CASE REPORT

Cutaneous infection with paucibacillary *Mycobacterium tuberculosis* treated successfully with a modified antituberculous drug regimen

Nicholas Laidler

Sir Charles Gairdner Hospital,
Nedlands, Western Australia,
Australia

Correspondence to
Dr Nicholas Laidler,
nicklaidler@gmail.com

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SUMMARY

Tuberculosis is a serious infection that is increasing in prevalence, affecting many people worldwide. The diagnosis of cutaneous tuberculosis is challenging and requires the correlation of clinical findings with often inconclusive diagnostic testing. Extrapulmonary tuberculosis comprises approximately 10% of all cases of tuberculosis, and cutaneous tuberculosis makes up only a small proportion of these cases. Discussed here is the case of a 61-year-old immunocompetent female with a large cutaneous lesion on her index finger secondary to *Mycobacterium tuberculosis*. Tissue cultures taken at biopsy were negative; however, empiric antimycobacterial therapy was initiated. The initial regimen was not tolerated, and antituberculous therapy was substituted for moxifloxacin and clarithromycin. The lesion improved significantly with a concurrent improvement in function.

BACKGROUND

Cutaneous tuberculosis is a relatively uncommon manifestation of tuberculosis, occurring in 1%–2% of infected patients.¹ Cutaneous manifestations of infection with *Mycobacterium tuberculosis* are varied and are influenced by the immune status of the patient, route of bacterial entry into the skin and the presence or absence of host sensitisation to *M. tuberculosis*.² The clinical findings include inflammatory papules, verrucous plaques, suppurative nodules and chronic ulcers.³ Cutaneous tuberculosis is often misdiagnosed due to its diverse clinical features and the difficulty demonstrating acid-fast bacilli on histology specimens.¹ Cutaneous inoculation with *M. tuberculosis* can occur from an endogenous source, lymphatic, haematogenous or contiguous spread⁴ and causes periorificial tuberculosis, tuberculous chancre, tuberculosis verrucosa cutis, lupus vulgaris, scrofuloderma, acute miliary tuberculosis and tuberculous gumma.⁵

CASE PRESENTATION

A 61-year-old immunocompetent female presented with a 1-year history of a solitary large black nodular lesion overlying her right proximal interphalangeal joint on her index finger, with associated swelling. Two months prior to presentation the lesion, which was initially hyperaemic, slowly became deeply discoloured and broke down, begun increasing in size and was associated with swelling at the base of the middle phalanx. There was no obvious preceding

event, in particular she emphatically denied injury in the garden, animal bite, penetrating trauma or other inciting events. She had a potentially relevant personal history in that she was born in Calcutta, India, and migrated to Australia 34 years ago. The patient's father may have had tuberculosis at an early age but other than this, there is no personal history of tuberculosis, and she did not have any symptoms to suggest pulmonary tuberculosis. The patient denied night sweats, fatigue and weight loss. She lives on a large rural property but does not keep livestock. The patient works full time in the hospitality and catering department of a large children's hospital.

On examination, the dorsal aspect of the index finger demonstrated areas of acutely inflamed tissue overlying chronically inflamed tissue ([figure 1](#)), consistent with an acute pyogenic bacterial infection. There was evidence of synovitis and restriction of movement at the joint. There was no locoregional lymphadenopathy nor any evidence of sporotrichoid spread.

INVESTIGATIONS

Baseline blood tests revealed a white cell count of 9.5 g/L and a C reactive protein (CRP) of 75 mg/L. Interferon gamma screening for tuberculosis returned a negative result. All other blood tests were normal. A chest X-ray to assess for pulmonary disease was reported as normal. MRI demonstrated a florid synovitis and soft tissue abnormality; however, there was no evidence of osteomyelitis ([figure 2](#)). Biopsy and debridement of the lesion was performed with generous soft tissue specimens sent for assessment. These included skin and synovial specimens for bacterial, mycobacterial, nocardial and fungal microscopy and culture as well as direct 16S and 18S ribosomal DNA sequencing, which were all negative. Histopathology revealed inflamed granulation tissue consistent with a mixed acute and chronic inflammatory reaction. Multinucleate giant cells with an area of granuloma formation showing central necrosis was seen; however, no organisms were seen on H&E sections, periodic acid–Schiff diastase stain, Fite's acid fast stain and Ziehl–Neelsen stain.

DIFFERENTIAL DIAGNOSIS

Infective differentials: mycobacterial infection other than tuberculosis, blastomycosis,

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Figure 1 Initial lesion on the dorsum of the right index finger prior to commencing treatment.

histoplasmosis, coccidioidomycosis, sporotrichosis, tularemia, cat scratch disease, leishmaniasis, chromoblastomycosis and fungal infection.⁶

Infiltrative or autoimmune differentials: pyoderma gangrenosum, cutaneous pseudolymphoma, sarcoidosis, discoid lupus erythematosus, squamous cell carcinoma and lymphoma.⁶

The diagnosis of cutaneous tuberculosis was favoured based on the patient's history and clinical picture in the absence of definitive diagnostic testing. Features consistent with cutaneous tuberculosis that narrowed the differential included the initial hyperaemic morphology that grew via peripheral extension, the development of fissures that exuded keratinous material, the peripheral location of the lesion and its slow and non-healing progression.

TREATMENT

Prior to biopsy and debridement, the patient was started on doxycycline 100mg twice daily for 2 weeks to treat secondary infection. The impression was that a mycobacterial infection

Figure 2 MRI of the right index finger demonstrating cutaneous and subcutaneous thickening and enhancement dorsal to the proximal interphalangeal joint and base of the middle phalanx.

Figure 3 Improving lesion on the dorsum of the right index finger after 10 weeks of treatment.

was the underlying cause of the chronic process, and doxycycline was chosen as it does not have activity against mycobacteria and therefore would not inhibit growth on tissue cultures. Tissue cultures taken at biopsy were negative. Despite this, it was felt that mycobacterial infection was likely to be paucibacillary and very unlikely to be drug resistant. Empirical antimycobacterial therapy consisting of isoniazid 300mg daily, rifampicin 600mg daily, ethambutol 800mg daily, pyrazinamide 1.5g daily and pyridoxine 25mg daily was started. Clinical response was observed at 1 month with the patient displaying slow resolution of the lesion; however, significant side effects from the antituberculous therapy were noted. Isoniazid was ceased because of a substantial alanine aminotransferase (ALT) rise from 32 U/L to 1120 U/L (with a normal bilirubin and *alkaline phosphatase*), consistent with isoniazid-induced hepatotoxicity. Pyrazinamide was ceased due to widespread arthralgias, and ethambutol was ceased as the patient repeatedly failed to attend her ophthalmology review for slit lamp examination and to have her visual acuity and colour discrimination tested. Antituberculous therapy was therefore substituted for moxifloxacin 400mg daily and clarithromycin 800mg twice daily to cover an atypical mycobacterial infection. Moxifloxacin and clarithromycin were chosen as they are relatively well tolerated medications that have proven in vitro susceptibility against *M. tuberculosis*.^{7,8} In addition to this, moxifloxacin has been shown to significantly improve culture conversion in the initial phase of tuberculosis treatment.⁸ The modified treatment was well tolerated, and the patient was able to remain on this antituberculous regimen without issue.

OUTCOME AND FOLLOW-UP

At week 10 of empirical treatment, tissue cultures returned a positive result for *M. tuberculosis*. In vitro susceptibility studies confirmed that the patient was receiving appropriate therapy. During this time, the lesions had improved significantly (**figure 3**) with a concurrent improvement in function. Repeat CRP at 10 weeks had reduced to 2.5 mg/L, and the white cell count remained normal at 6.35 g/L. At the same review, 6 weeks after isoniazid and pyrazinamide were ceased, the patients arthralgias had ceased, and ALT was normalising at 127 U/L. The treatment regimen was continued for a total of 6 months on the advice of the infectious diseases team consulting on the case. At the conclusion of the 6-month treatment course, complete resolution of the lesions was achieved. This persisted when the patient was followed up 2 months postcessation of therapy.

Learning points

- The clinical presentation of cutaneous mycobacterial infections is highly variable and any unexplained skin lesion, especially those with nodular or ulcerative components, may be due to tuberculosis.
- In the case of paucibacillary cutaneous tuberculosis, the number of acid-fast bacilli is usually scant, and failure to identify *Mycobacterium tuberculosis* in tissue cultures should not exclude the diagnosis as cultures will be positive in only slightly more than 50% of cases. Microscopy and culture have low sensitivity in paucibacillary conditions, and it may take weeks before results are returned, resulting in delay in initiation of therapy.
- In cases where there is a strong suspicion of *M. tuberculosis*, despite negative laboratory tests, a trial of antituberculous therapy may be considered.

DISCUSSION

M. tuberculosis has been reported in soft tissue infections that present as subacute or chronic, recurrent and resistant to treatment.^{5–7} Tuberculosis verrucosa cutis results from exogenous inoculation of *M. tuberculosis* at sites prone to trauma in previously sensitised individuals.^{9–10} One potential source of inoculation in this case is the patients place of employment where exposure to mycobacteria is certainly possible.

Diagnosis should be made through the culture of biopsied tissue that should be collected from the periphery of lesions. As exhibited in the above case, it is often difficult to demonstrate *Mycobacterium* in smears or tissue cultures because most cases are paucibacillary.¹¹ Therefore, the diagnosis of cutaneous mycobacterial lesions is challenging. The lesions are rarely pathognomonic, and there is a wide range of credible differentials. A high clinical suspicion coupled with microbiological and

histopathological examination is the key to prompt diagnosis and treatment.⁴ The demonstration of acid-fast bacilli in skin lesions is challenging, however, as tissue cultures provide such a small diagnostic yield.¹ As in this case, a therapeutic trial of anti-tubercular drugs can be used to confirm the diagnosis and treat the patient empirically when a diagnosis cannot be definitively established.³

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