Spontaneous cord transection due to invasive aspergillus spondylitis in an immunocompetent child

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Abstract Invasive spinal aspergillosis in an immunocompetent child is rare and often there is a considerable delay in diagnosis. A 13-year-old male child treated medically as tuberculosis of spine elsewhere for 1 year, came with complete paraplegia, dorsolumbar kyphosis and intermittently discharging sinus in the back. The child was taken up for surgical decompression and stabilization. Intraoperatively black granulomatous material was noted inside the canal extending anteriorly towards the vertebral body. There was complete cord transection with severe vertebral destruction and osteoporosis. The pathology and microbiology confirmed aspergillosis and the child was started on antifungal treatment. At further follow up, the infection was found to spread to the lung and caused further vertebral destruction. A change in the antifungal medication controlled further spread but failed to eradicate the infection at 2-year follow-up. In this patient, the delay led to extensive vertebral destruction with spine deformity and spontaneous cord transection. Retrospective review of the clinical and radiological findings suggests that this complication could have been prevented if these findings were carefully interpreted. In this era of transplantation and increase in use of immunosuppressive drugs the authors suggests having fungal infection as a differential diagnosis for infections of the spine.

Keywords Invasive aspergillus spondylitis · Immunocompetent · Vertebral destruction · Spontaneous cord transection

Introduction

Aspergillus is a rare cause of spondylitis. Though found throughout the world, it is usually pathogenic in immunocompromised hosts [1, 2]. Aspergillus spondylitis in a non-immuno compromised patient is rarely reported [1, 3, 4]. Due to its rarity, the lack of medical awareness and the similarity in clinical and radiological findings, it is often misdiagnosed as tuberculous spondylitis [1, 3, 4]. Since the management strategies of both are different, they should be differentiated at the early stage itself. Though there are reports of successful treatment of early aspergillus spondylitis with anti-fungal agents alone [2, 4], the invasive type usually responds poorly to the drug therapy [5]. The prognosis for disease cure in patients with invasive aspergillus spondylitis is poor [3, 6] especially when there is extensive vertebral destruction [6].

Case report

A 13-year-old male child presented with gradual onset paraplegia for 8 months, a painful dorsolumbar kyphosis of 6 months duration and bowel and bladder incontinence of 4 months duration. The child was apparently normal 1 year ago after which he developed mild low back pain, which was insidious in onset and progressive, there was no history of radiation of the pain. Two months later, he developed mild weakness in both legs which was insidious in onset and gradually progressive. He went to a local hospital for

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these symptoms where he was investigated and a diagnosis of T11–12 tuberculosis was made. He was started on anti-tuberculous treatment, spinal brace and rest. He had improvement in his back pain and weakness for the initial 2 months, later his back pain worsened and weakness in legs kept increasing gradually over 8 months. There was complete loss of power in the lower limbs for 2 weeks, after which he presented to us.

Examination revealed a tender dorsolumbar kyphosis with a midline sinus discharging sero-sanguinous fluid intermittently. The power was grade zero in both lower limbs, while sensation was preserved till T10 vertebral level. The X-ray (Fig. 1a) showed T11–12 vertebral destruction with lateral translation of T11 on T12 and retropulsion at the level of T11. The MRI (Fig. 1b) showed severe destruction of all three columns in T11, T12 with gibbus, osteolytic destruction from T9 to L3 vertebra, large intra spinal abscess from T9 to L2, multiple loculated pre and para spinal abscesses from T5 to L3, erector spinae abscess at L3 and subcutaneous abscess at T8, T9 level. The cord was not visualized at the apex of the deformity. The blood parameters were normal except for a increase in the total WBC count and ESR. There was no history to suggest immunocompromised status and the laboratory tests for immunodeficiency were negative. The sinus tract discharge was negative for acid-fast staining and the culture showed excessive growth of skin commensals. The child was then taken up for surgical decompression and stabilization to avoid further instability and to remove the elements causing spinal cord compression.

Through a posterior approach the soft tissues were carefully dissected and the spinal canal opened. There was plentiful infiltration of the deep layer of the para spinal muscles with black granulomatous material. There was extensive destruction of the posterior elements of the spine at the apex of the deformity. The canal was found to be completely filled up with black granulomatous material. The normal spinal cord was identified both proximally and

distally by doing partial laminectomy of T10 and L1. On careful removal of the intervening blackish material the cord was found to be completely transected at the apex of the deformity (Fig. 2). The transected ends were filled with blackish material. The transected ends of the cord were retracted and the material extending anteriorly was curetted to the maximum possible limits. Anteriorly through the gap, psoas muscle was visualized and found to be infiltrated with the granulomatous material. The material was sent for histopathological examination (HPE) and culture. Internal fixation was deferred because of severe vertebral osteoporosis and doubts about the diagnosis. The nibbled normal bone obtained during the surgery was placed between the decorticated transverse processes of T10–L1 and the spine was protected externally with a rigid thoracolumbosacral orthosis.

Histopathological examination (HPE) (Fig. 3) revealed fungal growth with acutely branching septate hyaline hyphae suggestive of aspergillosis. The culture report confirmed aspergillosis and the species was identified as *Aspergillus fumigatus*. The Lacto Phenol Cotton Blue mount of the growth showed (Fig. 4) uniseriate black and round conidiospores around the sporangium (globose vesicle) with germ tube formation.

The child was started on intravenous amphotericin B (0.25 mg/kg initially increased to 1 mg/kg at 3 weeks time) which healed the sinus and decreased the pain initially. But at the follow up of 2 months, the child presented with hemoptysis, blackish material in the sputum with infection spread to the lung (Fig. 5). The MRI showed increase in the fungal load with further vertebral destruction and deformity (Fig. 6a, b). The parents and the child refused further surgical intervention because of increased intraoperative mortality risk with no chance of neurological recovery. The child was then started on intravenous voriconazole (4 mg/kg every 12 h) for 2 months followed by oral voriconazole (100 mg every 12 h) which controlled the progression of infection but failed to cure it at the final follow up at 2 years.

Fig. 1 a X-ray of the child showing T12 vertebral destruction with lateral translation of T11 on T12 and retropulsion at the level of T11. **b** The coronal (T2-seq), sagittal (T1-seq) and axial (T1-seq) MRI (T12) showing destruction of the vertebra from T9 to L3. Large intra spinal abscess from T9 to L2, multiple loculated pre and para spinal abscesses from T5 to L3, erector spinae abscess at L3 and subcutaneous abscess at T8, T9

Fig. 2 The cut ends of the cord are shown by yellow arrows. The black granulomatous material was extending anteriorly and was removed to the maximum possible limits

Discussion

Aspergillus species are ubiquitous saprophytic fungi frequently found in the environment and are rarely pathogenic for humans. In humans, the most common portal of entry is by inhalation through the respiratory tract; however, entry

through the gastrointestinal tract, skin wound, and direct entry through the orbits or ears have been described [7]. Clinically, aspergillosis presents in one of three different ways: as superficial, locally invasive aspergillosis, or as invasive aspergillosis. The two milder clinical forms although rare can occur in normal immunocompetent subjects [7].

Aspergillus spondylitis is an opportunistic infection typically occurring in immunocompromised patients; however, it is increasingly reported in previously healthy patients without immunocompromise [3, 7, 8]. *Aspergillus* spondylitis typically presents with back pain, while neurological deficits may be seen in approximately 30% of cases [7]. Neurological deficits may occur due to compression of the cord by the *aspergillus* granulomatous mass, abscess or vertebral debris [3, 4, 8]. Few studies emphasized about the direct invasion of the spinal cord by the *aspergillus* causing extensive spinal cord necrosis [9, 10]. In one of the studies they found *aspergillus* hyphae filling the blood vessels of the necrotic spinal cord at autopsy [9]. The other showed *aspergillus* invading the anterior and lateral columns of the cord by penetrating into the myelin sheaths [10].

Spinal aspergillosis is often confused with tuberculous spondylitis [3, 4] as the clinical and radiological features of

Fig. 3 The low power view (left $\times 100$) showed fungal ball surrounded by inflammatory cells. The high power view (right $\times 430$) showed acutely branching septate hyaline hyphae typical of aspergillosis

Fig. 4 The Lacto Phenol Cotton Blue mount of the culture shows uniseriate conidia arranged around the sporangium (globose vesicle) on the left and the germ tube formation on the right

Fig. 5 At 2-month follow-up the infection spread to the right lung from the vertebra

Fig. 6 **a** The sagittal MRI (T2-seq) at 2-month follow-up shows deterioration in the deformity and further vertebral destruction with a large subcutaneous abscess. **b** The axial cuts at T11 (T2-seq) and L3 (T1-seq) show gross increase in the fungal load in retroperitoneal space with vertebral destruction and multiple abscesses

the both are similar [1, 3, 4]. However, identification at the early stage is important, as complete eradication of the disease is possible with antifungal agents and surgery [2, 4]. The delay in diagnosis and treatment can lead to extensive spread with high morbidity and mortality [3, 8, 11]. The long-term clinical outcome did not seem to be related to the specific species of fungus but rather to the time between the onset of the symptoms and the treatment of the infection [8]. Delay in diagnosis led to poorer results in terms of final neural recovery [3, 8].

The absence of sustained clinical improvement to anti-tuberculous treatment coupled with the following radiological findings suggests aspergillus spondylitis. In invasive aspergillosis the lesion spreads more circumferentially than longitudinally and destroys the vertebral body, neural arches and extend into chest wall and thoracic cavity as seen in our case and other reported cases [3, 6, 11]. Unlike tuberculous spondylitis which spreads longitudinally [12], we hypothesize that aspergillus spreads circumferentially as it is capable of invading fascia and neural tissues. Minimal

hyperintensity or isointensity of the vertebrae on T2-weighted MRI images and preservation of disc intranuclear cleft is suggestive of early aspergillus or candida spondylitis [13, 14]. However, none of the signs are specific for aspergillosis.

Since radiological studies are nonspecific, the definitive diagnosis of vertebral aspergillosis depends on isolation of the organism from biopsy [15]. Routine gram staining and acid-fast staining of tissue specimens are usually negative; thus, special procedures such as periodic acid-Schiff staining and Grocott-Gomori methenamine–silver nitrate staining are necessary to visualize fungal hyphae.

There are no clear guidelines available regarding the management of spinal aspergillosis since most of available literature are isolated case reports or case series including different fungal species. Although aspergillus osteomyelitis has been primarily treated medically, certain cases may require surgical intervention. In the presence of spinal instability or symptoms of spinal cord or radicular compression, surgical decompression is indicated [7]. If surgical

intervention is required, it should always be combined with pre- and postoperative medical treatment [7]. The drug of choice traditionally has been amphotericin B, because of its low bone penetrance and toxicity some investigators have advocated the use of voriconazole [16, 17]. In our case, voriconazole helped in preventing further progression of the disease and the patient was able to tolerate the drug well inspite of its long-term use. We suggest that in future voriconazole can be used as a first line therapy for invasive spinal aspergillosis and support the view by Mouas et al. [17].

Our patient was immunocompetent and yet developed aspergillus spondylitis further emphasizing that invasive aspergillosis is not rare in immunocompetent hosts. The patient was misdiagnosed and treated for tuberculosis and is yet another addition to the list of cases of delayed diagnosis. Progression of the disease process resulted in translation of the spine. The exact mechanism of cord transection is not known, as this is the first reported case. However, we hypothesize that invasion of the cord by aspergillus [9, 10] led to extensive necrosis and gradual translation of the unstable spine aided transection of the cord. This complication could have been prevented if there was an initial suspicion about fungal infection.

Conclusion

Invasive spinal aspergillosis although rare, can occur in immunocompetent individuals and is often confused with tuberculosis. The delay in diagnosis can cause multiple vertebral destruction and neurological damage up to cord transection. Radiologically, circumferential spread with destruction of all the columns of a vertebra and chest wall involvement is more suggestive of aspergillus spondylitis. It is important to have fungal spondylitis as a differential diagnosis in spinal infections as this condition is curable when detected early. Performing biopsies in cases of suspected tubercular spondylitis not responding to treatment will lead to earlier detection of the cause, thereby decreasing the morbidity and mortality of this condition.

The study was approved by the institutional review board and patient was counselled regarding the study and consent obtained.

Conflict of interest statement None of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article.

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