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Cutaneous tuberculosis: A clinicopathological study of 50 cases from a tertiary care referral hospital

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ABSTRACT

Background: Tuberculosis (TB) is a health problem worldwide. Cutaneous TB comprises a small fraction of all clinical forms of TB. **Objective:** The purpose of this study was to assess the disease pattern of cutaneous TB in an Asian country. **Materials and Methods:** Totally, 50 cases of cutaneous TB were diagnosed on histopathology in a tertiary care hospital over a period of 7 years. Relevant clinical details and available laboratory findings were correlated. **Results:** The patients ranged from 4 to 78 years with 26 males and 24 females. Neck was the most common site. 22 (44%) cases presented with erythematous plaques followed by papules in 9 (18%) cases. Classical epithelioid cell granulomas with Langhans giant cells were found in 46 (92%) patients, while caseation necrosis was seen in 18 (36%). On Ziehl-Neelsen staining, acid fast bacilli were demonstrated in 6 (12%). 24 (48%) patients were diagnosed lupus vulgaris, 11 (22%) scrofuloderma, 4 (8%) TB verrucosa cutis, 1 (2%) TB cutis orificialis, and 10 (20%) TB non-specific type. **Conclusion:** Lupus vulgaris is a most common presentation of cutaneous TB. Caseating epithelioid cell granulomas with or without positive Ziehl-Neelsen stain constitute the classical picture. Knowledge of different histopathological features and their variation is important for an accurate diagnosis.

KEY WORDS: Cutaneous, granuloma, histopathology, tuberculosis, Ziehl-Neelsen stain

INTRODUCTION

India is the country with highest tuberculosis (TB) burden in the world with 40% of population being infected with *Mycobacterium* TB. Not only in India, TB remains a worldwide health problem. In 2012, 8.6 million people fell ill with TB and 1.3 million died from it, including 3,20,000 people who were human immunodeficiency virus (HIV) positive [1]. Pulmonary TB is the most common form of TB, that being infectious, attracts global attention for its adequate control. In the latter half of the 20th century, TB burden showed a declining trend with the advent of effective chemotherapy and improvement in living standards. However, with the emergence of HIV and rise in multi-drug resistant TB, the incidence started increasing in the late twentieth century [2].

Cutaneous TB comprises a small fraction (<2%) of incident cases of all clinical forms of TB [3]. Similar to the pulmonary form, cutaneous TB has also showed an initial decrease in the incidence from 2% to 0.5% in different Indian studies [4,5]. It is characterized by diverse dermatological manifestations, as a result of which, its identification and classification purely on clinical grounds is difficult. Lupus vulgaris, scrofuloderma, and TB verrucosa cutis are among its most common clinical presentations. In view of poor bacterial isolation, histopathology remains the main modality for its diagnosis. Caseating epithelioid cell granulomas with Langhans type giant cells in dermis with or without positive Ziehl-Neelsen (ZN) stain for acid fast bacilli (AFB) constitute the classical picture of cutaneous TB. However, cutaneous TB is characterized by variations in the histopathological features including necrotizing granuloma, poorly formed granuloma, non-specific inflammatory infiltrate, and absence of caseation which make its diagnosis difficult [6]. We intend to present our 7 years retrospective data on cutaneous TB patients discussing their diverse clinical and histopathological features along with diagnostic correlation.

MATERIALS AND METHODS

The present study is a retrospective study comprising of 50 cases of cutaneous TB, which were diagnosed on the basis of histopathology findings. The study was conducted in the department of pathology, in a tertiary care hospital. The biopsy samples were sent from the dermatology department of our hospital. The ethical clearance was not taken on account of the retrospective nature of the study.

The case records and histopathology reports of selected TB patients, diagnosed between 2006 and 2012 were collected. Different parameters like age, gender distribution, site of involvement, clinical and microscopic findings, culture for *Mycobacterium* TB, AFB positivity among different clinical types of cutaneous TB were evaluated.

RESULTS

The patients ranged from 4 to 78 years of age (median age: 24 years). 32 patients (64%) were below or equal to the age of 30 years [Table 1]. Of 50 patients, 24 were females. Affected females were relatively younger than males (median age for females: 21.5 years; for males: 26 years). The neck was the most common site followed by face [Table 2]. The majority of patients with neck involvement had secondary skin involvement due to draining cold abscess. On evaluating the past history, 2 patients were old treated cases of pulmonary TB and 1 of skin TB. Three patients had a past history of trauma at the site of skin TB.

Erythematous plaque was the most common clinical finding seen in 22 (44%) patients [Figure 1]. 8 (16%) patients had sinus presentation that was secondary to draining cold abscess. On histopathological examination, epithelioid cell granulomas along with Langhans giant cells were seen in 46 (92%) patients while 4 (8%) cases showed granulomas devoid of giant cells [Table 3]. Of these four cases, caseation necrosis was seen in all. Of total 50 patients, caseation necrosis was seen in 18 (36%) patients. On ZN staining, AFB was demonstrated in 6 (12%) patients. Of these, three cases were of scrofuloderma [Figure 2]. Other causes for granulomatous inflammation were ruled out. Periodic acid Schiff stain for fungus was negative in all the cases. A careful search for organisms like leishmania on Giemsa stained sections was also negative.

Of 50 patients, 24 (48%) patients were diagnosed on histopathology as lupus vulgaris, 11 (22%) patients scrofuloderma, 4 (8%) patients as TB verrucosa cutis [Figure 3], 10 (20%) patients were labeled as "TB - non-specific type," and 1 (2%) patient was diagnosed as TB cutis orificialis [Table 3]. Median age of presentation for lupus vulgaris was 20 years with males being more affected than females (16 vs. 8 years). Face was the most common site of involvement [Figure 4]. In contrast to lupus vulgaris, scrofuloderma was more common in females. It was most commonly associated with a draining sinus due to underlying lymphadenopathy (8 out of 11 cases) [Figure 5]. 7 patients (64%) of scrofuloderma had evidence of caseous necrosis in contrast to 5 (21%) patients with lupus vulgaris. Rest of the 11 cases of scrofuloderma and 19 cases of lupus vulgaris [Figure 6] showed granulomas without caseation.

Table 1: Age-wise distribution of cases (n=50)

S. No	Age group (in years)	Number of cases (%)
1	0-9	5 (10)
2	10-19	11 (22)
3	20-29	16 (32)
4	30-39	6 (12)
5	40-49	7 (14)
6	≥50	5 (10)

Table 2: Site of involvement in cutaneous tuberculosis (n=50)

Site of involvement	Number of cases (%)
Neck	10 (20)
Face (ear, chin, lips)	9 (18)
Trunk (chest and back)	8 (16)
Knee	6 (12)
Foot	6 (12)
Forearm/arm	4 (8)
Axilla	3 (6)
Gluteal and perianal region	3 (6)
Thigh	1 (2)

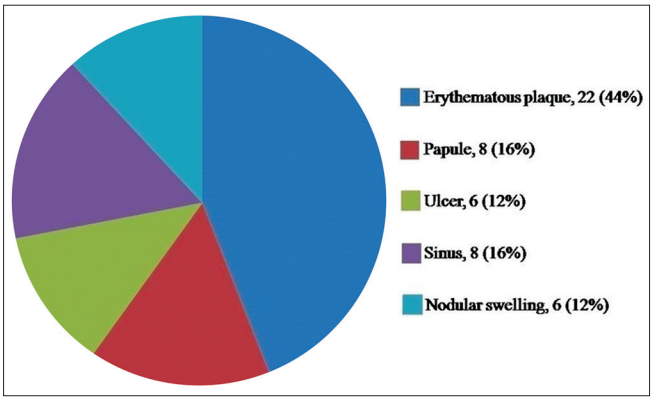

Figure 1: Spectrum of clinical appearances of lesions in cutaneous tuberculosis (n = 50)

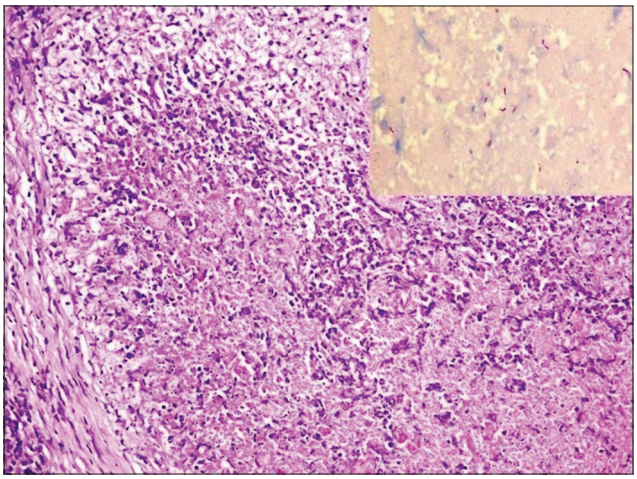

Figure 2: Caseating epithelioid cell granulomas in scrofuloderma (H and E, ×200). Inset shows acid-fast bacilli (Ziehl-Neelsen, ×1000)

Table 3: Composite features in different types of cutaneous tuberculosis (n=50)

Feature	Lupus vulgaris (%)	Scrofuloderma (%)	Tuberculosis verrucosa cutis (%)	Tuberculosis cutis orificialis (%)	Tuberculosis, non-specific (%)
Number of cases	24 (48)	11 (22)	4 (8)	1 (2)	10 (20)
Median age (years)	20	25	29.5	33	30.5
Male-female ratio	2:1	1:2.6	1:1	-	1: 1.66
Most common site involved	Face, 7 (29.2)	Neck, 5 (45.5)	Foot, 3 (75)	Face, 1 (100)	Lower limb, 4 (40)
Histopathology					
Epidermis					
Hypertrophy	18 (75)	2 (18.2)	4 (100)	-	3 (30)
Atrophy	2 (8.3)	1 (9.1)	-	-	2 (20)
Ulceration	4 (16.7)	8 (72.7)	-	1 (100)	5 (50)
Dermis					
Granuloma type	Tuberculoid	Tuberculoid	Tuberculoid	Tuberculoid	Ill-defined
Location	Upper dermis, 20 (83.3)	Entire dermis, 9 (81.8)	Mid dermis, 3 (75)	Entire dermis, 1 (100)	Variable
Langhans giant cells	23 (95.8)	10 (90.9%)	4 (100)	1 (100)	8 (80)
Inflammatory infiltrate	Lymphocytic, 21 (87.5)	Neutrophilic, 9 (81.8)	Neutrophilic, 3 (75)	Mixed, 1 (100)	Variable
Abscess formation	Absent	10 (90.9)	1 (25)	1 (100)	Variable
Caseation necrosis	5 (20.8)	7 (63.6)	3 (75)	1 (100)	2 (20)
AFB positivity	None	3 (27.3)	None	1 (100)	2 (20)

AFB: Acid fast bacilli

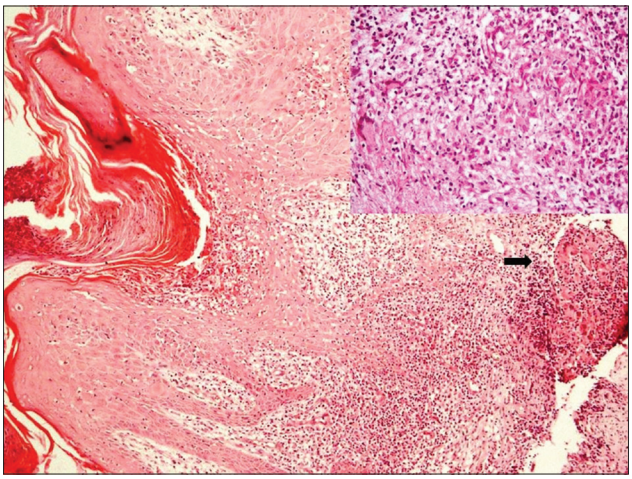

Figure 3: Hyperkeratotic acanthotic epidermis with epithelioid cell granulomas (black arrow) in tuberculosis verrucosa cutis (H and E, ×100). Inset shows Langhans giant cells (H and E, ×400)

Figure 4: Ulcerative lesion of lupus vulgaris on face

Figure 5: Scrofuloderma showing sinus tracts with onset of healing in response to anti-tubercular treatment

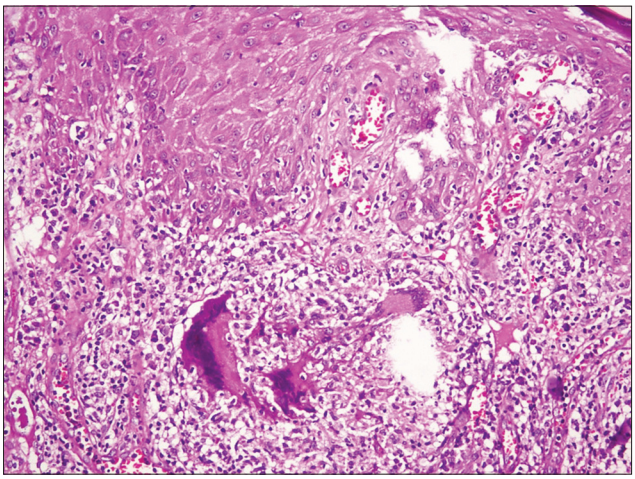

Figure 6: Histopathology of lupus vulgaris showing non-caseating epithelioid cell granuloma in the upper dermis (H and E, ×200)

In 42 patients, the clinical and histopathological diagnosis was similar with a positive correlation of 84%. Of these 42 patients, 22 patients had more than one differential diagnosis made on clinical grounds, which was later on confirmed as TB, on

histopathology. All the patients responded to standard therapy regimes under directly observed therapy short course with clinical response observed between 2 and 6 weeks of initiation.

DISCUSSION

Cutaneous TB is a rare form of extra-pulmonary TB. Non-specific and diverse clinical presentation, lack of knowledge, and histopathological variations are the factors leading to its under-estimation. Cutaneous TB is a chronic infective disorder of the skin with an estimated incidence of 0.1% of total patients visiting dermatology outpatient department [7]. In contrast to Europe and United States, the incidence is increasing in countries like India, Pakistan and other parts of Asia and Africa [8].

The infection is usually caused by *Mycobacterium* TB and rarely by *Mycobacterium bovis* or atypical mycobacteria [9]. As in other forms of TB, current or past history of TB is an important risk factor for the cutaneous presentation. It also shows a predilection for sites having skin trauma. In our study, three patients had a past history of TB and three gave a history of trauma at the site of infection. Based on the route of infection, Beyt *et al.* [10] classified cutaneous TB into exogenous and endogenous type which are also characterized by distinct clinico-histopathological features.

Cutaneous TB usually involves younger age group. In our study, 54% of patients were in 2nd and 3rd decade of life. Preponderance for the younger age has also been seen in other studies from India [11-13]. Skin trauma due to increased physical activity during younger age as well as contact with active TB cases at an early age may be the underlying factors for younger age predilection. However, average age of presentation is higher in few European studies [14,15]. This can be due to low TB prevalence in those geographical areas. In Indian subcontinent, males are more commonly affected than females whereas the situation is opposite in the western world [3,11,16,17]. However, male: female ratio was almost equal in our study, the cause of which can't be elucidated. The neck was the most common site of involvement in our study followed by the face and trunk. This was similar to the study by Solis *et al.*, [17] whereas limbs were the most common sites in other Indian studies [11,13]. The difference is partly due to the variation in the number of different clinical variants of cutaneous TB seen at different locations.

Based on the host immune response, the route of inoculation and previous sensitization, cutaneous TB can present in a number of clinical forms. Important varieties include TB chancre, miliary TB of the skin, lupus vulgaris, scrofuloderma, TB verrucosa cutis, tuberculous gumma, and TB cutis orificialis. Lupus vulgaris is considered to be the most common clinical variant of cutaneous TB [12,13,18,19]. It was also the most common form in our study. However a strong data from India and abroad, points toward scrofuloderma as the most common type [Table 4] [4,9,17]. Whereas a few researchers have reported TB verrucosa cutis, as the most frequent form in their studies [12,20].

Lupus vulgaris is a paucibacillary form of cutaneous TB that usually occurs by endogenous (hematogenous or lymphatic) spread of infection from an occult focus. It usually affects the immunocompetent patients. In contrast to our study, females are more often involved than males in lupus vulgaris [21]. In our study, out of total 24 patients with lupus vulgaris, around 50% had face and neck involvement and rest 50% had involvement of the lower limb and gluteal region. It may be related to differential route of spread in these groups. Scrofuloderma, another important clinical variant, occurs by contiguous (endogenous) spread of infection to the skin from underlying structures, most commonly lymph node, bone or joint. Understandably, neck, axilla, chest wall, and groin are the most probable sites involved. In our study, neck and axilla together constituted 75% of total cases of scrofuloderma. TB verrucosa cutis was the other common variant of cutaneous TB seen in our study. All 4 patients had lesions over their limbs which is commensurate with the evidence available in literature [11].

Due to non-specific clinicopathological picture and a low microbiological yield in tissue specimens, diagnosis of cutaneous TB is difficult as compared to other forms of TB. Most common differential diagnoses include leprosy, sarcoidosis, fungal infections, foreign body granulomas, leishmaniasis, and granulomatous syphilis. Histopathology is the best available diagnostic modality, which along with corroborative clinical features can give reasonable diagnostic confirmation. However, there is a lot of variability in the histopathological features in skin TB, which makes the job more difficult [4]. Moreover, it is not always possible to package cutaneous tuberculous lesions neatly into the specific categories and on occasion these are reported as "non-specific type," particularly in this current era of profound immunosuppression [22]. This was evident in our study also, where 10 patients could not be categorized and were labeled TB - non-specific type.

Table 4: Comparison of features of cutaneous TB among different studies

Feature	Patra *et al.* [17], 2006	Solis *et al.* [16], 2012	Chong *et al.* [18], 1995	Dwari *et al.* [10], 2010	Present study 2014
Number of cases	104	65	176	50	50
Male: Female ratio	2.25:1	1:3.6	1.2:1	1.2:1	1:1
Most common age group (in years)	5-15 and 16-25	-	44 (mean age)	16-25	20-29
Most common type	Lupus vulgaris	Scrofuloderma	Lupus vulgaris	Tuberculosis verrucosa cutis	Lupus vulgaris
Most common site	Lower limbs	Neck	Head and neck	Limbs and buttock	Neck
AFB positivity (%)	0	13.8	-	50.5	12

AFB: Acid fast bacilli, TB: Tuberculosis

Epithelioid cell granulomas with Langhans type giant cells constitute the classical histopathology of cutaneous TB. Important variations in the histopathological features seen among different clinical variants in our study included presence or absence of caseous necrosis and AFB positivity and well-formed or poorly formed granulomas. To a major extent, these variations are decided by the degree of host immune reaction. Hence, on one end of the spectrum histopathological picture is constituted by epithelioid granulomas with minimal necrosis and no AFB, indicating high immunity and on the other, the picture is of extensive necrosis with numerous AFB, indicating low immunity. In general, lupus vulgaris is seen at the high immunity end of spectrum, followed by TB verrucosa cutis and scrofuloderma toward the low immunity end [4]. Of 18 (36%) cases with caseous necrosis in our study, maximum proportion of cases was of scrofuloderma and TB verrucosa cutis (63.6% and 75%, respectively), whereas only 20.8% cases of lupus vulgaris demonstrated caseation. AFB were seen in 12% patients in our study which was similar to figures achieved by Solis *et al.* [17] and Gopinathan *et al.* [9]. AFB positivity was common in scrofuloderma and TB orificialis whereas no AFB was detected in cases of lupus vulgaris.

As already explained, a comprehensive evaluation of clinical and histopathological findings is the best diagnostic tool for cutaneous TB. Our study showed a significantly good correlation (84%) between the clinical and histopathological diagnosis. However, 8 (16%) patients in our study were detected to have TB on histopathology, even though the clinician did not suspect TB. A high index of clinical suspicion is often required.

CONCLUSION

The diagnosis of cutaneous TB is not straightforward as for other common bacterial infections. In view of the low probability of bacterial isolation, histopathology remains the best modality for its diagnosis. Knowledge about histopathological features of cutaneous TB and their variations among different clinical variants is important for an accurate diagnosis of this potentially treatable disease.

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