A Case Report of Aspergillus Fungal Spinal Infection in Immunocompetent Patient and Review of Literature

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Abstract

Background: Spinal aspergillus infection is rare but can cause significant morbidity and mortality. Sometime it may mis-diagnosed as pyogenic or tuberculous infection in immunocompetent patients. Therefore, it causes delay in diagnosis and leads to spinal instability, neurological deficit, and sometimes death.

Case Report: Here we discussed a case of 68-year-old female patient with severe back pain and difficulty in walking which was gradually increased over the period of time of two months. During this, she was diagnosed as koch's spine based on MRI report and she had been started on empirical anti-tuberculous medication. But her condition was deteriorated. After that patient underwent surgical management and infected tissue sent for culture and sensitivity and histopathological examination. The report was positive for aspergillus fungal infection. she was started with anti-fungal medication and course of treatment was uneventful.

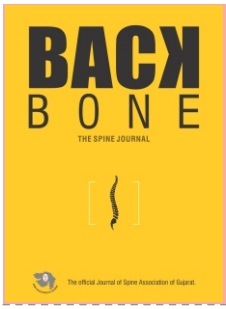
Conclusion: Early diagnosis of spinal fungal infection is often delayed in immunocompetent patients and it lead to delayed in anti-fungal management which lead to increase in morbidity and mortality.

Keywords: Aspergillus, Spinal fungal infection

Introduction

The cases of fungal infection have been increasing since 1980 and it is believed that it related to increase in immuno-suppressed patients [1]. Aspergillus is ubiquitous moulds and present in compost, air dust and ducts. The most commonly affected organ with aspergillosis is lung and extrapulmonary site is bone. Aspergillosis infection of spine is rarely encountered. Early diagnosis of fungal spinal infection is difficult and it is aggressive infection which may lead to spinal instability, neurological deficit, cauda equina syndrome and death [2, 3].

Here we describe a case of a 68-year-old female patient, diagnosed with aspergillus fungal infection of D5-D6 level and was treated with surgical decompression and fixation followed by oral anti-fungal medications. In addition, we reviewed all the available literature on fungal spinal infection and summarized the characteristics.



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Case Report

A 68-year-old female patient presented to outpatient department with history of severe back pain and radiating pain to ribs for the past 3 months. She was having difficulty in standing and walking due to severe pain. Pain was gradually increased with bending, standing, walking, or any posture change and was not relieved with rest and medications. There was no neurological deficit in lower limbs. There was no history of fall, trauma or fever. She had no history of weight loss. She was known case of diabetes and hypertension. There was no history of any infection or receiving steroids in the recent past. Other systemic examinations did not reveal any manifestation of any immunosuppressive conditions. Two months back, she was admitted to other hospital for the same and necessary investigations were done. After that she was diagnosed as spondylodiscitis (Koch's spine) D5-D6 and she had been started on empiric anti-\lar medications based on MRI report. However, the pain was not reduced and her condition deteriorated. She developed radiating pain to anterior ribs. Her physical examination revealed tenderness over dorsal region with normal neurology. After admission, routine investigations were done which showed increased ESR and CRP. MRI of spine showed altered signal intensity marrow edema in opposing end-plates D5-D6 with end-plates erosions and moderate wedging of D5 & D6 vertebra with pre and para vertebral fluid collection. Maximum width of pre-vertebral, right paravertebral, left paravertebral and anterior

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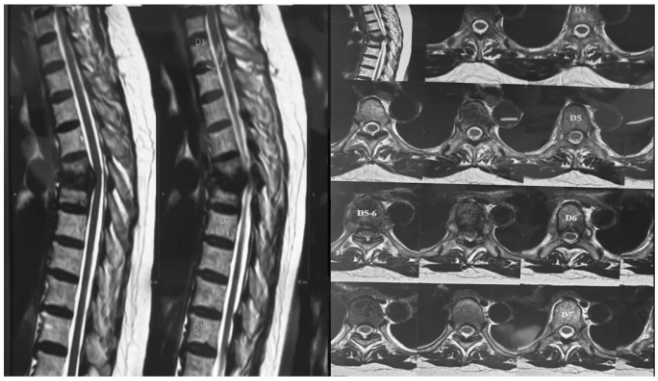

Figure 1: MRI of dorsal spine showed spondylodiscitis D5-D6 with pre and para vertebral fluid collection.

Figure 2: X-ray dorsal spine AP and Lateral showed endplate at opposing endplates of D5-D6 level with wedging of D5 and D6 vertebra

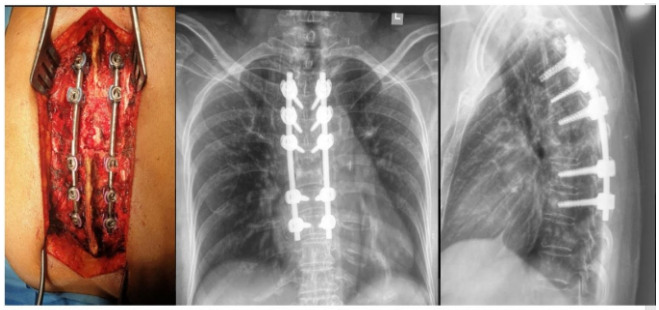

Figure 3: a) intra-operative, b) and c) show immediate post-op X-ray dorsal spine AP and Lateral view.

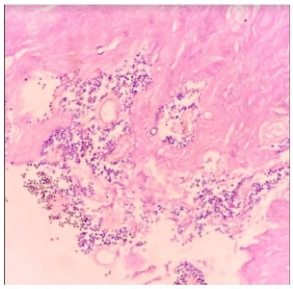

Figure 4: showed necrotic osteoid tissue with septate fungal hyphae and pigmented spores suggestive of aspergillus infection

Figure 5: Post-op X-ray at 6 months follow-up shows sclerosed opposing end-plates of D5-D6 and fusion of D5-D6 vertebra with implant in situ.

epidural collection measured approx. 3.3 mm, 6 mm, 5 mm and 3.6 mm, respectively. There was severe central canal stenosis and focal cord edema at D5-D6 level (Fig. 1). Chest x-ray was within normal limit. Dorsal spine x-ray showed endplate at opposing endplates of D5-D6 level with wedging of D5 and D6 vertebra. (Fig. 2). Patient underwent surgical management fixation and decompression with laminectomy (Fig. 3) and D5-D6 disc tissue was sent for culture and sensitivity and histopathological examination. Culture and sensitivity reported showed no growth. It was negative for GeneXpert and AFB. It was positive for fungal infection. HPE showed necrotic osteoid tissue with septate fungal hyphae and pigmented spores suggestive of aspergillus infection (Fig. 4). After that patient referred to infectious specialist and he advised for aspergillus antigen test and beta D glutan level fungitell. Both aspergillus antigen test and beta D glutan level fungitell were positive with value of 1.77 and 398.95 pg/mL respectively. After that she was started on tab voriconazole 200 mg BD for 3 months and her anti-tubercular medication was stopped. The patient withstood the antifungal medication well and course of treatment was uneventful. Back pain was reduced gradually and patient started walking without support. 6-month follow-up X-ray shows sclerosed opposing end-plates of D5-D6 and fusion of D5-D6 vertebra (Fig. 5).

Discussion

Spinal fungal infection is an uncommon condition and it is difficult to diagnose in early stage of vertebral infection. The incidence of aspergillus fungal infection is estimated of 12/10,00,000 population per year [4]. The incidence of fungal infection is increasing in recent years due to increase use of immunosuppressive medications, prolonged use of broad-spectrum antibiotics, prolonged neutropenia following chemotherapy, intravenous drug abusers, solid organ transplant recipient, patient with lung cancer and COPD, acquired immunodeficiency syndrome (AIDS). Recently the cases of aspergillus fungal infection also increase in immunocompetent patients with risk factors like pulmonary aspergillosis, tuberculosis, previous discectomy, diabetes, endometritis, fungal heart disease [5, 6]. Our patient was known case of diabetes mellitus and hypertension.

Aspergillus is a saprotropic fungus and its primary habitat is the soil, compost heaps, damp grain. This fungus can adapt, proliferate in the hostile environment and this can help fungus to resist and survive against human immune system. So that, aspergillus fungal infection is rare but one of the most devastating infections in term of morbidity and mortality [7]. Aspergillus fungus can cause three types of diseases based on host immune system like aspergillosis in the

immunocompetent patients, aspergillosis in the atopic patients and invasive pulmonary aspergillosis in the immunosuppressed patients [8]. Sometimes it is difficult to diagnose spinal fungal infection with aspergillus as it shares several common features as in pyogenic spinal infections like bimodal age distributions, more common in males, common in lumbar spine with back pain followed by thoracic and cervical spine [9]. The fungal infection can be spread to vertebra through exposure to contaminated blood (haematogenous spread), direct extension from adjacent pathology mainly from lung, and direct inoculation (trauma or iatrogenic) [5].

Clinical features of aspergillus vertebral osteomyelitis are non-specific and it may delay the diagnosis which increases morbidity and mortality. Low back pain is most common symptom with or without fever malaise and night sweat. Sometimes epidural abscess forms and it causes neurological symptoms and even lead to paraplegia and bladder and bowel involvement [10] of central nervous system can be lethal complication of aspergillus fungal infection and associated with mortality of more than 95% [11]. Early diagnosis of fungal spondylodiscitis can give better result and reduce the morbidity and mortality. Blood investigations like CBC, ESR, CRP are of little helpful in diagnosis of aspergillus vertebral osteomyelitis [12]. Even radiological findings are known to be non-specific for diagnosis and it may be confused with tuberculous spondylodiscitis. X-ray and CT scan finding are often non-specific. A CT-scan of thorax can be done to rule out suspicion of pulmonary invasive aspergillosis infection. MRI findings of spondylodiscitis includes hypointense signals from the vertebral body and the disc on T1-weighted (T1W) images, hyperintense signals of the disc on T2-weighted (T2W) images, and hyperintense signals from the involved endplates on T2-weighted (T2W) images. Non-pyogenic spondylodiscitis, such as tuberculous and fungal infection, tend to preserve the disc morphology, relatively [13]. The gold standard test for diagnosis is culture report and histopathological examination from the pus or tissue biopsy. So, during surgical management infective tissue should be send for culture and biopsy to confirm the diagnosis and sometimes percutaneous CT-guided biopsy may be useful in the diagnosis [14]. Su KC et al. [15] reported that the fungal beta-D glutan and aspergillus antigen tests are useful for both diagnosis and to detect efficacy of treatment on follow-up. Dai et. Al. [7] reported that blood culture should also be performed routinely. Although it's positive rate is low but it can guide for selection of anti-fungal medication. Other method is polymerase chain reaction (PCR). It has shown high sensitivity and specificity on research trials. Disadvantages of PCR are inability to differentiate between normal colonization and active infection and high false-positive rate [16]. In our case, initially the patient was diagnosed as spondylodiscitis (Koch's spine) D5-D6 and she had been started on empiric anti-tubercular medications based on MRI report by another surgeon. But the pain was not reduced and her condition deteriorated. She developed radiating pain to anterior ribs. Her ESR and CRP was high. MRI report was suggestive of spondylodiscitis D5-D6 and moderate wedging of D5 & D6 vertebra with pre and para vertebral fluid collection.

Treatment of fungal vertebral osteomyelitis includes medical management with anti-fungal therapy and surgical management [17]. According to infectious disease society of America's updated guideline recommended treatment is voriconazole as primary anti-fungal medication of aspergillus osteomyelitis and central nervous system aspergillosis. Lipid formulations of amphotericin B are reserved for those intolerant or refractories to voriconazole [18]. Herbrecht R et al. [19] reported that in comparison study of effect between amphotericin B and voriconazole, improvement of CNS aspergillosis was noted in patients who were treated with voriconazole. another one recent study showed that voriconazole gave better improvement and less toxicity than amphotericin [20]. For epidural aspergillosis, surgical decompression and anti-fungal medication are considered to be standard treatment [15]. Koehler P et al. [21] reported 78 % survival of patients treated with combination of medical and surgical management compared to 68% survival rate of patients treated with anti-fungal only. Duration of anti-fungal treatment has not established but it is recommended for minimum 8 weeks and not more than 6 months [18]. In this case, patient was treated surgically and infected tissues were sent for Culture and sensitivity and biopsy. Culture and sensitivity reported showed no growth. It was negative for GeneXpert and AFB but It was positive for fungal infection. HPE report was suggestive of aspergillus infection. After that she was treated with tab voriconazole 200 mg BD for 6 months.

Conclusion

Fungal spinal infection with aspergillosis is rarely encountered but it should be considered as differential diagnosis especially when bacterial cultures are negative. Rarely patients without immunosuppressive condition have been developed fungal spinal infection. Anti-tuberculous medication should not start on basis of MRI before confirm diagnosis in spinal infection. So, culture and sensitivity, biopsy and isolation of infective organisms require to confirm diagnosis and to start effective treatment. Delay in diagnosis may lead to severe morbidity and may lead to death. Surgical management followed by Anti-fungal medication for adequate duration gives a favourable outcome.

No.	Year	Authors	Total cases	Sex	Avg. Age	Location	Immunity	Anti-fungal used	Treatment	Complications	Outcome at follow up
1	2000	Van Ooij et al.[22]	4	2-Female, 2-male	39 yrs	1- dorsal 2-thoraco-doral 1-lumbar	immunosuppressed	1- amphotericin B and flucytosine, 2- amphotericin B, 1- amphotericin B f/b itraconazole	3- decompression and fusion with bone graft, 1- lumbotomy and brace for 3 months	1-pneumonia and respiratory insufficiency	2 patients died within 6 months of follow-up, 1 patient left with paraplegia, 1 patient-healed completely
2	2001	Gupta et al.[23]	1	Male	12 yrs	thoraco-lumbar	immunosuppressed	Amphotericin B and Itraconazole	laminectomy and decompression of granulation tissue	progressive paraparesis with recurrent of thoraco-lumbar abscess	wheel chair bound on follow-up after 3 months of re-admission
3	2003	Chi et al.[24]	1	Male	63 yrs	cervical	immunosuppressed	Amphotericin B and Itraconazole	decompression	intraventricular haemorrhage with fungal meningoencephalitis	patient died 2 weeks post-operative
4	2004	Saigal et al.[25]	1	Female	31 yrs	dorsal	immunocompetent	amphotericin B	surgical evacuation of abscess and decompression	re-infection with aspergillosis in lumbar spine	residual back pain - 8 months follow-up
5	2004	Vaishya et al.[4]	1	Female	35 yrs	dorsal	immunocompetent	Amphotericin B and Itraconazole	corpectomy and a strut iliac crest bone graft placed	rapid onset multiorgan failure	patient expired
6	2007	Son et al.[12]	1	Male	46 yrs	lumbar	immunosuppressed		curettage and debridement with fusion	re-infection with aspergillosis in cervical spine	
7	2009	Tew et al.[11]	1	Male	50 yrs	dorsal	immunosuppressed	voriconazole	decompression laminectomy, T4 costovertebral joint excision and anterior drainage of epidural abscess	multiorgan failure	multiorgan failure and died two weeks after the surgery.
8	2011	Zussman et al.[1]	9	5 females 4 males	57.4 yrs	5 lumbar 1 cervical 4 thoracic		voriconazole, fluconazole, compounding, Diflucan, Itraconazole,	5 patients - two staged surgery, 4 patients- one staged		19.2 months
9	2011	Batra et al.[3]	1	Male	45 yrs	lumbo-sacral	immunocompetent	itraconazole	decompression laminectomy	N/A	At the 36- month follow up, the patient was asymptomatic and complete neurological recovery.
10	2012	Chang et al.[26]	1	Male	17 yrs	lumbar	immunosuppressed	Amphotericin B and voriconazole	CT guided biopsy f/b medical management	N/A	10 months later MRI showed resolution of the paraspinal abscess, destruction of the L3–L4 vertebral discs and scoliosis of the lumbar spine
11	2013	Jiang et al.[27]	1	Female	40 yrs	dorsal	immunosuppressed	voriconazole	laminectomy and decompression of granulation tissue	not followed advice and developed recurrent dorsal osteomyelitis and epidural abscess	after proper anti-fungal therapy- no sign of recurrence on one-year follow-up
12	2013	Raj et al.[14]	1	Female	45 yrs	lumbo-sacral	immunocompetent	itraconazole	decompression laminectomy with C/S and HPE	N/A	clinically improving for 9 months after surgery
13	2015	McCaslin et al.[28]	1	Female	19 yrs	thoraco-lumbar	immunosuppressed	voriconazole	laminectomy and USG guided aspiration of her intra and extra medullary abscesses	intracranial extension of aspergillosis resulting in rapid progression of ventriculitis and cerebral vasculitis with diffuse vascular occlusion and cerebral infarction	Care was withdrawn shortly thereafter patient died
14	2015	Yoon et al.[13]	1	Male	53 yrs	lumbar	immunocompetent	vancomycin f/b amphotericin B failed medical management	1st- laminectomy and biopsy, 2nd corpectomy and fusion	N/A	recovered completely
15	2018	Shweikeh et al.[29]	1	Female	58 yrs	lumbo-sacral	immunocompetent	Micafungin and Voricanozole	medical management and abscess drainage from SI joint	N/A	Physical and occupational therapy noted the patient to progress well, returning very near baseline

Table 1: Table indicate literature review with pertaining case of fungal infection of spine according to year of publication.

No.	Year	Authors	Total cases	Sex	Avg. Age	Location	Immunity	Anti-fungal used	Treatment	Complications	Outcome at follow up
16	2018	Ono et al.[30]	1	Female	75 yrs	dorsal and lumbar	immunosuppressed	voriconazole	CT-guided thoracentesis	uncontrolled infection and multiple organ failure, including disseminated intravascular coagulation	died after 10 days of admission
17	2019	Senosain et al.[31]	1	Male	29 yrs	dorsal	immunosuppressed	amphotericin B	biopsy		died after 2 days of diagnosis
18	2019	Aghapoor et al.[32]	1	Female	63 yrs	lumbar	immunosuppressed	Itraconazole	corpectomy and discectomy with fusion	N/A	Pain, Parenthesis and lower extremity forces were improved
19	2019	Takagi et al.[33]	1	Male	74 yrs	dorsal	immunocompetent	Voriconazole	laminectomy with posterior fusion f/b anterior fusion with rib bone graft with rigid corset for 5 months	N/A	neurological dysfunction was completely recovered - 9 months follow-up
20	2020	Dai et al.[7]	6	5-Male, 1-Female	mean age 57 yrs	5-lumbar, 1 thoraco-lumbar	3-immunocompetent,3-immunosuppressed	6- Voriconazole	1- biopsy, 5-laminectomy, debridement and posterior fusion	N/A	1-patient reported left back pain, and 1 patient experienced left lower limb numbness-22 months
21	2021	Perna et al.[34]	1	Male	76 yrs	lumbar	immunosuppressed	amphotericin B f/b voriconazole	rigid fiberglass brace.	N/A	patient was pain free - 6 months follow-up
22	2021	Casanova et al.[2]	1	Male	56 yrs	dorso-lumbar	immunosuppressed	Voriconazole	emergency surgery-decompression and fixation	N/A	no back pain and normal walking on 7-month follow-up
23	2022	Makhdoomi et al.[35]	1	Male	85 yrs	lumbar	immunocompetent	amphotericin-B	laminectomy with debridement	N/A	lower limbs is normal at 3-months follow-up

Table 1: Table indicate literature review with pertaining case of fungal infection of spine according to year of publication.

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Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his/her consent for his/her images and other clinical information to be reported in the Journal. The patient understands that his/her name and initials will not be published, and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.

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