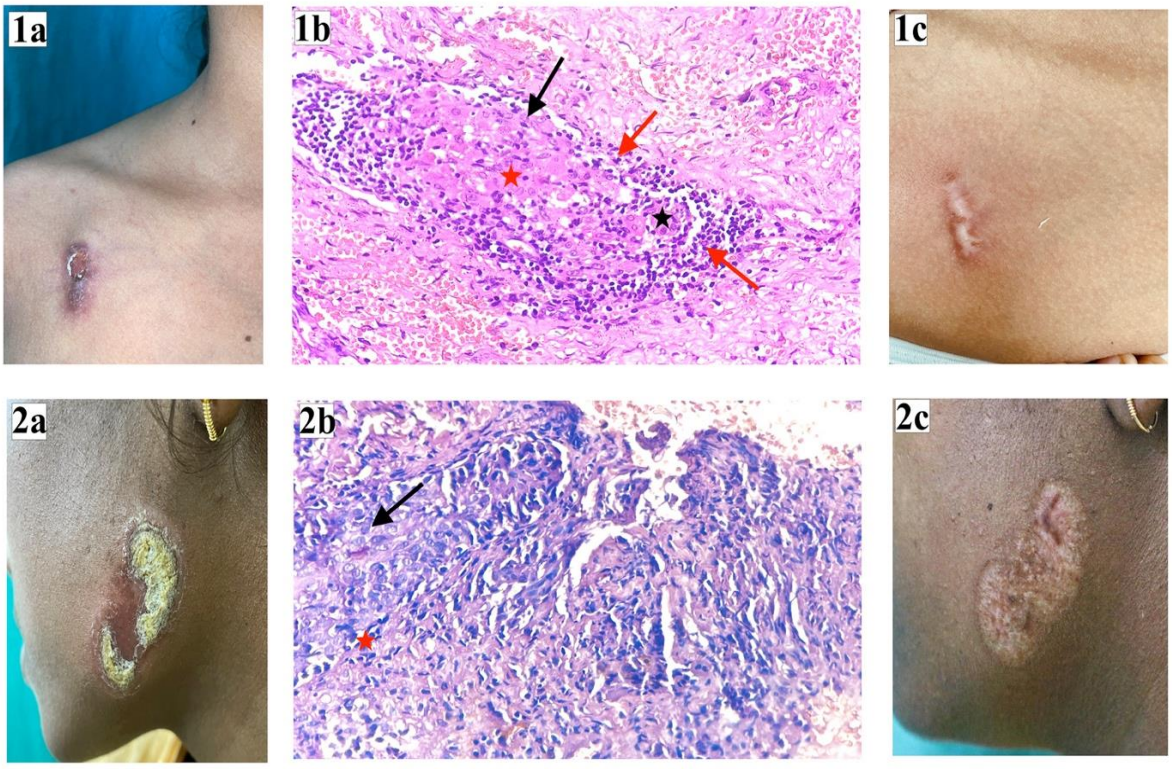

Figure 1a: A linear erythematous plaque measuring 0.5X2cm with ulceration and surrounded by a reddish-blue hue. Figure 1b: Histopathology revealing an epithelioid cell granuloma in the mid-dermis showing characteristic epithelioid cells (black arrow), a Langhans-type giant cell (black asterisk), mild necrosis in the center (red asterisk) and surrounding lymphocytes (red arrows) [Hematoxylin-Eosin stain, 40x]. Figure 1c: Healed linear scar on the chest after 9 months of anti-tubercular therapy

Figure 2a: Annular hyperkeratotic plaque-type lupus vulgaris of size 3cmX 7cm located over the left cheek. Figure 2b: Histopathology revealing a poorly defined tuberculoid granuloma in the mid-dermis showing epithelioid cells in the center (black arrow) and surrounding lymphocytes (red asterisk) [Hematoxylin-Eosin stain, 40x].Figure 2c: Post-treatment healed atrophic scar.

CASE 3

A 20-year-old male had a slowly progressive,round, smooth,non-tender and fluctuant subcutaneous swelling without local warmth located onthe right cheek [2.5x2.5 cm] and also had multiple sinus tracts on his abdomen that discharged caseous material and caused puckered scarringfor six months[Figure 3a]. According to patientthe lesions over abdomen were sequelae of multiple swellingswhich were similar to cheek lesion. He also experienced moderate fever and weight loss, but no cough for the same duration. Previous courses of oral antibiotics like amoxicillin+clavulanic acid and cefixime did not provide relief. Right-sided submandibular lymph nodes were enlarged. Investigations revealed a positive Mantoux test and normal blood results. Sputum for AFB was negative. High resolution ultrasonography of abdominal lesions showed a blind-ended tract extending to the subcutis.His fine needle aspiration cytology (FNAC) from the cheek swelling revealed epithelioid granulomas. Histopathology from abdominal lesion showed a well-formed epithelioid granuloma in the dermis [Figure 3b]. Thetuberculousgumma and sinuses completely healed with nine months of category 1 ATT [Figure 3c]. No recurrencenoted one-year post-treatment.

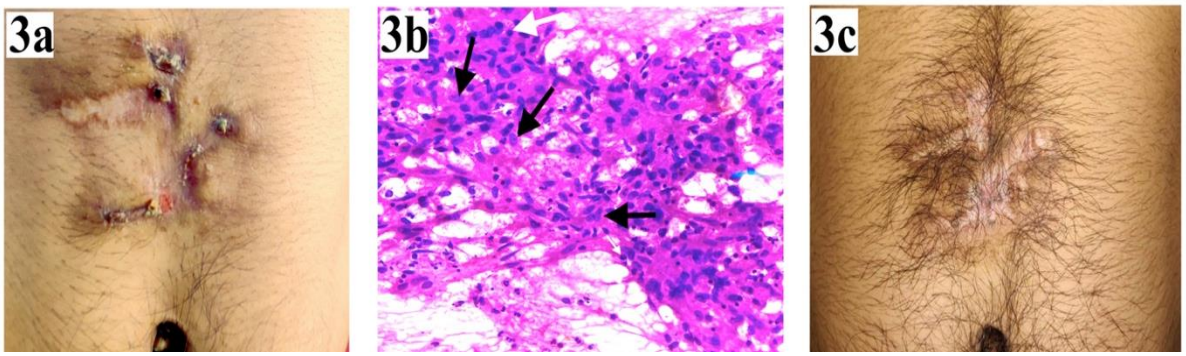

Figure 3a: Multiple sinus openings with ulceration and scarring present on the abdomen. Figure 3b: Histopathology revealing an ill-formed granuloma in deep dermis consisting of epithelioid cells (red arrows) and surrounding lymphocytes (white arrow) [Hematoxylin-Eosin stain, 40x]. Figure 3c: Healed abdominal atrophic scars after completion of antitubercular therapy.

CASE 4

A 32-year-old woman had slowly progressive non-healing ulcers on her left buttock for five months. The ulcers were round to oval, coalescing with each other, ranging in size from 0.5x0.5 to 2x4 cm and non-tender. They had a peripheral bluish hue, irregular undermined edgesand granulomatous floor[Figure 4a]. She also had a scar on her left buttock resulting from a deep ulcer that developed five months ago after an undocumented drug was injected intramuscularly into the affected site which led to ulcer formation three weeks later. There were no other symptoms or medical conditions reported. Routine blood tests and viral markers were normal. A Mantoux test was positive, and pelvis X-ray revealed a lytic lesion on the left ileum[Figure 4b]. The patient was referred to an orthopedic surgeon for further evaluation, but a magnetic resonance imaging (MRI) scan could not be done due to financial constraints; however, he advised treatment in line of bone TB. Histopathology from the edge of the ulcer also revealed changes suggestive of tuberculous chancre[Figure 4c]. As a result, category 1 ATT was initiated which led to complete healing of the ulcers within 8 weeks leaving behind residual scars [Figure 4d]. Patient is undergoing treatment with improvement.

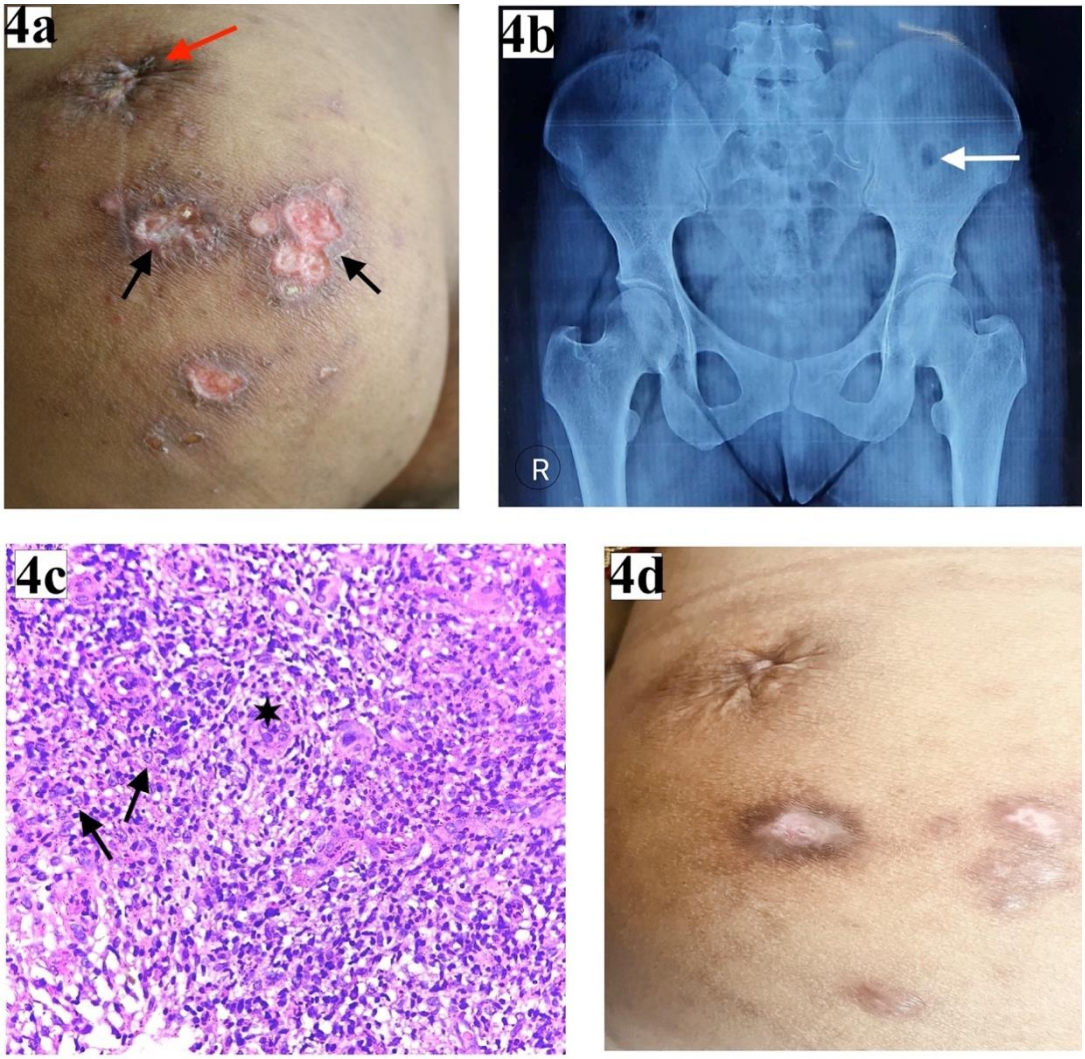

Figure 4a: Multiple non-healingulcers of varying sizes [0.5x0.5 to 2x4 cm] with clear granulomatous base and surrounded by a peripheral bluish hue (black arrows) on the left buttock. A deep puckered scar with mild ulceration present on the superior aspect of the ipsilateral buttock (red arrow).Figure 4b: X-Ray Pelvis [AP view] showing a lytic lesion on the left ileum bone (white arrow).Figure 4c: Histopathology demonstrating mid-dermal tuberculoid granuloma consisting of Langhans-type of giant cell in the center (black asterisk) and multiple epithelioid cells within the granuloma (black arrows) [Hematoxylin-Eosin stain, 40x].Figure 4d: Healed atrophic scars over left buttock after 6 weeks of antitubercular therapy.

CASE 5

A 63-year-old man with coronary artery disease presented with painful cutaneous necrotic ulcerated plaques on his forearms, thigh, and trunk for eight months. The plaques had dry scales and black discoloration at the center,ranging in size from 0.5x0.5 cm to 4x5 cm and,surrounded by a reddish-blue hue. Mild ulceration within the plaquescovered withhemorrhagic crusts was evident[Figure 5a & b]. The patient also experienced moderate grade fever in the evening and significant weight loss for three months. No history of offending drug intake like warfarin (which could develop necrotic skin ulcers) or respiratory symptoms were reported, but enlarged cervical lymph nodes were observed. Previous antibiotic treatments prescribed by a general physician had not provided relief. Routine blood investigations, viral markers, Mantoux test, and sputum for AFB were all inconclusive. A non-contrast computed tomography of the thorax revealed indications of pulmonary tuberculosis [Figure 5c]. The histopathological evaluation in hematoxylin-eosin stain was suggestive of CTB [Figure 5d]. The demonstration of AFB in Ziehl-Neelsen (Z-N) stain of biopsied tissue confirmed the diagnosis of CTB. Due to financial constraints, the patient declined cutaneous biopsy for TB culture and CBNAAT (cartridge-based nucleic acid amplification test) testing. Therefore,we began Category 1 ATT treatment for disseminated tuberculosis which resulted in partially healed ulcers within four weeks [Figure 5e]. The patient is improving withongoing treatment.

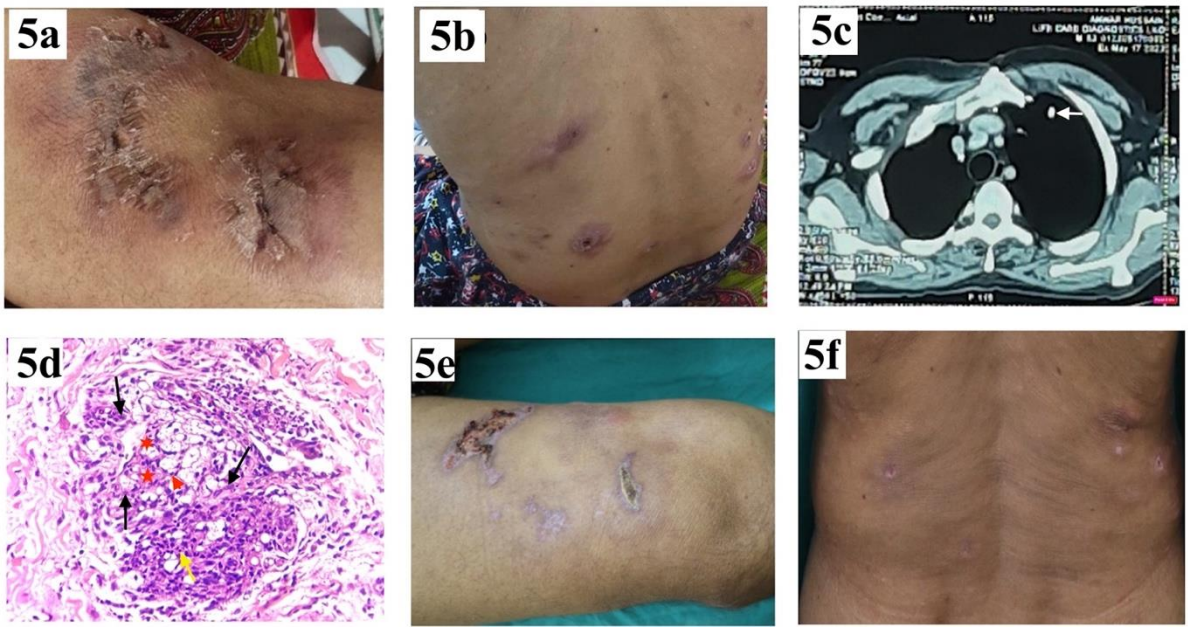

Figure 5a: Disseminated tuberculosis displaying ulcerated plaques with central necrosis and surrounding erythema over the right thigh.Figure 5b: Multiple ulcerated plaques covered with hemorrhagic crusts and surrounded by erythema and scales located over lower back. Figure 5c: Non-contrast Computed Tomography of Chest-[Axial] showing a calcific nodule in upper segment of left lung (white arrow). Figure 5d: Histopathology revealing dermal granuloma comprising of epithelioid cells (black arrows), lymphocytes (yellow arrow), neutrophils (red arrow head) with caseous necrosis (red asterisk) [Hematoxylin-Eosin stain, 40x].Figure 5e: Four weeks post antitubercular therapy showing partially healed ulcers covered with hemorrhagic crusts, surrounded by a bluish hue and scarred tissue present over the right thigh.Figure 5f: Four weeks post antitubercular therapy showing partially healed ulcers over lower back.

DISCUSSION

Lupus vulgaris (LV) is a chronic form of paucibacillary CTB that can occur through direct inoculation/extension from an affected organ or through hematogenous/lymphatic spread[2,3]. Common sites include the head, neck, and buttocks, while less common sites are the wrist and chest[2-4]. An ulcerative variety was found on the chest in our patient, which is uncommonly reported[2-6]. Another LV patient had an annular plaque on the left cheek, the annular configuration is less frequent according to literature[6]. Bacilli's DNA detection in cutaneous specimen through CBNAAT is known to be difficult in LV, but it was found to be positive in our ulcerative LV patient[2].

Tuberculous gumma is a multibacillary form of CTB that spreads either through the bloodstream or sometimes like in our case, may occur independently of other tuberculosis foci in the body[7]. Usually, tuberculous gummas occur in immunosuppressed individuals on the limbs, but this patient had multiple lesions on the cheek and abdominal wall despite not being immunocompromised[8,9]. The abdominal lesions resembled scrofuloderma, but there was no evidence of an underlying organ involvement at the affected site[10]. It was also necessary to differentiate this case from cutaneous actinomycosis, which has similar features. Table 1 provides points to distinguish between the two entities[9-11].

Tuberculous chancre or primary inoculation TB can be paucibacillary or multibacillary CTB, depending on the bacterial load[2]. There are three suggested routes of infection: exogenous inoculation through a break in the skin, breakout from an underlying foci, and hematogenous spread[12]. The incubation period for exogenous inoculation is 2-6 weeks[12,13]. Given the history of intramuscular injection on the affected area and a lytic lesion on left ileum bone probably of tubercular origin demonstrated in pelvis radiograph, it was difficult to determine the mode of infection as it could have been either exogenous or from the underlying bone foci, or a combination of both. Although more common in children, the patient in this case was an adult[12]. The tuberculous chancre is a shallow, friable ulcer with undermined edges and a granulomatous floor[12]. It is typically seen in individuals with low immunity, cancer, or malnutrition, but can also develop in those who are immunocompetent[12,13]. Our patient exhibited these clinical features and was immunocompetent with no health issues. The Mantoux test may initially be negative but later becomes positive[12,13]. Our patient had a positive reaction to the tuberculin antigen. Other bacterial infections like (Staphylococcus aureus, Pseudomonas aeruginosa etc), atypical mycobacterial infections and deep fungal infections were excluded based on histopathological and microbiological test results.

Disseminated TB involves infection in two or more non-contiguous sites[14]. The presence of multiple ulcerated plaques, histopathological evidence of AFB in biopsied skin tissue, lymphadenopathy, lung changes on radiology, and negative tuberculin test favoured a diagnosis of disseminated TB with skin involvement in our patient[14]. There is still controversy surrounding the terminology of disseminated TB and acute miliary TB. Some consider acute miliary TB to be a more advanced form of disseminated TB, while others view them as synonymous[15]. Acute miliary TB is characterized by immunocompetency, tubercles in histology, and a typical miliary pattern in lung radiology[15]. On the other hand, disseminated TB occurs in immunocompromised patients, with unorganized tissue granulomas and an absence of the typical miliary pattern in the lungs[15]. Contrary to the expected immunosuppressed characteristic in disseminated TB, our patient showed no evidence of it. This is an extraordinary case, as similar cases have rarely beenreported[15]. The presence of ill-formed granulomas without giant cells in the dermis and the absence of typical miliary changes in the lungs supported the diagnosis of disseminated TB in our patient[15]. Demonstration of acid-fast bacilli in biopsied skin tissue from ulcer ruled out papulonecrotictuberculid which is a hypersensitive phenomenon and chances of finding bacilli in Z-N stain is very low[1].Histopathological examination also aided in differentiating tubercular cutaneous ulcers from disseminated ulcerative pyoderma gangrenosum which could have a similar presentation and/or association[16].

In conclusion, the morphological variety of CTB, including chronic eroded plaques/ulcers/abscesses/sinuses, can present diagnostic challenges. Regardless of factors such as location, lesions' count, age of onset, fever, and immune status, a thorough work-up forsuspected CTB cases is crucial to prevent misdiagnosis and ensure appropriate treatment. However,larger studies are needed to validate these observations.Key takeaways of this case series includeconsidering CTB in cases of long-standing ulcers, excluding other possible causative infections, increasing awareness among clinicians and promoting collaboration with other specialities when dealing with such cases.

Table 1: Distinguishing features of tuberculous gumma from primary cutaneous actinomycosis[9-11]

S. No.	Features	Tuberculous gumma[9,10]	Primary cutaneous actinomycosis[11]
1.	Clinical pattern	Non-tender and fluctuant subcutaneous cold abscess, solitary or multiple[9]	Lumps with draining sinuses[11]
2.	Site	Trunk, extremities and often invade the skin[10]	Cervicofacial, thorax, abdomen, pelvic[11]
3.	Immune Status	Immunosuppressed state, but may occur in immunocompetent individuals[9]	Mostly immunocompetent, conditions linked to immunosuppression are associated with the disease[11]
4.	Source	Hematogenous spread[10]	Endogenous flora[11]
5.	Agent	*Mycobacterium tuberculosis*[9]	*Actinomyces israelii*[11]
6.	Discharge	Sometimes caseous material	Serosanguinous mostly with grains [grains- constitute of filamentous bacteria 'Splendore-Hoeppli Phenomenon']
7.	Staining	Acid-fast with 20% sulphuric acid (Ziehl-Neelsen stain)[9,10]	Gram-positive, Acid-fast in 1% sulphuric acid (Modified Zielh-Neelsen stain)[11]
8.	Tuberculin test	Negative or positive[10]	Negative
9.	Histopathological examination	Well-formed epithelioid granuloma[9]	Ray fungus surrounded by polymorphonuclear leucocytes associated with hyperkeratosis of the epidermis and dermal infilteration[11]
10	Treatment	Anti-tubercular drugs (rifampicin, isoniazid, ethambutol, streptomycin etc)	Amoxycillin+clavulanic acid

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