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Case report

Successful treatment of *Candida tropicalis* osteomyelitis with Micafungin in a leukemia patient

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Introduction

The incidence of invasive candidal infection is increasing. The widespread use of central intravascular catheters, invasive procedures, immunosuppression, diabetes mellitus, total parenteral nutrition, broad-spectrum antibiotics and drugs abuse predispose patients to the infection. Eye, kidney, liver, skin, cardiac and brain infections are the most common site of invasive candidiasis while vertebral osteomyelitis is rare. Most Candida vertebral osteomyelitis is caused by *Candida albicans*. Less common organisms include *C. tropicalis, C. glabrata and C. parapsilosis* [1]. Both amphotericin B and the azoles have a role in the treatment, but treatment failure with either agent had been reported [2,3]. Micafungin belongs to echinocandins, and interferes with the synthesis of fungal cell wall.

We report a *Candida tropicalis* infection manifested with osteomyelitis following a previous candidemia in a leukemia patient who was successfully treated by Micafungin.

Case report

A 52 year-old man with acute myeloid leukemia received IA (idarubicin + cytarabine) regimen of induction chemotherapy. His bone marrow showed remission, then he received another three consolidation chemotherapy. He experienced febrile neutropenia and septic shock after a course of mid-dose Cytarabine and recieved meropenem and voncomycin. Blood culture yielded *Candida tropicalis* and he was treated with Micafungin for 2 weeks. He had no fever and his leukocytes was nomal then he was discharged from hospital after recovery.

But a month later, he had lumber pain after heavy lifting. The pain became more and more serious and a low-grade fever developed. He couldn't walk because of the pain. Even he felt pain when he turned over. His physical examination was unremarkable except for diffuse lumber midline and paraspinal muscle tenderness. After his readmission, his lumbar MRI showed severe spondylodiscitis at L2–L3 and the formation of a vertebral abscess (Fig. 1).

The patient was operated with debridement of infected lesion and fusion of lumbar intervertebral space after general anesthesia. L2 as the center, took the middle incision about 8 cm, exposed the facet joints, opened, detected the pedicle was complete by probe, implanted guide needle, then completed L2, L3 pedicle positioning and implanted four screws. After decompression of vertebral plate, nerve root was seen to adhere with surrounding tissue. The intervertebral disc degenerated and the tissue was less than normal. The inflammatory granulation tissue was seen and a small amount of purulent package was sent to pathological examination. L2/3 intervertebral space lesion was completely removed, and the end plate was treated. The bones were cut into the size of rice for filling in cage. Two cages was implanted in the intervertebral space, fixed with rod, thoroughly washed the incision, completely stopped bleeding, stitched layer by layer, placed two tubes for postoperative drainage. Pus culture yielded *C. tropicalis* and he received Micafungin (150 mg/d, intravenous infusion) treatment for over four months.

His low back pain resolved progressively with treatment. A control lumbar MRI after four months of treatment and two months of follow-up showed gradual improvement radiologically and only the sequel lesions at the site of the infection (Fig. 2). His white blood cells were 2.0–2.5*10E9/L, but his bone marrow remained remission at the course of treatment and follow-up. Now he can walk freely and return to normal life.

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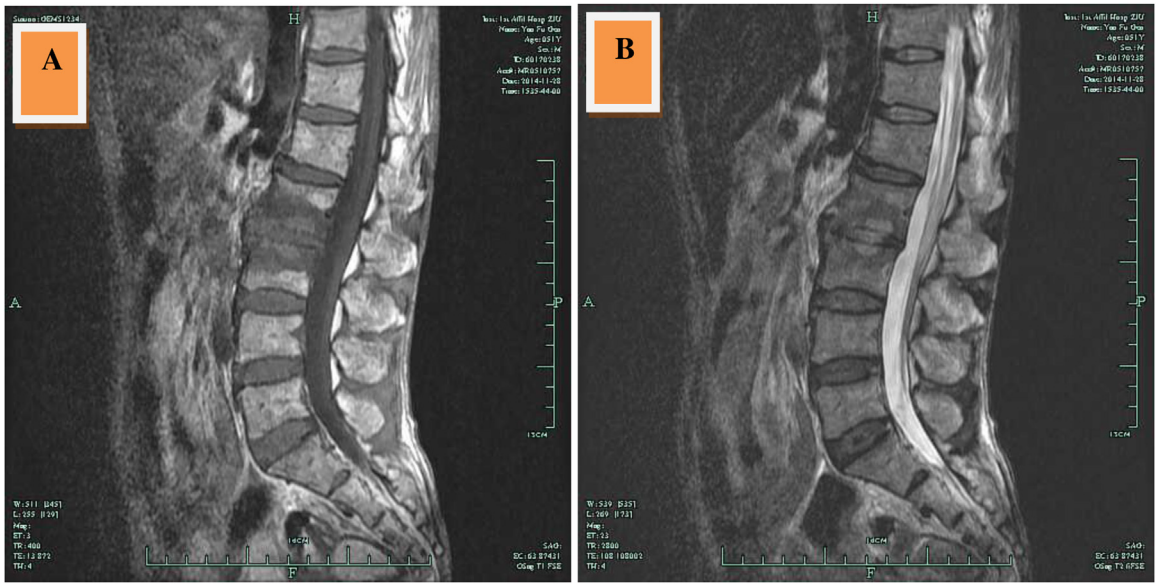

Fig. 1. Magnetic resonance image of the dorsal spine showing an L2–L3 spondylodiscitis: T1-sagittal MRI image of the lumber spine reveals hypointense signal within the L2-3 disc and associated destruction of vertebral bodies and compromise of the spinal cord at this level (A). T2 sagittal MRI reveals hyperintense marrow signal (B).

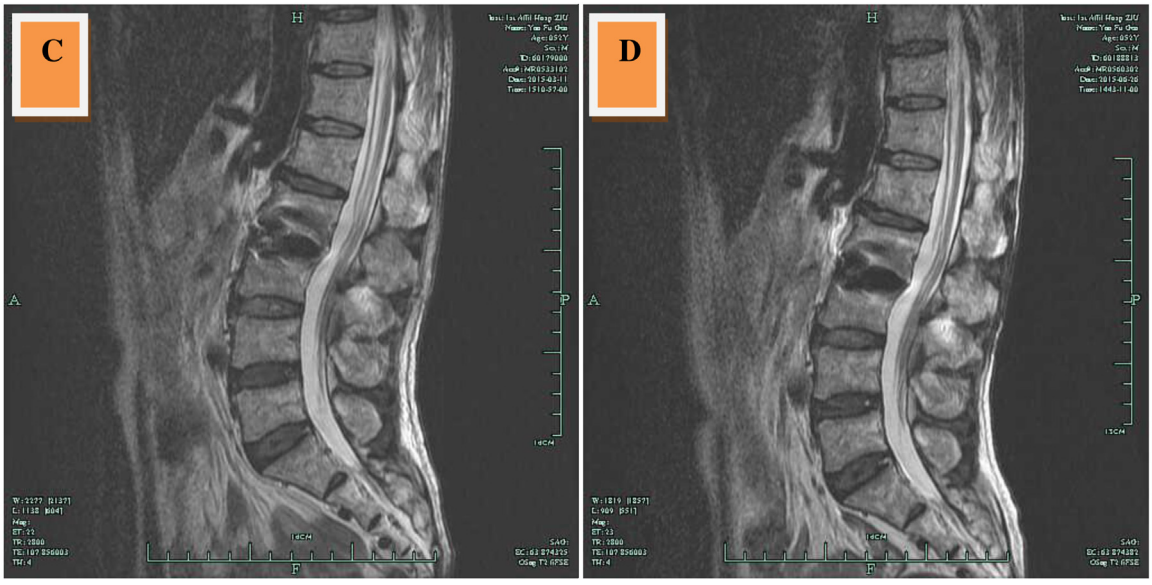

Fig. 2. A control lumbar MRI after two months of treatment (C) and four months of follow-up (D) showed gradual improvement radiologically and only the sequel lesions at the site of the infection (T2 sagittal).

Discussion

This patient was a middle-aged man with leukemia. Fever and lumber pain were his main complaint. He had several risk factors: broad-spectrum antibiotic usage, CVC, immunosusppression, malignancy and candidemia. The time interval from candidemia to identification of Candida osteomyelitis was about two months. It is possible that the complications experienced by this patient could have been averted with adequate treatment of the initial candidemia.

The diagnosis of candidal vertebral osteomyelitis begins with a high clinical index of suspicion, followed by appropriate radiographic studies and confirmation with microbiological tests [3]. MRI is more sensitive, specific and accurate than radioisotope bone scan or CT scan for early recognition and localization of infectious disease. Lifeso et al. found MRI to be 96% sensitive, 92% specific and 94% accurate in the diagnosis of vertebral osteomyelitis. In addition, MRI is an excellent way of demonstrating the presence of epidural or paraspinal extension of the infection [4]. Thus, MRI studies may lead to early diagnosis and differential diagnosis from degenerative disc disease, malignancy and tuberculosis.

A review of Candida osteomyelitis cases reported in the literature showed *C. albicans* as the predominant species (69%), followed by *C. tropicalis (15%) and C. glabrata* (8%). Fifty-seven percent of patients underwent a combination of surgical and antifungal therapy with therapy reported to be successful in 88% [5–7].

Amphotericin B has historically been the most commonly used antifungal therapy for Candida infections, but there appears to be a trend toward the use of azoles and echinocandins. However, there are very limited data available to support using echinocandins as therapy for candidal osteomyelitis. A review of literature revealed

only a small case series of four patients with candidal osteomyelitis, all treated successfully with caspofugin [5,8,9]. So far there is no reported cases of treatment with micafungin for C. tropical osteomyelitis.

Micafungin as one kind of echinocandins, is indicated for the treatment of candidemia, acute disseminated candidiasis, candida peritonitis, abscesses and esophageal candidiasis [10,11]. Micafungin has been approved for the prophylaxis of candida infections in patients undergoing hematopoietic stem cell transplantation. Micafungin works by way of concentration-dependent inhibition of 1,3-beta-D-glucan synthesis resulting in reduced formation of 1,3-beta-D-glucan, which is an essential polysaccharide comprising one-third of the majority of candida spp. cell walls. This decreased glucan production leads to osmotic instability and thus cellular lysis [10,11].

Micafugin are better than Amphotericin B in terms of nephrotoxicity, liver enzyme changes, and general side effects, including fever, chills, nausea, vomiting, and dyspnea. We reveal that micafugin has no evident side effect in this patient and plays a great role in his symptoms relief and radiografic improvement. Long-term therapy with micafugin is generally well-tolerated and can be continued for longer than 4 months.

Surgical intervention was generally used to make a definitive diagnosis when examination of biopsy specimen was not diagnostic, to decompress the spinal canal when radiographic or clinical features suggested spinal cord impingement, or to provide stability in the face of extensive disease [3]. Combination treatment of antifugal agents and surgical debridement and sufficient drainage is a better way to treat Candida osteomyelitis.

Prompt diagnosis and appropriate treatment are associated with a good prognosis. The prognosis for patients with candidal vertebral osteomyelitis appears to be favorable, with an overall cure rate of candidal vertebral osteomyelitis of 85%. The majority of patients were clinically cured in the absence of significant comorbidities [3].

Conclusion

To our knowledge, this is the first case report that Micafungin successfully treated *Candida tropicalis* osteomyelitis in a leukemia patient. Although *Candida tropicalis* are a rare cause of vertebral osteomyelitis, clinicians must suspect this entity in patients presenting with risk factors for candidiasis and low back pain of long duration. Once diagnosed, it should be aggressively treated with combination of medical and surgical management. Historically amphotericin B was the most frequently used agent, followed by flucytosine. Now more options are available. Micafugin as a new agent showed a great role in treatment of this patient. There is need for further research on the appropriate length of treatment with Micafugin for *Candida tropicalis* osteomyelitis [3].

Conflict of interest

The authors have no conflict of interest to declare.

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