

# A case of *Penicillium marneffei* osteomyelitis involving the axial skeleton

TS Pun, D Fang

**Fungal infection of bone by *Penicillium marneffei* is rare. We report on a case of *Penicillium marneffei* infection in a Filipino woman, which involved multiple soft-tissue abscesses and infection of the axial skeleton. Early diagnosis and treatment of this potentially reversible disease is emphasised. Such an approach is essential to prevent bony destruction from becoming too advanced and, more importantly, to prevent any damage to the spinal cord from occurring.**

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## Introduction

Osteomyelitis can be caused by bacteria as well as fungi. The disease is treatable with appropriate antibiotics or antifungal agents. During investigations, it is important to remember to look out for fungal infection. Doing so will allow a proper and accurate diagnosis to be made. In this way, appropriate treatment can be commenced and potentially serious complications can be avoided.

## Case report

A 30-year-old Filipino woman presented to the Queen Mary Hospital (QMH) in April 1993 with pyrexia of unknown origin and cervical lymphadenopathy. The patient had a history of mixed connective disease and had attended regular follow-up at the Department of Medicine of the QMH. Fever had developed 2 weeks before the hospital admission. On arrival at the QMH, she was emaciated, in a toxic condition, and had intermittent fever without any bone pain. A soft-tissue mass was felt over the forehead. Multiple firm and enlarged cervical lymph nodes were also palpable.

Laboratory investigations showed a white blood cell count of  $30.3 \times 10^9$  /L (normal range,  $3.2-9.8 \times 10^9$  /L) with 93.6% neutrophils, haemoglobin level of 86 g/L (normal range, 120-150 g/L), erythrocyte sedimentation rate of 133 mm/h (normal range, 0-30 mm/h), and C-

reactive protein level of 180 mg/L (normal range, 100-270 mg/L). Blood culture was negative for bacteria and fungi. All tests to detect viruses, including human immunodeficiency virus types 1 and 2, gave negative results. Antinuclear factor was present, at a titre of 1:1080; rheumatoid factor and antibodies to double-stranded DNA were absent. Biopsy examination of the bone marrow did not show any haematological diseases.

The X-ray of the cervical spine showed lytic lesions at the C2 vertebral body (Fig 1) and the head of left humerus. Multiple lytic lesions were also visible over the proximal shaft of the right femur. Gallium bone scanning detected multiple sites of abnormal uptake in the upper cervical spine, left shoulder, right side of manubrium, and right femur, which corresponded to multiple sites of infection. The chest X-ray showed no evidence of pulmonary infection.

An excisional biopsy examination of a cervical lymph node showed granulomatous lymphadenitis, but this finding was inconclusive. The biopsy site failed to heal and persisted as a skin ulcer. Staining for acid-fast bacilli and fungi were negative. The patient was given antituberculous drug treatment empirically. Fine-needle aspiration of the soft-tissue mass on the left side of the forehead revealed yeast cells. Histological examination of decalcified sections of a core biopsy sample from the left humerus showed diffuse fibrosis of the intertrabecular space and infiltration of histocytes. Well-formed granulomas or giant cells were absent. However, yeast-form fungi of 5 to 6  $\mu$ m in diameter were detected after special staining tests had been performed. These findings were consistent with tissue infection with *Penicillium* species.

Department of Orthopaedics and Traumatology, The University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong  
TS Pun, MB, BS, FRCS (Edin)  
306 Tak Shing House, 20 Des Voeux Road, Central, Hong Kong  
D Fang, FRCS (Edin), FHKAM (Orthopaedic Surgery)

Correspondence to: Dr TS Pun



Fig 1. X-ray showing bone destruction in the anterior part of the C2 vertebral body

The bony trabeculae were unremarkable and there was no evidence of lymphomatous infiltration. Microbiological examination revealed dimorphic fungus, and fungal culture was positive for *Penicillium marneffeii*. The culture of the fine-needle aspirate from the forehead mass was also positive for *P marneffeii*. The patient developed a left-arm abscess in the subcutaneous plane, which extended up to the axilla about 1 week after core biopsy of the left humerus. Fifty millilitres of pus was drained; its culture confirmed infection with *P marneffeii*.

Further abscesses developed despite the commencement of antifungal treatment. The patient was given intravenous amphotericin B and fluconazole. A retropharyngeal abscess presented itself with acute stridor and dyspnoea several days later. Another abscess developed at the lateral aspect of the right thigh, with underlying osteomyelitis of the femur (Fig 2). Both conditions were treated by performing surgical debridement. The involvement of the C2 vertebral body was treated with antifungal medication. There was no neurological deficit or progression of the bony erosions.

The fever then subsided, and the results of blood investigations such as white blood cell count and measurement of the erythrocyte sedimentation rate and C-reactive protein level gradually returned to normal over 3 to 4

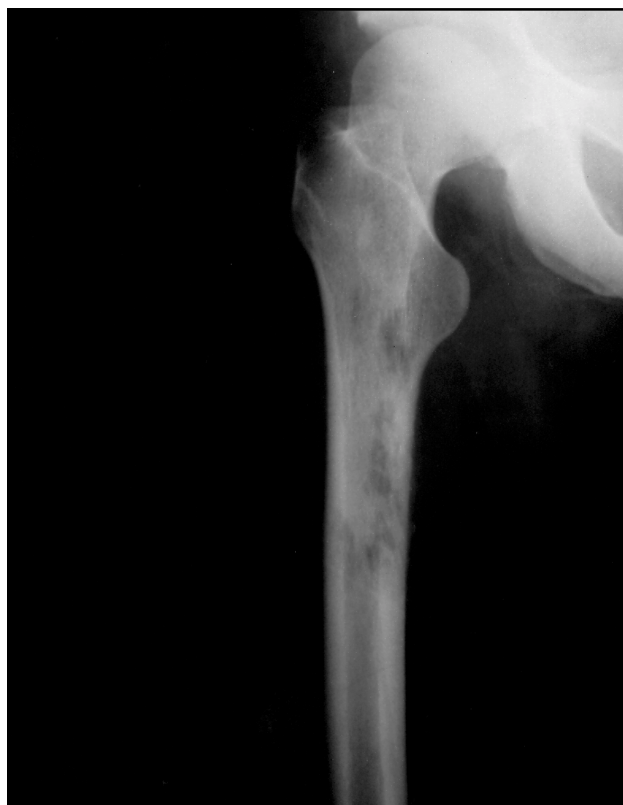


Fig 2. X-ray showing involvement of the right proximal femur

weeks. The patient's general condition improved, and she was able to walk with support. She later returned to the Philippines while continuing antifungal therapy.

## Discussion

Human infection with *P marneffeii* was first documented in 1956 by Capponi.<sup>1</sup> That case involved the accidental inoculation of the fungus into a laboratory investigator, and the infection subsided with antifungal drug treatment. The organism has been isolated from the liver of bamboo rats from Vietnam.<sup>2</sup> Other case reports showed that the patients with *P marneffeii* infection either lived in South-East Asia or had a history of travelling to this region.<sup>3</sup> Clinical infection with the organism has been reported in immunocompromised patients as well as in healthy individuals.<sup>4</sup>

The combination of fever, lymphadenopathy, and the development of abscesses are common manifestations of infection with *P marneffeii*. The lymphadenopathy may ulcerate and cause mediastinal compression—a situation that may often mimic tuberculosis. Lymph node biopsy is usually not helpful in distinguishing between the two diagnoses.<sup>5</sup> Without appropriate treatment, the infection may become disseminated to the lung and liver. Eventually, the infection may be fatal.<sup>2,6</sup> The clinician should bear this differential diagnosis in

mind when such clinical features are encountered. Most of the previously reported cases showed involvement mainly in soft tissues and abdominal organs.<sup>2,6</sup> Chan and Woo<sup>3</sup> reported on a patient with mainly peripheral skeletal involvement, which was manifested by multiple joint pain, swelling, and multiple radiolucent areas at the ends of various long bones and phalanges. Jayanetra et al<sup>6</sup> described involvement of the long bones, skull, and ribs in two patients of their series. Louthrenoo et al<sup>7</sup> reported that one of eight patients showed major involvement of the axial skeleton.

In the patient in this report, the *P marneffe*i infection progressed rapidly with bony destruction, soon after the onset of disease. When the spine is involved, this rapid progression can be potentially serious, result in severe neurological deficit, and eventually be fatal. Early treatment is very important to prevent any irreversible damage to the spinal cord. Despite giving full-dose antifungal treatment to this patient, more soft-tissue abscesses developed. These symptoms probably reflect a slow onset of the effect of antifungal agents. This delay further emphasises the need for early treatment.

## Conclusion

*Penicillium marneffe*i infection in bone is rare. When it occurs, systemic upset can be severe. There are multi-

focal bony lytic lesions, which can be rapidly progressive. Both the axial and peripheral skeleton can be involved, and the soft tissues are usually also affected. Recent contact in South-East Asia should raise suspicion of infection with *P marneffe*i. Early treatment is essential so that the bony destruction does not become too advanced and, more importantly, to prevent any damage to the spinal cord from occurring.

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