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A 33-Year-Old Refugee from Afghanistan With Recurrent Fever and Back Pain

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Clinical Presentation

History

A 33-year-old male refugee from Afghanistan presents to a German clinic with a 6-month history of recurrent fever, night sweats and progressive back pain. After leaving Afghanistan with his wife and two children, the family first lived in a refugee camp in Iran. There, the patient started feeling ill about 6 months ago and was treated with tablets for several weeks. Initially he also received intragluteal injections. His symptoms subsided whilst on medication but recurred after the treatment ended. After crossing Turkey and Eastern Europe, the family reached Germany 4 months ago. All medical documents were lost during the journey.

Clinical Findings

The patient is afebrile and in fair general condition. Vital signs are normal. On examination, there is marked spinal tenderness in the lumbar region. The remaining examination is unremarkable.

Laboratory Results and Imaging

Differential blood count, liver and renal function tests as well as LDH are normal. C-reactive protein and erythrocyte sedimentation rate are slightly raised at 26 mg/L (<5 mg/L) and 40 mm/hour (<20 mm/hour), respectively. Urinalysis is unremarkable.

MRI of the spine reveals signal enhancement of the L3 and L4 vertebral bodies, the corresponding vertebral disc and the right psoas muscle, as well as disc space narrowing and irregularities of both adjacent vertebral endplates (Fig. 81.1A and B). A chest x-ray shows no abnormalities.

Questions

1. What are the most likely differential diagnoses in this patient?
2. Which investigations are useful to determine the causative agent?

Discussion

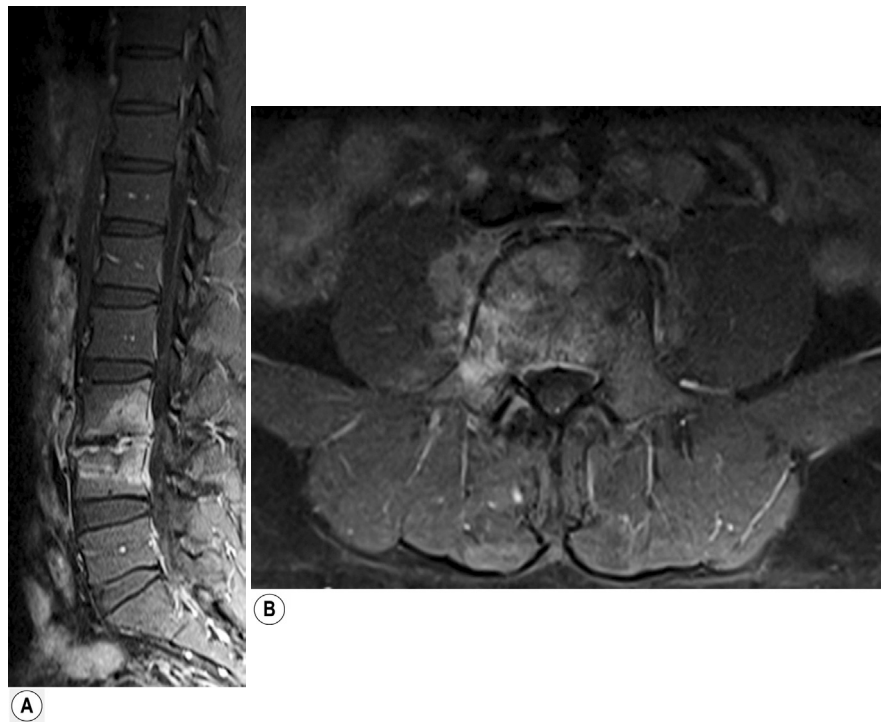
A male Afghan refugee presents with a 6-month history of recurrent fever, night sweats and progressive back pain. Physical examination reveals localized lumbar spinal tenderness. CRP and ESR are slightly raised and an MRI of the spine shows spondylodiscitis of L3/L4 with involvement of the psoas muscle.

Answer to Question 1

What are the Most Likely Differential Diagnoses in This Patient?

Spondylitis in a febrile young adult is likely to be infectious. Globally, tuberculosis is the main cause of infectious spondylitis. Spinal brucellosis may be equally common or even predominant in highly endemic countries, such as Afghanistan.

Other infectious causes of spondylitis mirror those of osteomyelitis and usually follow haematogenous spread from a distant site of infection. The spectrum of pathogens includes *Staphylococcus aureus*, pyogenic and non-pyogenic streptococci and Gram-negative bacteria such as *Salmonella* species. In addition, histoplasmosis, actinomycosis and melioidosis may be relevant causes depending on local epidemiology.



• **Fig. 81.1A and B** MRI of the spine reveals signal enhancement of the L3 and L4 vertebral bodies, the corresponding vertebral disc and the right psoas muscle, as well as disc space narrowing and irregularities of both adjacent vertebral endplates.

Answer to Question 2

Which Investigations are Useful to Determine the Causative Agent?

It is not possible to reliably distinguish spinal tuberculosis from brucellosis by x-ray or CT/MRI imaging; microbiological testing is required. In patients from highly endemic countries, serological testing and interferon gamma release assays (IGRA) are of limited diagnostic value, because they are not able to distinguish between active and latent/past infection. Definitive diagnosis requires isolation of the causative agent from blood or tissue samples.

Spinal tuberculosis is rarely accompanied by pulmonary involvement, and sputum samples often remain negative. In brucellosis, the sensitivity of blood culture is generally high in acute disease and decreases over time. Bone marrow cultures have a better yield at all stages of disease.

CT-guided percutaneous vertebral biopsy and subsequent tissue culture and molecular analysis is the diagnostic gold standard in infectious spondylitis. Histopathology should be performed simultaneously to rule out malignancy and to confirm granulomatous inflammation, which is a feature of both tuberculosis (caseous) and brucellosis (non-caseous).

It is important to notify laboratory staff that brucellosis is suspected: *Brucella* cultures are highly infectious and require biosafety level 3 handling; they may also have a prolonged

time to positivity (although this is less of an issue with modern automated blood culture systems).

The Case Continued...

Several blood cultures are taken but remain negative. Sputum samples are negative for acid-fast bacilli. A CT-guided biopsy of the lesion is performed without complications. Culture of the tissue sample reveals *Brucella melitensis* as the causative agent. No additional sites of infection are identified on imaging. Importantly, there is no sign of endocarditis on echocardiography.

The presentation is classified as “complicated brucellosis” with spondylitis and para-vertebral abscess formation according to WHO criteria, which requires a prolonged course of antimicrobial combination therapy. The patient is treated with doxycycline 100 mg twice daily and rifampicin 900mg daily for 16 weeks. Additionally, intramuscular streptomycin (1 g daily) is given for the first 3 weeks of treatment.

The fever subsides after several days and inflammation parameters return to normal several weeks after initiation of antimicrobial therapy. A second MRI at the end of treatment shows full resolution of the paravertebral abscess. One year post treatment completion, the patient shows no signs of relapse.

SUMMARY BOX

Brucellosis

Brucellosis is a common zoonotic bacterial infection and an important differential diagnosis in prolonged febrile illness. Currently, around 500 000 cases of brucellosis are reported to the WHO each year, with global incidence rates increasing. *B. melitensis* is the most common cause of brucellosis worldwide and mainly infects camels, sheep and goats. Frequent routes of animal-to-human transmission include consumption of unpasteurized dairy products as well as exposure to bodily fluids and aerosols during animal birth or slaughter. The possibility of airborne transmission requires special safety precautions while handling *Brucella* cultures in the laboratory (biosafety level 3).

In the early stages, brucellosis usually presents as a non-focal febrile illness. Clinical signs and symptoms are non-specific and may include night sweats, fatigue, lymphadenopathy and hepatosplenomegaly. Localized infection develops frequently during the course of disease and may affect the musculoskeletal, genitourinary, central nervous or cardiovascular system. Osteoarticular involvement is particularly common (up to 40% of cases) and often presents as peripheral arthritis, sacroiliitis or spondylitis.

Serological diagnostic tests are widely available but fail to distinguish current from past infection in areas of high endemicity. Blood culture has a high sensitivity in acute disease and tissue culture is considered the gold standard in localized infection.

Brucellosis therapy generally requires a combination of antimicrobials with activity in the acidic intracellular environment,

as well as a prolonged course of treatment to avoid treatment failure and relapse. Preferred drug combinations of brucellosis are doxycycline plus an aminoglycoside (streptomycin or gentamicin) or plus rifampicin. In neurobrucellosis, ceftriaxone is combined with doxycycline and rifampicin. If contraindications occur, ciprofloxacin and cotrimoxazole may be used. Treatment duration is between six weeks and several months depending upon organ manifestation and severity.

Although most osteoarticular complications can be treated with a standard course of 6 weeks' duration, brucella spondylitis requires prolonged treatment for at least 12 weeks to avoid relapse. Furthermore, surgical intervention may be required in cases of vertebral instability or epidural and paravertebral abscess formation.

Further Reading

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