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ABOUT COVER

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AIMS AND SCOPE

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CASE REPORT

Scedosporium apiospermum infection of the lumbar vertebrae: A case report

Xue-Wen Shi, Sheng-Tang Li, Jin-Peng Lou, Bo Xu, Jian Wang, Xin Wang, Hua Liu, Song-Kai Li, Ping Zhen, Tao Zhang

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Abstract

BACKGROUND

Scedosporium apiospermum (*S. apiospermum*) is a clinically rare and aggressive fungus mainly found in contaminated water, wetlands, decaying plants, stagnant water, and potted plants in hospitals. The lung, bone, joint, eye, brain, skin, and other sites are easily infected, and there is a marked risk of misdiagnosis. There have been few case reports of infection by *S. apiospermum* of the lumbar vertebrae; most reports have focused on infection of the lung.

CASE SUMMARY

An otherwise healthy 60-year-old man presented with a 4-mo history of lumbosacral pain, stooping, and limited walking. The symptoms were significantly aggravated 10 d prior to hospitalization, and radiating pain in the back of his left lower leg developed, which was so severe that he could not walk. Movement of the lumbar spine was significantly limited, anterior flexion was about 30°; backward extension, right and left lateral curvature, and rotational mobility were about 10°; tenderness of the spinous processes of the lumbar 3-5 vertebrae was evident, and the muscle strength of both lower limbs was grade IV. Imaging suggested bony destruction of the lumbar 3, 4, and 5 vertebrae and sacral 1 vertebra; in addition, the corresponding intervertebral spaces were narrowed and the lumbar 5 vertebra was posteriorly displaced and unstable. Lumbar

vertebral infection was also noted, and the possibility of lumbar tuberculosis was considered. We first performed surgical intervention on the lesioned lumbar vertebrae, cleared the infected lesion, and performed stable fixation of the lesioned vertebral body using a lumbar internal fixation device, which restored the stability of the lumbar vertebrae. Cytological and pathological examination of the lesioned tissue removed during surgery confirmed *S. apiospermum* infection of the lumbar vertebrae; on this basis, the patient was administered voriconazole. At the 6-mo follow-up, efficacy was significant, no drug-related side effects were observed, and imaging examination showed no evidence of recurrence.

CONCLUSION

S. apiospermum infection can occur in immunocompetent individuals with no history of near drowning. Voriconazole is effective for the treatment of *S. apiospermum* infection of the lumbar vertebrae for which it is suitable as the first-line therapy.

Key Words: *Scedosporium apiospermum*; Lumbar vertebrae; Fungal infection; Treatment; Voriconazole; Case report

Core Tip: *Scedosporium apiospermum* (*S. apiospermum*) infection can occur in immunocompetent individuals with no history of a near drowning event. *S. apiospermum* infection of the lumbar vertebrae is rare, leading to risks of misdiagnosis and mistreatment. Cytology and pathology of lesion tissue play a decisive role in diagnosis. Further cases would expand our understanding of this rare fungal infection.

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INTRODUCTION

Scedosporium apiospermum (*S. apiospermum*) is a rare and aggressive filamentous fungus widely distributed in contaminated water, wetlands, decaying plants, stagnant water, and potted plants in hospitals[1,2]. Immunocompetent individuals become vulnerable to this fungus following near drowning events[3]. In the case reported here, the patient had not experienced a recent near drowning event and had not been exposed to contaminated water or decaying plants. *S. apiospermum* infection occurs in patients with organ transplantation, acquired immunodeficiency syndrome (AIDS), long-term use of immunosuppressants, immune dysfunction of other causes, and invasion of the lung, bone, joints, eyes, brain, skin, and other organs[4-7] (Table 1). There have been no previous case reports of *S. apiospermum* infection of lumbar vertebrae; most reports have focused on infection of the lung.

CASE PRESENTATION

Chief complaints

An otherwise healthy 60-year-old man presented with a 4-mo history of lumbosacral pain, stooped back, and restricted walking with no obvious cause. The symptoms had become significantly aggravated 10 d prior to hospitalization.

History of present illness

This patient had a 4-mo history of lumbosacral pain with no obvious cause, along with stooped and restricted walking. He had visited a local hospital and received Chinese medicine. The patient's lumbosacral pain worsened, and oral pain medication was not effective. 10 d before admission, the symptoms were further aggravated and radiating pain developed in the back of his left lower leg, which was so strong he could not walk. The patient again visited a local hospital, and lumbar vertebrae computed tomography (CT) showed lumbar vertebral infection. The patient was referred to our hospital due to lumbar vertebral infection.

Table 1 Contrast in reports of infections caused by *Scedosporium apiospermum* around the world

Ref.	Age (yr), Sex	Pathogenesis	Site of infection	Symptoms	Diagnostic method	Characteristics of *S. apiospermum*	Therapeutic method	Therapeutic drugs	Duration of medication	Outcome
Agarwal *et al*[3], 2021	62, Male	Not reported	Right index finger	Swelling of the right index finger	Microscopy, culture, and identification of the pathogen	The surface of the colonies was brownish gray to black, the back surface was black, and microscopically, a single, oval, colorless, basal truncated ring spore could be seen germinating from the ring	Not reported	Not reported	Not reported	Not reported
Agarwal *et al*[4], 2021	62, Male	Not reported	Left eye	Redness and sudden loss of vision in the left eye	Bacterial culture and identification	Vitreous sample and the explanted intraocular lens inoculated onto BA, CA, and SDA showed colonies with a clear outer pale zone and central brownish growth with mycelial tufts suggestive of *S. apiospermum*	Medication	Voriconazole	6 mo	Recovery
Chen *et al* [5], 2016	62, Male	Near drowning	Brain and lungs	Persistent headache and urinary incontinence	Cerebrospinal fluid culture and strain identification	Not reported	Medication	Voriconazole and terbinafine	6 mo	Recovery
Todokoro *et al* [12], 2018	75, Male	Hypertension, colon cancer, and metastatic hepatic tumor	Left eye	Decreased visual acuity in the left eye	DNA sequencing, PCR	Microscopic features: septate hyphae 2 μm in diameter and branching irregularly, along with the production of lateral and terminal conidia, which were round or oval (3-5 by 5-10 μm)	Medication	Voriconazole	5 mo	Partial recovery
Oliveira *et al* [17], 2013	58, Female	Prior injury to foot while handling a dairy cow	Left foot	Swelling and pain in the left foot	Tissue culture	Not reported	Medication	Itraconazole	Not reported	Recovery
Girmenia *et al*[20], 1998	25, Male	Acute myeloid leukemia	Face	Pain in the face, multiple papular skin lesions	Bacterial culture and identification	Microscopic examination showed septate hyaline hyphae with conidia 9 by 5 mm in diameter borne terminally, singly, or in small groups on elongated simple or branched conidiophores or laterally on hyphae	Medication	Voriconazole	1 mo	Death

S. apiospermum: *Scedosporium apiospermum*; BA: Blood agar; CA: Chocolate agar; SDA: Sabouraud dextrose agar; DNA: Deoxyribonucleic acid; PCR: Polymerase chain reaction.

History of past illness

The patient had no relevant past medical history.

Personal and family history

No special personal and family history.

Physical examination

The patient was able to stand using crutches and did not have scoliosis. Movement of the lumbar spine was significantly limited, with approximately 30° anterior flexion, kyphosis, left-right scoliosis, and rotational mobility of about 10° and tenderness of the spinous processes of the lumbar 3-5 vertebrae bilaterally. Cutaneous sensation of both lower extremities was unremarkable, muscle tone was normal,

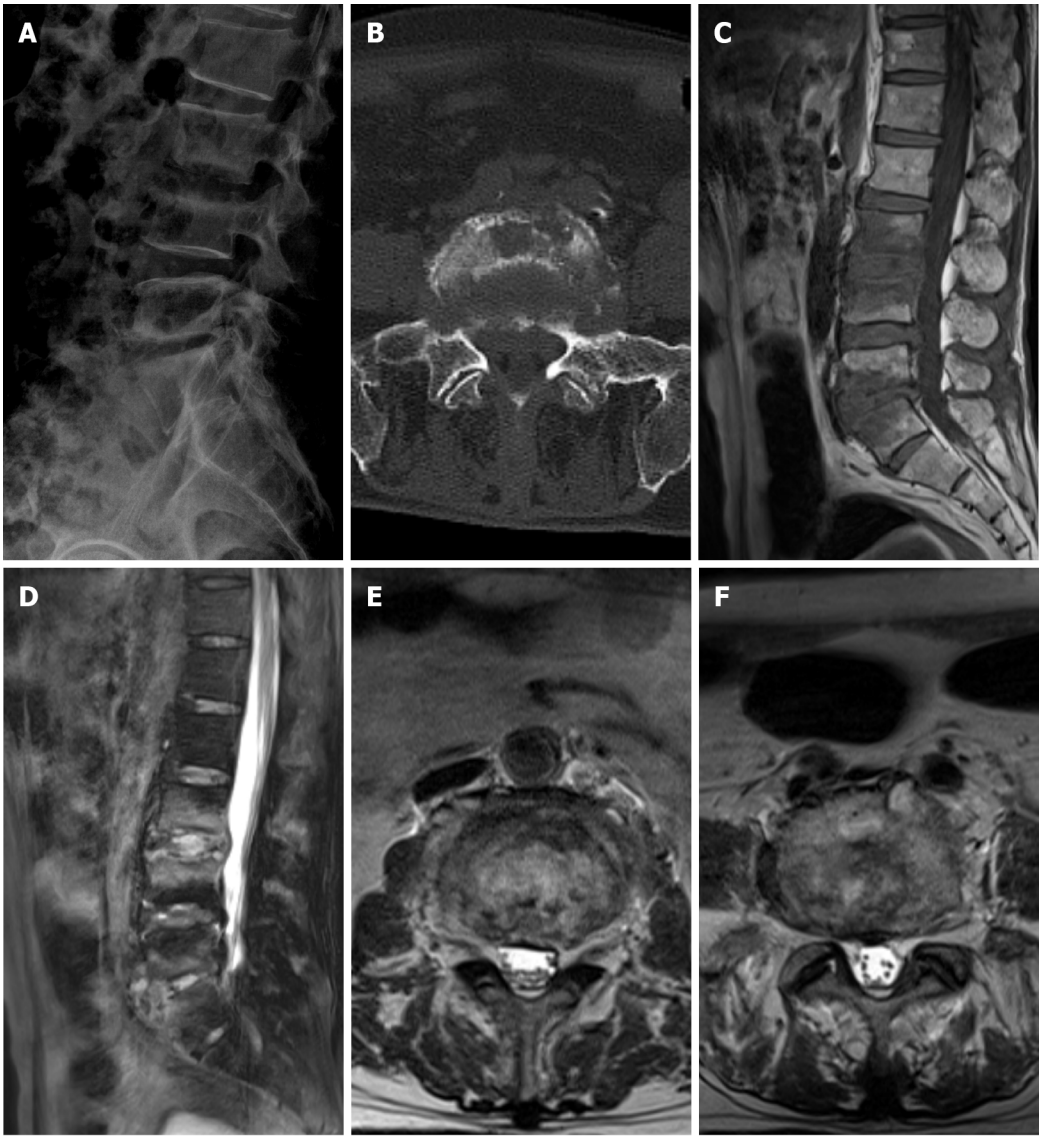

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Figure 1 Medical imaging examinations before therapy. A: X-ray image showing increased heterogeneity of bone density at the edge of the third lumbar (L3) vertebra to the first sacral (S1) vertebra. The fifth lumbar (L5) vertebra and S1 bodies had marginal hyperostosis with incomplete posterior border continuity, the L5 body was displaced slightly posteriorly, and the L5/S1 intervertebral space was narrowed; B: Axial computed tomography image showing bone destruction and hyperplasia at the edges of the L5 and S1 bodies, a small amount of low-density shadow encircling the paravertebral space, and bone destruction at the right sacroiliac joint surface; C and D: Sagittal T1WI and T2WI magnetic resonance imaging (MRI) showing abnormal bone signal at the margins of L3 and the fourth lumbar (L4), and L5 and S1, with a long T1 and mixed long T2 signal; E and F: Axial T2WI in MRI showing a decreased signal at the L3/L4 disc (E), L5/S1 disc (F), rim of the visible soft tissue shadow of the annular bulge, and slight narrowing of the spinal canal at the corresponding level.

and muscle strength was class IV. Range of motion was essentially normal at the hips, knees, and ankles bilaterally, although the movements were slowed by pain. Knee and Achilles tendon reflexes were normal bilaterally and the Babinski sign was negative.

Laboratory examinations

At admission, his laboratory data were as follows: Erythrocyte sedimentation rate (ESR) 120 mm/h (normal range 0-15 mm/h), C-reactive protein (CRP) 8.33 mg/dL (< 0.8 mg/dL), fibrinogen (FIB) 8.26 g/L (1.8-3.5 g/L), fibrinogen degradation products (FDP) 9.2 μg/mL (0-5 μg/mL), and D-dimer 3.5 mg/L (0-0.55 mg/L). However, tumor markers, brucellosis agglutination, tuberculosis cell immunoassay, and sputum acid-fast bacilli smear were negative.

Imaging examinations

X-ray analysis showed hyperostosis, sclerosis, and tapering of the fifth lumbar (L5) vertebra and the first sacral (S1) vertebral margins. The third lumbar (L3) vertebra to S1 vertebral margins showed local nonunion with slightly rough margins. The posterior border of L5 and S1 vertebra was incomplete, and L5 vertebra was displaced slightly posteriorly, not exceeding one quarter of the anterior posterior

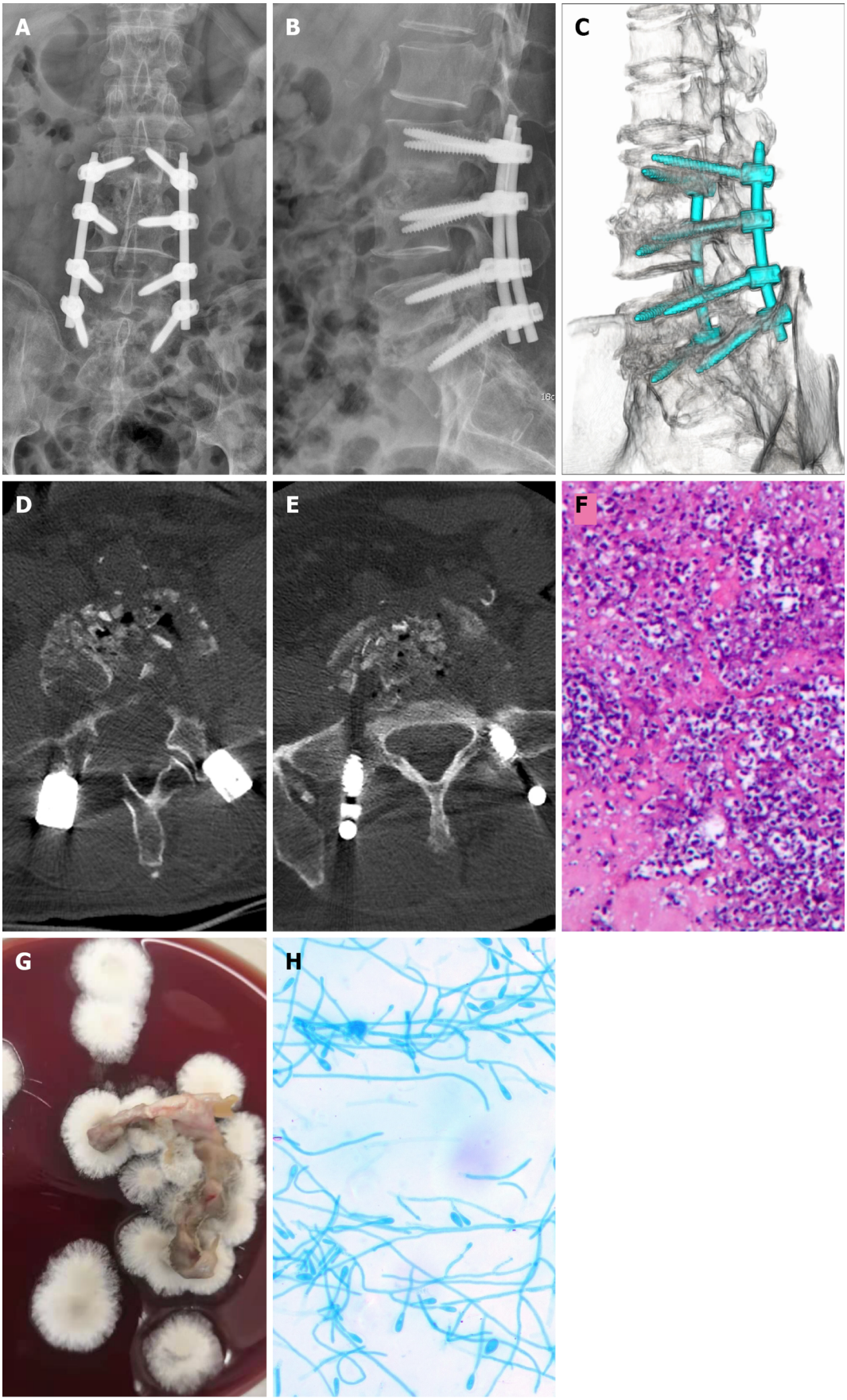

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Figure 2 Medical imaging, pathology and microbiology examination after surgery. A and B: X-ray image showing that the lumbar internal fixation device was in a good position; C-E: Three-dimensional computed tomography image showing sufficient bone grafting in the L3/L4 and L5/S1 intervertebral spaces; F:

Pathological examination results showing a large number of inflammatory cells in the tissues examined, and the staining revealed PAS (+), and acid resistance (-); G: Lesion tissue culture day 7 (blood agar medium, 30 °C, 7 d) showed that colonies were cashmere-like and the back was gray-black; H: Under the microscope (lactic acid phenol cotton blue staining, × 400), most of the hyphae were irregularly branched, producing round or oval lateral and terminal conidia.

diameter of the S1 vertebra; the L5/S1 intervertebral space was narrowed (Figure 1A).

CT revealed bone destruction and hyperplasia at the relative margins of the L3, L4, L5 and S1 vertebra, a small amount of low-density shadow encircling the paravertebral spaces, and bone destruction at the right sacroiliac joint surface (Figure 1B).

On magnetic resonance imaging (MRI), the bone signals of L3, L4, L5 and S1 vertebra were abnormal, showing long T1 and mixed long T2 signals. A small amount of equal-T2 signals surrounded the paravertebral space. The T2 weighted imaging signal of each intervertebral disc was weak. Annular soft tissue shadows were seen at the edges of the L3/L4, L4/L5 and L5/S1 vertebral discs. A soft tissue shadow with prominent limitations was evident at the posterior margin, and the corresponding spinal canal was slightly narrowed (Figure 1C-F).

FINAL DIAGNOSIS

S. apiospermum infection of the lumbar vertebrae.

TREATMENT

After 1 wk of hospitalization, the patient underwent surgical intervention. After induction of general anesthesia, a surgical incision was made at the median of the lower back, starting at the spinous process of the L3 vertebra and ending at the spinous process of the S1 vertebra (length about 15 cm). The right vertebral lamina and zygapophysial joint of the L3 to S1 vertebrae were first revealed. Next, the left L3 to S1 vertebral zygapophysial joint was exposed (Wiltze approach). After positioning *via* X-ray fluoroscopy, appropriately sized pedicle screws were implanted on both sides of the L3 to S1 vertebrae. Fluoroscopy showed that the individual pedicle screws were suitably positioned, and the L3/L4 and L5/S1 right hemivertebrae were sequentially decompressed and the articular processes of the lower right parts of the L3 and L5 vertebrae were resected. This showed destruction of the L3/L4 and L5/S1 discs and soft granulation-like tissue formation at the L3 and L5 vertebrae. In addition, destruction of endplates at the upper border of the lower, L4 and S1 vertebral bodies was evident. The lesion tissues in the intervertebral space were cleaned and sent for bacterial culture and pathological examination. This created a good bone graft surface, and medical gel foam mixed with isoniazid, rifamycin, and vancomycin was implanted into the intervertebral space. An appropriate amount of left iliac bone was removed through the incision and cut into bone blocks of appropriate size and mixed with allogeneic bone and bone induction material (recombinant human bone morphogenetic protein-2). During the operation, X-ray imaging showed sufficient bone grafting in the L3/L4 and L5/S1 intervertebral spaces. Next, we connected the bilateral posterior longitudinal connecting rod and fixed the lumbar vertebrae. Postoperative lumbar X-ray and CT imaging indicated good positioning of the lumbar internal fixation, and that bone graft placement was adequate in the L3/L4 and L5/S1 intervertebral spaces (Figure 2A-E). Pathological examination results showed a large number of inflammatory cells in the tissues examined, and staining revealed PAS (+), and acid resistance (-) (Figure 2F). Tissue culture on blood agar medium was performed twice (30°C, 7 d). The resultant colonies were cashmere-like and the back was gray-black (Figure 2G). Under the microscope (× 400), lactic acid phenol cotton blue staining showed that most of the hyphae were irregularly branched, producing round or oval lateral and terminal conidia (Figure 2H) (Table 1). Three microbiologists in our hospital confirmed the culture and microscopic examination results, and all agreed on the identification as *S. apiospermum*. The patient was given voriconazole (Pfizer, United States) 200 mg ivgtt every 12 h for antifungal treatment and cefoperazone sodium sulbactam (Pfizer, United States) 3 g ivgtt every 8 h to prevent postoperative infection. After 10 d, there were no abnormalities found during routine blood and biochemical analyses. The ESR was 34 mm/h (normal range 0–15 mm/h), CRP was 1.09 mg/dL (< 0.8 mg/dL), and PCT and interleukin-6 (IL-6) were within the respective normal ranges. The patient continued to take voriconazole for 6 mo.

OUTCOME AND FOLLOW-UP

At the 6-mo follow-up, the ESR, CRP, PCT, and IL-6 were all within the respective normal ranges. X-ray and MRI of the lumbar vertebrae showed that the fixation position of the L3-S1 vertebral body was

good, and the density in the L3/L4 and L5/S1 intervertebral spaces was increased, showing a short T1 signal on MRI (Figure 3). The patient was able to move with the assistance of a lumbar brace. However, the activity of the lumbar spine was limited, with anterior flexion of approximately 50°, posterior extension of about 15°, left–right scoliosis, and rotational activities of about 20°; nonetheless, walking and daily life were unaffected. The patient was satisfied with the outcome, but unfortunately refused further follow-up despite being informed of the risk of recurrence.

DISCUSSION

The *S. apiospermum* complex consists of *S. apiospermum*, *S. aurantiacum*, *S. boydii*, *S. minutisporum*, and *S. dehoogii*, of which the former three cause human infection[8]. *S. apiospermum* is distributed worldwide, but infections are rare. The clinical manifestations and imaging results differ according to the site of infection. Most doctors are unfamiliar with *S. apiospermum* infection, resulting in a risk of misdiagnosis. X-ray, CT, MRI, and other imaging examinations have limited diagnostic utility, typically showing only abscess formation; these modalities are mainly used for surgical planning and follow-up evaluation. Before surgery, histopathological and pathological examination, the patient was mistakenly believed to have *Mycobacterium tuberculosis* infection based on the imaging findings. The diagnosis of *S. apiospermum* infection was made by histocytology and pathology, and by isolation of the fungus in culture. Its pathological manifestations are similar to *Aspergillus* and *Fusarium* infection[9,10]. *S. apiospermum* colonies grow rapidly, and are cashmere like, white at first and subsequently gray black. Production of pigment or brown conidia, leads to gray/brown or black mature colonies. Microscopically, most *S. apiospermum* hyphae are irregularly branched, producing round or oval lateral and terminal conidia[11,12]. We analyzed lesional tissue removed at surgery *via* culture and microscopy, and the results were similar to those of previous reports. In immunocompetent patients, the diagnosis of *S. apiospermum* infection is delayed by almost 6 mo; significantly longer than in near drowning patients[13,14]. If hospital facilities are inadequate or the physician has insufficient experience, the probability of misdiagnosis increases significantly. *S. apiospermum* can form a fungal ball in human tissue due to fungal invasion and intravascular thrombosis, resulting in tissue necrosis[15,16].

The sites of *S. apiospermum* infection vary and the treatment modality differs according to site. In cases of limited infective focus and feasible surgical intervention, surgical removal of the infective focus improves the prognosis. We performed surgical intervention on the diseased lumbar vertebrae of this patient, cleared the infected lesion, and performed stable fixation of the diseased vertebral body using a lumbar internal fixation device, which restored spinal stability. *S. apiospermum* is resistant to most antifungal drugs, which makes treatment difficult and the prognosis poor. It is most sensitive to voriconazole, followed by posaconazole, itraconazole, and amphotericin B[17,18]; voriconazole is the first-line therapy[19-21] (Table 1). Due to the lack of prospective clinical studies, the dosage and duration of voriconazole for the treatment of *S. apiospermum* infection are unclear. We typically decide on treatments by following the drug manufacturer's instructions and the advice of clinical pharmacists. Our patient was discharged and took voriconazole tablets (200 mg po q12h) for 6 mo, and no drug-related adverse effects were observed. In addition, imaging revealed no evidence of recurrence. Micafungin is the second-line agent for the treatment of *S. apiospermum*. The combination of micafungin and voriconazole *in vitro* has a significant effect on *S. apiospermum*[22,23]. Our patient did not receive the micafungin and voriconazole combination but achieved a satisfactory outcome.

CONCLUSION

S. apiospermum infection can occur in immunocompetent individuals with no history of near drowning. Infection involving multiple vertebral bodies, intervertebral spaces, and paravertebral tissues cannot be diagnosed by imaging alone, and surgical intervention is the first-line treatment. Lesion tissues should be removed for cytological and pathological examination, and an accurate diagnosis is needed to prevent mistreatment. Multidisciplinary treatment promotes rehabilitation. Voriconazole is effective for the treatment of lumbar vertebrae infection by *S. apiospermum*.

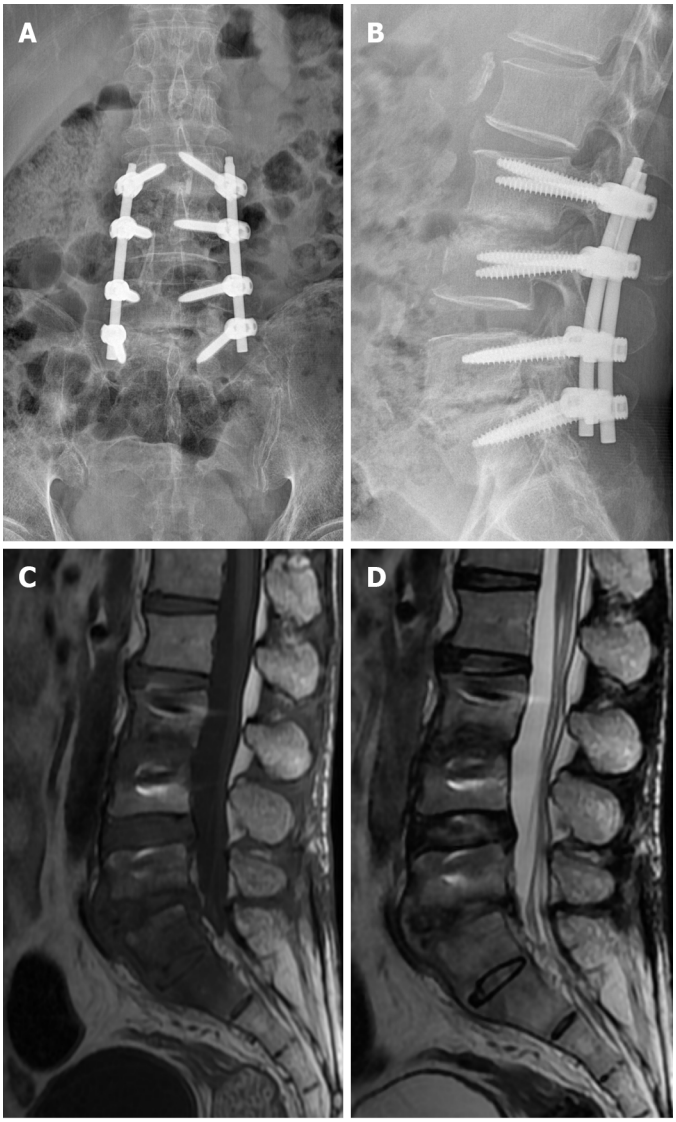

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Figure 3 Medical imaging examinations at follow-up. A and B: X-ray image showing that the position of fixation in the L3–S1 vertebral body was good; C and D: Magnetic resonance imaging showing increased density of the intervertebral spaces of L3/L4 and L5/S1, with a weak T1 signal. No recurrence was noted.

FOOTNOTES

Author contributions: Shi XW, Li ST, Lou JP, and Zhang T provided the concept for the study and drafted the manuscript; Xu B, Wang X, and Wang J provided the images; Liu H, Li SK, Zheng P, and Zhang T performed the operations; all authors have read and approved the content of the manuscript.

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