#### ARTICLE





# Aspergillus spinal epidural abscess: case presentation and review of the literature

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Received: 7 July 2017 / Revised: 8 January 2018 / Accepted: 11 January 2018  $\circledcirc$  International Spinal Cord Society 2018

#### Abstract

**Study design** In this review, we present a case of *Aspergillus* spinal epidural abscess (ASEA) and review the literature. **Objectives** To provide further insight on a rare condition.

Setting A description of a patient with ASEA in a 58-year-old woman that was successfully treated with conservative management is presented.

**Methods** Following case presentation, a literature search (MedLine and PubMed) and assessment of epidemiology, presentation, diagnosis, treatments, and outcomes is performed.

**Results** Review of the literature finds 26 reported cases. The infection occurs in males with a higher frequency (66.7%). The thoracic and lumbar regions are more likely afflicted (96.1%). Common symptoms are backache, neurological deficits, and fever. Most frequent comorbidities were malignancy, diabetes mellitus, and immunodeficiency. Complications were numerous and often catastrophic. Treatment entailed a combination of antibiotics and surgery. Overall, ASEA patients did poorly: death in majority (52%), minimal recovery in 22%, and others did attain full recovery (26%).

**Conclusions** Generally, this infection has high morbidity and mortality. Early identification is important to a successful outcome. Appropriate management with antifungals is central and proves to be effective as seen in the reported case though surgical intervention is usually a necessity as the literature suggests. From an epidemiological and public health perspective, particularly with recent outbreaks, understanding the treatment of this rare CNS infection becomes even more imperative.

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# Introduction

The fungus of the genus Aspergillus is an inhaled pathogen in humans that can result in various forms of pulmonary diseases [1]. It primarily effects those with chronic lung disease or who are immunocompromised. In some cases, the fungus may invade other loci outside of the lungs, occurring either contiguously or hematogenously. Invasive aspergillosis rarely affects bone structures, but when it does occur, the spine is the most common location [2-4]. Aspergillus infection of the spine can sequentially result in a spinal epidural abscess, typically occurring in young patients [3, 4]. Aspergillus spinal epidural abscess (ASEA) usually occurs via hematogenous spread from a respiratory focus, gastrointestinal focus, sinuses, or via contiguous spread following surgery or procedures in the same area [2, 5-9]. ASEA typically occurs in the thoracic or lumbar spine, but has also been reported in the cervical spine [2, 8, **9**].

As the rate of immunocompromised status among the general populace increases, the occurrence of fungal infections observes a proportional rise in prevalence [10–12]. In addition, fungal infections have been of epidemiological interest as their rarity yet increasing prevalence brings about an awareness in all of its aspects including pathophysiology and management. For instance, recently there was an outbreak of central nervous system fungal infections among patients receiving epidural or paraspinal glucocorticoid injections in multiple regions in the United States [13–15]. Patients reportedly developed fungal meningitis, spinal osteomyelitis, and epidural abscess. Multiple patients had confirmatory fungal infections, including cases with *Aspergillus* species.

Given the rarity of the condition, only a few patients with ASEA have been reported in the medical literature. Here, we present a fascinating case of ASEA that was successfully treated nonsurgically. We also review the current literature and provide a summary of clinical factors including risks, treatments and outcome.

## Methods

A case of a patient with an ASEA is presented followed by a review of the relevant literature. For the literature search, a query of the PubMed and MEDLINE databases was performed to identify articles reporting on ASEA. The Preferred Reporting Items for Systematically Reviews and Meta-Analyses (PRISMA) was utilized as a guide (Fig. 1).

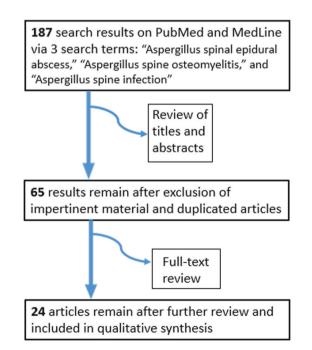


Fig. 1 Details of the literature search strategy using PRISMA guidelines

The search terms "Aspergillus spinal epidural abscess," "Aspergillus spine osteomyelitis," and "Aspergillus spine infection" were used and returned 187 results. These articles were then examined for relevant cases describing the infection. In addition, the reference lists from these articles were also inspected for other relevant articles. Only publications in English, peer-reviewed journals were selected. The criteria for inclusion into the review was: the article had to report demographic characteristics, clinical presentation, diagnostic information, and discussed treatment, complications, and outcomes at follow-up of patients with ASEA. In addition, articles that described spinal infections without frank epidural abscess, a different spinal disease entity, or lacked relevance were excluded. From the original search, 65 articles remained after exclusion of irrelevant content and duplicated material. Following removal of records that did not meet the inclusion criteria, the remaining 24 were included in this review. Articles were reviewed with an emphasis on predisposing factors, diagnosis, successful treatments, and prognosis. Microsoft Excel (Microsoft Corporation, Redmond, WA) was utilized for entry of data and its analysis.

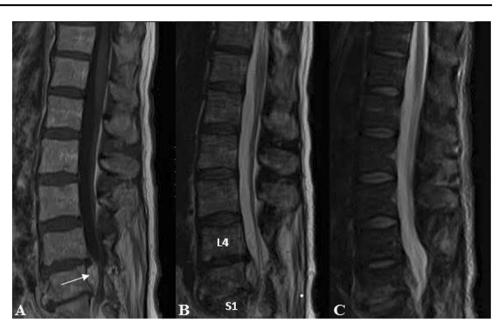
## Results

## **Case Presentation**

The patient is a 58-year-old woman with a past medical history of severe chronic obstructive pulmonary disease, chronic lower back pain, multiple back surgeries, and steroid epidural injections. She was also on chronic treatment with oral prednisone. She presented with a month long history of back pain and radicular symptoms. Patient had been seen a month prior by her orthopedist and diagnosed with mild-moderate L4–L5 foraminal stenosis. MRI done at that time was consistent with spinal stenosis without any evidence of other pathology, and she was treated medically with non-steroidal anti-inflammatory medication.

She presented to the emergency department for increasing and persistent back pain and new onset fevers and chills. She was found to be tachycardic but afebrile, with lumbar paraspinal and spinal tenderness as well as tenderness over the right thigh and leg. Her strength, sensation, and reflexes were within normal limits. She had normal rectal tone. Complete blood count was negative for leukocytosis or bandemia. Erythrocyte sedimentation rate was elevated at 91. Emergent MRI was indicative of an L4–S1 epidural abscess, diskitis and osteomyelitis (Fig. 2). In addition, she was found to have evidence of septic arthritis in the right sacroiliac joint with an additional small abscess anteriorly.

The patient was admitted and started on empiric treatment with antibiotics (Vancomycin and Clindamycin) for Fig. 2 MRI scans of the lumbar spine demonstrating epidural collection at L5 (arrow), enhancing soft tissue within the epidural space from L4–S1 suggestive of phlegmonous change and discitis/osteomyelitis. **a** Postcontrast sagittal T1-weighted MRI. **b** Sagittal T2-weighted MRI. **c** STIR image



what was thought to be a bacterial SEA. However, cytopathology of the CT-guided, percutaneously drained fluid from the epidural collection was positive for acute angle branching hyphae consistent with Aspergillus fungi, and treatment was initiated with intravenous antifungals (Voriconazole and Micafungin). Given that the patient lacked any neurological deficits or any signs of cauda equina syndrome, spinal decompressive surgery was not initiated at this time. Her condition remained stable over the next 2 days, at which point she received drainage of the right sacroiliac joint abscess and cytopathology was also positive for Aspergillus, indicating that both results were unlikely to be contaminants. Subsequent lumbar MRI performed 11 days later showed significant decrease in size of the epidural abscess, and invasive surgery was deemed unnecessary. Medical management with long-term intravenous Micafungin and Voricanozole was pursued, and patient was discharged to a skilled nursing facility to complete the planned 3-month course. Physical and occupational therapy noted the patient to progress well, returning very near baseline upon discharge.

### **Literature Review**

Searching the literature we found 26 previously reported cases summarized in Tables 1 and 2 [1–10, 16–18, 20–22, 24–26, 28–32]. These infections were found to occur in patients most commonly in their third to sixth decades of life, but the age of onset can vary at an average of 44 years and a range of 12–66 years. The incidence is much higher in males (66.7%). *Aspergillus* spinal abscess is most prevalent in the thoracic region of the vertebral column, but is also fairly frequently found in the lumbar spine (53.8% vs.

42.3%, respectively). Common symptoms on presentation are pain in the lower back, focal neurological deficits, and fever. MRI and CT myelography were most frequently used for diagnostic imaging. Most common comorbidities were cancer, diabetes mellitus, immunodeficiency, tuberculosis, and renal failure. Complications were disastrous in a number of instances and included intracranial hemorrhage, gastrointestinal hemorrhage, amphotericin B toxicity, meningoencephalitis, and multi-organ failure. Treatment usually entailed a combination of antibiotics and surgical intervention. Only a single case was treated with antibiotics alone [16].

In terms of overall clinical outcomes, death occurred in the majority (52%), with many dying in the immediate postoperative period or at mean follow-up of 1.8 months following discovery. In another outcome group there was full recovery (26%) and these patients attained their near preoperative baseline functional level at a mean follow-up of 14.4 months. In a subset of patients there was intermediate recovery (22%) of patients, in which minimal resolution of symptoms occurred but who are alive and functional at mean follow-up of 14.8 months.

### Discussion

The most common invasive *Aspergillus* is *Aspergillus fumigatus*, but other species have also been described in the literature [8, 34]. Despite its ubiquitous presence in the environment, invasive infection seldom occurs [24]. In the spine, it most commonly affects the vertebral bodies and intervertebral discs and often results in osteomyelitis [16]. In immunocompromised patients, in particular, *Aspergillus* 

AdditionAgentLorshUngling (description on MMLAthibits: studyType of operationComplicationsDistributionDistribu	Table 1 (	Characteris	tics of previou	Characteristics of previous reported cases of patients with Aspergillus spinal epidural abscess	Aspergillus spinal epidui	ral abscess		
35M         12-13         Lumbur coreconpetitis and divisits         Vancempcini initially comparison         Total Initiate comparison         NA           1         401         12-43         Lumbur coreconpetitis and comparison         Pointement and fission         Pointement and prison         Pointement and fission           1         10-11         Fission         Pointement and fission         Pointement and fission         Pointement and fission         Pointement and fission         Pointement and fission           1         10-111         Fission         Pointement and fission         Pointement and fission <th>Authors</th> <th>Age/sex</th> <th>Levels</th> <th>Imaging (description on MRI/ CT)</th> <th>Antibiotics used</th> <th>Type of operation</th> <th>Complications</th> <th>Outcome at follow-up time (yrs.)</th>	Authors	Age/sex	Levels	Imaging (description on MRI/ CT)	Antibiotics used	Type of operation	Complications	Outcome at follow-up time (yrs.)
10         11/1         Vertebra distrits and exempted in transaction resonance in transactin resonance in transaction resonance in transactin resonance in	Yoon et al. [22]		L2-L3	Lumbar osteomyelitis and diskitis	Vancomycin initially followed by Amphotericin B; failed medical therapy in initial 4 weeks;	Total laminectomy at L2 and biopsy; 2nd operation: corpectomy and fusion	N/A	7 months after discharge: patient recovered motor power and hypesthesia
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	McCaslin et al. [29]		T12-L1	Vertebral discitis and osteomyelitis, ring enhancing expansile intramedullary lesion T12–L1	IV voriconazole	Debridement and laminectomy; u/s guided aspiration	Intracranial extension, rapid progression of ventriculitis, vasculitis, widespread cerebral infarction	Care withdrawn shortly thereafter
40F         T1-T3         Osteomyclis of T1-T3         IV voiconazole paravetebral tissus. Low signal intensity on T1 and high paravetebral tissus. Low signal intensity on T1 and high signal intensity on T1 and high hyphosis, cord compression         Noncompression transhoracic         Noncomprises on transhoracic         T1-T3 laminectory and decompression         Noncomprises on transhoracic         Noncomprises on transhoracic         Noncompression         Noncompression           2]         104-T11         T10-T11 vertebral collapse, lay phosis, cord compression         200 mg/2 months         T10-T11         No           2]         1704         T10-T11 vertebral collapse, lay phosis, cord compression         200 mg/2 months         NA           3]         1704         T10-T11 vertebral collapse, lay collection extending front         No         NA           45M         L3-L4         L3-L4         No         NA         NA           45M         L3-L3         No surgeral         NA         NA           11         L3-L4         L3-R1         No         NA           13         S0M         L3-S1         No         NA           13-L4         L3-S1         No         No         NA           10         L3-S1         Na	Raj et al. [10]	45/F	L5-S1	L5–S1 endplate and intervertebral disc destruction, anterior epidural collection w/ spinal encroachment		Posterior decompression laminectomy at L5–S1	N/A	Clinical improvement since 9 months after surgery
al. 19M       T10-T11       T10-T11 vertebral collapse.       Transthoracic       N/A         21       Kyphosis, cord compression       200 mgx2 months       T10-T11       corpectomy and         17M       Paraspinal,       Initial spondylodiscitis of       Amphotericin B       NO surgery-       N/A         6       13-14       With a paraspinal/       Initial spondylodiscitis of       Amphotericin B       NO surgery-       N/A         17M       Paraspinal,       Li-14 with a paraspinal/       Ninitially to       N/A       N/A         45M       L3-14       Multiocular extradural       NO surgery-       N/A         11       L3-51       Multiocular extradural       N/A         al. 50M       L3-14       With a bacces       N/A         al. 50M       T2-79       None complete motor and sensory recovery         al. 50M       T2-79       Noteometolis and       Urgent surgical         al. 50M       T2-79       Noteometolis and       Proces         abscess       paradaregime       Condacada and       Urgent surgical       None Complete motor and sensory recovery         al. 50M       T2-79       Noteometolis and       Urgent surgical       Proceson and and and and and and and and and an	Jiang et al. [28]		T1-T3	~ <del> </del>	IV voriconazole >3 months	T1–T3 laminectomy and decompression	Noncompliance with antifungal. Abscess returned; voriconzole reinitiated for 6 months	At 1 year, back pain disappeared; well with no signs of recurrence
17MParaspinal, bidural abscessInitial spondylodiscifis of initially to epidural abscessMohotericin B voriconazole after s monthsNO surgery- voriconazole and s monthsNA45ML3-L4L3-L4 with a paraspinal/ epidural abscessL3-L4 with a paraspinal/ voriconazole afterNO surgery- trangal cutureNA45ML3-S1Multilocular extradural collection extending from L3Irraconazole after traconazoleNone. Complete motor and sensory recovery decompression dueNone. Complete motor and sensory recovery decompression dueal. 50MT2-T9Osteomyelitis involving otor and sequineVoriconazole decompression dueNone. Complete motor and sensory recovery decompression dueal. 46ML3-L5Osteomyelitis involving abscess,Voriconazole decompression dueDeveloped multi-organ failure and died decompression dueal. 46ML2-L5Surdia abscess extending abscess,NASurgical debridementResisteral. 46ML2-L5Band-like diffuseNASurgical debridementResisteral. 46ML2-L5Band-like diffuseNASurgical debridementResisteral. 46ML2-L5Band-like diffuseNASurgical debridementRe-infection and reoperational. 46ML2-L5Band-like diffuseNASurgical debridementRe-infection and reoperational. 46ML3-L5Band-like diffuseNASurgical debridementRe-infection and reoperational. 46ML3-L5MRIT1 vertehral bodyAmphotericin B a	Sethi et al 2012 [32]	M/01 .	T10-T11	T10–T11 vertebral collapse, kyphosis, cord compression	Itraconazole 200 mg×2 months	Transthoracic T10-T11 corpectomy and fusion, expandable cage, and rod fixation	N/A	NA
45/ML3-51Multilocular extradural collection extending from L3ItraconazoleUrgent surgical decompression due decompression due vithin 1 week.None. Complete motor and sensory recovery decompression due becompression dueNone. Complete motor and sensory recovery decompression due2011201collection extending from L3traconazoleUrgent surgical decompression dueNone. Complete motor and sensory recovery decompression due20172-T9Osteomyclitis involving abscess,VoriconazoleUrgent surgical decompression dueDeveloped multi-organ failure and died decompression due20172-T8epidural abscess extending osteomyelitisVoriconazoleUrgent surgical decompression dueDeveloped multi-organ failure and died decompression due14.6/ML2-L5L2-L5 band-like diffuse enhancement, epidural abscessNASurgical debridementRe-infection and reoperation20135/FMIT11 vertebral body destruction and an extraduralAmphotericin B and failure and an extraduralPeveloped rapidly progressive multi-organ	Chang et al. [16]		Paraspinal, L3–L4	Initial spondylodiscitis of L3–L4 with a paraspinal/ epidural abscess	Amphotericin B initially to voriconazole after fungal culture	NO surgery- voriconalzole and IFN-Y therapy for 8 months	N/A	10 month follow up showed resolution of abscess, with destruction on L3-L4
50/MT2-T9Osteomyelitis involving r2-T8 vertebral bodies with abscess, paravertebral tissue. Anterior T2-T8Voriconazole decompression due decompression dueDeveloped multi-organ failure and died decompression due46/M12-T8epidural abscess extending osteomyelitisVoriconazoleUrgent surgical decompression dueDeveloped multi-organ failure and died46/ML2-L5band-like diffuse enhancement, epidural abscessNASurgical debridementRe-infection and reoperation35/FMRI T11 vertebral body destruction and an extradural destruction and an extraduralAmphotericin B and radio radi intraconazoleDeveloped rapidly progressive multi-organ	Batra et al. 2011 [6]		L3-S1	Multilocular extradural collection extending from L3 to the S1 vertebrae	Itraconazole	Urgent surgical decompression due to cauda equine	None. Complete motor and sensory recovery within 1 week.	Itraconazole was given for 3 months post op. 36 month follow up asymptomatic
46/ML2-L5L2-L5 band-like diffuseNASurgical debridement Re-infection and reoperationenhancement, epidural abscessesabscessesEnhancement, epidural35/FMRI T11 vertebral bodyAmphotericin B and failure and an extraduralDeveloped rapidly progressive multi-organ	Tew et al. [4]		T2–T9 epidural abscess, T2–T8 osteomyelitis		Voriconazole	Urgent surgical decompression due to cauda Equina	Developed multi-organ failure and died 2 weeks later	Passed away 2 weeks post op
35/F MRI T11 vertebral body Amphotericin B and destruction and an extradural oral intraconazole	Son et al. 2007 [30]		L2-L5	L2–L5 band-like diffuse enhancement, epidural abscesses	NA	Surgical debridement	Re-infection and reoperation	NA
	Vaishya et al. [20]			MRI T11 vertebral body destruction and an extradural	Amphotericin B and oral intraconazole		Developed rapidly progressive multi-organ failure and expired after 2 month	

Table 1 (continued)	ontinued)						
Authors	Age/sex	Levels	Imaging (description on MRI/ CT)	Antibiotics used	Type of operation	Complications	Outcome at follow-up time (yrs.)
		T10–T12, with cord compression	mass compressing the cord T10–T12		Surgical decompression and corpectomy of T11		Passed away after 2 months of surgical and anti-fungal treatment
Saigal et al. [17]	31/F	T8-T9 to lower extent of thecal sac	MRI: Diffuse enhancement of Amphotericin B the lumbar subarachnoid space, 2 distinct intradural abscesses at T10–T11 and T12 to L1	Amphotericin B	Surgical evacuation of abscesses and decompression	No improvement. Repeat MRI showed large epidural abscess from L3–L4 to the S1 level, Osteomyelitis of L4–L5 vertebrae. Repeat surgery. 6 month hospitalization with residual back pain	Residual back pain- 8 month follow up
Chi et al. [8]	63/M	C2–C5, with cord compression	Paravertebral soft tissue lesion at the level of C2–C5 with cord compression	Oral intraconazole, later changed to IV Amphotericin B	Surgical decompression	Intraventricular hemorrhage and complicated fungal meningoencephalitis 2 weeks post decompression	Passed away 2 weeks post decompression
Gupta et al. [3]	12/M	T6-L2	T9–T11 vertebral involvement, destruction of the T10 vertebral body, multiloculated epidural abscess from T6–L2	Amphotericin B and itraconazole for 10 weeks and discharged on cotimoxazole and itraconazole	Extensive laminectomy and decompression of granulation tissue	Within a month, readmitted with progressive parparesis. MRI: T10 destruction and pre and paravertebral abscess, Epidural abscess at T6-L2.	3 month follow up after second admission and treatment with antifungal. Motor deficient, wheel chair bound
Ooij et al. 2000 [ <b>31</b> ]	39/F	L4–L5	Gross destruction of L4–L5 disc, epidural abscess formation	Antimycotics Lumbotomy, (unspecified) including for 3 months Amph B	brace	N/A	Death after 4 months
Delmas et al. [25]	66/M	T8-T9, with cord compression	MRI- large posterior epidural fusiform mass at T8–T9 compressing the cord	Itraconazole. Immunosuppression was not changed	Decompressive laminectomy and drainage	Complete neurological recovery	MRI 6 months showed resolution. Died 6 months after follow up due to immunosuppression
Dubbeld et al. [2]	30s-60s (3 pts.)	L1; T12-L1; L4-L5	L1; T12–L1; Vertebral destruction, L4–L5 paraveterbral extension of a process, spondylodiscitis	Amphotericin B+ Flucytosine; switched to itroconazole Amphotericin B+ Itroconazole Itroconazole	Surgical drainage in all 3	N/A	<ol> <li>Death at 5 months</li> <li>2 years later, free of infection, improved function (</li> <li>Only 10 days follow-up</li> </ol>
Witzig et al. [21]	36/F	T10-T11	MRI decreased signal intensity Itraconazole of T10 and T11 vertebrae	Itraconazole	Decompressive laminectomy with removal of subcutaneous mass	N/A	Rapid neurological improvement within 30 days, After 6 months rehab no incontinence. Remained wheel chair dependent.
Assaad et al. [5]	29/M	L5-S1	MRI- L5–S1 diskitis with a large inflammatory soft tissue extending in the anterior epidural space	Amphotericin B	Right L5 hemilaminotomy, L5 discectomy, and a right S1 partial foraminotomy	N/A	4 month follow up showed complete resolution and neurological baseline
	53/M	L3-L4					Patient died 4 days post op

**SPRINGER NATURE** 

Table 1 (continued)	ntinued)						
Authors	Age/sex Levels	Levels	Imaging (description on MRI/ Antibiotics used CT)		Type of operation	Complications	Outcome at follow-up time (yrs.)
Go et al. [26]			MR1-circumferential Amphotericit paraspinal abscess L3–L4 level to antibiotics with moderate compression of thecal sac; osteomyelitis of 13–14	Amphotericin B added Remitted with fever to antibiotics and on 9th day lumbar abscess was drained		4 days later found unresponsive; Intracranial hemorrhage with obstructive hydrocephalus. Patient passed later that day	
Hendrix et al. [1]	57/M	T1–T5	elogram: compression 15. With possible 1 abscess	Antifungal not mentioned	Decompressive laminectomy T1–T5 and drainage of epidural abscess	N/A	Gradual recovery, lower extremities; ambulate using a walker, urinary retention, constipation at 3.5 yrs
Sheth et al. [18]	53/M	T4	CT myelogram showed complete blockage of fluid at the level of T4	Amphotericin B	Laminectomy and removal of necrotic T3–T4 disc and drainage of adjacent abscess	Deterioration. Renal and respiratory complication	Died post op period
Chee et al. 54/M [7]	54/M	T3-T4	Radiographs of thoracic spine normal. Lumbar myelogram showed blocked flow at the T3-T4	Amphotericin B IV changed to Ketoconazole	Laminectomy with removal of epidural granulomatous tissue densely adherent to the dura	Passed 4 months after laminectomy. Could not tolerate amphoteric B.	No return of neurological function. Passed away four months past laminectomy
Byrd et al. 52/F [24]	52/F	L4–L5	Lumbar myelogram compression at L4–L5. Destruction of L5 vertebrae	Daily levels of azathioprine and prednisone reduced. Amphotericin B	Lumbar laminectomy Pseudomonas, DIC with drainage of abscess	Pseudomonas, DIC	Patient died of DIC
Ingwer et al. [9]	49/M	T8-T10	Myelogram shows mass compressing cord at T9–T10	Amphotericin B	Laminectomy with epidural abscess found from T8 to T10	No improvement of neurological status. Massive GI hemorrhage from multiple GI erosions	Died 55th day of hospitalization. Spread of Aspergillus

SPRINGER NATURE

Feature	Result
Mean age	42.3 years
Sex	66.7% male
	33.3% female
Location	Thoracic: 53.8%
	Lumbar: 42.3%
	Cervical: 3.8%
Comorbidities	•Immunodeficiency: 9
	•Aspergilloma:6
	•Cancer: 5
	•Diabetes Mellitus: 4
	•Tuberculosis history: 3
	•Renal failure and/or transplant: 3
	•History of epidural injections: 2
Complications	•Readmitted/Reoperation: 5
	•Intracranial extension/hemorrhage: 4
	•Multi-organ failure, DIC, other hemorrhage: 4
	•Amphotericin B toxicity: 1
Outcome	•Outcome Group 1 – Death (52%): at mean follow- up of 1.8 months (many in the immediate post- operative period)
	•Outcome Group 2 – Intermediate Recovery (22%): minimal resolution in symptoms but patient is alive and functional at mean follow-up of 13.8 months
	•Outcome Group 3 – Full Recovery (26%): patients made a full recovery, near to preoperative baseline at mean follow-up of 13.3 months

**Table 2**Summary of clinical features from previous papers describingpatientswith aspergillus spinal epidural abscess

can be contracted by inoculation during surgery or other procedures from the surrounding air [5]. A common theme among patients with ASEA is immunosuppression, which can be a result of various conditions, including intravenous drug abuse, corticosteroid therapy, and HIV status [5, 7, 24, 25]. Invasive *Aspergillus* is particularly prevalent in cases of damaged phagocytic function, as in chronic granulomatous disease [4, 6]. Other patients at risk for *Aspergillus* infection include those with a history of renal transplant, liver cirrhosis, and bodily prosthetics [4, 8, 25]. Diabetic patients have also reportedly developed ASEA with neutrophil dysfunction a likely contributor [8]. The most common source and route of infection is hematogenous spread from the pulmonary system and/or genitourinary system.

Recently, outbreaks of fungal spinal infections in patients receiving steroidal spinal epidural injections was reported [13, 14]. Smith et al. [15] reported on the outbreak of a series of fungal infections that occurred in patients receiving steroid injections at more than 70 facilities throughout the United States. Besides spinal infections, patients reportedly developed joint infections, meningitis, and strokes in one of the largest described outbreaks in the healthcare arena. The

result was 749 cases and 61 deaths [13, 15]. Patients with CNS involvement were more likely to have received a higher dose of methylprednisolone (>80 mg), a translaminar approach epidural injection, and an associated comorbidity such as diabetes mellitus and hypertension [13], with epidural abscess occurring at an estimated 39 days following administration of the steroid.

Similar to other causes of infection of the spine, typical symptoms on presentation include pain in the lower back and paresthesia of the lower extremities. Other common symptoms include pain in the lower extremities, urinary retention and fevers (Table 1). Because of the length of time required for the symptoms to become debilitating and the lack of specificity of the symptoms, diagnosis may be delayed as much as 5-7 months from the onset of the earliest symptom [7]. A recent paper alludes to the danger of late recognition with resulting disastrous consequences such as intramedullary involvement and intracranial spread [29]. In addition, not every patient presents with fever and neurological deficits, demonstrating the need for proper diagnostic testing [25]. The erythrocyte sedimentation rate (ESR) is generally increased and allows for a way for assessment at follow-up and treatment response [3].

Presently the gold standard for confirmatory diagnosis is histopathology and culture of the offending microorganism [3, 4]. However, obtaining a definitive culture can take many weeks, delaying diagnosis [4]. Because of the limitations in obtaining such a definitive diagnosis, methods with molecular biology have been utilized, including enzyme-based and PCR-based assays and are characterized by their earlier diagnostic results [4]. However, these are limited by either lower sensitivity or higher false positives. The primary imaging modalities used to determine the diagnosis are CT myelography and MRI (Table 2). Computerized tomography delineates bone and soft tissue damage in the surrounding area, but MRI is a better modality for diagnosing the phlegmonous lesion, although MRI results may vary for ASEA [4, 8, 33]. Characteristically, SEA of the Aspergillus type can be differentiated by its shape, which is irregular and thick-walled and two other features on imaging: band-like subchondral T2 hypointensity and vertebral endplate irregularities on T1 [17] (see Fig. 2). Importantly, image-guided biopsy can be a powerful diagnostic and therapeutic tool. This was demonstrated impressively in our patient.

The primary mode of treatment in patients listed in Table 2 was a combination of antifungals and surgical decompression and debridement. Standardizing management is difficult for this condition, though surgical drainage combined with intravenous antifungal therapy seems to be the most common approach [6, 8, 16]. While amphotericin B was frequently used in earlier reported cases, it is nephrotoxic and has reportedly been found to be ineffective in

some cases of invasive *Aspergillus* because of lack of entry into bone [3, 6, 9, 16]. Second generation triazoles, like Voriconazole, have been shown to be more efficacious and less toxic for the patient on long-term treatment [16]. Flucytosine may also be a good addition to the treatment regimen for vertebral infections concurrent with abscess [2, 6, 16]. Treatment must be administered until symptoms resolve with concordant clearance of the abscess on imaging and continued for multiple months [8]. In addition, symptomology dictates the protocol for surgery—those lacking neural compression may be treated medically, but only with very close monitoring [7, 28].

Unfortunately, despite treatment, the condition is associated with a high long-term mortality rate, and many patients have persistent symptoms, such as paraplegia and various serious complications ranging from hemorrhage to multi-organ failure. In fact, as seen in Table 2, more than half the patients died and only 7 patients made a complete recovery (one dying soon after). In addition, 5 patients made partial recovery, but remained wheel chair bound and two others had significant residual symptoms. These dismal findings highlight the need for better recognition of this disease entity, improved treatment modalities, and safer interventions. This becomes even more important from a public health standpoint during times of infectious disease outbreaks, such as the recent series of fungal infections that occurred in mid-late 2012 [13–15]. The high mortality rate is likely for a number of reasons such as many patient comorbidities (immunosuppression being at the top of the list) and patient status on presentation to the hospital (those with a poor functional status likely having a worse outcome). It is interesting to note the finding of hemorrhage (i.e. intracranial or gastrointestinal) as one of the recurring complications of this unique infection. As to whether surgery correlates with a higher mortality rate is difficult to determine as almost all previous cases were treated via surgery and many had high mortality while others had a better outcome.

In our case, the patient was treated successfully without amphotericin B, eliminating the unpleasant and potentially risky side effects. Additionally, she was treated conservatively without surgical intervention. This was decided based on lack of neurological deficits on presentation and significant improvement of the abscess on MRI following administration of antifungal therapy. This supports the view that effective treatment for ASEA and osteomyelitis should be centered on systemic antifungal therapy, with surgical intervention acting as a supplementary role to ensure complete clearance of the infection [3, 19, 28]. Voriconazole and Micafungin were used and the authors report an adequate outcome with this combination of antifungals. Being a fungal cell wall inhibitor, Micafungin, part of the Echinocandin class of antifungals, has a relatively benign side effect profile with very minimal toxicity [34–36]. Duration of antifungal treatment should be at least 3–6 months or a longer length of time [16, 27]. While surgical excision should be considered in cases with cord compression and for relief of neurological symptoms and those that don't resolve with drug treatment alone [3, 6, 23, 28]. Additionally, we recommend surgery for large collections, patients with neurological symptoms, especially those that are progressive, when diagnosis is very uncertain, and there is lack of response to medical management alone. Location of the epidural collection is also of significance, with more invasive management to likely be undertaken on cervical and thoracic abscesses than those in the lumbar spine.

## Conclusion

We describe a patient with a history of chronic back pain treated with spinal epidural injections who presents with symptoms of a probable spinal infection and was subsequently diagnosed with ASEA. She was successfully treated with conservative, nonsurgical management, and we report success with a Voriconazole and Micafungin combination. Confirmatory diagnosis has to be with histopathological and microbiological analysis, though earlier diagnosis is crucial and enzyme/PCR assays are alternatives. Understanding the management of aspergillus is also essential from a public health standpoint, as outbreaks involving fungal spinal infections have been reported in patients receiving invasive spinal interventions.

#### Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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