

# The picture of cutaneous tuberculosis today: New diverse clinical manifestations in the absence of the old lupus vulgaris in a series of 72 patients

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## Abstract

**Background** Lupus vulgaris as the main picture of the old cutaneous tuberculosis is no more existing at the time being but replaced by different and diverse cutaneous clinical features that can mimic other skin diseases.

**Objective** To record all patients with skin tuberculosis and to do full clinical and histopathological evaluation.

**Methods** This is case series descriptive study where all patients with cutaneous tuberculosis were recorded during the period from 2015-2021 years. Full demographic features were recorded and full clinical assessment was carried out. Classifications of clinical presentations were done. Skin biopsies for histopathological examination were performed. Tuberculin testing was done as confirmatory diagnostic aid especially when it is needed.

**Results** Seventy-two patients with cutaneous tuberculosis were seen and evaluated, their ages ranged from 6months-60 years with a median 28 years, with 42(58.33%) males and 30 (41.66%) females. The course of disease was chronic and the duration of rash ranged from 0.5-10 years. All parts of the body were affected, with limbs predominance 38(52.77%).The lower limbs were affected in 22 (30.55%) cases followed by upper limbs 16 (22.22%) cases , trunk 15 (20.83%), face 13(18%) and neck in 6 (8.33%) cases. In many patients, the initial lesions were inflammatory red cutaneous lumps and plaques that overtime change into different clinical lesions. The following clinical types were identified: cold abscesses and discharging sinuses were the most commonly diagnosed clinical variants as seen in 38 (52.77%) patients, followed by tuberculous chancre in 17 (23.61%), tuberculosis verrucosa cutis (warty TB) in 11 (15.27%) and orificial tuberculosis in 6 (8.23%) patients. No systemic involvement was documented in all patient apart from one patient with lung TB. No cases with classical lupus vulgaris were observed. The pathology of lesions were characteristically inflammatory lymphocytic granulomatous reactions.

**Conclusion** The old picture of cutaneous tuberculosis in form of lupus vulgaris is now no more existing and rarely observed but replaced by different cutaneous chronic pyogenic lesions like pictures of cold abscesses, cutaneous lumps, ulcers, sinuses and scarring, lupus pernio like and warty lesions. Chronic leishmaniasis should be regarded as the most common and an important differential diagnosis. Sarcoidosis although a rare disease but remains an important challenging differential diagnosis.

## Key words

Mycobacterium tuberculosis, cutaneous, cold abscesses, lupus vulgaris, scrofuloderma, tuberculin skin test, chronic leishmaniasis.

## Introduction

Tuberculosis (TB) is a major international health

problem and an important cause of morbidity and mortality throughout the world.<sup>1</sup> TB is still endemic in many countries, including Iraq.<sup>2</sup>

Cutaneous tuberculosis (CTB) is usually an uncommon form of extrapulmonary mycobacterial infection comprising 1-2% of all TB cases, mainly caused by *Mycobacterium TB*, and sometimes *Mycobacterium bovis*.<sup>3</sup>

Route of infection, the immune status of the host and virulence of the bacillus, are all these factors that determine the clinical types of CTB.<sup>4,5</sup>

CTB has diverse clinical forms. Endogenous infection of the skin may appear as scrofuloderma, tuberculous gumma, acute miliary TB, orificial TB, and lupus vulgaris (LV). Also, exogenous infection from direct inoculation of *Mycobacterium TB* can lead to tuberculosis verrucosa cutis (TVC) tuberculous chancre, and occasionally, LV. In addition, there are cutaneous tuberculids, which represent immune reactions against *Mycobacterium TB* or its antigens.<sup>6</sup>

The commonest old clinical pictures of CTB were LV and scrofuloderma. LV typically presents in adult life as erythematous patches and plaques commonly on the face consisting of papules and nodules so called apple jelly nodules especially when pressed by slide glass. On time there will be clearance at the center and extending peripherally leaving an unhealthy scar so called fire in a field. The head and neck area

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is the most commonly involved site. Without treatment, complete remission of LV rarely occurs. While lesions of scrofuloderma initially and clinically appear as lymphadenopathy typically of the neck and overtime rupture leaving chronic discharging sinuses and this is commonly seen among children. After remission, retracted tethered scars and keloids appear at the sites of infection.<sup>6,7</sup>

*Mycobacterium TB* is a straight, non-motile, non-sporulated, aerobic, threadlike rod measuring from 1 to 10µm long by 0.2 to 0.6µm wide. It is an acid- and alcohol-fast bacillus and the presence of high lipid content in its cellular wall makes it resistant to degradation after phagocytosis.<sup>8</sup>

The clinical presentations of CTB are varied, the causative bacterium is rarely identified by culture or staining, and atypical cutaneous lesions are common, all these factors make the diagnosis of CTB challenging. Several conditions may propose the diagnosis of CTB including: history, physical signs, pathology of the lesion, positive tuberculin skin test (TST), the presence of active tubercular lesion in any other organs and the responsiveness to anti-TB treatment.<sup>9</sup>

The histopathological examination of skin lesion might be enough to confirm the diagnosis of CTB. While the non-specific results of histopathological evaluation of many cases make the diagnosis doubtful and hence not helpful for diagnosis.<sup>10</sup> But the presence of histopathological granuloma at the positive TST is more suggestive for diagnosis of CTB, principally the active disease or has high risk of developing TB soon as well documented by a recent study.<sup>2</sup>

Diagnosis of CTB becomes difficult when the following differential diagnoses are taken into

thoughtfulness that include skin lesions due to chronic cutaneous leishmaniasis, atypical mycobacterium, deep fungal infections, sarcoidosis, staphylococcal abscess, syphilitic gumma, nocardiosis, leprosy and acne conglobata.<sup>11</sup>

So the aim of the current work is to do full clinical and histopathological study of all patients with skin TB and classify the different clinical pictures.

## **Methods**

This is case series descriptive study where all patients with cutaneous TB were recorded during the period from 2015-2021 years. Full demographic features were recorded and full clinical assessment was carried out. Clinical classifications of the different presentations were done. After informed consent from the patients, a thorough history and examination were made for every one including name, age, sex, address, profession, duration and site of the lesion, morphology and number of the lesions, associated tubercular lesion in any other organs, past medical and drug history, history of Bacillus Calmette Guérin (BCG) vaccination. Also family history of pulmonary or extrapulmonary TB were recorded.

Complete blood count (CBC), erythrocyte sedimentation rate (ESR), skin biopsy and chest X-ray were performed for all patients. TST was carried out for 28 (38.88%) selected cases in The Specialist National Center for Pulmonary Diseases to be seen after 48 to 72 hours and it is regarded positive when the diameter of the induration  $\geq 10$ mm.

When non-specific pathology of the TB lesion was seen, tuberculin testing was indicated and carried out. When it was positive, biopsy was done for histopathological assessment, and

when granuloma was seen in lesion of tuberculin test, this was diagnostic for active TB. This confirmatory testing was done for 12 (16.66%) cases and after 10 days of positive tuberculin, punch biopsies were done and sent for histopathological examination using Hematoxylin and Eosin (H&E) stain. Screening IGRA test was done for 10 (13.88%) patients.

Diagnosis of CTB was based on: (1) history; (2) clinical pictures confirmed by histopathology, TST, granulomatous reaction at the site of positive TST or Interferon Gamma-Release-Assay (IGRA); and (3) responsiveness to anti-TB drugs as a therapeutic testing.

Hence doubtful cases and when confirmatory testing was negative, therapeutic trial using anti-TB treatment was recommended.

## **Results**

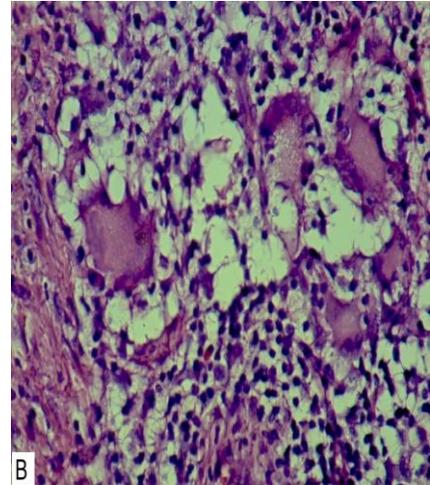
Seventy-two patients with CTB were seen and evaluated, their ages ranged from 8 months-60 years with a median 28 years, with 42 (58.33%) males and 30 (41.66%) females. The course of disease was chronic and the duration of lesions ranged from 0.5-10 years with a mean of 13 months. Multiple lesions were seen in 49 (68%) patients while solitary lesions were recorded in 23 (31.94%) patients. All parts of the body were affected, with limbs predominance in 38 (52.77%) patients. The lower limbs were affected in 22 (30.55%) cases, followed by upper limbs 16 (22.22%) cases, trunk in 15 (20.83%), face in 13 (18%) and neck in 6 (8.33%) cases. In many patients, the TB lesions started as panniculitis like picture and clinically appeared as red tender lumps and plaques (**Figure 1**) anywhere on the body with some fever and these lesions might stay for weeks and months with resolution with or without rupture and appearance of new lesions. The red lumps that rupture, will change over time into



**Figure 1** 25 year old female patient showing red lumps on chest and abdomen, some of them ruptured leaving atrophic pigmented lesions. Family history was positive as her sister had similar disease.



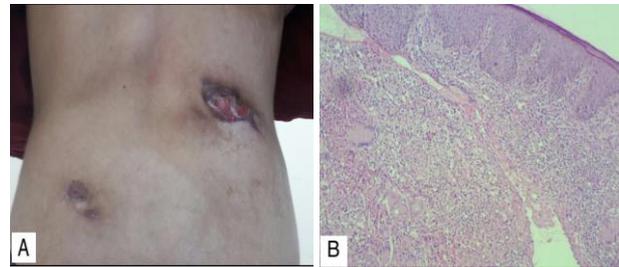
**Figure 2** Eighteen years old female patient showing multiple cold abscesses and discharging sinuses affecting both hands and forearms (A) and Hematoxylin and Eosin stained section from the same patient showing granuloma with epithelioid cells surrounding center necrosis and enveloped by lymphocytic infiltrate. (B; X 40).



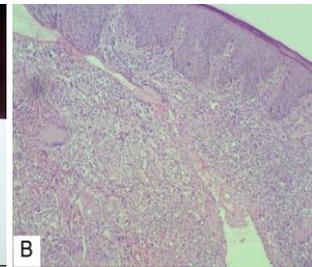
**Table 1** Showing the clinical types of cutaneous tuberculosis in relation to sex.

Clinical type	Sex	Number (%)
Cold abscesses; discharging sinuses	Male: 20	38 (52.77%)
	Female:18	
Tuberculous chancre	Male: 11	17 (23.61%)
	Female: 6	
Tuberculosis verrucosa cutis	Male: 7	11 (15.27%)
	Female: 4	
Orificial tuberculosis	Male: 4	6 (8.33%)
	Female: 2	

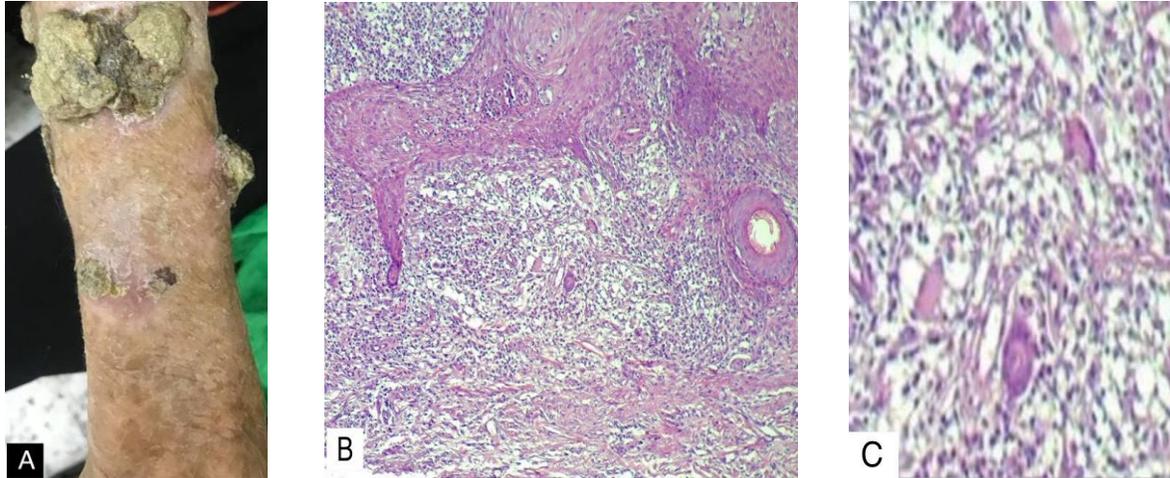
discharging sinuses and ulcers and some of these lesions become warty in appearance and according to depth and chronicity of lesions. Accordingly, the clinical presentations of the lesions were mainly multiple chronic cutaneous pyogenic like lesions in a form of cold abscesses, nodules, lumps, verrucous plaques, chronic ulcers, discharging sinuses and scarring. These lesions could be classified into the following types or variants (**Table 1**): cold abscesses and discharging sinuses was the most commonly diagnosed form as seen in 38 (52.77%) cases (**Figure 2**) followed by T. chancre in 17 (23.61%) (**Figure 3**), tuberculosis verrucosa cutis (TVC) in 11 (15.27%) cases (**Figure 4**) and orificial TB in 6 (8.23%) patients (**Figure 5**). These cases of orificial TB were



**Figure 3** Seventeen years old female patient showing multiple tuberculous chancre involving the trunk (A) and Hematoxylin and Eosin stained section from the same patient showing poorly developed granuloma with diffuse lymphocytic infiltrate through the entire dermis with single giant cell (B; X 10).



clinically similar to lupus pernio and appeared as a red lump inside nostrils. BCG scar was observed in 48 (66.66%) cases and BCG CTB in a form of scrofuloderma was detected in two infants. No systemic involvement was documented in any patient apart from one patient who showed pathological changes of lung TB on chest X-ray with the typical sign and symptoms of this disease. CTB was recorded in two sisters at the same time with no history of other family members for pulmonary or extrapulmonary TB. No cases with old lupus vulgaris were observed. Regarding the pathology of CTB, three pathological patterns



**Figure 4** Eleven years old female patient with skin tuberculosis showing multiple hyperkeratotic warty plaques involving the left forearm (A), Hematoxylin and Eosin stained section showing diffuse lymphocytic infiltrate where giant cells are embedded (B; 1X10) and higher magnification showing two small giant cells in the center of inflammatory reaction (C; X 40).

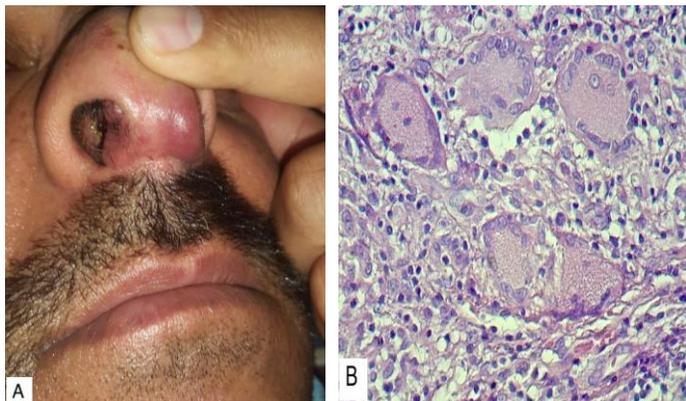
were seen and as follow:

1-18 (25%) patients showed granuloma with epithelioid cells surrounding central necrosis and enveloped by lymphocytic infiltrate (**Figure 2**).

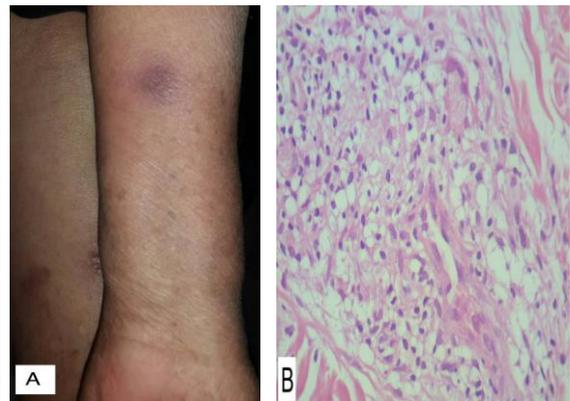
2-28 (38.88%) patients showed well-developed granulomatous reaction consisting of lymphocytic infiltrate surrounding giant cells but without epithelioid cells. 3-26 (36.11%) patients revealed no granuloma but there was diffuse lymphocytic infiltrate throughout the entire dermis including even the panniculus with

scattered giant cells inside the infiltrate (**Figure 3**).

The histopathological features of positive tuberculin testing also showed superficial and deep perivascular and periadnexial lymphocytic and lymphohistiocytic infiltrate, dermal edema and vascular dilatation with positive granuloma that was seen in 9(75%) out of 12 cases (**Figure 6**). ESR was high in 50(69.44%) cases. Of 30 cases, 21 (70%) revealed TST positivity (**Figure 6**) while IGRA was positive in 11 (91.66%) out of the 12 examined patients.



**Figure 5** Thirty-Five years old male patient showing orificial tuberculosis (pernio like) inside the nostril(A) and Hematoxylin and Eosin stained section from the same patient showing multiple giant cells inside diffuse lymphocytic infiltrate but without granuloma formation (B; X 40).



**Figure 6** Showing positive tuberculin skin test (A) and its histopathology revealed granulomatous reaction with single giant cell (B; X 40).

## **Discussion**

Tuberculosis is still a major health problem in the developing countries and the overall incidence of CTB is about 1-2% among all forms of TB.<sup>12</sup>

The present study showed that the age of the patients ranged from 8 months-60 years with a median 28 years with male predominance (58.33%). In addition, around 60% of patients in our study belonged to second and third decades of life although all age groups were affected. These results were comparable to other published articles.<sup>13-15</sup>

Overcrowding as a result of socioeconomic conditions may be an important contributory factor for this wide range of the affected ages.<sup>16</sup>

In Iraq and in the old days of TB and especially before 1980, pulmonary TB was a common and endemic while cutaneous TB was in a form of lupus vulgaris in adult age while TB of cervical lymph glands with discharging sinuses so called scrofuloderma was common among children. But since then these clinical pictures of cutaneous lesions were completely changed and replaced by new clinical patterns and variants as well documented by the present work.

Cold abscesses and discharging sinuses accounting for 52.77% of patients were the most commonly recorded clinical form, this finding also was reported in some published articles.<sup>17,18</sup> While in other studies LV was still the most commonly recorded clinical form.<sup>19,20</sup> The second presentation was tuberculous chancre (23.61%) and TVC (15.27%) of cases. While orificial tuberculosis was seen in 8.33% of patient. These findings were comparable with another study.<sup>21</sup>

The scenario of evolution of cutaneous pyogenic like infection of skin TB could be summarized

as follow: The TB lesions start as panniculitis and clinically appear as red tender lumps anywhere on the body with some fever and this might stay for weeks and months with resolution with or without rupturing and appearance of new lesions. These ruptured lumps might change into discharging sinuses and ulcers and some of these lesions become warty in appearance and according to the depth and chronicity of lesions. Regarding the lupus pernio lesions, these appear as red nodules and continue like that but rarely rupture into sinuses and ulcers.

The classical histopathological features of CTB are well-developed granulomas with or without caseous necrosis with multiple giant cells. The type of inflammatory infiltrating cells depends on the clinical type of CTB lesion and duration of the lesion whether acute or chronic.<sup>22-25</sup> While in the current study, 25% of cases showed granuloma with epithelioid cells surrounding center necrosis and enveloped by lymphocytic infiltrate while the remaining 75% of cases showed poorly developed granuloma consisting of well-defined lymphocytic infiltrate surrounding giant cells but without epithelioid cells and this variant was named lymphocytic granuloma. The other pathological presentation was in a form of severe diffuse inflammatory reaction mainly lymphocytic infiltrate invading through the entire dermis including even the panniculus but with a single or few giant cells embedded inside the infiltrate. This difference in the clinical presentation and histopathological pattern between our study and other published studies<sup>19-25</sup> could not be explained well, but we can speculate that there is either a change in the type of the bacilli from typical mycobacterium TB to atypical mycobacterium TB, or some immunological differences due to host genetic factors and socioeconomic circumstances.<sup>5,26</sup>

Another possible explanation that could explain this change in the behavior of TB is through the

epigenetics as through this mechanism, microbes can weaken the immune system and thus helps mycobacterium TB to survive in a better condition and environment and become more resistant to therapy. Through this epigenetics, we can also explain the epidemic of dermatophytes skin infection that is running now in Iraq, as fungi can change gene expression thus making skin more vulnerable for infection and chronicity of the disease and turning the skin into sabouraud culture media like.<sup>27,28</sup>

In the present work, 31.94% of patients had single lesion while 68% had more than one lesion. These results are comparable to Saher *et al.* study<sup>29</sup> and differ from Padmavathy *et al.* study<sup>30</sup> in which solitary lesions were the most common findings. This difference can be attributed to variation in the clinical types between current study and previous study and also, to differences in social habits.

In the current study, limbs were the most commonly affected sites as seen in 52.77% patients and this finding is in correspondence with another study conducted by Punia RS *et al.*<sup>15</sup> and this could be attributed to trauma sites.

Histopathological granuloma was seen at the positive site of TST in 75% of patients with positive tuberculin although the biopsy from the active skin lesion showed no granuloma in some patients and this is consistent with Sharquie *et al.* study.<sup>2</sup> So the presence of this tuberculin positive granuloma is a very helpful for diagnosis of active TB, especially in suspected cases in comparison with other laboratory investigations.

ESR was elevated in 69.44 % of our cases which is similar with another published article conducted by Supekar BB *et al.*, who recorded elevated ESR in 71.15% of cases.<sup>31</sup>

Although BCG scar was observed in 48 (66.66%) cases but it failed to protect from CTB for unknown reasons.

TST was positive in 70% of the examined patients. The sensitivity of this test varies widely among the diverse clinical pictures of CTB and it usually ranges from 33-96%.<sup>32</sup>

In 3 doubtful cases, clinically diagnosed as CTB but the histopathology and laboratory investigations did not confirm the diagnosis, in such cases, trial of an anti-TB treatment as empiric therapy was started. One month after treatment these cases showed marked improvement and continued the course of anti-TB treatment until complete remission. These results encourage dermatologists not to trust only laboratory investigations but clinical suspicion with the responsiveness to anti-TB treatment may give a good clue for diagnosis of CTB even in case of non-specific pathological results or negative results of laboratory investigations.

A large number of differentials needed to be excluded before reaching the final diagnosis such as chronic cutaneous leishmaniasis including leishmania recidivans,<sup>33,34</sup> sarcoidosis, deep fungal infections, staphylococcal abscess, atypical mycobacterial infections, nocardiosis, leprosy, syphilitic gumma, acne conglobata and panniculitis.<sup>11,35</sup> The possibility of CTB was raised in our cases due to high prevalence of TB in this country and the cutaneous lesions were chronic. In addition, laboratory investigations, histopathological results. Furthermore, the responsiveness to anti-TB treatment in doubtful cases as confirmed by the present work was very helpful for diagnosis and management.

## **Conclusion**

Lupus vulgaris represents the old picture of

cutaneous tuberculosis is now almost completely vanished and replaced by chronic pyogenic skin infection like and in pictures of cold abscesses, skin lumps, ulcers, sinuses and scarring ,lupus pernio like and warty lesions. Chronic leishmaniasis as a common disease especially leishmania recidivans is the most common important differential diagnosis. Sarcoidosis although a rare disease but still remains challenging differential diagnosis. Tuberculin-positive granuloma and responsiveness to anti-TB treatment are supportive diagnostic methods used to confirm the diagnosis in doubtful cases.

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