

## Soft Tissue Manifestations of Mycobacterial Infection in Patients with Rheumatic Diseases

Dear Sir

Patients with rheumatic disease are at risk of opportunistic infections as a result of immunosuppressive therapy and the underlying disease. These infections (including mycobacterial infections) can present in unusual ways, mimic disease exacerbations and pose a diagnostic and therapeutic challenge to physicians. We describe 3 patients who presented with soft tissue mycobacterial infection to our institution over a 1-year period.

### Case 1

A 54-year-old female with newly diagnosed anti-synthetase antibody syndrome was treated with 30 mg/day of prednisolone for 1 month but her disease remained active. Prednisolone was thus increased to 50 mg/day and 2 mg/day of tacrolimus was added. She defaulted follow-up and was admitted 8 months later with fever of 2 weeks' duration and right gluteal cellulitis that progressed rapidly over next few hours to involve her right thigh. A diagnosis of necrotising fasciitis was made. Immunosuppressants were withdrawn, she was treated with broad-spectrum antibiotics and underwent surgical debridement urgently. Tissue sections revealed acid-fast bacilli (AFB) and culture grew *Mycobacterium tuberculosis* (MTB), sensitive to isoniazid, rifampicin, ethambutol and streptomycin. She was treated with isoniazid, rifampicin and pyrazinamide for 2 months and subsequently isoniazid and rifampicin for 1 year. Although initial bacterial cultures were negative, she developed secondary bacterial infection of her wound requiring repeated debridements and prolonged antibiotics. She gradually recovered and at the end of 1 year, cultures from a residual small sinus were repeatedly negative for MTB. There was no evidence of pulmonary or miliary tuberculosis (TB).

### Case 2

A 37-year-old female with long-standing systemic lupus erythematosus (SLE) (arthritis, oral ulcers, subcutaneous LE and Class IV lupus nephritis) presented with fever and tender soft tissue swellings over her right lower abdominal wall and left thigh for 2 weeks. Prior to this, recurrent flares of arthritis and nephritis marked her clinical course necessitating prolonged use of high dose prednisolone (40 to 60 mg/day). Various immunosuppressants (azathioprine, methotrexate and cyclosporine) were stopped because of side effects. Her disease was eventually controlled with

oral cyclophosphamide 100 mg daily. A computerised tomography (CT) scan of the abdomen and pelvis revealed subcutaneous stranding in the right lower abdominal wall suggestive of inflammation. A subsequent biopsy revealed features suggestive of chronic inflammation, but cultures were negative. Despite empiric antibiotics the swellings enlarged. Magnetic resonance imaging (MRI) of the left thigh (Fig. 1) showed features suggestive of myositis and a subsequent biopsy revealed panniculitis and the presence of AFB. Although there were no respiratory symptoms and the chest radiograph (CXR) was normal, sputum smears and cultures were positive for MTB, sensitive to all anti-tuberculous drugs. Despite triple therapy (isoniazid, rifampicin and ethambutol), she developed pharyngeal and multiple soft tissue lesions involving the lower abdominal wall, right shoulder and right foot. In view of non-compliance, she was placed on directly-observed therapy (DOT) with the addition of pyrazinamide. After 2 months of DOT, she was discharged with isoniazid and rifampicin for another 6 months. She completed her course of anti-tuberculous therapy and has remained symptom-free on follow-up at 1 year.



Fig. 1. Axial magnetic resonance imaging (MRI), T2-weighted image of distal left thigh showing diffuse muscle oedema of vastus lateralis suggestive of myositis.

### Case 3

A 55-year-old female with overlap syndrome (rheumatoid arthritis and polymyositis), which was previously well controlled on prednisolone (12.5 mg/day) and weekly methotrexate (20 mg/week), developed lesions consistent with panniculitis/erythema nodosum over her lower limbs and a flare of her arthritis. Despite an increase in prednisolone dose, her skin lesions continued to progress. Four months later, she was admitted in neutropenic sepsis with acute renal failure secondary to obstructive uropathy due to renal papillary necrosis. Methotrexate was discontinued and folinic acid rescue given. She required dialysis, inotropic and ventilatory support. Skin biopsy revealed infective panniculitis with the presence of AFB and tissue cultures confirmed non-tuberculous mycobacterial infection. Her condition deteriorated rapidly despite aggressive broad-spectrum antimicrobial treatment and granulocyte macrophage colony stimulating factor (GM-CSF) support. She succumbed to overwhelming *Acinetobacter baumannii* septicemia 5 days later. Post-mortem examination revealed disseminated infection with cardiac valve vegetations, hepatic and splenic abscesses.

### Discussion

Patients with rheumatic disease have a higher predisposition to infection as a result of immunosuppressive therapy and underlying abnormalities of the immune system such as impaired phagocytosis or deficient cell-mediated immunity.<sup>1</sup> Infection remains a major cause of morbidity and mortality in these patients. These range from common infections to more unusual ones, in terms of presentation and/or causative pathogen. TB is one of the key opportunistic infections that should be considered in these patients, especially in endemic areas.

Along with an increased risk of developing TB, clinical presentations may be unusual and the disease may be more severe and widespread. Although the most common presentation of TB in such patients remains pulmonary, a higher incidence of extra-pulmonary involvement (15% to 45%) has been reported in the literature.<sup>2</sup> The majority had concomitant pulmonary and/or military TB. These findings were mirrored in an earlier local study of SLE patients.<sup>3</sup>

Extra-pulmonary TB involving the musculoskeletal system is uncommon with a quoted incidence of 1% to 3%.<sup>4</sup> Of this, TB spondylitis, osteomyelitis and septic arthritis account for up to 80% of cases. Soft tissue involvement as the primary manifestation has been infrequently described, the majority of which are miliary or contiguous spread.<sup>5,6</sup> All our patients initially presented with soft tissue

involvement. The infection was confined to soft tissues in case 1; disseminated in case 3 and possibly 2, several months after initial presentation.

Some important issues can be highlighted from this series. Firstly, infections may mimic underlying disease activity. Second, both processes may occur concurrently. Third, immunosuppressed individuals may present atypically. All these can contribute to diagnostic delay with resultant disseminated infection and poor outcome.

In conclusion, mycobacterial infection should be considered in patients with rheumatic disease who present with unexplained soft tissue swellings, particularly in those who are on immunosuppression or have active disease. A high index of suspicion, prompt diagnosis and treatment, as well as judicious use of immunosuppression, are crucial to patient survival and outcome.

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