CASE REPORT

Sternal osteomyelitis caused by Aspergillus fumigatus in a patient with previously treated Hodgkin’s disease

D Allen, S Ng, K Beaton, D Taussig

This report details the case of a 67 year old woman with sternal osteomyelitis caused by Aspergillus fumigatus. She was diagnosed with Hodgkin’s disease in 1975 and was successfully treated with chemotherapy. A lobectomy for recurrence localised to the left lung was complicated nine years later by severe bronchiectasis, for which she required a total left sided pneumonectomy. At surgery, a non-invasive aspergillus was found. She presented eight years later with symptoms that were initially attributed to recurrence of Hodgkin’s disease, but on investigation were found to be caused by fungal sternal osteomyelitis. Treatment with itraconazole suspension at a dose of 400 mg daily was successful.

A 67 year old woman presented in August 2000 with a one year history of loss of 10% body weight and a four week history of night sweats, fever, and general malaise. She also complained of pain in the region of the left clavicle and sternum, which was worse with movement or palpation. This pain had been intermittently present for the previous year and after a negative exercise test had been diagnosed as “musculoskeletal”.

In 1975 she had been treated for stage IIIIsB Hodgkin’s disease. After a staging splenectomy, she was given six cycles of combination chemotherapy with mustine, vinblastine, prednisolone, and procarbazine to complete remission. Two years later she relapsed with right cervical lymphadenopathy and received mantle radiotherapy at a total dose of 30 Gy in 15 fractions. She relapsed again in 1983, with Hodgkin’s disease localised to the lower lobe of the left lung, for which she had a lobectomy and received combination chemotherapy with chlorambucil, vincristine, prednisolone, procarbazine, doxorubicin, and etoposide, achieving a complete response. In 1992, she presented with fever, night sweats, and a cough with purulent sputum. A computed tomogram of the chest was compatible with bronchiectasis of the remaining left lung with the presence of a loculated fluid collection. This was aspirated at bronchoscopy and found to be sterile. Several courses of antibiotics and a trial of antibiotics did not lead to an improvement in her symptoms. Therefore, she underwent a completion pneumonectomy, using the posterolateral thoracotomy scar, in 1994. Histology revealed bronchiectasis and a cavity containing aspergillus, with no evidence of invasion. The operation resulted in gradual resolution of her symptoms and until presentation she had appeared well in routine follow up, apart from mild exertional dyspnoea.

On examination, she was pale and cachetic with a low grade fever. There was no palpable lymphadenopathy or hepatomegaly. She had a tender sternum with minimal overlying erythema, which extended to the right sternoclavicular joint (fig 1). Blood tests showed a haemoglobin of 107 g/litre, neutrophils of $10.3 \times 10^9$/litre, and platelets of $504 \times 10^9$/litre.

The infecton scan suggested a bacterial osteomyelitis and therefore no specific request for fungal culture was made. Gram’s staining and auramine staining of the pus were sterile. An isotope bone scan showed increased tracer uptake in the clavicle and sternoclavicular joints. A computed tomography scan undertaken to exclude recurrent Hodgkin’s disease showed a non-specific but pronounced abnormality of the bony texture of the manubrium and proximal body of sternum.

A technetium-99m radiolabelled ciprofloxacin (“infecton”) scan was performed. This showed focally increased uptake in the region of the right sternoclavicular joint and sternum (fig 2). This was followed by diagnostic sternal biopsy, at which removal of overlying necrotic bone revealed a collection of purulent material. Extensive debridement was not done at the time of biopsy. The infecton scan suggested a bacterial osteomyelitis and therefore no specific request for fungal culture was made. Gram’s staining and auramine staining of the pus and bone biopsy revealed no organisms. Bone and pus were cultured at 37°C on blood agar, both aerobically and anaerobically, and on chocolate agar in a 5% carbon dioxide incubator. Aspergillus fumigatus was grown in pure culture on the three samples of bone after 48 hours of incubation. The pus samples were sterile. Aspergillus fumigatus was also isolated from a Lowenstein-Jensen slope after five days of culture. The Public Health Laboratory Service Fungal Reference Laboratory, Bristol confirmed the identification and reported minimum inhibitory concentrations of 1.0 mg/litre for amphotericin (sensitive) and 0.25 mg/litre for itraconazole (sensitive). Grocott staining of the bone biopsy showed fungal hyphae within the bone material, consistent with invasive Aspergillus fumigatus infection.

A cardiothoracic surgical review suggested that the patient’s previous pneumonectomy and frail state precluded further extensive debridement. Treatment was therefore started with liposomal amphotericin at a dose of 1 mg/kg. However, she was unable to tolerate this and was changed to 200 mg twice daily of itraconazole.
daily of itraconazole suspension. After 10 weeks of treatment, she had responded well, with resolution of the rash and a C reactive protein of < 5 mg/litre. Because of general malaise and abnormal liver function tests while on itraconazole, treatment was stopped. She continued to improve clinically with resolution of her pain and night sweats and weight gain. Her C reactive protein remained within normal limits and the wound healed well. Unfortunately, she became acutely unwell eight months later with a chest infection that was thought to have exacerbated type II respiratory failure as a result of her previous pneumonectomy and kyphoscoliosis. She required ventilation at another hospital and died. A necropsy was not performed. There had been no evidence of osteomyelitis or aspergillus infection clinically or on microbiological samples, and her death was not thought to have been caused by a recurrence of her fungal infection.

DISCUSSION

This case highlights how, despite an initial non-invasive pathology, *Aspergillus fumigatus* infection recurred in an unusual site after an eight year interval. Our patient had no obvious immune deficiency (lymphocyte numbers, neutrophil function, and immunoglobulin values were normal) and no evidence of recurrence of her original cancer.

Osteomyelitis occurring in the sternum is uncommon and most cases are seen after sternal trauma or surgery. Spread from a contiguous focus in the lung, pleura, or mediastinum is also recognised. The most common organisms are *Staphylococcus aureus*, Gram negative organisms, and mycobacteria. Aspergillus predominantly causes osteomyelitis in the immunocompromised; however, it was first recognised as a cause of sternal osteomyelitis in patients who had undergone sternectomy as part of a cardiothoracic procedure. Such an insidious history is typical, but in most cases presentation is within months of surgery, and also in the context of sternal manipulation and wiring. Several cases of aspergillus sternal osteomyelitis in otherwise immunocompetent intravenous drug abusers have also been reported.

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The abnormal technetium-99m radiolabelled ciprofloxacin scan is unusual because there was no microbiological evidence of bacterial infection. This imaging has been shown to be sensitive and specific for bacterial infection, but only in comparison with normal controls. Further evaluation in the presence of fungal infections may be needed.

Optimum treatment involves debridement and antifungal treatment with amphotericin B, although this drug has relatively poor bone penetration and a high incidence of side effects. Oral itraconazole has been used as a single agent in patients with invasive and osseus aspergillosis and in aspergillus osteomyelitis, including that of the sternum. Although it only causes an improvement and not cure in many cases, it is usually very well tolerated and is therefore a good alternative to intravenous treatment.

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