

# A Case Report: Classical Clinical Presentation of Scrofuloderma Confirmed with Novel Laboratory Workups

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Abstract: Scrofuloderma, can develop on the skin through direct extension from an endogenous source of tuberculosis such as lymph node. This report presents a case of scrofuloderma in its classical presentation in a 41-year-old man, who suffered from a three-week history of a painless swelling that ulcerated. Physical examination revealed two tender nodules on the left anterior neck and armpit. The diagnosis was confirmed by the presence of an underlying focus of infection tuberculous lymphadenitis, positive results of *Mycobacterium tuberculosis interferon-gamma release assay* (IGRA), Xpert MTB/RIF, and histopathological examination. Treatment with anti-tuberculosis regimen resulted in an excellent outcome.

## 1 INTRODUCTION

Cutaneous tuberculosis is a chronic infection of the skin by *Mycobacterium tuberculosis*, and less commonly by *M. bovis* and *M. atypical*. (Santos JB et al., 2014). It is relatively rare and accounts for 1% of extrapulmonary tuberculosis. In the Asian community, most cases are between the ages of 10 and 50 years. (Ho SCK, 2003). Scrofuloderma, also known as *tuberculosis cutis colliquative*, is a common form of cutaneous tuberculosis followed by other forms e.g., tuberculosis verrucosa cutis and lupus vulgaris (Sethi et al., 2012; Haase O et al., 2014).

The development of clinical manifestations in scrofuloderma should be understood as the result of interactions among the environment, agent, and host. (Santos JB et al., 2014). It most commonly occurs in the neck from underlying tuberculosis in a deeper structure, usually a lymph node, bone, and joint. Starting with lymphadenitis, lymph node attachment with surrounding tissue causes peri adenitis, which becomes doughy and progresses to liquefaction. A cold abscess is formed, and the skin erodes to form a discharging sinus and fistula formation. The fistula estuary extends and forms an ulcer. It is

characterized by elongated, irregularly shaped, granulated tissue at the base, and covered with seropurulent discharge. The ulcer may be healed with scarring (Santos JB et al., 2014; Sethi et al., 2012; Lai-Cheong JE et al., 2007).

Diagnostic steps usually begin with history taking, physical examination, and confirmation tests, e.g., polymerase chain reaction, tissue culture, tuberculin skin test, and histopathology.<sup>2,6</sup> Treatment of scrofuloderma is similar to pulmonary tuberculosis. World Health Organization (WHO) recommends regimens consisted of four drugs, isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) given to intensive and continuation phases. (Ho SCK, 2003; Kar S et al., 2011).

The following report showcases several techniques, some with their shortcomings, that may be utilized to improve the accuracy of diagnosis in a clinically characteristic presentation of scrofuloderma.

## 2 CASE

A 41-year-old man presented with a three-week history of multiple ulcers on the upper chest and neck (Figure 1). It started from a painless neck masses six

months before a consultation, that gradually increased in number and size. They suppurated and broke down, forming ulcers with granulating tissue. There was no other trauma.

Systemic examination did not reveal drenching night sweats and unexplained pyrexia. Nonetheless, approximately 2 kilograms of weight loss in the last two months was admitted. He had neither significant childhood lung disease or tuberculosis background and had received BCG vaccination.

Physical examination from the upper chest and bilateral supraclavicular skin revealed multiple ulcers measured approximately 4x3 cm, with suppuration and granulation tissue at the base and deeply undermined edges.

Routine laboratory work-ups were unremarkable except for an elevated erythrocyte sedimentation rate (ESR) 25 mm/hr. *Mycobacterium tuberculosis* interferon-gamma release assay (IGRA) was positive (1.61 IU/mL). Histopathological examination showed epithelioid granulomas with a variable number of Langhans giant cell and lymphocytes (Figure 2)

On a subsequent visit, there were new two fixed tender swelling in the left anterior neck and left axillary (Figure 3). Physical examination showed multiple nodular swelling measuring approximately 4x3 cm and 3x3 cm, fixated, doughy, without signs of acute inflammation. The patient was consulted to pulmonology division.

Further investigations had been carried out, such as fine-needle aspiration biopsy (FNAB). The result showed abscess material with lymphocytes, histiocyte, neutrophil, with marked caseation necrosis area. *Mycobacterium tuberculosis* was detected using the Xpert MTB/RIF. Chest x-ray was normal. Another workup, including polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*, mycobacterial culture, *Mycobacterium* other than tuberculosis culture, sputum culture, and tuberculin skin test showed negative findings.

Furthermore, the patient started standard anti-tuberculosis treatment consisting of four drugs, rifampicin, isoniazid, pyrazinamide, and ethambutol. After two months of therapy with anti-tuberculosis regimens, he reported improved symptoms. No new nodules had evolved (Figure 4).



Figure 1. An ulcerated lesion with purulent fistula in the supraclavicular region.

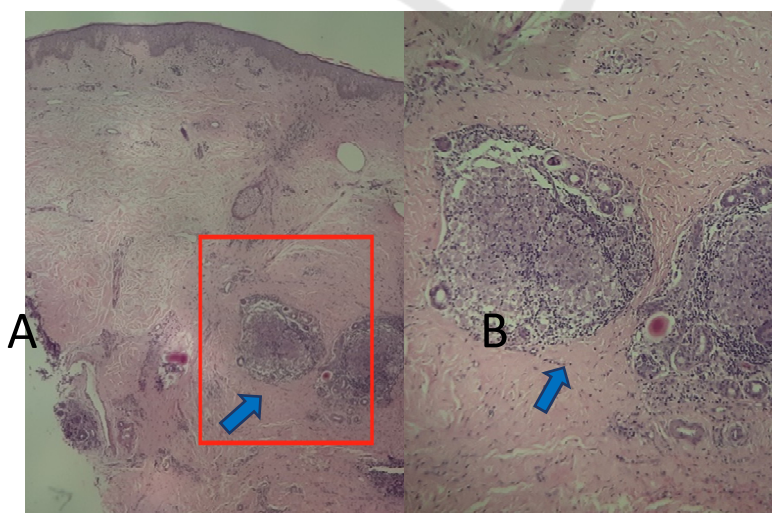


Figure 2. Epithelioid granulomas, 100x (A), 400x (B) (hematoxylin-eosin)



Figure 3. Cervical and axillary tender fixed masses

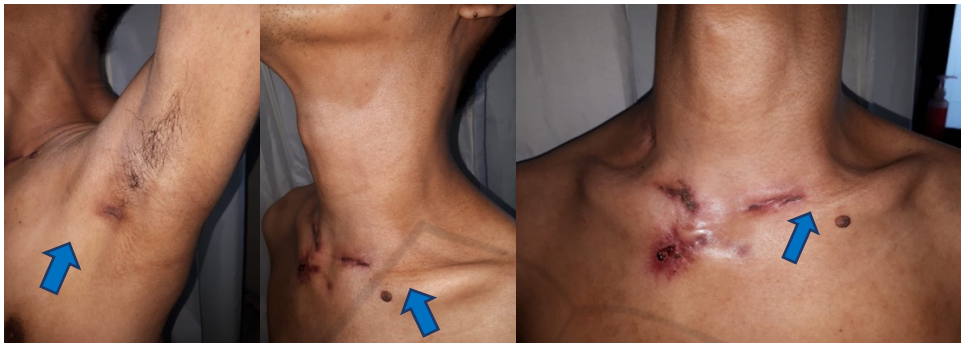


Figure 4. Lymphadenopathy has improved after two months of treatment.

### 3 DISCUSSION

Scrofuloderma is increasingly recognized as the most common form of cutaneous tuberculosis in adults (Pasmayathy L et al., 2008). This patient was 41 years old, included in the profoundly affected population who often have scrofuloderma. The presentation of cutaneous tuberculosis depends on the pathogenicity of the mycobacteria, route of infection, and the level of host cell-mediated immunity (CMI). Scrofuloderma lesions begin as subcutaneous nodules which become doughy and progressive liquefaction. (Santos JB et al., 2014; Ho SCK, 2003; Frankel A et al., 2009). The fistula estuary extends and forms an ulcer. It is characterized by suppuration and granulation tissue at the base and deeply undermined edges.<sup>2</sup>In our case, they started as painless swelling overlying his upper chest and neck six months ago. The masses gradually enlarged into cold abscess formation. It suppurates and breaks down, forming an ulcer with granulation tissue at the base covered with purulent discharge.

Scrofuloderma is caused by dormant tuberculosis reactivation. There is contiguous involvement of overlying skin from the underlying focus infection such as tuberculous lymphadenitis. Scrofuloderma

from tuberculous lymphadenitis often affects the neck, axillae, chest wall, and groin. (Ho SCK, 2003; Aliaagaoglu et al., 2015). As can be seen in the present case, the area of predilection was the neck and axillae, which were the familiar site of scrofuloderma. Moreover, there were two tender swellings occurred in the left supraclavicular and axillary region, which were tuberculosis lymphadenitis. The left supraclavicular and axillary nodes receive lymphatic drainage from the thoracic duct causing of a lesion at multiple sites. In scrofuloderma, the host has moderate cell-mediated immunity. Following infection, macrophages that circulate to lymph nodes and then haematogenic spread to other parts of the body phagocyte the mycobacteria. (Santos JB et al., 2014). Macrophages act as antigen-presenting cells and interact with T lymphocyte. (Ho SCK, 2003). When the mycobacteria survive, in which they divide within the macrophages. It is inducing the production of cytokines such as IL-6, IL-12, IL-1 $\alpha$ , and IL-1 $\beta$ , resulting in the recruitment of monocytes, lymphocytes, neutrophils, and dendritic cells.<sup>1</sup>The persistent presence of these interleukins stimulating macrophages will ultimately lead to their differentiation into epithelioid and giant cells, which will be more or less organized into granulomas



according to individual host factors. (Santos JB et al., 2014) This explains the histopathology finding that may show marked caseation necrosis and abscess material with mixed inflammatory infiltrations dominate the center of the lesion. (Santos JB et al., 2014). Besides, a presence of characteristic tubercular granulomas with epithelioid cells in the dermis is observed in 57%–96% of the samples. (Rahman et al., 2018) showed only 16.7% cases whereas granuloma with caseous necrosis found in the dermis. On the other hand, 55.6% the majority of the cases showed granuloma without caseous necrosis.<sup>12</sup> Although not typical, a histopathological examination from skin showed the presence of epithelioid cell granulomas with a variable number of Langhans giant cell and lymphocytes infiltrates in the dermis. Central caseation necrosis was found from FNAB, therefore support the diagnosis of tuberculosis lymphadenitis. Some acid-fast bacilli can be found (Ho SCK, 2003). This patient's bacteriological examination showed no acid-fast bacilli. This is in line with the literature which stated that bacteriological examination did not always find acid-fast bacilli although a higher bacterial load. (Ho SCK, 2003). Mycobacterial culture is the gold standard for determining the presence of active TB infection. (Ho SCK, 2003). However it is not always possible to obtain a positive result. Positivity is lower in an exclusively cutaneous presentation, that is around 23% (Santos JB et al., 2014; Frankel A et al., 2009). Polymerase chain reaction is used primarily as a complement to clinicopathological evaluation. It was reported in another study that one out of three scrofuloderma patients had a positive PCR finding (Santos JB et al., 2014; Tan WP et al., 2007). Positive PCR result is not always obtained. In the diagnosis of cutaneous TB, the sensitivity and specificity of PCR vary greatly from literature. Detection of *Mycobacterium tuberculosis* by a PCR in this patient turned out to be negative.

A diagnosis of tuberculous lymphadenitis with a cutaneous extension (scrofuloderma) has been made. It was confirmed by history taking, clinical features, a positive result on IGRA, Xpert MTB/RIF, and histopathological findings. The patient was quickly started on an anti-tubercular treatment regimen that included isoniazid, rifampicin, ethambutol, and pyrazinamide. The cutaneous lesion regressed, and the ulcer starts healing.

#### 4 CONCLUSION

In this patient, scrofuloderma occurs as a result of extension from underlying tuberculous

lymphadenitis. By proper history taking and morphologic features examination, a preliminary diagnosis can be made, that must be followed by the best methods available. Here our case had shown that although mycobacterial culture and PCR test failed to yield positive findings, IGRA, Xpert MTB/RIF, and histopathological evaluations provided the conclusive results. That the patient responded well to treatment was another proof of the infection.

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