

# Multiple diagnostic examinations are effective for the early diagnosis of scrofuloderma

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## ABSTRACT

Although scrofuloderma is the most common subtype of cutaneous tuberculosis, its diagnosis is often delayed. In this case, ciprofloxacin was first administered as only *Pseudomonas aeruginosa* was detected by initial culture tests. *Mycobacterium tuberculosis* is usually susceptible to quinolone antibiotics, hence the partial improvement in inflammatory symptoms and subsequent delay in diagnosis. Our case serves as a reminder that we should always be aware of the possibility of cutaneous tuberculosis being the cause of an abscess, especially when the abscess is not completely resolved by antibiotics. Moreover, our case reminds us that it is necessary to conduct repeated culture tests, rather than relying purely on polymerase chain reaction (PCR) results, given that cases of PCR-negative acid-fast bacilli (AFB) culture-positive scrofuloderma have been reported. Fine needle aspiration is a less invasive and useful way to collect culture samples.

**KEYWORDS:** scrofuloderma, tuberculosis, acid-fast bacilli, polymerase-chain reaction, fine needle aspiration

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## Case presentation

A man in his 50s visited our department with a 3-month history of an erythematous swelling in the right neck. The lesion gradually ulcerated, with discharge. Anterior cervical discectomy and fusion had been performed 7 months earlier. He had a history of cervical spondylosis and was on peritoneal dialysis for chronic kidney disease. He had no history of immunosuppressant use or tuberculosis contact. At the first visit, a painless erythematous swelling was observed in the right cervical region (Fig 1a). A cervical computed tomography (CT) scan indicated a subcutaneous abscess, with enlarged lymph nodes (Fig 1h). One

week after the first visit, the symptoms had progressed and he was hospitalised. *Pseudomonas aeruginosa* was detected by pus culture, and oral ciprofloxacin and intravenous ceftazidime were administered. A skin biopsy from the swelling revealed necrosis and epithelioid granuloma in the papillary dermis, but no bacteria. Four days after discharge, the symptoms had improved, but two nodules remained in the right neck. A skin biopsy from a nodule revealed granulomatous inflammation with necrosis. Since neither fungi nor bacteria were observed by Grocott staining or Ziehl-Neelsen staining, and the biopsy specimens were culture-negative, antibiotics were terminated 1 week after discharge. Five weeks after discharge, a subcutaneous mass with an erythematous surface appeared in the right axilla (Fig 1b). The patient was re-examined and hospitalised. Cervical and chest CT showed a suspected subcutaneous abscess in the right axilla (Fig 1i). Bloods showed a white cell count of 11,800/ $\mu$ L (of which 73% neutrophils), and a C-reactive protein level of 9.86 mg/dL. Methicillin-resistant *Staphylococcus epidermidis* grew from a pus culture. The patient was treated with vancomycin for 2 weeks, after which the inflammatory symptoms improved, and the subcutaneous mass developed into hard nodules. He was subsequently discharged. One day later, severe pitting oedema appeared over the entire right arm (Fig 1c). The nodules seemed to compress the lymphatic vessels and had caused lymphoedema.

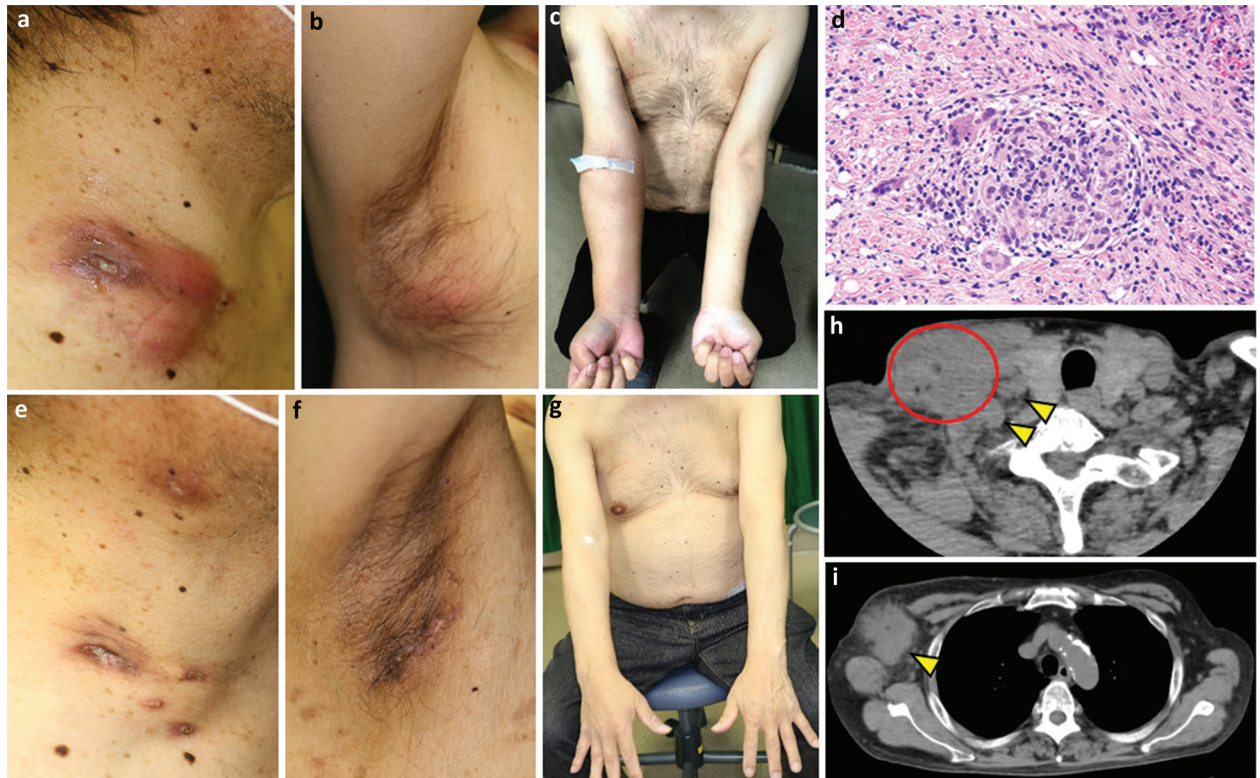
## Diagnosis

Differential diagnoses included a post-operative wound-related infection (initially), suppurative cervical lymphadenitis, an undiagnosed immunodeficiency, or an acid-fast bacillus (AFB) infection. A post-operative infection was quickly dismissed after abscesses appeared from sites unrelated to the cervical fusion. Suppurative cervical lymphadenitis was a likely differential, with abscesses in the anterior triangle of the neck and axilla. However, the growth of *Pseudomonas*, rather than *Staphylococcus aureus*, was somewhat unusual for the development of suppurative cervical lymphadenitis. Any immunodeficient state could predispose patients to recurrent infections and is always worth considering, but we found absolutely no evidence of the sort in this patient. The remaining differential diagnosis was AFB infection.

## Case progression and outcome

A needle biopsy from a nodule in the right axilla showed granulomatous lymphadenitis suspicious of AFB infection. A PCR

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**Fig 1. Clinical features and histopathological findings.** (a) At the first visit, egg-sized swelling with redness in the right neck was recognised, accompanied by yellowish-white drainage. (b) Erythematous swelling was seen in the right axilla, and the yellowish discharge observed by incision. (c) Pitting oedema was observed over the entire right arm prior to treatment, and the arm diameter difference is significant (right arm diameter: 29.3 cm; left arm diameter: 25.1 cm). (d) Epithelioid cell granuloma with caseous necrosis was recognised, and multinucleated giant cells were also observed in a tissue sample from the right axillary lesion (hematoxylin-eosin stain, original magnification  $\times 200$ ). (e,f) After 3 weeks of anti-tuberculosis medication administration, the redness and swelling have improved, leaving slight scarring on the neck (e) and the subcutaneous mass is almost unpalpable in the axilla (f). (g) The oedema in the right arm has improved and the forearm diameters have become almost the same. (h) On a CT scan at the first visit, a large soft-tissue mass (red circle) is observed from the subcutaneous region in the right cervix to the upper clavicle. From some low-density areas, the mass was suspected of being an abscess. Multiple swollen lymph nodes (yellow arrowheads) are recognised around the mass. (i) In a CT image obtained when the axillary swelling appeared, an irregularly shaped subcutaneous mass (yellow arrowhead) of 5.5 cm in diameter is seen in the right axilla. Non-uniform low-density areas are observed in the mass, and the density of the adipose tissue surrounding the mass is increased. Thus, the mass was also suspected of being an abscess.

test for *M tuberculosis* was negative, but T-SPOT was positive. Chest CT showed no lesions suggesting tuberculosis, and sputum cultures were negative. *M tuberculosis* complex was detected from the long-term culture of the cervical pus collected by fine needle aspiration (FNA), and from partially resected right axillary tissue. A partial biopsy from the right axilla demonstrated epithelioid cell granuloma with caseous necrosis (Fig 1d). Thus, the patient was finally diagnosed with scrofuloderma. Isoniazid, ethambutol, rifampicin and pyrazinamide combination was started with good response. Rapid shrinkage of the right axillary and cervical nodules, and recession of right arm oedema were observed after a week (Fig 1e, f, g).

## Discussion

In our case, since the lesion emerged at the cervical fusion surgery site, post-operative infection was first suspected. Since only *P aeruginosa* was detected by culture tests, ciprofloxacin was initially administered. *M tuberculosis* is usually susceptible to quinolone antibiotics,<sup>1</sup> hence the partial improvement in inflammatory symptoms and subsequent delay in diagnosis.

PCR tests for *M tuberculosis* are 88% sensitive and 83% specific,<sup>2</sup> and PCR-negative AFB culture-positive cases of scrofuloderma have been reported previously.<sup>3</sup> Rather than relying purely on PCR results, we feel it is important to conduct repeated tissue and pus culture tests, which are essential for an accurate diagnosis. Additionally, FNA is a less invasive and useful way to collect culture samples,<sup>4</sup> and interferon-gamma release assays are helpful in detecting early-stage AFB infection.<sup>3,5</sup> ■

## Summary

- > Recurrent subcutaneous abscesses are associated with a wide variety of differential diagnoses.
- > Scrofuloderma is an infection by *M tuberculosis* which is difficult to diagnose clinically.
- > PCR for *M tuberculosis* are not always reliable, and multiple tissue and pus cultures are useful for diagnosis.
- > FNA and interferon-gamma release assays are also helpful in achieving a diagnosis.

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## References

- 1 Pranger AD, van der Werf TS, Kosterink JGW, Alffenaar JWC. The role of fluoroquinolones in the treatment of tuberculosis in 2019. *Drugs* 2019;79:161–71.
- 2 Abdalla CM, de Oliveira ZN, Sotto MN *et al*. Polymerase chain reaction compared to other laboratory findings and to clinical evaluation in the diagnosis of cutaneous tuberculosis and atypical mycobacteria skin infection. *Int J Dermatol* 2009;48:27–35.
- 3 Haase O, von Thomsen AJ, Zillikens D, Solbach W, Kahle B. Recurrent abscesses of the neck scrofuloderma. *JAMA Dermatol* 2014;150:909–10.
- 4 Fontanilla JM, Barnes A, von Reyn CF. Current diagnosis and management of peripheral tuberculous lymphadenitis. *Clin Infect Dis* 2011;53:555–62.
- 5 Chen Y, Jiang H, Zhang W *et al*. Diagnostic Value of T-SPOT.TB test in cutaneous mycobacterial infections. *Acta Derm Venereol* 2018;98:989–90.

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