CASE REPORT

Case Report: Culture negative cutaneous tuberculosis [version 1; peer review: 1 approved with reservations, 1 not approved]

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Abstract
Cutaneous tuberculosis (TB) can present in a number of ways, making it difficult to diagnose. It most commonly presents as scrofuloderma, which commonly affects the supra-clavicular region, axilla and the cervical region. All the different presentations of cutaneous TB should be known to clinicians, in order to diagnose it early. The objective of this article is to describe a case of scrofuloderma presenting with different cutaneous lesions at the same time, which were culture negative. We present a 23-year-old male with no known co-morbidities, presenting to us with fever and multiple swellings on the body. Cultures of pus and blood were negative for TB; GeneXpert detected the microorganism. Cutaneous TB, although a rare disease with wide spectrum of cutaneous lesions, should be considered in differential diagnosis of cold abscesses and nodules, especially of the head and neck region.

Keywords
Tuberculosis, Scrofuloderma, Cutaneous Tuberculosis, Cold Abscesses

This article is included in the World TB Day collection.
Introduction

Tuberculosis (TB) is a systemic illness caused by a rod-shaped bacillus, *Mycobacterium tuberculosis*. It is usually pulmonary. Cutaneous TB constitutes 1–2% of extrapulmonary TB and 0.15% of skin diseases; this is significant, considering the overall prevalence of TB is 2% per year\(^1\–^4\).

Cutaneous TB can present in a number of ways clinically, during histopathology as well as in treatment response, making it difficult to diagnose. These cases should be recognized early for timely and accurate management\(^4\–^5\). Cutaneous TB most commonly presents as Tuberculosis cutis colliquativa (also known as scrofuloderma), a type of cutaneous TB presenting with cold abscesses and commonly affecting the supraclavicular region, axilla, and the cervical region\(^6\). Lupus vulgaris (LV) is another less common manifestation of TB\(^7\). Some rarer ones include inguinal scrofuloderma, ulcerative type of LV, and acute military cutaneous TB\(^3\). Cutaneous TB is usually confined to the skin but can be multifocal\(^8\).

Here, we describe a case of scrofuloderma presenting with different cutaneous lesions at the same time, which were culture negative for TB.

Case presentation

A 23-year-old male laborer, with no known co-morbidities was admitted to Jinnah Postgraduate Medical Centre, Karachi, Pakistan in March 2018, with complaints of fever for 18 months and multiple swellings on different parts of the body for 12 months.

According to the patient, he had developed a fever, which was gradual in onset, low grade (100°F), intermittent, occurring mostly in the evening and relieved by taking Paracetamol. The fever was not associated with rigors or chills. After six months of fever, the patient noticed multiple swellings of variable size on different parts of body, which included the right lower back, left lower base of neck, upper part of middle chest, front of right ear and upper surface of right foot. The largest swelling was over the back. Swelling was gradual in onset, increasing in size, ranging from lemon size (upper surface of foot) to melon size (abdomen), associated with discharge from left lower neck and chest swelling. Discharge was yellowish in color with no blood in it and was not associated with itching or pain.

The patient had a history of undocumented weight loss for one year and using antipyretics and proton pump inhibitors (Omeprazole, 20mg once daily). The rest of the history was unremarkable.

On general physical examination, the patient was average height and thinly built, cooperative, with visible parotid swelling, which was non-tender, soft in consistency, size ranging from 5cm to 7cm, associated with discharge from left lower neck and chest swelling. Discharge was yellowish in color with no blood in it and was not associated with itching or pain.

The patient had a history of undocumented weight loss for one year and using antipyretics and proton pump inhibitors (Omeprazole, 20mg once daily). The rest of the history was unremarkable.

On ultrasound of the abdomen, the liver was 14cm and spleen was 11.7cm in size with normal borders. A psoas abscess was found measuring 11×11.9cm with septations and calcifications. Fine-needle aspiration cytology of the cheek swelling showed necrotizing inflammation. Fungal stain was negative and skin
split test for Leishmania donovani bodies was also negative. Mycobacterium tuberculosis was detected after GeneXpert analysis of the pus from the psoas abscess, which had previously shown no growth on culture. Blood culture was also negative. Computed tomography of chest with contrast showed multiple fluid collections at right supraclavicular region, anterior chest wall and along with bilateral psoas abscess formation predominantly on right side.

Initially, a differential diagnosis of deep fungal infection (actinomycosis), cutaneous leishmaniasis, lymphoma and TB was made. After GeneXpert, HIV serology, and fungal stain were performed, cutaneous tuberculosis (scrofuloderma) was the final diagnosis and anti-tuberculous therapy was started. After consulting the Dermatological Department, Lupus vulgaris was also ruled out. A standard regimen of four drugs, i.e. Isoniazid (5 mg/kg), Rifampin (10 mg/kg), Ethambutol (20 mg/kg), and Pyrazinamide (24 mg/kg), in combined form, i.e. Tablet Myrin-P-Forte 4 x daily, was given for two months and converted to the combination of Isoniazid and Rifampin in combined form, i.e. Tablet Rifna 4 x daily, for a further 8 months. The patient was discharged after 8 days and kept on regular follow-up.

### Discussion

The incidence of TB is increasing worldwide, which may be due to the growing number of HIV cases and resistance to antituberculous drugs⁴. Immunocompromised individuals have a greater propensity to get this disease. Cutaneous TB is either transmitted via a hematogenous route or direct extension from a primary focus, which is elsewhere in the body, usually pulmonary. However, primary infection can also occur by direct introduction of the microbe into the skin or mucosa of a susceptible individual by trauma or injury⁵.

In our case, no primary source was found in any organs and there was no history of TB contact. Moreover, there was no reason to identify the patient as immunocompromised.

### Table 1. Patient laboratory results on admission and 8 days later.

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Initial examination after admission</th>
<th>8 days after admission</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>9.5 g/dL</td>
<td>10.9 g/dL</td>
<td>13.8–17.2 g/dL</td>
</tr>
<tr>
<td>Total leukocyte count</td>
<td>10 ( \times 10^9 )/L</td>
<td>7 ( \times 10^9 )/L</td>
<td>4.5–11.0 ( \times 10^9 )/L</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>85%</td>
<td>59%</td>
<td>50-70%</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>12%</td>
<td>36%</td>
<td>30-45%</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>1%</td>
<td>3%</td>
<td>0-3%</td>
</tr>
<tr>
<td>Monocytes</td>
<td>2%</td>
<td>2%</td>
<td>0-6%</td>
</tr>
<tr>
<td>Platelet count</td>
<td>530 ( \times 10^9 )/L</td>
<td>251 ( \times 10^9 )/L</td>
<td>150–400 ( \times 10^9 )/L</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>28.7%</td>
<td>34.7%</td>
<td>37–47%</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td>78.2 fl</td>
<td>82.4 fl</td>
<td>80–98 fl</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>13 mg/dL</td>
<td>-</td>
<td>7–20 mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.9 mg/dL</td>
<td>-</td>
<td>0.6–1.2 mg/dL</td>
</tr>
<tr>
<td>Sodium</td>
<td>139 mEq/L</td>
<td>-</td>
<td>135–145 mEq/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.6 mEq/L</td>
<td>-</td>
<td>3.5–5.5 mEq/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>96 mEq/L</td>
<td>-</td>
<td>97–107 mEq/L</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.72 mg/dL</td>
<td>0.46 mg/dL</td>
<td>0.1–1.2 mg/dL</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>0.12 mg/dL</td>
<td>0.12 mg/dL</td>
<td>0.1–1.2 mg/dL</td>
</tr>
<tr>
<td>Indirect bilirubin</td>
<td>0.6 mg/dL</td>
<td>0.34 mg/dL</td>
<td></td>
</tr>
<tr>
<td>SGPT</td>
<td>24 units/L</td>
<td>25 units/L</td>
<td>7–56 units/L</td>
</tr>
<tr>
<td>Gamma-glutaryl transpeptidase</td>
<td>87 units/L</td>
<td>78 units/L</td>
<td>8–40 units/L</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>435 units/L</td>
<td>450 units/L</td>
<td>150–480 units/L</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>10.2 seconds</td>
<td>-</td>
<td>9.1-13.1 seconds</td>
</tr>
<tr>
<td>Activated partial thromboplastin time</td>
<td>25 seconds</td>
<td>-</td>
<td>22.9-34.5 seconds</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>1.0</td>
<td>-</td>
<td>0.9-1.3</td>
</tr>
</tbody>
</table>
Cutaneous TB rarely involves the region of head and neck, especially lymph nodes, larynx, oropharynx, salivary glands, nose, ear, skin, and paranasal sinuses. Our patient had bilateral cervical and inguinal lymphadenopathy, parotid swelling, an ulcerated lesion on the chest, a right lumbar swelling, and a scar on the left supra-clavicular region. This distribution also favored our final diagnosis of scrofuloderma.

Due to the different type of lesions, correct diagnosis may be delayed because investigations fail to detect TB, as in our case where cultures were negative and TB was only detected by GeneXpert.

Conclusion
Our case illustrates that scrofuloderma, although a rare disease with a wide spectrum of cutaneous lesions and higher rates of false negative investigations, should still be considered in differential diagnosis of cold abscesses and nodules, especially of the head and neck region.

Data availability
No data are associated with this article.

Consent
Written informed consent for publication of their clinical details was obtained from the patient.

Grant information
The author(s) declared that no grants were involved in supporting this work.

References


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Version 1

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- The author wants to discuss cutaneous tuberculosis, but the case is not fitting in any spectrum of cutaneous tuberculosis.

- Irrelevant case history has been mentioned without diagnostic features of cutaneous tuberculosis.

- Histopathology of any lesions has not been mentioned.

- There is more description of cold abscess rather than cutaneous tuberculosis.

- Ideally culture for AFB is positive in hardly 5% cases of cutaneous tuberculosis. So what is the meaning of given title and conclusion?

- The case looks like extrapulmonary tuberculosis, rather than cutaneous tuberculosis.

- The morphology of cutaneous lesions is not fitting in description of cutaneous tuberculosis. So, with this title and description, this manuscript is not acceptable for indexing.

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Partly

Is sufficient discussion included of the importance of the findings and their relevance to
future understanding of disease processes, diagnosis or treatment?
No

Is the case presented with sufficient detail to be useful for other practitioners?
No

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Dermatology and Leprosy.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to state that we do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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Scrofuloderma itself is not uncommon in countries endemic for TB. The main reason for the presentation of the case is the multiplicity of abscesses, a rare presentation of the scrofuloderma. Some sentences need to be better built and emphasize this point: “a type of cutaneous TB presenting with *solitary or few* cold abscesses and commonly affecting the supraclavicular region, axilla, and the cervical region." Here, we describe a case of scrofuloderma *with an uncommon presentation* (presenting ) with many cutaneous lesions at the same time, which were culture negative for TB.

The authors contradict themselves when writing in the introduction “Cutaneous TB *most commonly* presents as Tuberculosis cutis colliquativa (also known as scrofuloderma), a type of cutaneous TB presenting with cold abscesses and commonly affecting the supraclavicular region" and then in the discussion “Cutaneous TB *rarely* involves the region of head and neck, especially lymph nodes, larynx, oropharynx, salivary glands, nose, ear, skin, and paranasal sinuses”. These sentences should be rewritten or remove the phrase from the discussion.

Rewrite the phrase “Our case illustrates that scrofuloderma, although a rare disease with a *wide spectrum of cutaneous lesions* and higher rates of false negative investigations, should still be considered in differential diagnosis of cold abscesses and nodules, especially of the head and neck region...” There is no “wide spectrum of cutaneous lesions“ but rather different locations of lesions, some rare as the lesion of the chest and foot.
Clarify the phrase “After GeneXpert, HIV serology, and fungal stain were performed, cutaneous tuberculosis (scrofuloderma) was the final diagnosis and anti-tuberculous therapy was started.” Did you investigate HIV, fungus only after the TB diagnosis? There was no emphasis in the text that HIV serology was negative.

The following phrases should be deleted from the text:
- “Cutaneous TB can present in a number of ways clinically, during histopathology as well as in treatment response, making it difficult to diagnose. These cases should be recognized early for timely and accurate management⁴,⁵.”
- “Lupus vulgaris (LV) is another less common manifestation of TB⁷.”
- “After consulting the Dermatological Department, Lupus vulgaris was also ruled out.”
- “Moreover, there was no reason to identify the patient as immunocompromised.”
- “Some rarer ones include inguinal scrofuloderma, ulcerative type of LV, and acute military cutaneous TB3. Cutaneous TB is usually confined to the skin but can be multifocal⁸.”

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Tuberculosis, leishmaniasis, psoriasis.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
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