Case Report

Candida vertebral osteomyelitis in the setting of effectively treated candidaemia A Case Report

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Abstract

Candida vertebral osteomyelitis (CVO) is a rare and frequently misdiagnosed condition which can be complicated with neurological deficits. The incidence of CVO has risen, particularly among patients predisposed by immune suppression, resulting in candidaemia that leads to haematogenous seeding of the vertebrae. Here, we report a case of CVO in a patient with chronic kidney disease, on regular haemodialysis via a central venous catheter, who had a recent history of effectively treated central line-associated bloodstream infection (CLABSI) due to *Candida parapsilosis*. She presented with lower back pain and fever, and culture of aspiration biopsy yielded *Candida parapsilosis*. The patient was successfully managed with nine months of antifungal therapy. This case report emphasises the occurrence of CVO following effectively treated *Candida* CLABSI and highlights the importance of establishing the fungal aetiological agent of vertebral osteomyelitis in patients with risk factors that require prolonged antifungal therapy.

Keywords: vertebral osteomyelitis, candidaemia, Candida parapsilosis, central venous catheter, chronic kidney disease

Introduction

Vertebral osteomyelitis (VO) in adults is primarily caused by haematogenous seeding from a distant focus. *Candida* vertebral osteomyelitis is rare. Diagnosis is often delayed for months and can be complicated with neurological deficits due to the destruction of the vertebral bodies and spinal cord compression. Risk factors for CVO including immunosuppression, indwelling central venous catheter and use of broad-spectrum antibiotics.[1] Patients typically present with back pain unresponsive to conservative measures, and elevated inflammatory markers with or without fever.[2]

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Reported cases of VO due to *Candida* spp. are scarce. Here we report a case of CVO due to *Candida parapsilosis* in an elderly woman with chronic kidney disease (CKD).

Case Report

A 62-year-old woman was admitted with back pain and fever. She had a history of progressive lower back pain for four weeks affecting movements and being wheelchair bound. She developed focal segmental glomerulosclerosis when she was 37 years old, which progressed to end-stage renal disease associated with hypertension. She was undergoing regular haemodialysis (HD) via a central venous catheter (CVC) while awaiting kidney transplantation.

Three weeks previous to her admission she was treated for a central line-associated bloodstream infection due to C*andida* species and was treated with removal of the central line and IV fluconazole for 14 days from the last negative blood culture. The blood culture isolate was identified at the National Reference Laboratory as C*andida parapsilosis.* Antifungal susceptibility testing facility was not available.

On examination, there was tenderness over the lower back. The patient was febrile (38.3 °C) with no change in vital signs. Neurological examination was normal. The white cell count (WBC) was 5.57 × 10 3/µl, ESR and CRP were 102 mm/1st hour and 19 mg/L respectively. Serum *candida* mannan antigen was negative, *candida* mannan antibody was positive and blood cultures had no growth.

MRI of the lumbar spine (19/09/2023) demonstrated spondylodiscitis at L4-L5 with a small prevertebral collection and degenerative changes at L3/L4 with no evidence of nerve root compression (Fig 1A). CT-guided spinal biopsy histologically showed unremarkable fibroconnective tissues.

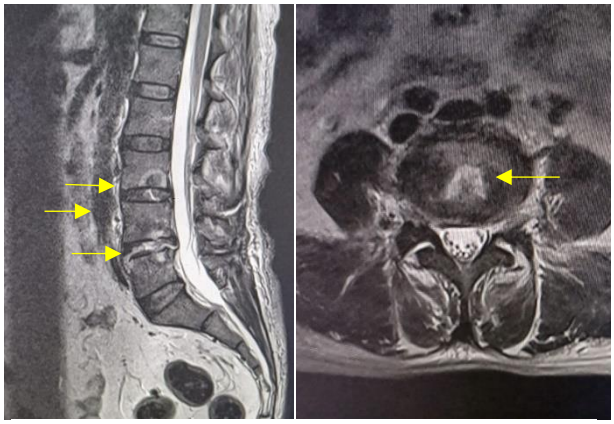

Figure 1 A: Initial MRI (19/09/2023) showing spondylodiscitis of the L4/L5 disc with a small prevertebral collection, degenerative changes at the level of L3/L4

TB PCR was negative. Culture of the biopsy yielded *Candida* species, identified at the National Reference Laboratory as *Candida parapsilosis*, similar to the recent CLABSI isolate, which was sensitive to fluconazole (MIC). A diagnosis of *Candida* vertebral osteomyelitis was made.

Empirical antimicrobial therapy was started with IV meropenem and IV teicoplanin and converted to antifungals after spinal biopsy yielded *Candida* spp. As per guidelines, the initial antifungal regimen included IV anidulafungin 200 mg (loading dose) followed by 100 mg daily dose for 2 weeks and IV fluconazole was added (loading dose 400mg 12 hourly followed by 400 mg on haemodialysis (HD) days and 200mg on non-HD days for a further 2 weeks). HD was continued as renal replacement therapy with multiple central lines replacements during this period.

Repeat MRI (10/10/2023) was done in 3 weeks due to clinical deterioration and elevated inflammatory markers, which was subsequently managed as a cannula site infection. Repeat MRI showed the previously noted destructive process involving the intervertebral disc and vertebral end plate at the level of L4/L5 with mild interval progression in size of previously appreciated prevertebral collection and degenerative changes at the level of L3/L4 with no evidence of nerve root compression (Fig 1B).

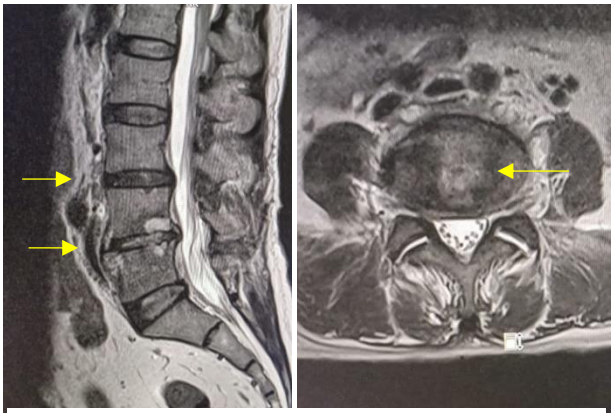

Figure 1 B
Repeat MRI (10/10/2023) showing previously noted spondylodiscitis at L4/L5 with mild interval progression in size of prevertebral collection, degenerative changes at the level of L3/L4

The patient gradually improved after 4 weeks of IV antifungal therapy,. She was discharged in 4 weeks on oral fluconazole which was continued for a further 8 months. She was followed up with full blood count, inflammatory markers and liver function tests (LFT) throughout the course of antifungal treatment. Tolerability was good with only mild LFT elevation which was subsequently normalised. A total duration of nine months of antifungal treatment was given, and she clinically recovered with complete resolution of back pain and normalisation of the inflammatory markers with confirmed one-year survival without recurrences.

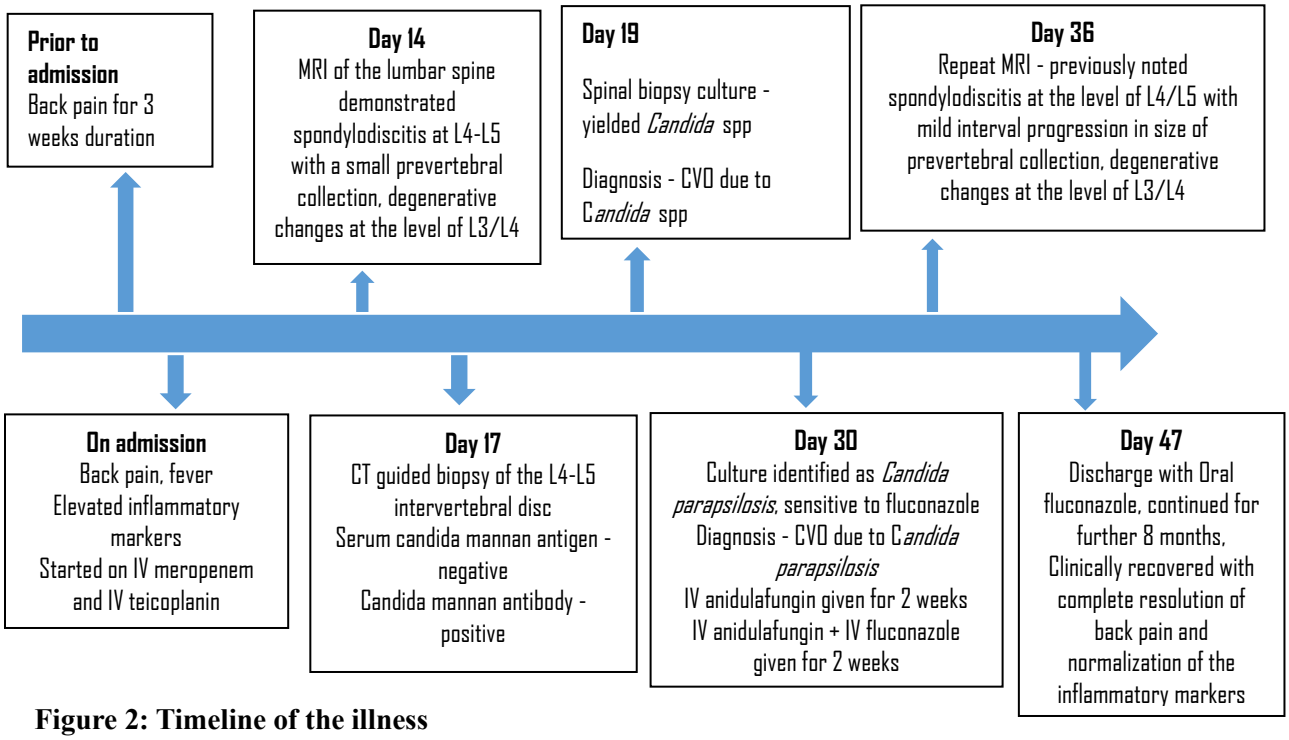

Figure 2: Timeline of the illness

Discussion

Invasive *candida* infections are rising due to increased immunocompromised patients with risk factors such as central intravascular catheters, use of broad-spectrum antibiotics, recent surgery, intravenous drug abuse, chemotherapy and parenteral nutrition.[1] Candida vertebral osteomyelitis is rare and represents approximately 1% of infectious spondylodiscitis which primarily develops haematogenously and can present up to 3 years after a bloodstream infection.[3,4]

CVO often presents with back pain in the lower thoracic to lumbosacral spine, usually with months of symptoms before diagnosis.[1] Early diagnosis is associated with an 85% cure rate, while diagnosis in later stages leads to the destruction of the vertebral bodies and abscess formation in the bony and epidural areas causing neurological deficits.[5]

Diagnosing CVO may be difficult and requires serologic, radiographic, and microbiologic diagnostic tests together with a high index of clinical suspicion. MRI is considered the imaging modality of choice for VO.[2] Williams et al.1999) reported several characteristic MRI features to differentiate fungal from bacterial osteomyelitis.[6] Every effort must be taken to achieve a definitive diagnosis by isolating the pathogen from the lesion through repeated needle biopsies. If negative, an open biopsy is warranted, as treatment for bacterial, mycobacterial, or fungal osteomyelitis is vastly different and requires prolonged therapy with close monitoring for potential toxicities. The *Candida* species should be further identified to guide therapy, as some may have reduced susceptibility to azoles. Blood cultures rarely yield the pathogen after the acute haematogenous stage and is more challenging due to the indolent nature of *C. parapsilosis*, with only 30-50% of blood cultures being positive.[7] In our case, although blood cultures were negative, spinal biopsy yielded *C. parapsilosis*, the same organism linked to the recent CLABSI, supporting the diagnosis of CVO with CLABSI being the probable focus.

Three weeks prior to this admission, central venous catheter (CVC) and peripheral blood cultures were collected simultaneously before routine dialysis to investigate an episode of fever. Both blood cultures were positive for *Candida* species suggestive of CLABSI. The peripheral blood culture isolate was identified as *Candida parapsilosis.* Repeat CVC blood culture was positive for *Candida* species while the peripheral blood culture was negative, indicating transient or intermittent candidaemia from the CVC. She was treated for CLABSI caused by *Candida parapsilosis* with IV fluconazole for 2 weeks after documented clearance from the bloodstream, with removal of CVC, which is adequate therapy for candidaemia.[8] However, the patient developed CVO, which could have been due to transient candidaemia causing haematogenous seeding of the vertebrae at the time of CLABSI detection. This challenges the effectiveness of current guidelines on the treatment of candidemia in preventing complications such as VO by haematogenous seeding.

Recommended antifungal therapy for CVO is with fluconazole or echinocandins for 6 to 12 months until the ESR and clinical symptoms improve. Repeat imaging studies should be reserved for patients failing to show clinical and laboratory improvement to assess complications and requirement for surgical intervention.[5] A recent systematic review reports a median duration of antifungal treatment of six months, primarily with fluconazole, and 80% two-year survivorship free of death. Younger age and prolonged treatment appeared protective, while older age, use of

haemodialysis, diabetes, liver cirrhosis, malignancy and infective endocarditis were associated with higher in-hospital mortality rates in patients with VO.[9,10]

Conclusion

Candida vertebral osteomyelitis is a rare condition, and fungal pathogens should be suspected in patients with risk factors. This case emphasises the importance of suspecting CVO in a CKD patient presenting with back pain undergoing regular HD, despite adequately treated recent CLABSI due to *Candida* species. Blood cultures can be negative in CVO and repeated biopsy sampling is warranted to make a definitive diagnosis to direct therapy together with MRI.

Declarations

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Ethics statement: Consent was obtained from the patient for publication of this case report
Author's contribution: All the authors have contributed to collecting information and preparation of manuscript

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