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ORIGINAL RESEARCH

Differences in Haematological and Imaging Features of Lumbar Spine Fungal and *Brucella* Infections

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Objective: To observe the clinical characteristics of fungal and *Brucella* infections of the lumbar spine and explore the key points for their differential diagnosis.

Methods: The clinical data of 12 patients with fungal infection (the fungal group) and 31 patients with *Brucella* infection (the *Brucella* group) of the lumbar spine confirmed by microbiological culture and antigen test were retrospectively analysed. The differences in the clinical characteristics and imaging manifestations were observed between the two groups.

Results: The peripheral blood neutrophil ratio, erythrocyte sedimentation rate, serum total protein and serum globulin levels in the fungal group were higher compared with the *Brucella* group, while the peripheral blood lymphocyte count, lymphocyte ratio and albumin-globulin ratio were lower in the fungal group compared with the *Brucella* group ($P < 0.05$). As for imaging examinations, the proportion of bone destruction centred on the intervertebral disc with surrounding osteosclerosis on computed tomography (CT) imaging showed a statistical difference between the *Brucella* group and the fungal group ($P < 0.05$). Fungal infection patients showed more osteosclerosis-free areas around the bone destruction on magnetic resonance imaging (MRI) than *Brucella* infection patients.

Conclusion: There are certain similarities in clinical manifestations between fungal and *Brucella* infections of the lumbar spine, but the haematological indices and image features of CT and MRI can effectively differentiate between them, providing guidance for the clinical differential diagnosis.

Keywords: mycosis, brucellosis, imaging, differential diagnosis

Introduction

Infectious diseases of the spine (IDS) are common clinical conditions, and their pathogens include bacteria, fungi and viruses. The incidence of IDS is approximately 1/100,000–1/250,000 per year, and they are more common in males and mainly occur in the lumbar spine.[1,2] Fungal spondylitis is rare and often occurs in individuals with an immunosuppressive status or low immunity. Its risk factors include acquired immunodeficiency syndrome, long-term antibiotic use, malignant tumours, organ transplantation, use of immunosuppressive drugs, previous fungal infections, catheterisation and previous surgical procedures.[3–5]

The pathogens of fungal infections include symbiotic and endemic fungi. The former, including *Candida, Aspergillus* and *Cryptococcus*, mostly outbreak during a decline in immunity.[6–8] Brucellosis is an infectious zoonotic disease that has become a global public health issue. The annual number of new cases worldwide is expected to grow to 1.6 million–2.1 million.[9] In China, the incidence of brucellosis has also gradually increased,[10] reaching 3/100,000.[11] The spine is

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a common site of *Brucella* infection, with more than half occurring in the lumbar spine.[12–14] Most brucellosis patients have a history of contact with livestock, such as cattle and sheep. However, in recent years, infections caused by the consumption of dairy products have also increased,[9] which has brought difficulties to clinical diagnosis.

Fungal spondylitis and brucellosis spondylitis mainly manifest as fever and lower back pain in the clinic. Laboratory examination may suggest elevated inflammatory markers, and imaging may display vertebral and intervertebral disc destruction. However, specific clinical diagnostic criteria are lacking. In addition, some patients have a low pathogen positivity rate, which can easily lead to missed diagnosis or misdiagnosis, thus aggravating the condition. There are many reports on the clinical characteristics of the two diseases, both domestically and internationally. However, there is a lack of a systematic summary of the key points for their differentiation. On this basis, this study retrospectively analyses the clinical data of patients with lumbar spine fungal infection and *Brucella* infection in our hospital, assessing the differences between the two in haematological examination and imaging, with a view to providing a reference for the differential diagnosis of clinical lumbar spine fungal infection and *Brucella* infection.

Materials and Methods

General Data

Patients with infectious diseases of the lumbar spine admitted to the Third People's Hospital of Kunming and the People's Hospital of Lincang from 1 January 2022 to 31 December 2023 were included consecutively. After excluding patients with incomplete data, 43 patients were enrolled. Among them, 12 patients were confirmed as having a fungal infection (the fungal group) and 31 as having a *Brucella* infection (the *Brucella* group) through aetiology and pathology. This study was approved by the Ethics Committee of the authors' hospital (approval no. KSLL20230711001), and all patients signed informed consent forms.

Diagnostic Criteria

(1) The diagnostic criteria for fungal spondylitis were as follows:[15] (a) a histopathological examination identifying fungal hyphae and spores and (b) a positive fungal culture in pus and tissue samples. (2) The diagnostic criteria for brucellosis spondylitis included:[6] (a) a positive serological *Brucella* agglutination test ($\geq$ 1:100) and (b) a bacterial culture positive for *Brucella* in pus and tissue samples.

Methods

Clinical Data

The general information (gender and age), clinical symptoms, medical history, laboratory tests (peripheral blood leukocyte count and classification, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serological test, etc)., lesioned spinal segment and diagnostic basis of the patients were collected. The clinical data were acquired through the hospital's electronic medical record system.

Imaging Examination

All the patients underwent lumbar X-ray, computed tomography (CT) plain scanning and magnetic resonance imaging (MRI) plain scanning. After downloading the patients' imaging data from the hospital's PACS platform, X-ray, CT and MRI images were read using the Radiant DICOM Viewer (Poland) to analyse imaging manifestations. Vertebral bone destruction and intervertebral stenosis were observed on the lumbar X-rays. The areas affected by bone destruction were observed on the lumbar CT scans. The bone involvement of the lesioned vertebral bodies and the anterior and middle columns of the spine were observed in the abdominal and dorsal directions. Referring to the classification of bone destruction in spinal tuberculosis,[16] bone destruction with the vertebral body or intervertebral disc as the centre was observed in the capitopedal direction. Whether there was osteosclerosis around and sequestration inside the bone destruction was noted. Additionally, whether the diseased bone was accompanied by compression fractures was recorded. On the lumbar MRI scans, signals on T1WI, T2WI and fat-suppressed T2WI of bone destruction and surrounding osteosclerosis, granuloma beneath the paraspinal ligament, anterior longitudinal ligament and posterior longitudinal

ligament, as well as the presence of a psoas abscess were observed. Images were read by 2 physicians with intermediate or higher professional titles who had been engaged in the imaging diagnosis of infectious diseases for many years using the blind method. In the event of inconsistent conclusions from the 2 physicians, the images were read by the third physician to reach a consensus through joint consultation.

Lumbar X-ray was performed using United Imaging uDR 780 at a tube voltage of 75 kV (posteroanterior position) and 85 kV (lateral position) and a tube current of 500 mA. Computed tomography scans were carried out with United Imaging uCT 960 with a tube voltage at 120 kV, automatic tube current modulation, a scanning layer thickness of 5 mm and a layer thickness of bone reconstruction of 0.55 mm, with coronal and sagittal images reconstructed. Magnetic resonance imaging was taken with United Imaging uMR 780 using sagittal T1WI, T2WI and fat-suppressed T2WI sequences and horizontal T2WI and T1WI sequences, with TR = 500 ms, TE = 9 ms, layer thickness of 4 mm, TR of T2WI sequence = 2500 ms, TE = 100 ms, layer thickness of 4 mm, TR of T2WI sequence with fat suppression = 2400 ms, TE = 90 ms and layer thickness of 4 mm.

Statistical Methods

The data were analysed using SPSS version 23.0 statistical software. Measurement data were expressed as mean ± standard deviation ($\overline{x} \pm s$) or median (interquartile range) (M [P25, P75]) and intergroup comparisons were carried out using the independent samples *t*-test or the rank-sum test. Enumeration data were expressed as n (%) and analysed with the $\chi 2$ test or Fisher's exact test. $P < 0.05$ was considered as statistically significant.

Results

Comparison of Clinical Characteristics

In the fungal group, there were 8 males and 4 females, aged 46–63 years (with an average age of 55.9 ± 4.9 years). The *Brucella* group had 27 males and 4 females, aged 37–78 years (with an average age of 55.1 ± 10.2 years). The two groups showed no statistically significant differences in gender ratio or age ($P > 0.05$). The proportions of fever and lower back pain in the *Brucella* group were higher than those in the fungal group without statistically significant differences ($P > 0.05$). In the fungal group, 5 (41.7%) patients had a history of local surgery, which was significantly more than 1 (3.2%) patient in the *Brucella* group ($P < 0.05$).

Comparison of Laboratory Results

The peripheral blood neutrophil ratio, ESR, serum total protein and serum globulin levels in the fungal group were significantly higher compared with the *Brucella* group, while the peripheral blood lymphocyte count, lymphocyte ratio and albumin-globulin ratio were lower in the fungal group compared with the *Brucella* group, with statistically significant differences ($P < 0.05$). No statistically significant differences were found in the CRP or serum globulin levels between the two groups ($P > 0.05$), as Table 1 shows.

Table 1 Comparison of Laboratory Results Between the Two Groups

	Fungal group (n = 12)	Brucellar group (n = 31)	*P*
WBC	5.66(5.25, 10.53)	5.90(4.35, 7.29)	0.369
NEU	3.93(3.34, 8.21)	3.26(2.26, 4.69)	0.045
NEU%	69.58(63.64, 76.68)	55.31(51.86, 63.79)	0.000
LYM	1.21(1.09, 1.30)	1.57(1.34, 2.29)	0.002
LYM%	18.51±4.78	30.51±9.14	0.000
MO	0.66±0.24	0.62±0.23	0.621

(*Continued*)

Table 1 (Continued).

	Fungal group (n = 12)	Brucellar group (n = 31)	*P*
MO%	9.19±2.04	10.28±2.66	0.162
ESR	73.00(60.00, 100.00)	28.00(15.00, 26.00)	0.000
CRP	19.86(10.46, 69.70)	29.25(16.19, 38.88)	0.800
TP	69.35±5.95	61.06±5.01	0.000
ALB	35.80(29.10, 37.10)	31.70(30.1, 34.70)	0.254
GLOB	35.85(35.10, 37.90)	28.90(27.70, 31.90)	0.000
A/G	1.01(0.73, 1.07)	1.08(0.96, 1.52)	0.030

Note: Data were shown as mean ± SD or median (interquartile range).
Abbreviations: WBC, total number of white blood cells in the peripheral blood (× 10^9); NEU, peripheral blood neutrophil count (× 10^9); NEU%, peripheral blood neutrophil percentage (%); LYM, peripheral blood lymphocyte count (× 10^9); LYM%, peripheral blood lymphocyte percentage (%); MO, peripheral blood monocyte count (× 10^9); MO %, peripheral blood monocyte percentage (%); ESR, erythrocyte sedimentation rate (mm/h); CRP, C-reactive protein (mg/L); TP, serum total protein (g/L); ALB, serum albumin (g/L); GLOB, serum globulin; A/G, serum albumin-globulin ratio.

Comparison of Imaging Results

X-Ray

There were 4 (33.3%) patients with intervertebral stenosis and 6 (50%) patients with vertebral bone destruction in the fungal group (n = 12), while there were 18 (58.1%) patients with intervertebral stenosis and 20 (64.5%) patients with vertebral bone destruction in the *Brucella* group (n = 31), presenting no statistically significant differences ($P > 0.05$), as Figure 1 shows.

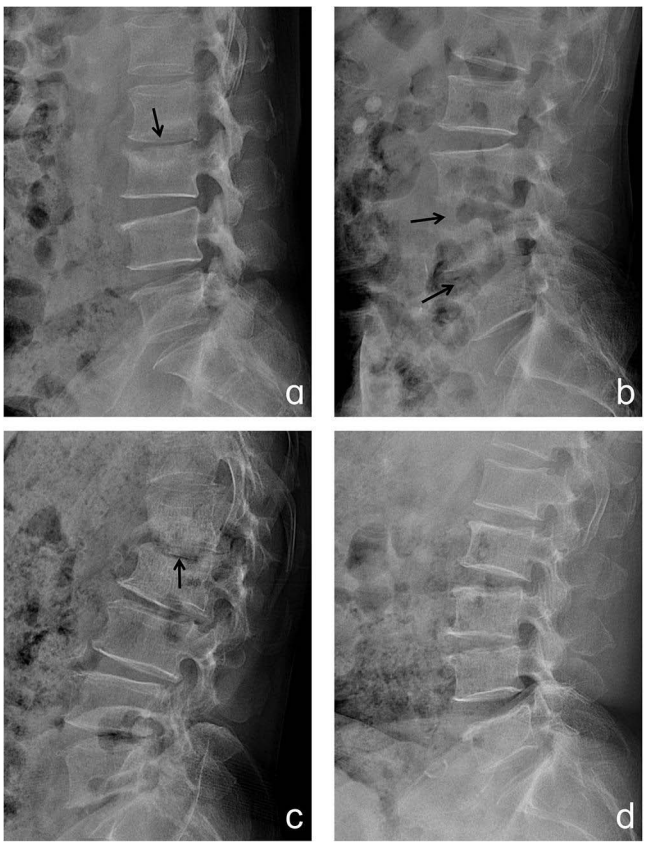

Figure 1 (**a**) Lumbar X-ray of fungal spondylitis in the lateral view shows L2-3 intervertebral stenosis (black arrow); (**b**) Lumbar X-ray of fungal spondylitis in the lateral view shows no L3-4 or L4-5 intervertebral stenosis (black arrow); (**c**) Lumbar X-ray of brucellar spondylitis in the lateral view shows L1-2 intervertebral stenosis (black arrow); (**d**) Lumbar X-ray of brucellar spondylitis in the lateral view shows no obvious intervertebral stenosis.

CT Plain Scanning

In the fungal group (n = 12), a single segment was involved in 10 (83.3%) patients, and osteosclerosis was found around the bone destruction in 1 (8.3%) patient. In the *Brucella* group (n = 31), a single segment was involved in 26 (83.9%) patients, and bone destruction centred on the intervertebral disc was found in 31 (100.0%) patients with surrounding osteosclerosis in 15 (48.4%) (Table 2 and Figure 2). The proportion of patients with bone destruction centred on the intervertebral disc and surrounded by osteosclerosis in the *Brucella* group was significantly higher than in the fungal group ($P < 0.05$).

MRI Plain Scanning

Of 12 fungal infection patients, 11 (91.7%) showed no osteosclerotic area around the bone destruction on MRI, while 16 (51.6%) *Brucella* infection patients showed osteosclerosis around the bone destruction on MRI ($P < 0.05$). All patients showed an equal signal on T1WI, a high signal on T2WI, a high signal on fat-suppressed T2WI, a high signal on T2WI around the bone destruction and a high signal on fat-suppressed T2WI. Patients with no osteosclerotic areas around the bone destruction showed an equal signal on T1WI for bone destruction, and the osteosclerotic regions around the bone destruction showed a low signal on T1WI on MRI (Figure 3).

Discussion

The spine is a common site of infections, of which fungal spondylitis has a relatively low incidence, although an upward trend has been seen in recent years.[17] Issa et al[18] reported that fungal spondylitis in the United States increased from 3.4/100,000 in 2000 to 5.6/100,000 in 2012. Brucellosis spondylitis is the most common complication of bones and joints in brucellosis, with an incidence of 10%–60%.[19–21] However, the lack of specific clinical manifestations in the two diseases makes them prone to misdiagnosis or missed diagnosis. Gündüz et al[22] have found that the median time is 6 months for diagnosing brucellosis spondylitis in children. Consequently, clarifying the clinical characteristics and key points for differentiation of the two diseases is crucial for their early diagnosis and treatment.

The present study's results showed no statistically significant differences in gender or age distribution between the fungal and *Brucella* infection groups, suggesting similar populations are prone to the two diseases. Regarding clinical symptoms, the proportions of patients with lower back pain and fever showed no statistically significant differences between the two groups, but the proportion of patients with a history of surgery was significantly higher in the fungal group compared with the *Brucella* group. The potential causes may be as follows: fungi often appear in patients with low immunity, and surgery can trigger a decrease in the body's immune function. In addition, iatrogenic infections during surgical procedures are also an important cause.[23,24] Therefore, patients with spinal infections who have a history of surgery should be alert to the possibility of fungal infections. Among the 12 patients with fungal infections in this study, only 50% were immunocompromised and had a previous history of surgical procedures. In future clinical practice, paying attention to fungal infections of the spine in immunocompetent populations is necessary.

In this study, it was found that the peripheral blood neutrophil ratio, ESR, serum total protein and serum globulin levels in the fungal group were higher compared with the *Brucella* group, while the peripheral blood lymphocyte count, lymphocyte ratio and albumin-globulin ratio were lower in the fungal group compared with the *Brucella* group. This indicates that patients with fungal infections have more severe inflammatory responses, mainly dominated by neutrophils and with relatively reduced lymphocytes. In addition, due to the combination of inflammation and the decline in immune function, albumin synthesis is reduced. The changes in the above indicators, to a certain extent, reflect the differences in pathological and physiological changes between the two diseases. Nevertheless, they still lack specificity and cannot be used as a direct basis for their differential diagnosis.

Table 2 Lumbar CT Manifestations of the Two Groups

Group	Single-Segment Involvement	Centered on the Intervertebral Disc	Surrounded Osteosclerosis
Fungal group (n = 12)	10(83.3)	8(66.7)	1(8.3)
Brucellar group (n = 31)	26(83.9)	31(100.0)	15(48.4)
P	1.000	0.004	0.017

Notes: Data were shown as number (percent).

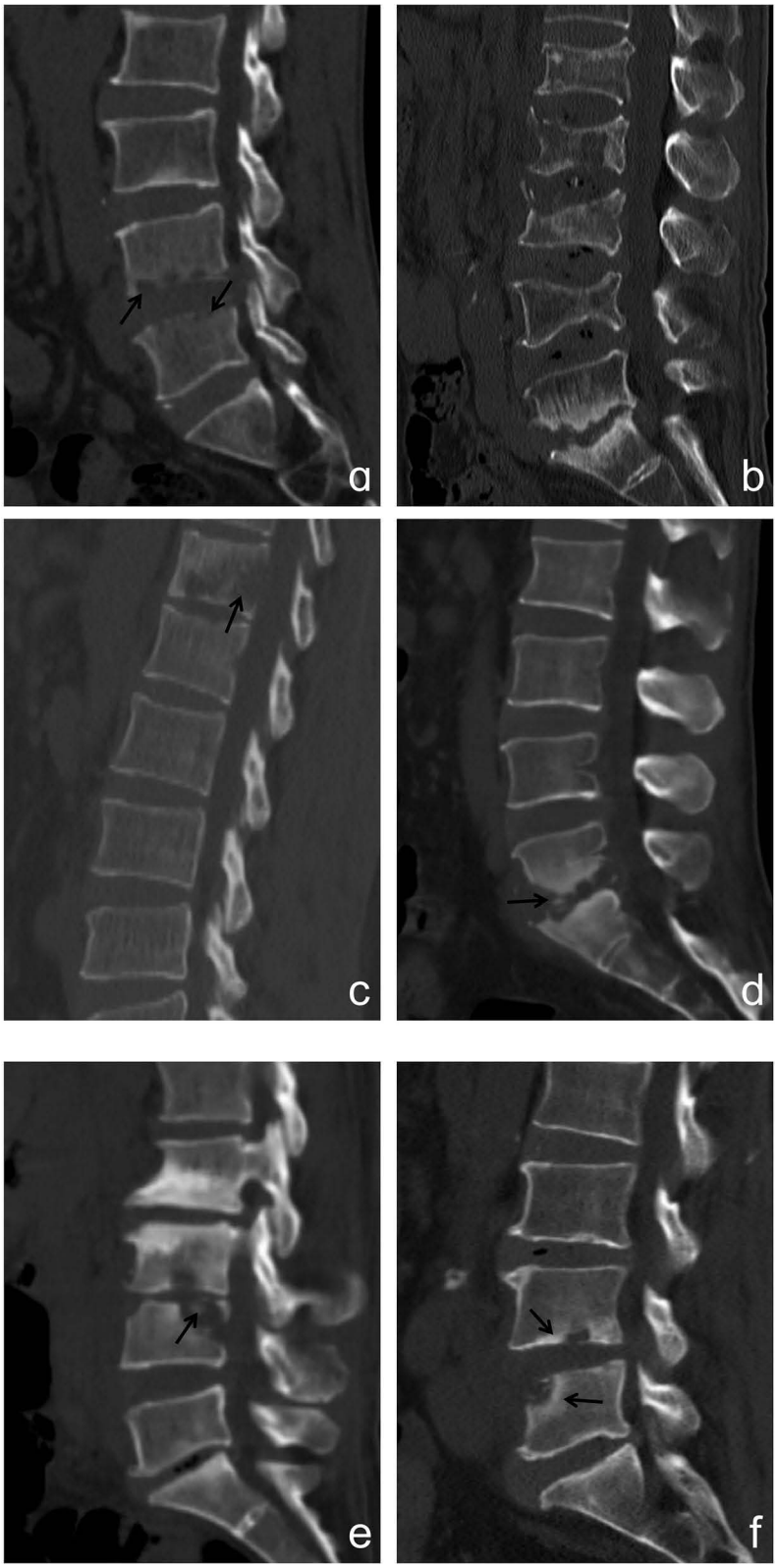

Figure 2 (**a**) CT scan with sagittal reconstruction of fungal spondylitis shows single segment involvement of bone destruction, worm eaten-like bone destruction beneath the L4-5 vertebral plates, no obvious intervertebral stenosis, and no osteosclerosis around the bone destruction (black arrow); (**b**) CT scan with sagittal reconstruction of brucellar spondylitis shows multiple segment involvement of bone destruction; (**c**) CT scan with sagittal reconstruction of fungal spondylitis shows bone destruction centered on the vertebral body at L1, and no osteosclerosis around the bone destruction (black arrow); (**d**) CT scan with sagittal reconstruction of brucellar spondylitis shows bone destruction centered on the intervertebral disc at L5 and S1, and osteosclerosis around the bone destruction (black arrow); (**e**) CT scan with sagittal reconstruction of brucellar spondylitis shows bone destruction at L3-4, punctate sequestration inside the bone destruction (black arrow), and no osteosclerosis around the bone destruction; (**f**) CT scan with sagittal reconstruction of brucellar spondylitis shows bone destruction at L4-5, and osteosclerosis around the bone destruction.

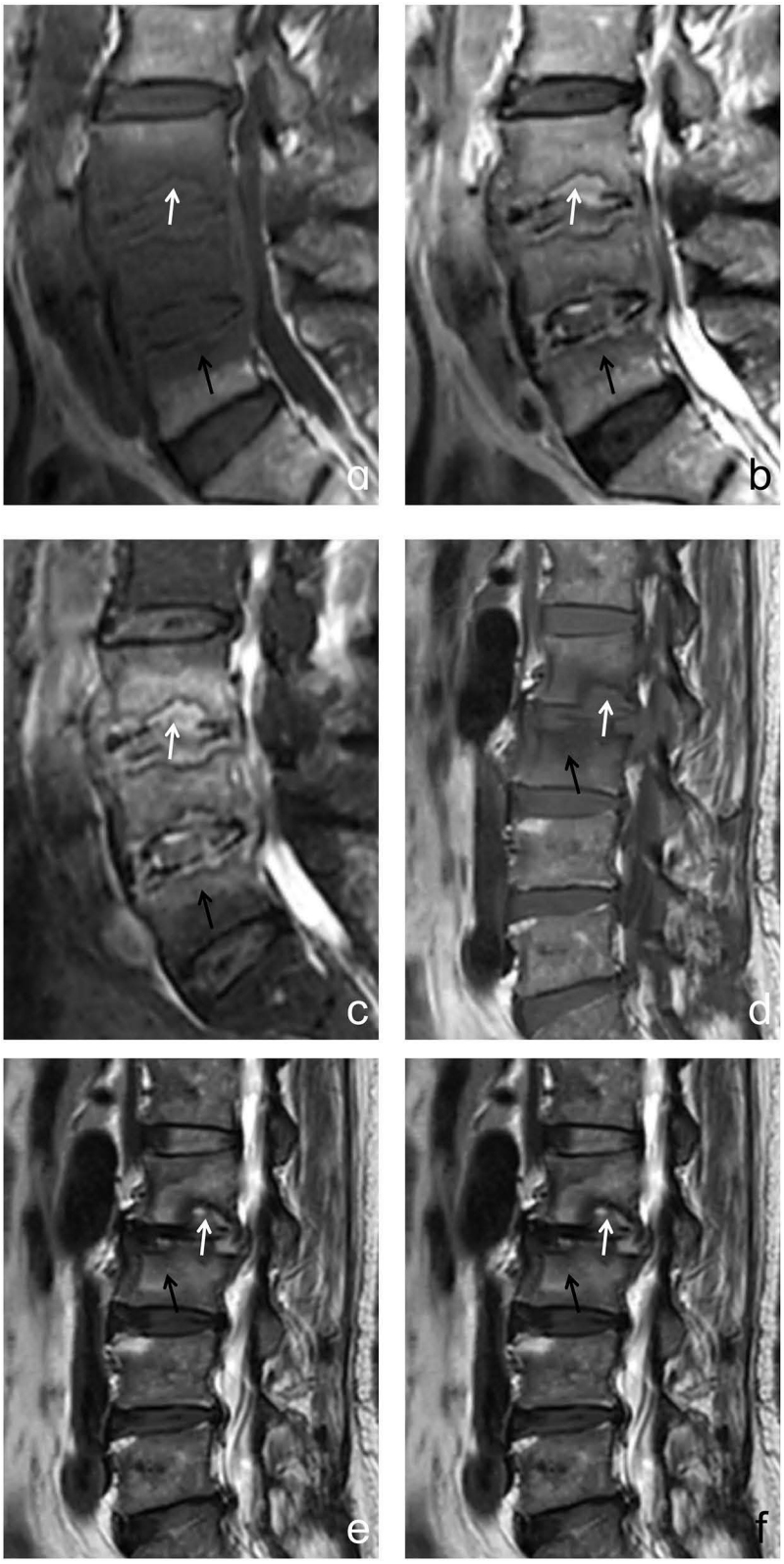

Figure 3 (**a**–**c**) Fungal spondylitis (**a**) Sagittal T1WI of the lumbar spine, bone destruction shows equal signal (white arrow), and bone around the bone destruction shows low signal (black arrow), (**b**) Sagittal T2WI of the lumbar spine, bone destruction shows high signal (white arrow), and bone around the bone destruction shows low signal (black arrow), (**c**) Sagittal fat-suppressed T2WI of the lumbar spine, bone destruction shows high signal (white arrow), and bone around the bone destruction shows high signal (black arrow); Figure d-f Fungal spondylitis (**d**) Sagittal T1WI of the lumbar spine, bone destruction shows equal signal (white arrow), and bone around the bone destruction shows low signal (black arrow), (**e**) Sagittal T2WI of the lumbar spine, bone destruction shows high signal (white arrow), and bone around the bone destruction shows low signal (black arrow), (**f**) Sagittal fat-suppressed T2WI of the lumbar spine, bone destruction shows high signal (white arrow), and bone around the bone destruction shows high signal (black arrow).

Imaging examination is an important means of diagnosing spinal infections. In our study, the diagnostic sensitivity of X-rays for the two diseases was not high, and the difference in the proportion of visible abnormal manifestations was not statistically significant, indicating that an X-ray has limited diagnostic value for early lesions. Regarding CT, the proportions of patients with bone destruction centred on the intervertebral disc with surrounding osteosclerosis in the *Brucella* group were higher than those in the fungal group. The reason may be that *Brucella* is prone to invading intervertebral discs and subsequently affecting adjacent vertebral bodies, thus leading to osteosclerosis as a disease progression. Fungi often directly invade the vertebral bodies, causing osteolytic damage.[16] Magnetic resonance imaging is the preferred imaging method for diagnosing spinal infections. The main MRI findings of the two groups in our study were as follows: fungal infections often affected the vertebral bodies without obvious surrounding osteosclerosis, presenting low signals on T1WI and T2WI, possibly related to fibrous tissue proliferation. *Brucella* infections mostly involved the intervertebral discs with surrounding osteosclerosis and low T1WI and high T2WI signals, suggesting mainly oedematous changes. In the *Brucella* group, granulation often spread to adjacent soft tissues, while in the fungal group, it was mostly limited to the diseased vertebral bodies. Therefore, CT combined with MRI findings have certain differential diagnostic values for the two diseases.

This study is retrospective and has some shortcomings. Firstly, the sample size is relatively small due to the low incidence of these diseases. In addition, the long-term follow-up data on patient prognosis and outcomes are lacking, which limits the evaluation of the prognostic differences between the two diseases. In the future, prospective studies should be conducted with larger sample sizes to dynamically monitor patients' clinical outcomes and further explore the prognostic factors of the two diseases.

In conclusion, lumbar spine fungal infections and *Brucella* infections remain clinically distinct. Fungal infections occur predominantly in patients with a history of surgery and laboratory tests, suggesting an elevated neutrophil ratio and decreased albumin. Computed tomography scans showed a higher percentage of patients in the *Brucella* group with bone destruction centred on the intervertebral discs with surrounding osteosclerosis compared with the fungal group. On MRI, patients with fungal infections showed more osteosclerosis-free areas around the bone destruction than patients with *Brucella* infections.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the declaration of Helsinki.The studies involving human participants were reviewed and approved by Kunming Third People's Hospital/Yunnan Clinical Medical Center for Infectious Diseases (approval No.: KSLL20230711001). The patients/participants provided their written informed consent to participate in this study.

Consent for Publication

The manuscript is not submitted for publication or consideration elsewhere.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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