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ABOUT COVER

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CASE REPORT

Thoracic spine infection caused by *Pseudomonas fluorescens*: A case report and review of literature

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Abstract

BACKGROUND

The clinical incidence of spinal infection is gradually increasing, and its onset is insidious, easily leading to missed diagnosis and misdiagnosis, which may lead to serious complications such as nervous system dysfunction, spinal instability and/or deformity, and cause a huge burden on society and families. Early identification of the causative agent and precision medicine will greatly reduce the suffering of patients. At present, the main pathogenic bacteria that cause spinal infection are *Staphylococcus aureus*, Streptococcus, Pneumococcus, *Escherichia coli*, and Klebsiella. There are no reports of spinal infection caused by *Pseudomonas fluorescens*.

CASE SUMMARY

We report a 32-year-old female patient with spinal infection. She presented with flank pain, initially thought to be bone metastases or bone tuberculosis, and had a family background of tumors. Her clinical features and changes in imaging and laboratory tests led to the suspicion of thoracic spine infection. Histopathology of the lesion showed inflammation, tissue culture of the lesion was negative several times, and the possible pathogen - *Pseudomonas fluorescens* was found after gene sequencing of the lesion. The patient recovered completely after a full course of antibiotic treatment.

CONCLUSION

This report increases the range of pathogens involved in spinal infections, highlights the unique advantages of gene sequencing technology in difficult-to-diagnose diseases, and validates conservative treatment with a full course of

antibiotics for spinal infections without complications.

Key Words: Thoracic spine infection; *Pseudomonas fluorescens*; Spinal infection; Case report

Core Tip: Vigilance regarding unexplained spinal infection is required. Detailed physical examination, puncture biopsy, pathological examination and genetic testing can play a very important role in clinical diagnosis. Needle biopsy and genetic testing are effective methods for identifying unexplained spinal infections, and appropriate antibiotic therapy with a full course of treatment is critical to prognosis. Due to the hidden nature of unexplained spinal infections, regular follow-up over a long period of time is recommended.

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INTRODUCTION

Spinal infection is common in the thoracic spine. Spinal infections include vertebral osteomyelitis, discitis, paravertebral musculoskeletal infections, and refractory spinal abscesses[1], accounting for 2%-7% of all musculoskeletal infections[2]. Common presenting symptoms are fever and chest and back pain. Common pathogens are mainly cocci and bacilli, and infections with specific bacteria have also been reported. As bone metastasis, tuberculosis, rheumatic diseases, brucellosis, osteoporosis and other diseases can lead to different degrees of bone destruction, imaging can show abnormal manifestations of the spine; thus, spinal infection is easily misdiagnosed and missed. In the case of delayed diagnosis or surgery, potential early destructive and late disabling complications may occur[3], and can even lead to the risk of mortality, seriously affecting the normal life and work of patients, and result in serious economic burdens to society and families. If a patient has serious complications, debridement and fusion surgery can only be performed to eliminate the infected lesion and stabilize the spine[4], and if the infection is holospinal, surgery should be performed as soon as possible to achieve better neurological recovery and infection control[5]. However, regardless of the treatment chosen, antibiotics are required throughout the course of treatment. Although the optimal duration of antibiotic therapy remains controversial, it should not be less than six weeks[2].

CASE PRESENTATION

Chief complaints

A 32-year-old female patient presented with pain in her left flank of 1 wk.

History of present illness

The patient presented with pain in her left flank of 1 wk, the nature of the pain was undescribed, and was obvious at night, persistent, severe, was worse when breathing and changing position, and was slightly relieved when her position was maintained. Pain was accompanied by chest tightness and decreased appetite. No fever, chills, cough with sputum, dyspnea, or aches in other parts of the body were observed. Nausea and vomiting, abdominal pain, diarrhea, abnormal urine and bowel movements, palpitations, precordial pain, back pain, and left upper limb pain were absent. In addition, no rash was noted. From disease onset, her diet, sleep, and spirit were poor, and no significant weight reduction was observed. Self-administration of analgesic drugs (details unknown) before presentation were ineffective.

History of past illness

She was usually in good health.

Personal and family history

The patient reported a family history of malignancy.

Physical examination

Physical examination showed that she was conscious, had poor mental status, was helped into position, and supported by others. Pain was associated with breathing and trunk movement. Occasional palpable tenderness in the left flank and mild tension in the left back muscles and left flank muscles were observed with no obvious tenderness. The patient

showed no obvious deformity in the thoracolumbar segment of the spine, limited movement of the thoracic spine, interspinous tenderness at T 7-10, suspicious positive percussion pain, and a positive thoracic crush test. Examination of the cardiopulmonary tract, abdomen, and other areas showed no obvious positive signs.

Laboratory examinations

Laboratory tests showed the following: leukocytes were 10.62 × 10^9/L, neutrophil percentage was 76.80%, lymphocyte percentage was 17.80%, eosinophil percentage was 0.30%, neutrophil absolute value was 8.16 × 10^9/L, platelets were 381 × 10^9/L, C-reactive protein (CRP) was 37.35 mg/L, erythrocyte sedimentation rate was 44 mm/h, aspartate aminotransferase was 11.6 U/L, globulin was 42.0 g/L, the leukoglobulin ratio was 1.0, prealbumin was 138.7 mg/L, glucose was 6.42 mmol/L, urine ketone body 3+, urine occult blood+-, urine protein+, urine specific gravity was 1.033, urine leukocytes 32.50/μL, urine leukocytes in the high power field were 5.8/HP, liver and kidney function, blood lipids and blood glucose were not significantly abnormal. The patient underwent a tissue biopsy for bacterial culture and pathology smear. The bacterial culture of the lesion was negative, and the pathology (Figure 1) showed trabecular bone degeneration and necrosis, and the fibrous tissue of the intertrabecular granulation tissue revealed hyperplasia with inflammatory cell infiltration, and a few cytoplasmic transparent round cells were found. Symptomatic analgesic treatment was administered, but as the specific causative agent could not be identified, the patient attended Shandong Chest Hospital for inpatient treatment. After admission, re-examination of laboratory tests showed a *Mycobacterium tuberculosis* IgG antibody positive reaction, activated partial thromboplastin time of 50.6 s, albumin 37.9 g/L, creatine kinase 22 U/L, lactate dehydrogenase 116 U/L, triglycerides 1.76 mmol/L, magnesium 0.74 mmol/L, anion gap 6.8 mmol/L, and angiotensin-converting enzyme 5 U/L. Plasma D-dimer, routine blood tests, tiger red plate agglutination test, brucellosis test tube agglutination test, Brucella antibody IgG, Aspergillus galactomannan antigen, liver and kidney function, blood glucose, immunoglobulins (IgG, IgA, IgM), complement C3, complement C4, *Mycobacterium tuberculosis* IgM antibody, eight items before surgery, and the T-SPOT were also performed. There were no obvious abnormalities in the TB test, erythrocyte sedimentation rate, CRP, rheumatoid factor, anti-O, (1,3)-β-D-glucan, gram-negative lipopolysaccharide, and routine urine and bowel movements.

Therefore, a local needle biopsy of the lesion was performed again for relevant examination and culture. The results showed that no fungal or bacterial growth was found in the lesion tissue culture, and no mycobacteria were detected, and the DNA of *Mycobacterium tuberculosis* complex was also negative. The pathological evidence showed that the biopsy tissue (thoracic vertebrae) contained cartilage, bone and fibrous tissue with minimal inflammation.

Therefore, genetic sequencing (Tables 1 and 2) was performed and showed that *Pseudomonas fluorescens* had the largest number of total fragments, a small number of *Escherichia coli* and *Staphylococcus aureus*, and no mycobacteria, fungi, viruses, parasites, mycoplasma/chlamydia, and drug resistance genes were detected.

Imaging examinations

Imaging studies (Figures 2 and 3) showed that the T7-9 vertebrae were slightly flattened, and the T8 vertebra was predominant, with reduced smooth margins. The T7-9 vertebral body and adnexal bones showed patchy long T2 long T1 signals, STIR hyperintensity, and the corresponding vertebral space was slightly narrowed. Multiple bone destruction of the T7 vertebral body and T8 vertebral body, bilateral vertebral arches, left transverse process, and left rib cage with swelling of the surrounding soft tissues were thought to be caused by infectious lesions, and positron emission tomography-computed tomography (PET-CT) or needle biopsy was recommended to rule out neoplastic lesions. Mild inflammation of the middle and lower lobes of the right lung, with signs of bilateral pleural effusion were also seen.

FINAL DIAGNOSIS

Thoracic vertebral body infection caused by *Pseudomonas fluorescens*.

TREATMENT

According to the patient's symptoms, signs, imaging data and laboratory test results, and considering the inflammatory bone structural abnormalities caused by *Pseudomonas fluorescens*, antibiotic therapy with moxifloxacin 0.4 g intravenously once a day was given for 4 wk, followed by oral moxifloxacin 0.4 g once a day for 2 wk.

OUTCOME AND FOLLOW-UP

The patient's symptoms resolved after treatment, and she went through pregnancy, delivery, and breastfeeding over the next two years; thus, no second-generation sequencing was performed. After stopping breastfeeding, the patient returned to the clinic in June, 2023, and did not complain of significant back pain or oblique rib pain. Magnetic resonance imaging (MRI) of the thoracic vertebra indicated that the original lesion site was significantly improved (Figure 4).

Table 1 Precision medicine high-throughput sequencing (clinical infection gene analysis report): List of bacteria detected

Bacterial genus name (total number of fragments, abundance%)	Bacterial species name	Number of fragments detected (species)	Total fragment length (species, bp)	Homologous matching degree (%)
Pseudomonas spp. (67, 57.27%)	Pseudomonas fluorescens	44	17534	99
Escherichia coli (10, 8.55%)	Escherichia coli	10	3979	98
Staphylococci (7, 5.98%)	Staphylococcus aureus	5	2142	100

Table 2 Precision medicine high-throughput sequencing (clinical infection gene analysis report): Other list

Serial number	Name	Result
1	Mycobacterium and other important pathogens	0
2	Fungus	0
3	Virus	0
4	Parasite	0
5	Mycoplasma/chlamydia trachomatis	0
6	Drug resistance gene	0

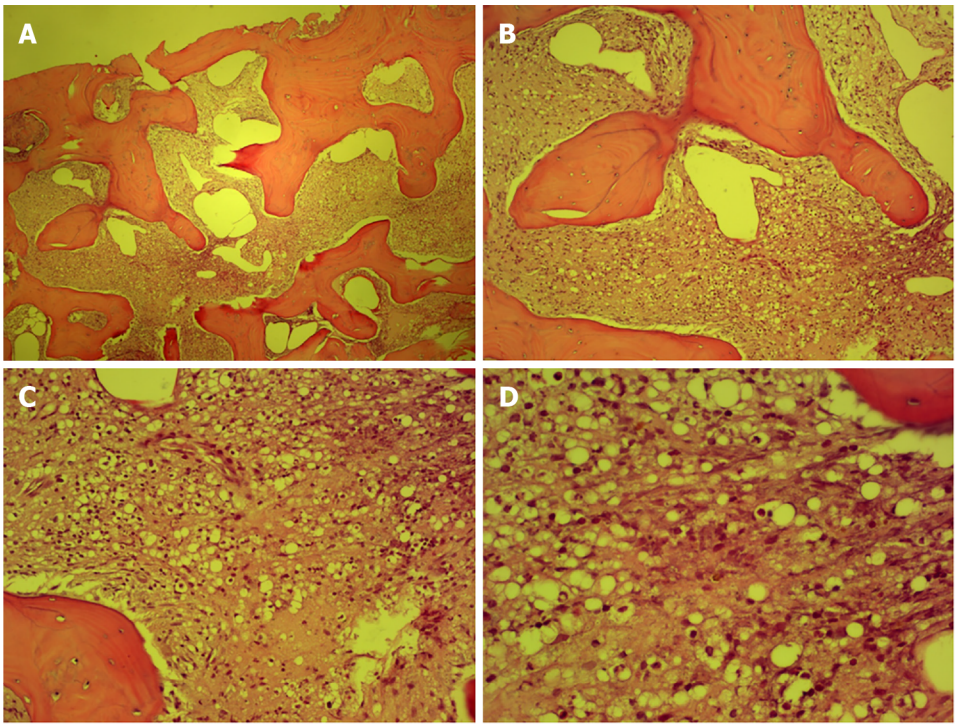

Figure 1 Pathology of the local puncture biopsy in Zibo Central Hospital. A: 4 × 10 times; B: 10 × 10 times; C: 20 × 10 times; D: 40 × 10 times.

DISCUSSION

Spinal infections are common in adults, but can also occur in younger[6] and older adults[7]. Studies[7] predict that the number of patients over the age of 80 years with spinal infections will increase rapidly in aging populations. These infections are not clinically prevalent but may lead to serious complications such as neurologic dysfunction, spinal instability and/or deformity due to skeletal destruction, and in severe cases, death[3,8]. As it is difficult to identify the causative pathogen, diagnosis is often delayed[9], resulting in a serious burden on the life and economy of patients and society. Spinal infections can occur in single-segments or contiguous multi-segments or non-contiguous multi-segments [10] and can occur throughout the spine, most commonly in the lumbosacral spine (39.1%), followed by the thoracic spine (27.1%), and less frequently in the cervical spine[11,12]. Studies have found that the occurrence of spinal infections is

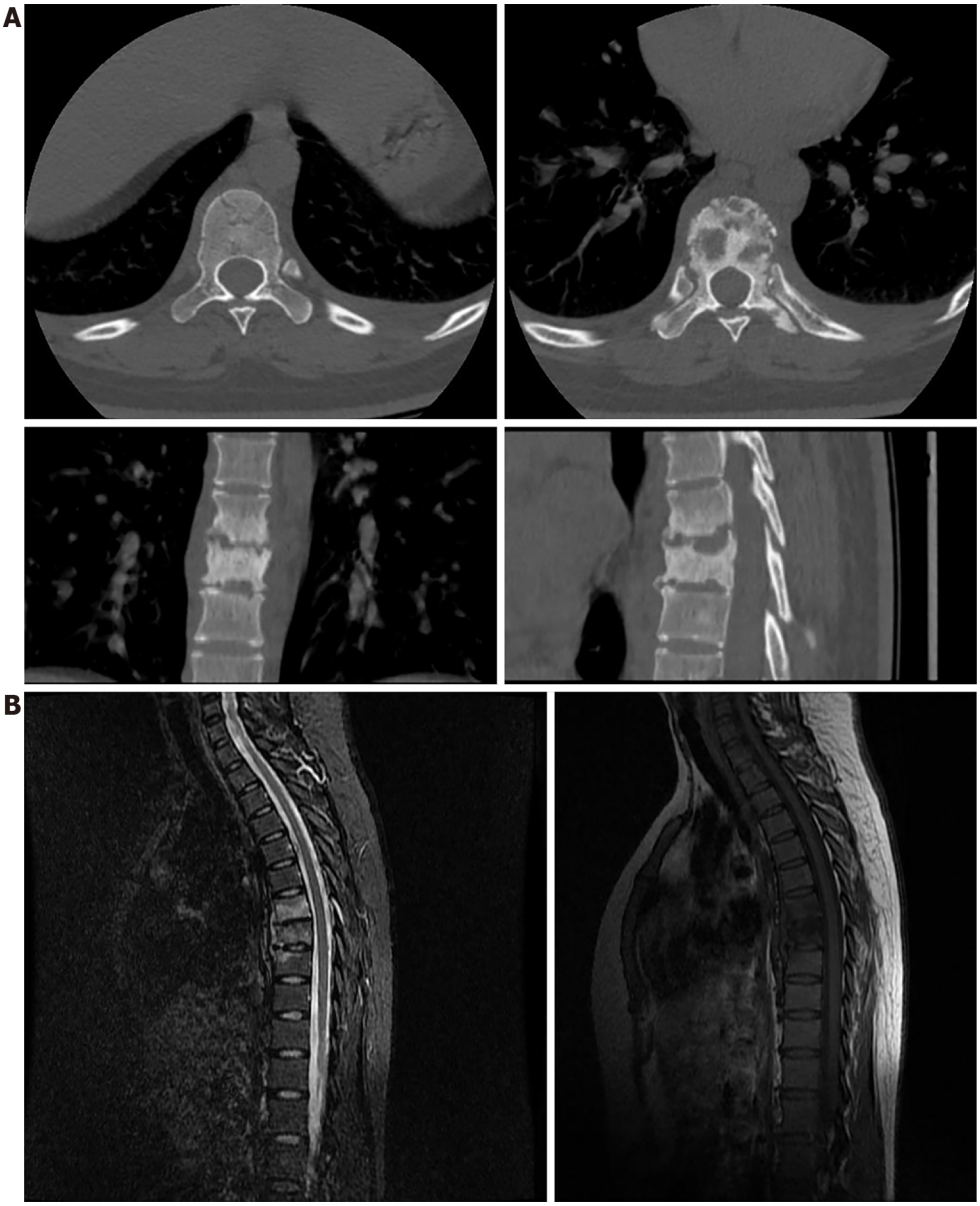

Figure 2 Computed tomography and magnetic resonance imaging of the thoracic spine. A: Thoracic vertebral computed tomography shows bone destruction in T7-9, with T8 being the most significant; B: Magnetic resonance imaging of the thoracic vertebra showed signs of bone abnormalities in T7-9, with T7 and T8 being the most significant.

mostly related to immunosuppression[13], diabetes mellitus[14], intravenous drug abuse[15], osteoporotic vertebral fractures[16], recent soft tissue infection or bacteremia[17], and spinal surgery[18]. As spinal infections often lead to morphological abnormalities of the bone and accessory structures of the spine the clinical diagnosis and differential diagnosis of tumors, tuberculosis, brucellosis, ankylosing spondylitis, *etc.*, are particularly important. With the development of MRI and PET-CT, these two techniques can distinguish between the types of spinal infections, and of these two techniques, PET-CT has shown better sensitivity and specificity in the diagnosis and treatment evaluation of spinal infections[19-21]. However, pathological analysis and bacterial culture are still important in the diagnosis of infected tissue[22]. The common pathogens in these infections[23-26] are *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus*, *Pneumococcus*, *Klebsiella*, and less commonly, *Salmonella*[27], *Aspergillus*[28], *Fungi*[29], *Actinomycetes*[30], and *Gram-positive bacteria*[25]. Due to the limitations of bacterial culture conditions and the number of samples, it is not always possible to obtain relevant pathogens even by local bacterial culture and biopsy pathology[9], which leads to challenges in clinical diagnosis and treatment. With the rapid development of genomics technology, such as high-throughput DNA sequencing, big data and gene editing technology, precision medicine is getting closer. For bacterial infections, effective treatment is only possible by accurate identification of pathogenic microorganisms. It has been found[31-33] that gene sequencing can detect pathogens that are negative using traditional cultures, is more sensitive and time-consuming than traditional cultures, and has unique advantages in the identification and detection of clinically rare bacteria, fastidious bacteria, and bacteria that do not grow in solid media. For example, Dong *et al*[34] identified 190 suspected tuberculosis sputum culture isolates by genetic technology, and found that among the 190 isolates, 186 were *Mycobacterium tuberculosis* , while the remaining 4 were non-tuberculous mycobacteria. In addition, gene sequencing technology is also used in the

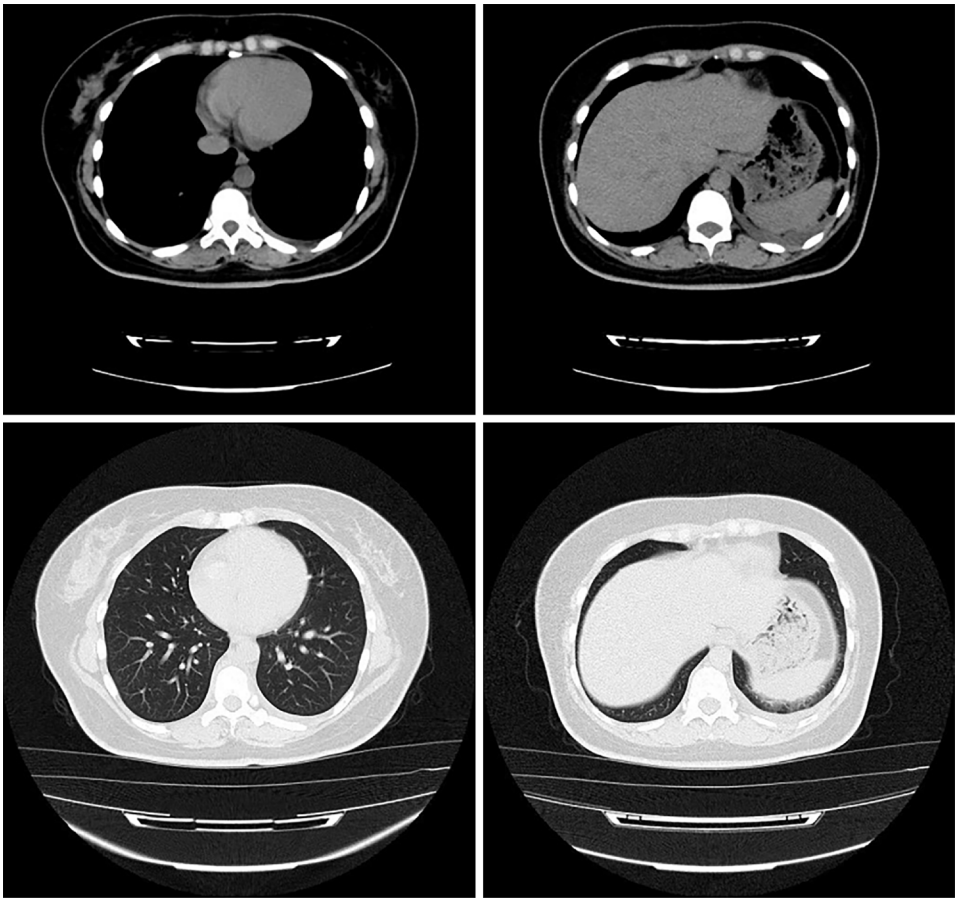

Figure 3 Computed tomography of the lungs. Chest computed tomography shows mild inflammation in the middle and lower lobe of the right lung and a small amount of pleural effusion on both sides.

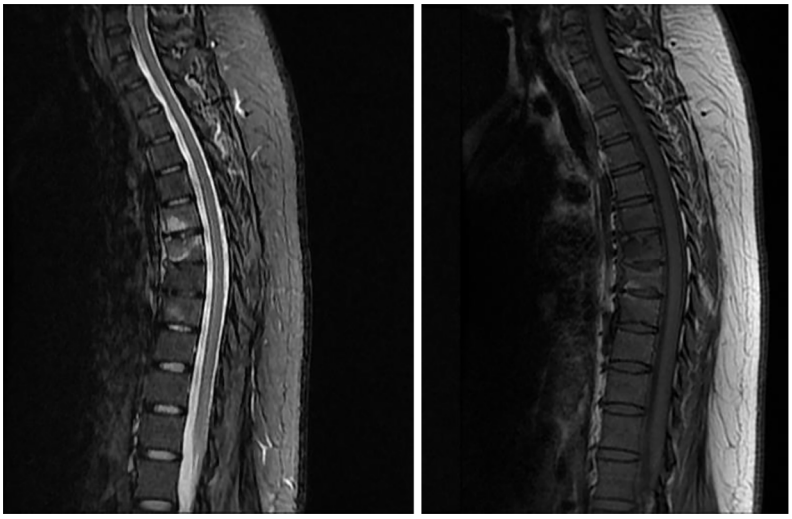

Figure 4 Magnetic resonance imaging showed that the lesions of the T7-9 vertebrae were significantly reduced after treatment.

identification of intestinal flora, the detection of tumor markers and mutant genes, the diagnosis and prognosis of diseases, and the evaluation of diagnosis and treatment effects, which is an important part of modern technologies. In the present case, gene sequencing technology was also used to detect pathogens that could not be cultured using conventional bacterial culture, in order to determine the final diagnosis and treatment plan.

Treatment of spinal infections is divided into surgical and conservative treatments, and the choice of treatment depends on whether there are clear complications. Korovessis *et al*[3] evaluated English language peer-reviewed clinical trials on purulent spinal infections published before 2009. They found that the most basic treatment for uncomplicated spondylitis was intravenous antibiotics, followed by oral antibiotics and braces. In complex cases, surgery can improve

the balance of the sagittal plane, restore nerve damage, and relieve severe pain. Duarte *et al*[22] selected the appropriate literature on spinal infections using databases from the US National Library of Medicine and the US National Institutes of Health, and stated the need for consistent antibiotic therapy, emphasizing that antibiotic use must be initiated after the etiological diagnosis is made. Surgery is used only in the presence of neurological deficits or sepsis, spinal instability and/or deformity, epidural abscess, and failure of conservative treatment. Aljawadi *et al*[35] conducted a comprehensive search of relevant literature published from 1990 to 2018 and found that adequate non-surgical treatment with antibiotics can achieve satisfactory results with low recurrence rates. In the present case, the patient had an acute onset, a short disease course, and limited lesions, and satisfactory results were achieved following non-surgical treatment with antibiotics. It is important to note that regardless of whether conservative or surgical treatment is chosen, rehabilitation at all stages has a positive effect on the improvement of neurological, motor, and sensory impairments in patients with spinal infections[36].

Compared with common spinal infections, the case reported in this article had certain specificities which were mainly manifested in the following aspects: First, the onset of symptoms was atypical. The patient did not have obvious symptoms of fever, back pain, or neurological dysfunction, but presented with severe flank pain, which was related to postural changes and breathing, and could easily be misdiagnosed as herpes zoster and visceral disease. Careful physical examination revealed tenderness and percussion pain in the thoracic spine, but no significant tenderness in the flanks, no obvious rash or paresthesia, a negative thoracic crush test, and no obvious positive signs in the lungs or abdomen. MRI of the thoracic spine and CT of the lungs were completed before the lesion was localized to the thoracic spine. Second, there was no history of obvious underlying medical conditions, immunodeficiency or suppression, and no abnormal contact or recent history of trauma, infection, and surgery. Spinal infections have been found to result from distal skin or visceral infections followed by the bloodstream route[37]. Our patient was a young woman who had previously been in good health and had no history of travel, other illnesses or unusual contacts, and no significant trauma or distal skin infection or surgery. As there was a genetic history of tumor in the family, it was not possible to determine whether the lesion was a tumor or an infection using MRI. At this time, clinicians are prone to misdiagnosis, and how to communicate with patients when there is no good and clear diagnosis, how to stabilize the patient's mental status, and what the next diagnosis and treatment plan are problems faced by clinicians. A clear source of infection was traced in this patient, and it is speculated that there may have been superficial skin lesions over a long period of time that led to colonization by the pathogen and activation of the causative agent when the body became immunocompromised, leading to morbidity. Third, pathological analysis of the biopsy and bacterial culture failed to identify the causative organism. The patient underwent biopsy for pathological analysis and bacterial culture in our hospital and Shandong Chest Hospital, and both results showed inflammatory lesions, while no obvious positive results were found in both bacterial cultures. These results are similar to those in many clinical reports[23,26], which has resulted in a bottleneck in terms of diagnosis and treatment when the true pathogen cannot be found. This poses a further challenge in the diagnosis and treatment of the disease. There were three reasons for failure to culture positive bacteria in this patient. First, few samples were obtained by puncture and the transfection rate was low. Second, a fluorescence test was not carried out. Third, culture is less sensitive than gene sequencing. Bacterial culture requires live bacterial growth, and in the progressive or active stage of the disease, the lesion site has obvious inflammatory infiltration and cytophagocytosis, inanimate bacteria or decomposed nucleic acid fragments which does not provide culture positive results or biochemical identification. For gene sequencing, the sensitivity is higher, both live bacteria and decomposed nucleic acid fragments can be detected; thus, culture and biochemical tests failed to detect *Pseudomonas fluorescens*, while gene sequencing could detect this pathogen. Fourth, the pathogenic bacteria found by gene sequencing are special. With the development of omics technology, the application of new genomics, metabolomics, and proteomic technologies has brought opportunities for clinicians to break through bottlenecks. The patient's cultures were negative, and pathology only showed inflammatory cell infiltration, and the specific pathogen was unclear. It was not until after gene sequencing was conducted that infection with *Pseudomonas fluorescens* was suggested. According to the results of gene sequencing, the presence of *Pseudomonas fluorescens*, *Escherichia coli* and *Staphylococcus* may have been due to co-infection. As the content of *Pseudomonas fluorescens* was much higher than that of the other two bacteria, *Pseudomonas fluorescens* was considered to be the main pathogen. However, this pathogen is a rare in humans, and there have been no reports of spinal infection caused by this bacterium. *Pseudomonas fluorescens* is widely distributed in nature, such as in soil, water, plant and animal environments, and can antagonize plant pathogens and promote plant growth[38], and is an important plant root growth-promoting bacterium, which is mainly used in agricultural production, and has been occasionally found to infect humans[39]. *Pseudomonas fluorescens* is an opportunistic pathogen, and the most common clinical infection is *via* blood and blood products[40-42]. From 2004 to 2006, 80 people in the United States were reported to have been infected by products contaminated with the bacterium[43]. *Pseudomonas fluorescens* can exist in urine, bile, skin and skin infected secretions[44-45], and can also enter the blood and cause pyogenic pus, osteomyelitis, pyogenic ganglitis and lung infection. It even leads to severe after-effects such as septicemia, infected huke and intravascular coagulation, with a high mortality rate[46]. *Pseudomonas fluorescens* is temperature-sensitive and does not grow below 37 °C or 42 °C during bacterial culture[47]. However, it is possible to develop transient strains that are tolerant to high temperature, for example *Pseudomonas psychrophila*, which is widely distributed in nature, and can cause human and animal disease. It has also been found[48] that *Pseudomonas fluorescens* is an important spoilage bacterium that causes spoilage of meat and can be detected in such meat. The cause of infection due pathogenic bacteria is unknown, and the source of the infection is unclear. In our patient, it may be related to the consumption of spoiled food, as the number of gene fragments of the bacterium obtained by gene sequencing was not large, but could have been due to the small amount of sampling. Fifth, the treatment of the patient was relatively smooth as she fully recovered and returned to normal work and daily life with no obvious sequelae after treatment with intravenous and oral antibiotics. This was related to the relatively young age of the patient, the short disease duration, the absence of significant comorbidities, and the use of adequate antibiotics, which is consistent with previous studies[2]. In this case, bacterial

culture was negative and drug susceptibility testing could not be performed. Ciprofloxacin was empirically selected for treatment. The Department of Pharmacology, Shantou University Medical School in China carried out a drug resistance study on the strain of *Pseudomonas fluorescens*, and found that the strain was resistant to penicillin, ampicillin, amoxicillin, cefuroxime, ceftazidime, cefotaxime, cefazolin, imipenem, meropenem, amtronam and tetracycline, and only sensitive to ciprofloxacin[49]. Liu *et al*[47] carried out a drug sensitivity test on a patient infected with *Pseudomonas fluorescens* secondary to finger skin trauma, and found that the bacterium was sensitive to ceftazidime, amiamkanamycin, amtronam, levofloxacin, ciprofloxacin, imipenem, meropenem, tobramycin, netimicin, *etc*., and resistant to piperacillin, cefoperazone, polymyxin B and ticacillin. Thus, we empirically selected ciprofloxacin in the absence of drug sensitivity, and achieved good clinical efficacy.

This case indicates that clinicians should pay attention to detailed physical and other examinations. When the patient's complaint is not consistent with their condition, appropriate physical and auxiliary examinations are important in helping to identify the cause as soon as possible. The existence of special diseases requires clinicians to continue to explore, recognize and improve, to use the continuous developments of new technologies, and to work together with multidisciplinary unity and cooperation, so that patients can obtain an early diagnosis and precision treatment, and reduce or avoid serious complications or sequelae.

CONCLUSION

This report increases the range of pathogens involved in spinal infections, highlights the unique advantages of gene sequencing technology in difficult-to-diagnose diseases, and validates conservative treatment with a full course of antibiotics for spinal infections without complications.

FOOTNOTES

Author contributions: Guo LL was the doctor in charge, and provided detailed information on the patient; Guo LL and Li L wrote the manuscript; Zhang BH provided and modified the pathological data; Cao JF provided and modified the imaging data; Guo LL, Li L, Zhang BH and Zhang LJ jointly revised the manuscript; All authors read and approved the final manuscript.

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