CASE REPORT

Candida albicans osteomyelitis as a cause of chest pain and visual lossRita Magano,¹ Joana Cortez,¹ Evelise Ramos,² Luís Trindade¹¹Department of Infectious Disease, Coimbra's Hospital Centre and University, Coimbra, Portugal²Clinica Vida Cligeste, Luanda, Angola

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SUMMARY

Candida albicans osteomyelitis is a rare disease that occurs in immunocompromised individuals, sometimes with a late diagnosis related to the mismatch between symptoms and candidemia. This case refers to a 36-year-old male patient with a history of oesophageal surgery for achalasia with multiple subsequent surgeries and hospitalisation in the intensive care unit for oesophageal fistula complication. Four months after discharge, the patient was admitted to the infectious diseases department with pain in the 10th–12th left ribs, swelling of the 4th–6th costal cartilage and decreased visual acuity. An MRI study showed thickening and diffuse enhancement, with no defined borders in the cartilage and ribs, compatible with infection. After performing a CT-guided bone biopsy, isolated *C. albicans* sensitive to antifungal agents was detected. The patient started therapy with liposomal amphotericin B and maintenance fluconazole for 6 months and showed clinical and radiological improvement within this time.

BACKGROUND

Candida is a ubiquitous organism whose pathogenicity is enhanced by the involvement of individual defence mechanisms.^{1 2} Candidemia has frequently been diagnosed after oesophageal/mediastinal surgery; however, the bone and joint involvement associated with vitreous infection by this agent are rare. A high level of suspicion and early institution of therapy with amphotericin B, followed by an oral azole,^{2 3} are of foremost importance to prevent osteoarticular functional impairment and retinal necrosis resulting in blindness.^{4 5}

CASE PRESENTATION

A Caucasian 36-year-old male patient was admitted to the infectious diseases department in April 2011 with pain and swelling in the left hemithorax. He reported pain in the left hemithorax during the previous 1 month, persistent on a daily basis and not related to physical exercise. In addition, he also noted decreased visual acuity of the right eye during the previous 3 months.

On physical examination, several scars at the level of the 10th–12th ribs and left upper quadrant with inflammatory signs were noted. Clinical observation showed thick abdominal wall, non tender and painful on light palpation at the level of 4th–6th costal cartilage left and right anterior axillary line of the 10th–12th ribs. The remaining physical examination showed no other abnormalities and the patient was afebrile and in good condition.

His history was relevant; 6 months before this episode, he underwent oesophagocardiomyotomy for treatment of achalasia in the surgical department, complicated by oesophageal fistula to the chest wall that led to several subsequent surgeries: right thoracotomy, cervical oesophageal exclusion, feeding jejunostomy and bilateral thoroscopic decortication. As a complication, he developed severe sepsis by methicillin-resistant *Staphylococcus aureus*, isolated from an abscess in the parietocolic gutter. The patient was subsequently admitted to the intensive care unit where he was started on vancomycin 500 mg 12/12 h and later given linezolid for 21 days. Necrotising pneumonia was diagnosed and treated with piperacillin/tazobactam 4.5 g 6/6 h. No aetiological agent was identified. Blood cultures and tracheal aspirate grew *Candida albicans* treated with caspofungin 50 mg/day for 17 days. Follow-up blood cultures and tracheal aspirate showed no microorganisms.

INVESTIGATIONS

Laboratory tests showed haemoglobin 11.8 g/dL, leucocytosis with neutrophilia (leucocytes 11 400/mm³ with 62.3% neutrophils) and elevation of C reactive protein (7.3, a normal value of <0.5 mg/dL). Serology for HIV was negative. The sagittal chest plan (figure 1) showed well-defined osteolytic lesions in multiple ribs bilaterally. The initial CT of the chest revealed a heterogeneous formation at the level of the fourth left costal cartilage and costochondral joint, with a central area which was the

Figure 1 Sagittal chest plan, March 2011.

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most hypodense. There was also increased density of the surrounding tissues, causing some destruction of the architecture of the bone and chondral structures above. Similar changes were also identified in previous segments of the sixth and seventh ribs and surrounding areas (figure 2).

MRI studies showed a thickening in the left anterior chest wall with ill-defined limits involving the muscles, subcutaneous tissue and the fourth costal cartilage and costochondral joint, compatible with infection. Overlapping changes in segments of the sixth and seventh ribs and surrounding areas were also noted with a liquid collection in the centre (figure 3). A CT-guided bone biopsy was performed and bone tissue was grown in blood agar base media and Sabouraud in aerobic and anaerobic conditions at 37°C. *C. albicans*, sensitive to all tested drugs (azole, polyene and azole derivatives), was isolated.

The patient also underwent an ophthalmological examination which diagnosed vitritis with probable fungal aetiology. The fundus could not be visualised, and as such surgery at a later stage was proposed.

TREATMENT

A diagnosis of *C. albicans* osteomyelitis with involvement of the vitreous was established. The patient started therapy with liposomal amphotericin B 300 mg/day intravenously for 37 days, with linezolid 600 mg 12/12 h orally for 24 days, due to the presence of inflammatory signs suggestive of an abscess in the fourth costal cartilage and the 6th–7th ribs.

OUTCOME AND FOLLOW-UP

There was a progressive clinical and radiological improvement of the eye and ribs without the need for surgical intervention and normalisation of the infection parameters. The patient was referred for a follow-up consultation and treated with fluconazole 400 mg 12/12 h orally during 12 months. MRI of the chest (figures 4 and 5) was repeated at 3, 6 and 12 months after initiation of therapy which has shown slow but progressive recovery of bone tissue.

DISCUSSION

This case is an excellent example of the intrinsic difficulty in diagnosis and therapy of fungal osteomyelitis. The massive use of broad-spectrum antibiotics, immunosuppressants, parenteral nutrition and invasive techniques exposes patients to an increased risk of systemic fungal infections.^{6 7} Cardiothoracic surgery is associated with increased risk of infection by

Figure 3 Chest MRI, March 2011.

contiguity.^{8 9} In these patients, *Candida* infections have increased in hospitals in recent times; however, the bone and joint achievement is still uncommon. The predisposing risk factors for this type of infection should be remembered in the clinical context.⁸ Considering a long follow-up period, up to 3 years, is necessary on isolation of *Candida* in blood cultures to develop the first clinical signs and symptoms of osteomyelitis; it is essential to have a high level of suspicion. In this case report, it is possible to identify clearly the period with blood cultures positive for *C. albicans* during which the patient was treated with caspofungin for 16 days; although the patient has completed 14 days of echinocandin to treat candidemia, however this antifungal was not used until 1 week after negative blood cultures, as recommended.⁷

For the treatment of chronic osteomyelitis caused by *C. albicans*, the guidelines^{3 10} suggest as first-line treatment liposomal amphotericin B 3–5 mg/kg, 2–6 weeks, followed by fluconazole; or fluconazole 6 mg/kg over 6–12 months from the beginning without the

Figure 2 Chest CT scan, March 2011.

Figure 4 Chest MRI, October 2011.

Figure 5 Chest MRI, October 2011.

initial phase of liposomal amphotericin B.¹¹ Phospholipid vesicles, known as liposomes, allow continuous use of this effective drug but with less renal toxicity. Currently, amphotericin B deoxycholate is not the first option. Some authors^{1 12} propose the use of itraconazole in combination with liposomal amphotericin B (as antagonism is observed with the combination of fluconazole and amphotericin B). Use of fluconazole from the beginning of treatment is still controversial. Ketoconazole has been used successfully in patients with a history of intravenous drug use and disseminated candidiasis, while treatment failures have been reported with the exclusive use of fluconazole throughout treatment in patients with sternal osteomyelitis.² Regarding vitritis caused by *C. albicans*, intravenous treatment and subsequent extended oral antifungal treatment, associated with early surgery with intravitreal injection of voriconazole or amphotericin B, could improve the prognosis.⁴

Some authors argue that in view of the potential complications of inadequate treatment, the choice of a parenteral antifungal to initiate treatment, followed by a less toxic agent administered orally, is the ideal.^{11 13}

Management of *Candida* osteomyelitis is usually associated with prolonged antifungal therapy alone or complemented with surgical intervention.¹⁴ Despite the possibility of an invasive technique in complicated cases: neurological impairment, spinal instability or clinical deterioration, these specific conditions have not been identified in this patient.¹⁴ The guidelines suggested as the best option for treatment, the combination of antifungal with surgical debridement of the affected area; this is best documented for vertebral osteomyelitis or joint arthritis,^{7 15} while for *Candida* mediastinitis the evidence is based on a small number of case reports.¹⁶ A revision of 62 cases of vertebral osteomyelitis shows that 31 patients (50%) received only medical therapy, 3 (5%) only surgical treatment and 28 (45%) combined treatment. Of these 28 patients, 13 had early surgery while the other 15 had initial conservative treatment failure.¹⁵

The diagnosis of this disease requires a high index of suspicion, resulting from the combined results of clinical, laboratory

and imaging findings. In the case presented, the existence of risk factors for infection by this organism, associated with isolation of *C. albicans* in the thoracic biopsy, was of foremost importance in establishing the diagnosis and in directing the therapy.

Learning points

- ▶ Chronic osteomyelitis caused by *Candida* is a rare condition that should be considered in a patient with clinical findings, predisposing risk factors and candidemia.
- ▶ The best treatment options include a minimal 2 weeks of an induction regimen with amphotericin B (intravenous), followed by 6–12 months of an oral azole, which can be associated with a surgical intervention.
- ▶ Follow-up needs clinical and imaging criteria.

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