Journal of Pakistan Association of Dermatologists. 2020; **30(1)**: 190-197.

Case Report

Cutaneous tuberculosis with uncommon presentation: A case report and review of literature

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Abstract Tuberculosis is a serious infection that affects many people worldwide, with a recent increasing prevalence especially in high-risk patients, such as HIV infection, intravenous drug abuse, diabetes mellitus, immunosuppressive therapy, malignancies, end-stage renal disease, and and/or with multiple comorbidities. Although the incidence of Cutaneous Tuberculosis (CTB) is rare, it should be considered in patients presenting with atypical skin lesions suggestive of an underlying infectious etiology. Most often TB is an airborne transmissible disease with skin manifestations presenting as a result of hematogenous spread or direct extension from a latent or active foci of infection. However, primary inoculation may occur as a direct introduction of the mycobacterium into the skin or mucosa of a susceptible individual by trauma or injury. Although rare, it is important for clinicians to recognize the many clinical variants of CTB to prevent missed or delayed diagnoses. It is imperative that physicians have a high index of suspicion in order to quickly and effectively diagnose and treat these substantially morbid skin conditions. We report here a case with atypical presentation that we saw in our Out Patient Department (OPD). The aim of this communication is to bring to attention this often overlooked, but definitely curable clinical entity. This case report demonstrates the importance of a proper history and physical examination as well as diligent laboratory and diagnostic testing in determining the etiology of a suspicious and treatment-resistant skin lesion. Prompt consideration leads to a swift diagnosis and proper treatment resulting in high patient satisfaction.

Key words
Tuberculosis, cutaneous tuberculosis, lupus vulgaris.

Introduction

The high prevalence of Tuberculosis (TB) worldwide, its transmissible nature, and the significant morbidity and mortality associated with this infection account for the status of TB as a major public health concern.[1,2] Cutaneous tuberculosis occurs rarely, despite a high and increasing prevalence of tuberculosis worldwide. *Mycobacterium tuberculosis, Mycobacterrium bovis*, and the Bacille Calmette-Guérin vaccine can cause tuberculosis involving the skin.[3] Cutaneous lesions are relatively uncommon manifestations of TB, occurring in only 1 to 2 percent of infected patients.[4,5] A resurgence of cutaneous TB has been noted in parts of the world where human immunodeficiency virus (HIV) infection and multidrug-resistant TB are prevalent. The clinical findings vary; inflammatory papules, verrucous plaques, suppurative nodules, chronic ulcers, or other lesions may be seen. Factors such as the pathway of bacterial entry into the skin, the host's immune status, and the presence or absence of host sensitization to *M. tuberculosis* influence the morphologic presentation of TB in the skin. Cutaneous TB was first documented in

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1826, when Laennec reported his own "prosector's wart," a lesion that likely represented tuberculosis verrucosa cutis, a variant of TB that results from direct entry of the organism into the skin.[6] However, the causative organism of TB was unknown until Robert Koch discovered *Mycobacterium tuberculosis* in 1882.[7] Subsequently, the bacillus was detected in cutaneous lesions. Exogenous inoculation occurs after the direct inoculation of *Mycobacterium tuberculosis* into the skin of a person who is susceptible to infection. This leads to TVC, tuberculosis chancre and some cases of LV. Endogenous infection occurs in patients who were previously infected either by lymphatic spread, hematogenous spread, or contiguous extension. Lymphatic spread is seen occasionally in LV. Hematogenous spread is seen in acute miliary TB, metastatic TB abscess (gummatous TB) and LV. Contiguous extension is seen in scrofuloderma and orificial tuberculosis.[8]

Primary inoculation TB (tuberculous chancre) typically follows a penetrating injury that results in the direct introduction of mycobacterium into the skin or mucosa of an individual with no previous TB infection.[9,10] Scrofuloderma is the most common form of CTB in children and historically was seen after consumption of milk contaminated with *Mycobacterium bovis*.[11] TB cutis orificialis (TBCO) affects individuals with dramatically impaired cell-mediated immunity and advanced TB in other organs, such as the gastrointestinal tract and lungs.[10,12] Miliary TB (disseminated TB) is characterized by a wide dissemination of *Mycobacterium tuberculosis* into the body and shows a distinctive pattern on chest x-ray of multiple, tiny lesions (millet-sized) distributed throughout the lung fields.[9] Metastatic TB abscesses (TB gumma) can arise from breakdown of an old healed tubercle that still contains live organisms or from cell-mediated immune defense inhibition that reactivates.[8,9] TVC occurs after direct inoculation of TB into the skin of people who were previously infected.[13] LV is a chronic and progressive form of CTB that is widely described as the most common form of CTB with a multitude of presentations. Clinical variations exist and are defined as 1) classic plaque or keratotic 2) hypertrophic 3) ulcerative and 4) vegetating. The plaque type begins as discrete, red-brown papules that coalesce and form plaques with a slightly elevated verrucas border and central atrophy. The consistency of the plaque is soft and gelatinous and has a classic apple-jelly appearance on dermoscopic examination. Persistent lesions may damage underlying tissue and ulcerate causing severe disfigurement and an increased risk of cancer formation.[14]

Diagnosis of CTB is complicated and requires a full work-up, including a detailed history and physical examination; careful consideration of clinical presentation; TST; Serum QuantiFERON-TB Gold (QFT-G); skin biopsy with histological analysis and special staining methods for identification of AFB; and the use of other diagnostic tests, such as chest x-ray and sputum culture.[15] Mycobacterial culture remains the most reliable method to determine the presence of mycobacteria.[16,17] With the advent of polymerase chain reaction (PCR), even the smallest tissue sample can be analyzed and amplified for mycobacterial DNA sequences, confirming its presence.[18] In developing countries, PCR is not always readily available and therefore physicians must rely on a positive response to anti-TB drugs to confirm difficult cases.[18,19] CTB treatment is the same as that for systemic TB and consists of long, multidrug therapy. The most commonly used drugs are isoniazid, rifampin, pyrazinamide, and either ethambutol or streptomycin.[10,20] After eight weeks of therapy, the patients are considered no

longer infectious, but still require longer term treatment for eradication.[10,12]

Case report

Mrs. Nurjahan Begum, 60 year old female, hailing from Keraniganj, presented to us with multiple fleshy weepy foul smelling masses over left inguinal region. According to the patient's statement, she was reasonably well 8 months back. Then she noticed few tiny papules over anterior aspect of the left upper thigh which were red in colour, severely pruritic and painless. In the following days new papules began to appear, some of them were discrete, some were grouped, coalesced together and formed plaques. Due to continuous rubbing, the overlying skin surfaces became eroded and turned to beefy, weepy, red masses. In the successive days new papules appeared continually, the masses were extended peripherally, fused to each other gradually and became massive in size finally. She was so embarrassed with the continuous oozing of purulent foul smelled discharge from that area and the tendency of occasional bleeding during scratching. She has history of low grade intermittent fever with highest recorded temperature of 101^0F for last 1 year. She has lost one fourth of her body weight during this period. The patient is depressed and mildly anaemic. She has bilateral inguinal lymphadenopathy, having 3-4 enlarged lymph nodes on each side; the largest one is 3 cm in diameter, firm to hard in consistency, non tender, not fixed to underlying structure and overlying skin without any surface changes. On Integumentary system examination, there are multiple, fleshy, beefy red colored, mal odorous, closely set plaques of various sizes with an peripheral descrete arrangement of few red brown papules distributed over anterolateral aspect of left upper thigh extending downwards in an inordinate pattern up to beginning of mid thigh and medially towards the groin up to beginning of pubic region. The larger plaque is 7x9 cm in diameter, serpiginous bulbous in shape, have well demarcated darkly brown everted indurated border. The base is fleshy, lobulated, soft, mildly tendered covered with thick purulent exudate along with few foci of necrotic & haemorrhagic spot over the surface. She has no history of contact with TB patient and all the family members are healthy and she took BCG vaccine in her childhood. She is nor-motensive and non diabetic. Her bowel and bladder habits are normal. Before coming to this hospital she was treated with Cap. Flucloxacilline, Tab.Ceevit, Tab. Fexo fenadine, Topical Mupirocin from local physicians without any improvement. On general physical examination her appearance was depressed, cooperative, body built below average, pulse was 84 b/min, blood pressure (BP) 120/80 mm Hg, Temperature 98^0 F and respiratory rate 18 breaths/min on day of examination. Regarding investigation, Complete blood count finding on 5 June 2017 showed Haemoglobin: 10.6g/dl, ESR:69mm in 1st hour, Red blood cells: 7x10^12/L, White blood cells:7.8x1o^9/L, Platelets:260x10^9/L, SGPT: 35 U/L, S. Creatinine : 0.6 mg/dl, RBS: 4.4 mmol/l and HbsAg was Negative. Regarding Urine R/M/E: Pus cell 0-5/ HPF, Epithelial cell-2-3 /HPF and RBC was Nil. X-Ray chest P/A view showed Normal. Mantoux (Tuberculin) Test on 08 June 2017 showed positive result where Dose of PPD was 10 TU in 0.1 ml, induration appeared after 72 hours and diameter of skin induration was 16 mm. Skin Biopsy for histopathology was done on 31 May 2017. Specimen was skin from left inguinal region and microscopic appearance reveals area of ulcer with surface necrosis. The dermis shows multiple granulomas with Langhans type giant cells. Single focus shows early caseous necrosis and no malignancy is seen. Final comment was Granulomatous inflammation, suggestive of tuberculosis. Fine Needle Aspiration Cytology

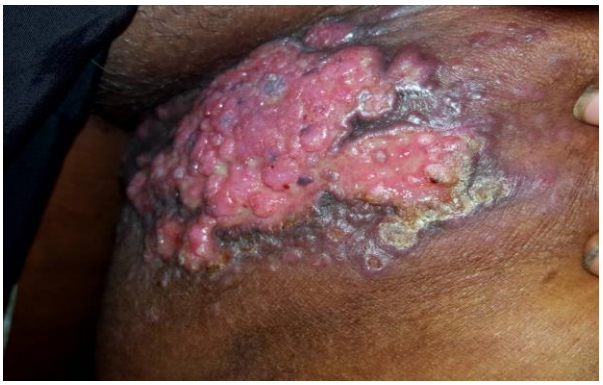

Figure 1 Multiple, fleshy, beefy red colored, plaques of various sizes distributed over anterolateral aspect of left upper thigh up to beginning of pubic region. The larger plaque is 7x9 cm in diameter, have well demarcated everted indurated border. The base is lobulated, covered with thick purulent exudate along with few foci of necrotic & haemorrhagic spot over the surface.

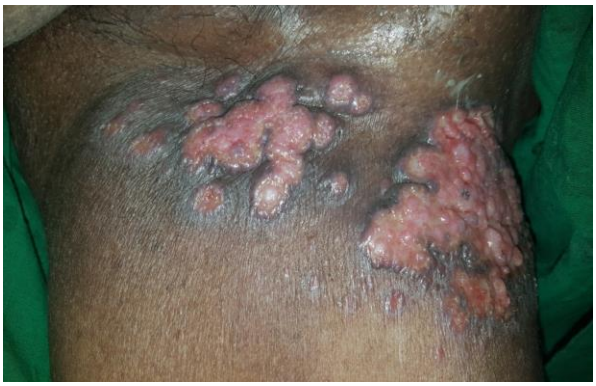

Figure 2 Multiple closely set plaques of various sizes with an peripheral discrete arrangement of few red brown papules distributed in an inordinate pattern medially.

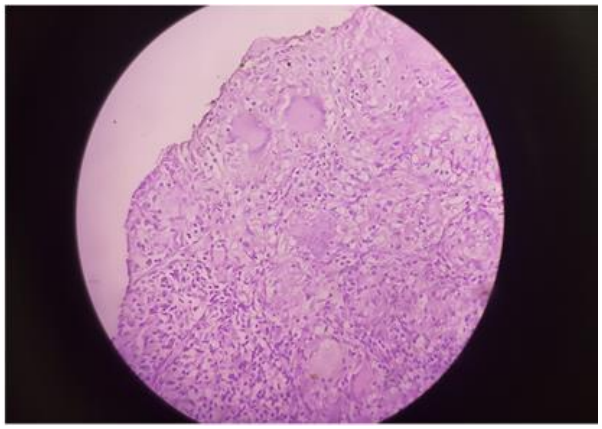

Figure 3 Histopathological examination findings revealed the upper dermis with multiple granulomas with Langhans type giant cells.

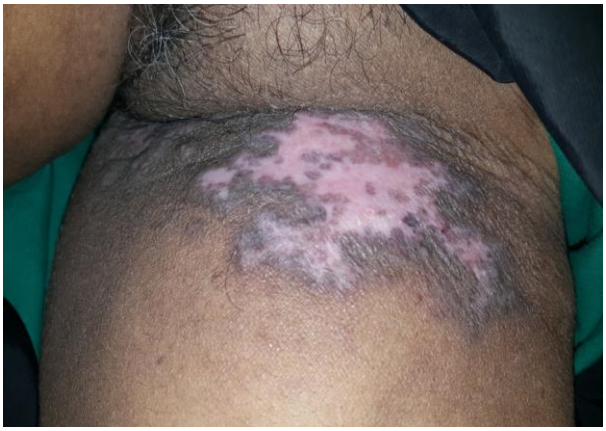

Figure 4 Clinical improvement of patient when patient on anti-tubercular drug therapy

(FNAC) of Inguinal lymph node was done and showed mycobacteria. The patient is on anti-tubercular drug therapy and improving day by day.

Discussion

Amylynne Frankel presented a 24-year-old Hispanic woman, with a painful lesion on her right buttock that began during her pregnancy four years prior. The lesion appeared as a large, reddish-brown, scaly plaque with well-defined borders and central atrophic changes covering the entire surface of the right buttock. The lesion was tender and warm with notable expression to light touch of purulent material through multiple fissures along the periphery. The patient reported no other symptoms, such as fever, chills, cough, or fatigue. On physical examination, vital signs were within normal limits, the skin demonstrated no other significant changes, and the patient had no notable lymphadenopathy. On history, the patient reported the skin lesion had progressively increased over the past four years. She had been previously diagnosed with psoriasis and was treated with multiple topical therapies, including salicylic acid and potent topical corticosteroids

without any relief. Further, the patient reported having a similar lesion (which was on her neck) as a child that was surgically removed in Mexico. She had been Bacille Calmette-Guérin (BCG)-vaccinated in the past. Serum QuantiFERON®-TB Gold (QFT-G; Cellestis Inc.,Valencia, California) testing was performed along with tissue cultures and skin biopsy with histological analysis. Histopathology of the plaque showed pseudoepitheliomatous hyperplasia and neutrophilic microabscesses in the epidermis. The dermis contained a mixed neutrophilic and granulomatous infiltrate. Acid-fast bacillus (AFB) staining showed rare elongated acid-fast structures suggestive of TB infection. Culture from lesional tissue grew *Mycobacterium tuberculosis* and serum QFT-G testing was positive. The patient was referred to infectious disease to rule out active TB infection. Sputum cultures were negative and a chest x-ray showed no active pulmonary disease. A diagnosis of CTB was made based on the patient's history, clinical picture, and diagnostic testing. Although an explicit classification of CTB could not be specified, lupus vulgaris (LV) and tuberculosis verrucosa cutis (TVC) are two variants of CTB that have been shown to occur in a previously sensitized individual, and her diagnosis was assumed to be one of these two variants. The patient was treated by infectious disease with multidrug TB therapy (pyrazinamide, rifampin, ethambutol, and isoniazid) resulting in lesion clearance at three months. Currently, the patient remains free of tuberculous disease.[3]

Agada et al presented a 70-year-old Asian man with noninsulin-dependent diabetes presented with a 4-month history of left-sided otitis externa and right-sided facial palsy. Physical examination of the left ear revealed a punched-out ulcerative lesion on the tragus, an edematous and inflamed external auditory canal, and a purulent nonmucoid discharge. Computed tomography of the brain and neck demonstrated a large retropharyngeal abscess, an abscess in the left parapharyngeal space, and a small collection adjacent to the right carotid sheath at the level of C4; the cervical vertebrae and lungs were normal. Microscopy of drained pus and histology of left ear and neck node biopsies identified tuberculosis. The patient was started on antituberculosis drug therapy, but he died within 2 weeks of treatment.[21]

Saritha et al presented 3 cases of lupus vulgaris with atypical presentations. The cases mimicked other chronic skin lesions like actinomycosis, mycetoma, and so on. Strong clinical suspicion, histopathology, and response to antituberculous treatment led to the diagnosis and all three had excellent response to treatment.

Case 1

A 14-year-old boy presented with multiple ulcers involving bony prominences of his body of 1-year duration. Onset was insidious with multiple remissions and exacerbations. The most prominent ulcer was present around his nose and mouth. It had healed and broken open many times leading to severe scarring, microstomia and disfigurement. Other ulcers (nine of them) were present over various bony prominences on his limbs. A few had healed with severe hypertrophic scars. The boy had occasional low grade fever, difficulty in eating and breathing (as a result of scarring around the nose) and episodes of pain over the ulcers. Preliminary workup revealed a raised erythrocyte sedimentation rate (ESR) and positive Mantoux test. Culture for myco-bacteria was negative and tissue smear did not reveal acid fast bacilli (AFB). Skin biopsy revealed a dense tuberculoid granuloma in the mid-dermis with Langhans giant cells and minimal central caseation. The boy was started on empirical anti-tuberculosis treatment (ATT) with excellent response. All

ulcers healed in a month. Surgical correction of microstomia was done with considerable improvement in patient's morbidity. Our final diagnosis was disseminated lupus vulgaris.

Case 2

An 18-year-old girl presented with a soft tissue swelling over her left gluteal region of 5 years' duration. Onset was insidious with no preceding trauma. The mass slowly grew in size with recent formation of multiple sinuses exuding serous fluid. Her preliminary workup was unremarkable except for a positive Mantoux test. Skin biopsy showed a tuberculoid granuloma in mid-dermis with Langhans giant cells. Empirical ATT was started with excellent results. The mass reduced in size and sinuses healed during the course of ATT.

Case 3

A 35-year-old man presented with a chest wall growth of 8 months' duration. He too had an insidious onset of disease, with formation of numerous sinuses extruding serous discharge without any history of discharge of grains. A potassium hydroxide (KOH) mount from the discharge was negative. We proceeded with skin biopsy, which showed a typical dense tuberculoid granuloma with numerous Langhans giant cells in the dermis but no AFB being demonstrated. On further investigation, he revealed history of contact with tuberculosis (father was on ATT). His chest radiograph revealed an area of consolidation but sputum for AFB was negative. He was also started on empiric ATT with good results confirming our diagnosis of lupus vulgaris mimicking actino-mycosis.[22]

Sehgal et al presented a Bacillus Calmette-Gue´rin (BCG) vaccinated 26-yearold well-nourished woman reported with numerous, progressive, elevated lesions for the past 8 months. A few of them broke up to form raw, exuding, painful infected ulcers, unresponsive to systemic and/ or topical antibiotics. The lesions were progressive and had advancing borders leaving behind scars. There was no history of evening rises of temperature, night sweats, cough, or weight loss. General physical examination was normal. However, the skin surface examination revealed the presence of multiple, round, soft, 0.5-mm nodules and ulcers, distributed over the face, under the breast, abdomen, flanks, and the wrist. The ulcer over the upper outer quadrant of the right breast, just above the nipple, was round and 2.4 cm in size, with undermined margins, and was well demarcated. Its floor was erythematous, raw, and exuding. BCG vaccination scar on the left deltoid was conspicuous. Standard tuberculin purified protein derivative 6 tested highly positive; 20-mm (normal: 6–10 mm) erythrocyte sedimentation rate (Westergren) was 44 mm/ 1 hr; total and differential leukocyte count, hemogram, blood sugar, HbA1C x-ray of the chest, and ultrasound of abdomen were normal. Ziehl–Neelsen stained smears for acid fast bacilli were negative from the ulcer. Mycosure polymerase chain reaction (PCR) DNA analysis for Mycobacterium tuberculosis and nontuberculous mycobacteria done on the peripheral blood was negative, whereas Mycobacterum TB immunoglobulin (Ig)-M enzyme linked immunosorbent assay (ELISA) (A 60 TB test) done on peripheral blood was 1.58 (positive.1.00). Antibodies/antigen for human immunodeficiency virus (HIV), HIV 1 and II, was nonreactive. Hematoxylin-eosin–stained sections from the nodules depicted marked hyperkeratosis, follicular plugging, thinning, and focal atrophy of the epidermis. Epithelioid cell granulomas comprising giant cells occupying the upper dermis was prominent. Chronic inflammatory infiltrate formed by lymphocytes and increased vascularity was

another feature confined mostly to the upper dermis. Although the sections revealed an ulcer, the surface of which was covered by acellular and granular necrotic material, caseation was conspicuous by its absence. A few underlying scattered epithelioid cells (white arrow) and giant cells with peripheral arrangement of nuclei (black arrow) were also seen. The lesion was lined by inflammatory granulation tissue and underlying fibrosis. There was destruction of all cutaneous appendages. Stain for acid fast bacilli, however, was negative, so also was the culture on Lowenstein–Jensen medium. Accordingly, an antitubercular therapy comprising 800 mg of ethambutol hydrochloride, 300 mg of isoniazid, 1500 mg of pyrazinamide, and 450 mg of rifampicin was instituted, and the patient was asked to come for follow-up every week for 6 weeks. The perceptible regression of all the lesions during the period prompted to continue the treatment to complete the scheduled regimen for a period of 9 months. A complete resolution of lesions was recorded after completion of the therapy. The same was supported by laboratory investigations (IgM titers declined to 0.82 by ELISA).[23]

Conclusion

Atypical presentations of cutaneous tuberculosis are not so uncommon and are frequently overlooked in clinical practice, leading to late diagnosis and increased morbidity. We report a case of cutaneous tuberculosis with atypical presentations. Strong clinical suspicion, histopathology, and response to antituberculous treatment led to the diagnosis and she had excellent response to treatment. Today, when tuberculosis threatens to burst into pandemics again, early diagnosis and treatment are more important than ever for control and prevention of morbidity.

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