

Aspergillus spinal epidural abscess: A case report and review of the literature

ABSTRACT

Aspergillus spinal epidural abscess (ASEA) is a rare entity that may mimic Pott's paraplegia as it commonly affects immunocompromised patients. We present one institutional case of ASEA with concomitant review of the literature. A 58-year-old female presented with intermittent low back pain for 10 years recently aggravated and with concurrent spastic paraparesis, fever, and weight loss. Emergent magnetic resonance imaging (MRI) showed T11–T12 epidural abscess with discitis and osteomyelitis. After empirical treatment with antibiotics, computed tomography-guided, percutaneous biopsy with drainage was performed, showing granulomatous tubercular-like collection. Antitubercular therapy was initiated, but after 1 month, the patient's condition deteriorated. Repeat MRI showed growth of the spinal epidural abscess with significant cord compression and vertebral osteomyelitis. T11–T12 laminectomy and tissue removal were performed with a posterior midline approach. Tissue histopathology showed necrotic debris colonies of *Aspergillus* spp. Antifungal therapy was started, and the patient rapidly improved. ASEA may mimic Pott's disease at imaging, leading to immediate start of antitubercular treatment without prior biopsy, leading to severe worsening of patients' clinical status. Cases of ASEA should be considered at pretreatment planning, opting for biopsy confirmation before treatment initiation so to prevent the occurrence of fatal infection-related complications.

Keywords: *Aspergillus* infection, spinal epidural abscess, spine infection, spine osteomyelitis

INTRODUCTION

Aspergillus species inhabit the soil and plants worldwide and may become pathogenic only in immunocompromised hosts.^[1,2] Inhaled by humans, *Aspergillus* infections may result in severe pulmonary diseases with human-to-human spread via blood contact. Invasive aspergillosis rarely affects bone structures, with the spine being the most common site.^[3] In immunocompromised patients, *Aspergillus* spinal epidural abscesses (ASEAs) may occur via hematogenous route or contiguous spread following any surgery or procedure in the respiratory system, gastrointestinal tract. ASEAs are typically found in the thoracic or lumbar spine but have been reported also in the cervical spine.^[4] In 1.9% of patients, they may also involve the skeletal muscle system.^[5] Due to their delayed onset and nonspecific clinical manifestations, ASEAs are often misdiagnosed at initial presentation as tuberculous spondylitis, especially due to the imaging similarities between the two entities. However, accurate differential diagnosis is


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mandatory as their management strategy differs, and severe risks of fatal complications may follow the initiation of inappropriate therapeutic plans.^[6] Owing to the rarity of this condition, only a few patients with ASEA have been reported. We present one institutional case of ASEA successfully treated with a combination of antifungal and surgical management and further review the current literature.

CASE ILLUSTRATION

Clinical history

A 58-year-old female normotensive, nonasthmatic, and diabetic presented intermittent low back pain for 10 years recently aggravated. The pain gradually increased in the last 4 months, radiating down to the anterior left leg and associated with decrease in walking distance. Intermittent fever and prolonged weight loss were also referred. Physical examination revealed spastic paraparesis with normal sensation and reflexes. She had normal rectal tone. Complete blood count was negative for leukocytosis or anemia, and erythrocyte sedimentation rate was elevated at 75.

First hospitalization

Emergent magnetic resonance imaging (MRI) showed a T11–T12 epidural abscess with discitis and osteomyelitis [Figure 1]. The patient was admitted and started an empirical antibiotic treatment with meropenem, linezolid, and metronidazole for a presumed bacterial spinal epidural abscess. Percutaneous computed tomography (CT)-guided abscess aspiration and fluid cytopathology were positive for granulomatous tubercular-like infection [Figure 2]. Smear showed adequate cellular material containing plenty of degenerative polymorphs, lymphocytes, and histiocytes, and few epithelioid cell granulomas of tubercular origin. Decompressive surgery was not indicated because the patient lacked any neurological deficits or signs of cauda equina syndrome. Antitubercular therapy was initiated with rifampicin, pyrazinamide, ethambutol, isoniazid, and pyridoxine.

Second hospitalization

After 1 month of antitubercular therapy, the patient's condition worsened, with aggravating pain and increased weakness in the left lower limb. A new MRI study showed T11–T12 paravertebral soft-tissue intensity with central liquefaction consistent with spinal epidural abscess, and concurrent significant cord compression with vertebral osteomyelitis. The patient underwent partial T11–T12 laminectomy and subtotal removal of the granulation tissue via a posterior midline approach [Figure 3]. Tissue was sent for histopathology, showing negative bacteriological findings but revealing necrotic debris of *Aspergillus* spp. [Figure 4]. Long-term oral voriconazole was administered together with the antitubercular therapy. The patient was discharged to a skilled nursing facility to complete the planned 3-month course of antifungal therapy. Physical and occupational therapy noted the patient to progress well.

Literature review

A literature search was performed on PubMed and returned 21 articles reporting patients with ASEA [Table 1]. Most patients were males in their third to sixth decade of life. The most common comorbidities were diabetes mellitus, tuberculosis, immunodeficiency, cancer, and kidney failure. The thoracic spine and the lumbar spine were the most affected. Common presenting symptoms were lower back pain, neurological deficits, low-grade fever, and weight loss. Diagnostic management mostly consisted of MRI imaging and/or CT-guided fine-needle aspiration. The most common pathogen was the *Aspergillus fumigatus* (60%) [Table 2]. Treatment commonly comprised a combination of antibiotics and surgical intervention. Only a few cases were treated with antibiotics alone.^[15] Most patients recovered completely or partially at a mean follow-up of 14.4 months. Some patients developed drug-related complications and died at a mean of 1.8 months.^[15]

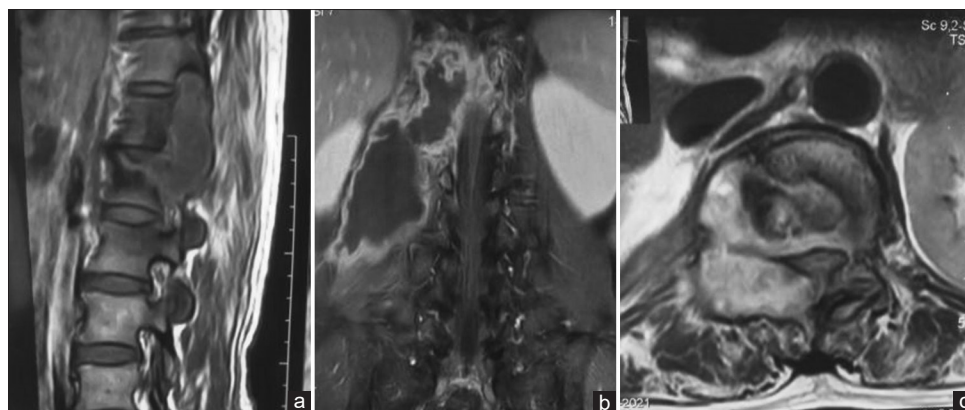


Figure 1: Sagittal (a), coronal (b), and axial (c) magnetic resonance imaging T2WI scans showing T11–T12 epidural abscess with concurrent discitis

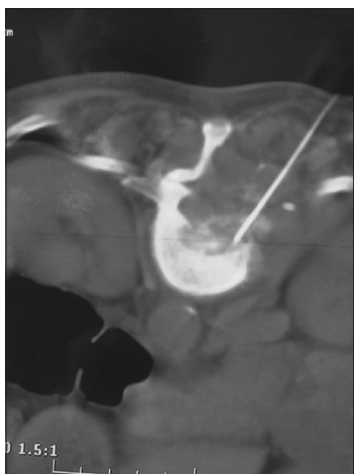


Figure 2: Computed tomography-guided fine-needle aspiration cytology of the T11 lesion suggestive of a granulomatous tubercular-like inflammation

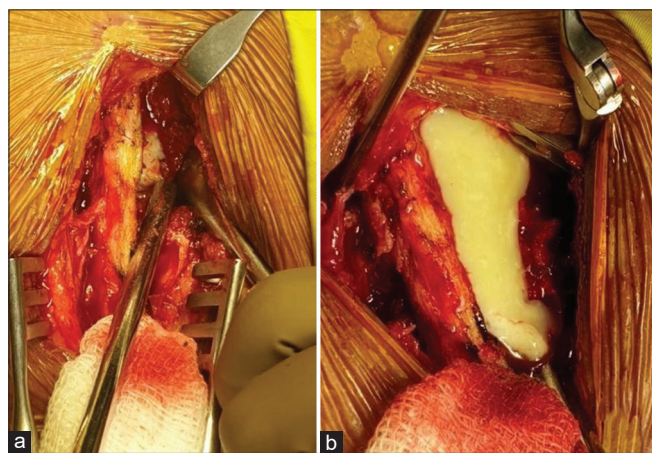


Figure 3: Perioperative findings showing granulation tissue with purulent collection (a) evacuated via a posterior midline approach (b)

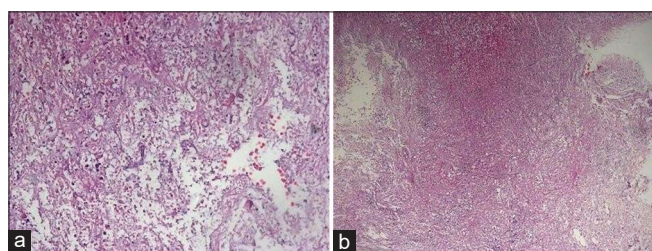


Figure 4: Histological specimen stained with H and E showing necrotic debris and infection from *Aspergillus* spp

DISCUSSION

ASEA is a rare entity with a recent increase in incidence owing to raising prevalence of systemic diseases responsible for immunosuppressive states (e.g., diabetes, kidney failure, and cancer). Corticosteroid therapy and intravenous drug abuse also play a major role in the development of these opportunistic infections.^[25] In immunocompromised patients, *Aspergillus* may spread to the spine from continuous lung

foci, exposure to contaminated blood, or direct inoculation from the surrounding air during trauma or surgery and involve vertebral bodies with intervertebral discs causing osteomyelitis.^[26] Clinical features are nonspecific, mostly characterized by lower back pain with or without fever. Symptoms of spinal cord compression may occur after time. Men are most frequently affected, with involvement of their thoracic and lumbar spine regions.

For diagnostic confirmation, routine fungal culture, microbiological testing, imaging examinations, and histopathology need to be combined to exclude differential diagnoses. White blood cell counts have poor sensitivity and specificity. Specific genetic *Aspergillus* examinations often fail to rule out *Aspergillus* infection because immunocompromised patients cannot produce a significant inflammatory response, but inflammatory markers monitoring may help to assess response to treatment.^[5,7,8,27] The differential diagnosis between spinal aspergillosis and tuberculosis is challenging only based on clinico-radiological examinations, but delay in diagnosis and treatment may be responsible for the development of invasive aspergillosis with high morbidity and mortality burden. From a radiological perspective, spinal tuberculosis frequently begins in the antero-inferior portion of the vertebral body and then spreads beneath the anterior longitudinal ligament to involve the adjacent vertebral body with secondary narrowing of the disc space.^[1,9] In invasive aspergillosis, the lesions often expand circumferentially destroying the surrounding spinal structures (vertebral bodies and discs) and the contiguous structures (ribs, thoracic wall, and lungs), as seen in our case. This imaging feature may support in the correct differential diagnosis. If the diagnosis is missed or delayed until there is extensive paravertebral, para-aortic, chest wall, or skull base invasion, complete eradication of disease by antifungal agents or surgery is not possible.^[1,4,10] For this reason, expedite diagnosis and distinction from the more common tubercular spondylitis are mandatory. The most reliable diagnostic methods for ASEA are histopathological examination and bacterial culture. When hematological and imaging examinations are doubtful, CT-guided fine-needle biopsy should be promptly performed to confirm the suspicion and start the appropriate therapy. Methods of molecular biology including enzyme-based and polymerase chain reaction-based assays can aid in the earlier diagnosis, but these are limited by lower sensitivity and higher false positives. In our case, the granulomatous inflammation detected at CT-guided biopsy posed some challenges in the differential diagnosis. Indeed, CT-guided biopsy is less invasive than intraoperative biopsy, but provides an insufficient number of specimens to make a proper diagnosis.

Table 1: Overview of all studies reporting patients with *Aspergillus* spinal epidural abscess

Authors	Year	Age/sex	Spinal level	Radiology	Hematology/microbiology	Co-morbidities	Causative organism	Type of Treatment		Outcome
								Antibiotics	Surgery	
Ur-Rahman et al. ^[1]	2000	40/W	T6–T8	Destruction of T6–7 with epidural abscess extending T6–T8	Nothing significant	Pulmonary TB	<i>A. flavus</i>	Amphotericin B	Left posterolateral costotransversectomy at D6–D8 and 6 weeks later re-operation with instrumentation and bone graft	Died after prolonged hospital stay
van Ooij et al. ^[7]	2000	45/male	T3–T7	Spondylodiscitis of T4–T5 with a soft-tissue swelling anterior to the spine from T3–T7 spondylodiscitis at T12–L1	N/A	Acute myeloid leukemia	<i>A. fumigatus</i>	Total dose of 3800 mg amphotericin B	Right thoracotomy, curettage of anterior part of ossified disc, and iliac crest bone graft	3 month follow-up radiographic fusion of T4–T5, with a local kyphosis of 26°
		69/male	T12–L1			Acute myeloid leukemia	<i>A. fumigatus</i>	Amphotericin B 2.07 g and 5-flucytosine changed to Itraconazole 400 mg after 6 weeks	Decompression via left thoracoabdominal approach and iliac crest and rib bone graft	Neurologically improved without any pain, good fusion
		39/female	L4–L5	Destruction of L4–L5 disc, epidural abscess formation		Remission from acute myeloid leukemia	<i>A. fumigatus</i>	Amphotericin B with unspecified antimycotics	Lumbotomy with brace for 3 months	Death after 4 months
Gupta et al. ^[8]	2001	12/male	T9–T11, Abscess T6–L2	T9–11 vertebral involvement, destruction of T10 vertebral body with angulation, multiple loculated abscesses extending from T6–L2	Anemia with normal leukocyte count; ESR: 120 mm in the 1 st h	Undernourished, chronic granulomatous infection, cervical abscess, osteomyelitis of left 10 th rib	<i>A. niger</i>	Amphotericin B 700 mg itraconazole 200 mg Co-trimoxazole	D7–L1 laminectomy and decompression of all the loculi and partial removal of granulation tissue	3-month follow-up patients motor power improved 2–3/5 from paraplegia wheelchair bound
Auletta and John ^[9]	2001	15.5/ female	T9–10	T9–T10 anterior mild thecal compression with paravertebral soft-tissue shadow	Anemia with ESR: 84 mm in the 1 st h, neutrophilic leukocytosis (WBCL11, 10 0/microL, N: 87%)	Nothing significant	<i>A. flavus</i>	Amphotericin B Rifampicin for 6 weeks	Right-sided thoracotomy and abscess evacuation	Cured
Chi et al. ^[6]	2003	63/male	C2–C5	Cord compression at C2–C5 with paravertebral soft-tissue lesion	Normal WBC with no anemia	DM	<i>A. flavus</i>	Itraconazole PO changed to IV amphotericin B	Decompression and evacuation of abscess	Died after 2 months due to IVH with complicate fungal meningoencephalitis
Saigal et al. ^[10]	2004	31/female	T8-T9 and T12-L1	2 distinct intradural abscesses at T10–T11 and T12–L1	Normal WBC count with no anemia	Nothing significant	<i>A. fumigatus</i>	Amphotericin B	Surgical evacuation of abscess and decompression	Residual back pain at 8-month follow-up
Vaishya and Sharma ^[11]	2004	35/female	T10-T12	T11 vertebral body destruction with extradural mass compressing the cord from T10–T12	Hgb: 10.8 g/dl, WBC Normal, HIV: Negative	Nothing significant	<i>A. fumigatus</i>	Amphotericin B	T11 corpectomy, spinal stabilization with an iliac bone strut graft, "Z" plate, and screw fixation	Died at 2-month follow-up due to multiorgan failure

Contd...

Table 1: Contd...

Authors	Year	Age/sex	Spinal level	Radiology	Hematology/microbiology	Co-morbidities	Causative organism	Antibiotics	Type of Treatment	Outcome
Son et al. ^[12]	2007	46/male	L2–L5	L2–L5 diffuse band-like enhancement with epidural abscess and paravertebral soft-tissue shadow C4–5 osteolytic lesion and T2–4 signal change	Normal WBC with no anemia	History of liver transplantation due to HBV induced liver cirrhosis with pulmonary aspergillosis	<i>A. fumigatus</i>	Not mentioned	Surgical debridement and biopsy	Re infection and re-operation for 2 times. Follow-up not mentioned
Tew et al. ^[13]	2009	50/male	T2–T9	T2–T9 epidural abscess with osteomyelitis with paravertebral soft tissue	Neutrophilic leukocytosis (WBC: $16.2 \times 10^9/L$, N: 84.8%); albumin reduced to 25 g/L ESR: 65 mm in the 1 st h, WBC normal, CRP normal	Pulmonary TB, DM, Bronchiectasis	<i>Aspergillus</i> spp.	Voriconazole	T2–T8 decompression laminectomy, T4 costovertebral joint excision, and anterior drainage of epidural puss	Died 2 weeks postoperative due to multiorgan failure
Batra et al. ^[14]	2011	45/male	L3–S1	Multilocular extradural collection from L3–S1 vertebra	ESR: 65 mm in the 1 st h, WBC normal, CRP normal	Nothing significant	<i>A. fumigatus</i>	Itraconazole for 3 months	Decompression by laminectomy due to cauda equine syndrome	Complete motor and sensory recovery at 3-year follow-up
Chang et al. ^[15]	2012	17/male	L3–4	Initial spondylodiscitis of L3–L4 with a paraspinal/epidural abscess	WBC: 5220/microL; N: 71.1%, Hgb: 4.4 g/dl, CRP: 4.4 g/dl	Chronic granulomatous disease, left maxillary sinusitis with mucormycosis, and periorbital cellulitis	<i>A. flavus</i>	Amphotericin B initially, later voriconazole	No surgery	10-month follow-up showed destruction of L3–4 with resolution of abscess and scoliosis of lumbar spine
Sethi et al. ^[16]	2012	25/male	L4–L5	Destruction of L4–L5 vertebral region with abscess formation and cauda equine compression	No biochemical or hematological abnormalities	Nothing significant	<i>A. fumigatus</i>	Antitubercular therapy with Itraconazole 200 mg BD for 3 months	Posterior decompression of L4–L5 with instrumentation and interbody fusion with tricortical bone graft from iliac crest	1-year follow-up no back pain
Jiang et al. ^[17]	2013	40/female	T1–T3	Osteomyelitis involving T1–T3 vertebral bodies and associated paravertebral tissue with abscess extending T1–T3. T1 hypo, T2 hyper, and contrast homogenous enhancement	Anemia with normal leukocyte count; ESR 48 mm in the 1 st h; CRP: 21.8 mg/l	Lung fungal granuloma and brain cysticercosis	<i>A. nidulans</i>	Voriconazole 4 mg/kg for 2 month	T1–T3 laminectomy and wound debridement	1-year 6-month follow-up shows back pain but no recurrence
Raj et al. ^[18]	2013	45/female	L5–S1	Intervertebral disc with endplate destruction at L5–S1 with epidural abscess 7.4 mm in thickness	HIV and HBV negative, routine investigation normal	DM	<i>A. fumigatus</i>	Itraconazole PO 200 mg BD×3 months	Posterior decompression laminectomy	9-month follow-up showed clinical improvement

Contd...

Table 1: Contd...

Authors	Year	Age/sex	Spinal level	Radiology	Hematology/microbiology	Co-morbidities	Causative organism	Type of Treatment		Outcome
								Antibiotics	Surgery	
Yoon and Kim ⁽³⁾	2015	53/male	L2–L3	Osteolytic lesion in the inferior endplate of L2 and superior endplate of L3 with discitis	CRP level of 0.86 mg/dl and WBC of 5540/ μ l (differential count: neutrophils, 64.0%; lymphocytes, 22.2%)	Nothing significant	<i>A. fumigatus</i>	Vancomycin 2 g BD followed by amphotericin B (25 mg/day for 30 days)	Total laminectomy of L2 and biopsy followed by operation corpectomy and fusion	7-month follow-up-recovered motor power and hypoesthesia
McCaslin et al. ⁽²⁰⁾	2015	19/female	T12–L1	Vertebral discitis and osteomyelitis from T12–L1 with small epidural fluid collection with rim enhancing expansile intramedullary lesion within distal spinal canal	CSF study showed RBC 20 cells/micro L, WBC: 1459 cells/microL, protein: 367 mg/dl, glucose: 19 mg/dl	Active acute lymphoblastic leukemia	<i>A. fumigatus</i>	Voriconazole	Laminectomy and ultrasound-guided aspiration of intra- and extramedullary abscess	Patient died postoperatively due to intracranial invasion and ventriculitis
Sathyapalan et al. ⁽²¹⁾	2016	35 years/male	T5–T9	Partial collapse of T8 vertebra with epidural abscess extending from T5–T9	Normal routine investigation. CSF: Glucose 31.6 mg/dl (corresponding 120 mg/dl), 12 cells/HPF with 30% polymorphonuclear and 70% mononuclear	Pulmonary TB	<i>A. fumigatus</i>	Voriconazole later changed to amphotericin B with steroid and antitubercular drugs	T5–T8 laminectomy, debridement of epidural tissue, and posterior stabilization from T22–T12	2-year follow-up complete cure with able to stand with support, CNS infection resolves
Yang et al. ⁽²²⁾	2019	48/male 51/male (2 patients)	T3–T5, T5–T10	Vertebral body osteomyelitis, gross destruction of vertebral body, and extension of abscess in segmental level	Anemia with ESR 65 mm and 70 mm in the 1 st h	DM and chronic pulmonary disease	<i>A. fumigatus</i>	Amphotericin B and voriconazole	Laminectomy and corpectomy and instrumentation	Bilateral leg weakness persists another patient died due to recurrence
Dai et al. ⁽³⁾	2020	67/male 68/male 50/female 48/male 43/male 66/male	T3–5 T12–L2 L3–4 L4–5 L4–5 L2–3	2 patients had spinal nerve compression symptoms, 3 patients had spinal instability	ESR 66 ESR 34 ESR 115 ESR 23 ESR 32 ESR 45	Diabetes, chronic renal disease	<i>A. fumigatus</i> , <i>A. niger</i> <i>Aspergillus</i> spp.	Voriconazole 200 mg 12 hourly 16–20 weeks 1 patient managed conservatively	Laminectomy, debridement, and instrumentation	20–24-month follow-up all patients cured with 2 cases had lumbar pain
Tavakoli et al. ⁽²³⁾	2020	10/male	T4–T5	Destructive lesion in T4-5 with adjacent paravertebral soft-tissue mass involving central spinal column	ESR 75 mm in the 1 st h, CRP 69, Hgb: 7.8 g/dl, normal WBC count	Chronic granulomatous disease, pulmonary TB	<i>A. nidulans</i>	Amphotericin B 1 mg/kg/day and changed to Voriconazole 9 mg/kg/day Caspofungin 50 microg/m ²	Laminectomy and wound debridement Right parietal V-P shunt for CNS infection	Died within 1 year
Takagi et al. ⁽²⁴⁾	2019	74/male	T11–T12	Contrast enhancing T11–T12 vertebral body lesion causing destruction of vertebral body with severe cord compression and epidural abscess	CRP 0.51 mg/dl, Normal WBC count	Nothing significant	<i>A. terreus</i>	Voriconazole 600 mg PO for 3 months	Partial laminectomy at T11 and posterior fusion at T9–L2 followed by anterior fusion at T11–T12 with a rib bone graft	2-year follow-up shows complete cure

A. fumigatus – *Aspergillus fumigatus*; *A. flavus* – *Aspergillus flavus*; *A. nidulans* – *Aspergillus nidulans*; *A. niger* – *Aspergillus niger*; *A. terreus* – *Aspergillus terreus*; N/A – Not available; IV – Intravenous; TB – Tuberculosis; ERR – Erythrocyte sedimentation rate; DM – Diabetes mellitus; CRP – C-reactive protein; WBC – White blood cell count; CNS – Central nervous system; PO – Oral, IVH – Intraventricular hemorrhage, HBV – Hepatitis B virus; CSF – Cerebrospinal fluid; HPF – High power field

Table 2: *Aspergillus* species found in the 30 patients with *Aspergillus* spinal epidural abscess

Species	Value (%)
<i>A. fumigatus</i>	18 (60)
<i>A. flavus</i>	4 (13.3)
<i>Aspergillus</i> spp.	3 (10)
<i>A. nidulans</i>	2 (6.7)
<i>A. niger</i>	2 (6.7)
<i>A. terreus</i>	1 (3.3)

A. fumigatus – *Aspergillus fumigatus*; *A. flavus* – *Aspergillus flavus*; *A. nidulans* – *Aspergillus nidulans*; *A. niger* – *Aspergillus niger*; *A. terreus* – *Aspergillus terreus*

A review of the available literature shows that combined operative and medical treatment in early cases offers the best chance for the patient.^[1,4,10] Surgery is usually indicated for spinal cord compression, microbiological diagnosis, and stabilization of the spine. Biopsy and decompression by posterior approach followed by antifungal therapy may be successful in most cases. In our case, this strategy was pursued as the disease was limited in only two spine segments with no spine instability. However, extension of the pulmonary aspergillosis infection to the chest wall and mediastinum carries higher risks of morbidity and mortality burden.^[11,12]

As regards antifungal therapy, amphotericin B was used in earlier cases of ASEA but later disregarded because of its high nephrotoxicity and its ineffectiveness in invasive aspergillosis, owing to the lack of entry into bones. As shown in more recent cases, second-generation broad-spectrum triazoles are often tolerated well and favor survival improvement in ASEA patients.^[8,13,15] The aspergillosis treatment guidelines^[28] proposed by the Infectious Diseases Society of America recommend voriconazole as primary therapy for extrapulmonary central nervous system aspergillosis including *Aspergillus* osteomyelitis, while itraconazole can be used in patients who cannot tolerate voriconazole. Voriconazole is associated with higher survival rate and higher remission rate than amphotericin B. In our patient, we started voriconazole obtaining optimal clinical improvement with no neurological deficit in postoperative period.

CONCLUSION

ASEA represents a rare cause of compressive myelopathy, which shows clinico-radiological similarities with tubercular spine disease. Early definitive diagnosis is challenging, but surgery with antifungal drugs is often indicated to establish the definite diagnosis and decompression of the spine in severe cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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