

CASE REPORT

Candida parapsilosis osteomyelitisRekha Lopez,¹ Alistair Robert Hunter,² Orla Geoghegan,³ Elli Demertzi¹

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SUMMARY

A 51-year-old previously fit and healthy gentleman sustained a circular saw injury to his right thumb with partial amputation and an open multifragmentary fracture of his distal phalanx. He underwent open reduction and internal fixation under the hand surgery team. He developed a postoperative infection discharging pus 2 weeks postoperatively, which later grew *Candida parapsilosis*. He underwent radical debridement and removal of a K-wire, then a further second debridement 2 days later. Ceftriaxone was started empirically while awaiting cultures. Tissue and bone biopsy samples obtained in theatre all grew *C. parapsilosis* and he was started on caspofungin for 1 week, and switched on to oral fluconazole to complete a 6-week course. He has progressed well and has regained function in his thumb after 3 months, without any sign of ongoing infection.

coamoxiclav for 72 h and was discharged on a further weeks course of oral co-amoxiclav. He returned to the hand trauma clinic 2 weeks post-operatively with an infected wound that was discharging pus. He was taken to theatre for a radical debridement of the infected tissues and removal of the infected K-wire, and a further debridement 2 days later. He was started on intravenous ceftriaxone pending culture of bone biopsies which subsequently grew a yeast 3 days later. Following the isolation of *C. parapsilosis* from bone cultures, he was started on an echinocandin, caspofungin while awaiting sensitivities. This was then changed to oral fluconazole and the patient was discharged on a 6-week course. He has regained full function of the hand and is back at work with no relapse of infection.

BACKGROUND

Candida osteomyelitis is a rare clinical entity, has significant morbidity and is often difficult to treat. Out of all species of *Candida*, *Candida albicans* is the most common cause of *Candida* osteomyelitis with *Candida parapsilosis* accounting for only 7% in a recent case series of 207 cases of *Candida* osteomyelitis.¹

Most cases of *Candida* osteomyelitis occur in patients who are not immunocompromised, and bone biopsies should be performed to make the diagnosis.¹⁻⁴

Haematogenous spread to the highly vascular vertebral bodies is the most common mechanism occurring in adults, however direct inoculation from trauma occurring in this case is also well recognised.¹⁻³

A multidisciplinary approach using a combination of surgical debridement, removal of infected metalwork and antifungals has led to a good outcome in this case, highlighting the need for combined medical and surgical intervention. This has allowed a shorter duration of antifungals to be used and return of function with minimal side effects.

CASE PRESENTATION

A 51-year-old manual worker, presented to the emergency department with a partial amputation to the right thumb after an accident with a circular saw at work. He sustained an open, multifragmentary fracture of the distal phalanx of the thumb and was admitted under the hand surgery team. He had no other significant medical history. He was taken to theatre for washout and debridement of his wounds and open reduction and internal fixation of his fractures. He was started on intravenous

INVESTIGATIONS

The patient had a normal white cell count and the C reactive protein (CRP) was not raised at any stage of his infection.

Plain radiographs of the thumb diagnosed the multifragmentary element to his bony injury (figure 1).



Figure 1 Preoperative radiographs showing and lateral view of a multifragmentary open fracture of the distal phalanx of the thumb.



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Figure 2 Postoperative radiographs showing lateral view of the open reduction and internal fixation operative procedure.

Metalwork in the form of K-wires was used to stabilise the fracture (figure 2).

Bone biopsy was performed following debridement which isolated *C. parapsilosis* after 3 days. Sensitivity testing using minimum inhibitory concentrations was performed and the isolate was found to be sensitive to fluconazole and caspofungin.

Liver function tests were monitored while he was on fluconazole therapy for 6 weeks and showed no abnormality.

TREATMENT

Treatment of *Candida* osteomyelitis in this case involved a combination of radical surgical debridement, removal of infected metalwork and antifungal therapy. The infected K wires and a large, loose, necrotic fragment of bone were removed from distal phalanx of the right thumb, thus removing biofilms and potential sources of infection. Returning to theatre for multiple debridements is common in severe infections such as this to ensure all necrotic tissue is removed. Coamoxiclav intravenous 1.2 g thrice daily was started empirically for osteomyelitis while awaiting culture results and the patient was instructed to elevate his hand.

A peripherally inserted central catheter line was inserted to allow for long-term antibiotic administration. Coamoxiclav was changed to ceftriaxone 2 g once daily after 72 h to ease

administration via the outpatient antibiotic therapy (OPAT) service and rifampicin was added at a dose of 300 mg twice daily to cover for biofilms which may have formed on the remaining metalwork. There was a plan for 4–6 weeks of antibiotics with the choice of therapy to be reviewed when microbiology cultures and sensitivities were available.

Following isolation of *Candida* species from the bone, the case was discussed with the medical microbiologist and it was decided to start caspofungin intravenous, pending identification and susceptibility testing of the *Candida* species. All *Candida* species, with the exception of *C. parapsilosis*, are generally sensitive to echinocandins. The patient was administered a loading dose of 70 mg on the first day followed by 50 mg once daily. This was also administered in the OPAT setting.

C. parapsilosis has been demonstrated to possess less in-vitro sensitivity to echinocandins, with elevated minimum inhibitory concentrations (MIC) levels, however this isolate was sensitive to caspofungin on invitro testing.⁵ *C. parapsilosis* isolates are generally susceptible to fluconazole, and studies have shown no increase in resistance rates of *C. parapsilosis* to azoles over time.⁶ It is worth noting that resistance rates vary throughout the world with Africa and the Middle East having a lower overall susceptibility to those from Europe.⁶ However, if the patient has an indwelling device an echinocandin should be used as an increased resistance to azoles has been demonstrated by *C. parapsilosis* biofilms.^{7 8}

As the isolate was shown to be sensitive to fluconazole and the infected bone and K-wire had been removed, the decision was made to stop caspofungin therapy and switch to oral fluconazole 400 mg once daily. Although the literature suggests a treatment course of 6–12 months for patients with *Candida* osteomyelitis,^{1 4} although there are no definitive guidelines, it was decided that a shorter course of 6 weeks would be appropriate as the necrotic bone and infected K wires had been removed.

OUTCOME AND FOLLOW-UP

He was followed up in the hand trauma clinic after his two surgical debridements, when his wounds were noted to be healing well without any sign of infection. Six weeks postoperatively, he continued to do well, with reduced swelling, a 20° range of movement at the interphalangeal joint of the thumb and a normal CRP. At this point his antimicrobials were stopped. He has continued to recover well with regular hand therapy and has almost normal thumb function 3 months postoperatively. He has been discharged from the hand trauma clinic and has returned to work.

DISCUSSION

Candida osteomyelitis is still a relatively rare but important disease with significant morbidity and mortality.^{1–3} In a recent review, *Candida* osteomyelitis had an attributable mortality rate of 6%.² *Candida* osteomyelitis arises most commonly from haematogenous spread but can also occur through direct inoculation in up to 25% of cases as demonstrated in a recent case review.¹ In all the reviews of *Candida* osteomyelitis, *C. albicans* is the most frequently isolated pathogen.^{1–3}

C. parapsilosis accounted for 7% of osteomyelitis cases in a recent review of 207 cases of *Candida* osteomyelitis,¹ and 18% in a review of 53 cases in North America.² *C. parapsilosis* is a skin commensal and is the most frequently isolated yeast from the hands and subungual spaces.^{7 9} Its pathogenicity is usually limited by integrity of the skin. The penetrating nature of the injury to the thumb in this patient allowed inoculation of the

soft tissues. *C. parapsilosis* also has the capacity to form biofilms on catheters and other implantable devices which accounts for its pathogenicity in deep infections.^{7 8} In this case; the infected metalwork was removed, which helped eliminate the biofilm and aid in successful treatment.

There is no current consensus on duration or selection of treatment of *Candida* osteomyelitis and there is considerable variation in practice. Current Infectious Diseases Society of America (IDSA) guidelines are based on case reports and case series. IDSA guidelines recommend the combination of surgical debridement of the affected area and antifungal therapy as the best treatment for *Candida* osteomyelitis.⁴ A reported case of *C. parapsilosis* causing vertebral osteomyelitis was successfully treated with fluconazole 400 mg/day for 3 months postsurgical debridement and they recommend a shorter duration may be possible post proper debridement in the immunocompetent patient, which was what we decided to do in this case to shorten treatment duration with good outcome.¹⁰

White cell count and CRP were not raised in this case and are usually only moderately raised in cases of *Candida* osteomyelitis.² Index of suspicion should remain high in the immunocompetent host with localised symptoms despite treatment with antibiotics as occurred in this case. Prompt diagnosis is important to prevent treatment failures and relapses which occur in up to 66% of cases,² and is made based on direct culture of *Candida* species from bone material from bone biopsy or removed hardware from the infected bone in keeping with radiological and clinical features suggestive of osteomyelitis, as was seen in this case.

The importance of concomitant surgical intervention in achieving a good outcome should be highlighted. There is also limited data on the bone penetration of the antifungals. Animal studies suggest good penetration of fluconazole into the vertebrae of rabbits, but there is no comparable human data available.¹¹ In one study, *C. parapsilosis* was most frequently isolated

from skin and soft tissue and blood culture samples and less from other sites such as urine, and the azoles such as fluconazole and voriconazole were active against >90% of *C. parapsilosis* irrespective of site.⁸

In one study, treatment of *C. parapsilosis* for 14 days combined with surgical intervention was associated with good clinical outcome.³ Shorter duration of antifungals combined with surgical intervention, as was used in our case, was associated with favourable clinical outcomes. Side effects from the prolonged use of antifungals, such as hepatotoxicity, were also avoided, although fluconazole is associated with less hepatotoxicity than the other antifungal agents.^{5 12}

In this patient, *C. parapsilosis* was isolated from bone biopsy and deep tissue cultures. MICs for various antifungals were measured and the isolate was found to be sensitive in vitro to fluconazole and caspofungin. The patient was discharged after 1 week on intravenous caspofungin with a 6-week course of oral fluconazole following debridement, removal of infected bone and infected wires. A good clinical result was achieved with return of function of the hand and return to work with no relapse 3 months after stopping therapy.

Contributors RL selected case to write up and wrote main case body, discussion, literature review and corrections. ARH wrote clinical case details, provided images and obtained patient consent. OG wrote treatment section, reviewed all treatment patient was on and literature review on treatment. ED reviewed and approved final version.

Competing interests None.

Patient consent Obtained.

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Learning points

- ▶ *Candida parapsilosis* is a rare cause of *Candida* osteomyelitis and there is limited data available on best treatment guidelines.
- ▶ Treatment with antifungals can be shortened with no adverse outcome if radical surgical debridement with removal of infected bone and metalwork is performed.
- ▶ *Candida* osteomyelitis should be considered in patients who have sustained traumatic injuries and fail to improve on standard antibiotics.
- ▶ Bone biopsies and cultures coupled with imaging remain gold standard for making the diagnosis of *Candida* osteomyelitis
- ▶ *Candida* species isolated on bone cultures should always be regarded as significant and treatment should not be delayed.

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