

A Rare Case of Aspergillus Spondylodiscitis In B-Cell Acute Lymphoid Leukemia

Keywords: Aspergillus spondylodiscitis; Invasive aspergillus infection; Voriconazole; Liposomal amphotericin B; Isavuconazole

Abstract

Introduction: Spondylodiscitis is an infection of the disc space and surrounding vertebrae. Mycobacterium tuberculosis and bacterial infections are the most prevalent causes, but fungal spondylodiscitis is comparatively uncommon. Mycotic infections are most commonly caused by Candida and Aspergillus species. Aspergillus is a saprophytic fungus that lives mostly in soil and plants. The incidence of Aspergillus affecting the bone among all cases of invasive aspergillosis is estimated to be 3%. They infiltrate the spine in immunocompromised patients, such as those who have had an organ transplant, are on chronic steroid medication, or are undergoing chemotherapy.

Case Report: An adult male with Type 2 Diabetes Mellitus, Hypertension and alcoholic liver disease was diagnosed with B-Cell Acute Lymphoblastic Leukemia with CALLA positive, FISH Negative. He was started on chemotherapy with G-MALL 07/03 regimen. During BFM 76/79 Re-intensification phase II the patient complained severe lower back pain. A CT guided biopsy from the area previously diagnosed to have Discitis (T4-T5 disc bulge soft tissue) showed negative for malignancy. In view of persistent backache, MRI of whole spine and pelvis was done, which revealed L4-L5 disc inflammation of infectious etiology. Surgery for L4-L5 stabilization and biopsy from the same region analyzed with molecular PCR revealed Aspergillus spp. Patient was initiated on Anti-fungal agents.

Conclusion: Invasive aspergillosis most commonly affects the sinopulmonary tract, with the lung being the most common location of infection, while Aspergillus osteomyelitis is rare. Contiguity, hematogenous spread, and direct implantation are all factors that affect bone tissues. The prevalence of Aspergillus disrupting the bone is believed to be 3% of all cases of invasive aspergillosis, with rates ranging from 1 in 10,000 to 1 in 250,000. Treatment outcomes are greatly influenced by a variety of factors, including neurological illnesses, underlying conditions, and early detection and management.

Introduction

Spondylodiscitis is an infection of the disc space and surrounding vertebrae. *Mycobacterium tuberculosis* and bacterial infections are the most prevalent causes, but fungal spondylodiscitis is comparatively uncommon. Mycotic infections are most commonly caused by *Candida* and *Aspergillus* species. *Aspergillus* is a saprophytic fungus that lives mostly in soil and plants. The incidence of *Aspergillus* affecting the bone among all cases of invasive aspergillosis is estimated to be 3%. They infiltrate the spine in immunocompromised patients, such as those who have had an organ transplant, are on chronic steroid medication, or are undergoing chemotherapy [1]. Invasive aspergillosis can migrate from the lungs to the brain, kidneys, heart, and bones, with the spine being a main target. It is frequently misdiagnosed at first presentation because to its potentially delayed start and non-specific clinical symptoms [2]. Medical therapy alone or surgery with medical therapy is the mainstay of treatment [3,4]. Here, we report the case of an immunocompromised 53-year-old male with L4-L5 spondylodiscitis caused by *Aspergillus*.



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Case

A 53 year old gentleman with Type 2 Diabetes Mellitus, Hypertension and alcoholic liver disease was diagnosed with B-Cell Acute Lymphoblastic Leukemia with CALLA positive, FISH Negative. He was started on chemotherapy with G-MALL 07/03 regimen. During G-MALL 07/03 induction phase 1 he developed vincristine induced pseudo-obstruction which was managed with conservative treatment. During Induction with G-MALL 07/03 phase II, the patient had increased transaminase level, biopsy showed features of alcohol induced liver dysfunction also he was found to have secondary haemochromatosis with deposition of iron in liver and heart managed with Deferoxamine in view of this the treatment was changed to BFM 76/79 chemotherapy protocol with appropriate hepatic dose modification. While on the chemotherapy, post PEG asparaginase (BFM 76/79 Reintensification Phase I) he had an episode of elevated liver enzymes. Later he developed transient loss of vision further examination revealed occipital lobe abscess for which he underwent surgical excision and was also treated with empirical antibiotics and antifungal. The chemotherapy continued as per schedule and he was post BFM 76/79 consolidation, BFM 76/79 Re-intensification phase I and II.

At the last cycle of BFM 76/79 Re-intensification phase II the patient complained severe lower back pain. A CT guided biopsy from the area previously diagnosed to have Discitis (T4-T5 disc bulge soft tissue) showed negative for malignancy. In view of persistent backache, MRI of whole spine and pelvis was done (Figure 1), which revealed L4-L5 disc inflammation of infectious etiology. The patient underwent posterior spinal decompression with wit L4-L5 debridement with instrumentation and stabilization. Intraoperative findings showed unstable L4-L5 vertebra. Biopsy from the same region analyzed with molecular PCR revealed *Aspergillus* spp. The patient was initiated on empirical antifungal treatment with Liposomal Amphotericin B with necessary premedication but after the third

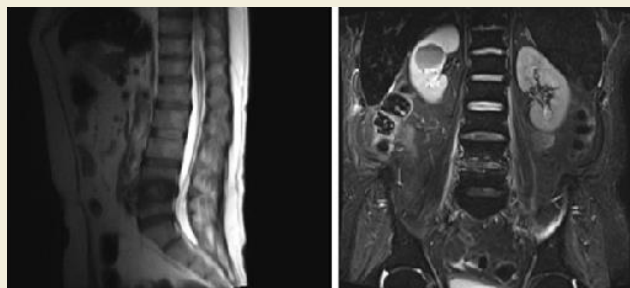


Figure 1: Interval Development of L4/L5 Spondylitis with associated prevertebral, paravertebral enhancing soft tissue, small paravertebral abscess and thin enhancing soft tissue causing mild canal stenosis of infectious etiology.

dose he developed hypersensitivity reaction and the treatment was interrupted. His treatment was thus changed to Voriconazole, after the first dose of which he developed an episode of hallucination. Following this, Isavuconazole was prescribed for 6 months and he tolerated it with significant symptomatic improvement. After 2 weeks of isavuconazole therapy, during the next follow up visit voriconazole was re-challenged and the patient tolerated it well which was done in view of financial constraints. He is now on follow up with voriconazole maintenance therapy.

Due consent was taken from the patient before publication procedures..

Discussion

Aspergillus species are saprophytic microbes that are ubiquitous. Invasive aspergillosis most commonly affects the sinopulmonary tract, with the lung being the most common location of infection, while *Aspergillus osteomyelitis* is rare. Contiguity, hematogenous spread, and direct implantation are all factors that affect bone tissues. The prevalence of *Aspergillus* disrupting the bone is believed to be 3% of all cases of invasive aspergillosis, with rates ranging from 1 in 10,000 to 1 in 250,000.[5] Men are 3 times as likely as women to be affected [5,6].

Although *Aspergillus* spondylodiscitis is an uncommon opportunistic fungal infectious illness, it has recently overtaken *Candida spondylitis* in terms of occurrence. It most commonly arises in an immunocompromised host as a result of AIDS, organ transplantation, chemotherapy, or immunosuppressive medication, among other factors [2,7]. The patient in this case was immunocompromised, and the predominant focus of *Aspergillus* appeared to be pulmonary.

Aspergillus spondylodiscitis is characterised by a lack of particular clinical characteristics. Lower back pain with or without fever, neurologic impairments due to cord damage, or kyphosis are the most prevalent symptoms. The majority of patients developed spondylodiscitis or epidural abscess at one or more vertebral levels. Diagnosing aspergillus spondylitis early is difficult and requires a

high level of suspicion. Histopathological investigation and bacterial culture are the most reliable diagnosis procedures for *Aspergillus spondylitis*. Diagnostic imaging, such as CT and/or MRI, is necessary for disease staging and guiding orthopaedic and/or neurosurgical intervention [2,4,7]. In our case, the patient is known ALL, and radiological findings suggested infective spondylodiscitis at L4-L5. The diagnosis was confirmed by a surgical biopsy.

Surgical decompression in combination with antifungal therapy is advised for *Aspergillus* spondylodiscitis patients who have spinal instability or symptoms consistent with spinal cord or radicular compression or abscess formation. The Infectious Diseases Society of America (IDSA) recommends an antifungal treatment regimen of at least 8 weeks, with longer courses (>6 months) frequently required. Voriconazole has been recommended as a first-line treatment, either alone or with surgical debridement. Amphotericin B or Isavuconazole is an alternative primary treatment. Itraconazole has been used subsequent to a course of Amphotericin B. Posaconazole or echinocandins have been used in the treatment of *Aspergillus* spondylodiscitis with limited results [4]. In the present case, *Aspergillus* spondylodiscitis was treated with Isavuconazole as patient could not tolerate Voriconazole and Amphotericin B. Isavuconazole have numerous benefits over existing azoles, including comparable effectiveness with fewer adverse effects, favorable pharmacokinetic characteristics, and good absorption when administered orally but affordability as maintenance therapy remains a disadvantage to be addressed [8]. The patient tolerated and is symptomatically better with the current medication. Treatment outcomes are greatly influenced by a variety of factors, including neurological illnesses, underlying conditions, and early detection and management.

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