CASE REPORT

Spontaneous bacterial peritonitis by *Brucella* in a cirrhotic patient

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SUMMARY

Spontaneous bacterial peritonitis (SBP) is a frequent form of decompensation of end-stage liver disease, with an incidence of 15–20% and a short-term mortality of 10–33%. The usual causative agents (90% of SBP) are enteric Gram-negative bacteria—*Escherichia coli* and *Klebsiella pneumoniae*. *Brucella* is known to be a possible, but exceedingly rare, causative agent of SBP. We present the case of a 47-year-old Egyptian man, with hepatitis C cirrhosis, and a 2 week history of ascites, jaundice, encephalopathy, fever and pain on his right shoulder that started while travelling in the Middle East. Laboratory and imaging studies were undertaken and he was diagnosed an SBP that failed to respond to Imipenem. *Brucella* was identified both in the ascitic fluid and blood; he was started on doxycycline plus rifampin with immediate clinical improvement. The antibiotic regimen was kept for 8 weeks. The patient is currently under evaluation for liver transplantation.

BACKGROUND

Spontaneous bacterial peritonitis (SBP) is a frequent complication of end-stage liver disease usually caused by enteric Gram-negative bacteria. *Brucella* sp. is an exceedingly rare causative agent with a few reports of *Brucella* peritonitis in cirrhotic patients.^{1–6}

Brucellosis is one of the most common zoonosis worldwide, with an incidence of 500 000 cases per year. It is transmitted to humans through contact with fluids from infected animals (sheep, cattle and other mammals) or by ingestion of unpasteurised milk and dairy products.^{7–9}

Acute brucellosis is a systemic infection that usually follows a period of incubation of 1–4 weeks and has very wide clinical spectra, varying from an asymptomatic to fatal disease.¹⁰ It can be acute and become chronic, after 1 year from diagnosis. Usually, acute illness consists of non-specific symptoms such as fever, night sweats, arthralgia, weight loss, fatigue, malaise, headache and anorexia.^{11–13} Focal infection is present in 30% of all cases^{10 14 15} and can affect any organ system, with osteoarticular involvement the most common focal presentation,^{16 17} and spondylitis being the most frequent severe complication. Other organ systems involved include genitourinary, pulmonary, haematological, neurological, cardiac, dermatological and gastrointestinal, including hepatitis.¹⁰

Gastrointestinal involvement is infrequent (3–6%)¹³ with peritonitis in cirrhotic patients being rarely reported.

CASE PRESENTATION

A 47-year-old Muslim, born in Egypt was admitted to our hospital for ascites, jaundice and encephalopathy in July 2012. He had been previously followed for hepatitis C infection (previous non-responder to ribavirin and pegylated interferon therapy) and type 2 diabetes mellitus. He lived in Portugal for 20 years, but in the last 4 years he has been living and working as a businessman in China.

He had travelled to the Middle East, 2 months earlier, where he had his first liver disease decompensation with ascites and hepatic encephalopathy. He was transferred to our institution after 2 weeks. He denied travelling to rural areas, having contact with animals or drinking of unpasteurised milk.

At admission, he was symptomatic for abdominal and right shoulder pain, jaundice and encephalopathy.

The physical exam revealed a conscious, but lethargic and grossly disoriented icteric man, with obvious flapping. He was tachypnoeic, tachycardiac and febrile (38.5°C). His abdomen was diffusely painful with a moderate volume ascites. His right shoulder was painful, but did not have any visible inflammatory signs.

INVESTIGATIONS

Blood was taken for analysis including blood cultures. Paracentesis was performed and assessed for cytology, biochemistry and microbiology. Laboratory data were as follows: haemoglobin 14.1 g/dl (13.0–17.5); white blood count $12\,400 \times 10^6$ /litre ($4.0\text{--}11.0 \times 10^6$); platelets 93×10^9 /litre ($150\text{--}450 \times 10^9$); international normalised ratio 1.44; creatinine 0.7 mg/dl (0.7–1.3); sodium 121 mEq/l (135–145); aspartate aminotransferase 103 U/l (<34); γ -glutamyl transferase 282 U/l (<73); lactate dehydrogenase 806 U/l (208–378); total bilirubin 7.2 mg/dl (<1.0); albumin 2.2 g/dl (3.2–4.8); and C reactive protein 4.3 mg/dl (<0.5). Serology was positive for HBs-Antigen, HBe-antibody (Ab) and HBe-Ab. Hepatitis B DNA was below the lower level of detection.

The ascitic fluid had a serum-ascitic albumin gradient >1.1 and the cytology indicated the presence of 1514 polymorphonuclear leukocytes/ μ l.

The abdominal ultrasound (US) showed an enlarged heterogeneous liver and signs of portal hypertension, as shown by splenomegaly and small volume ascites.

The Child-Pugh classification was class C with a Model for End-Stage Liver Disease (MELD) of 18 points.

He was started on Imipenem/cilastatin for SBP without symptomatic or laboratory improvement.

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By the fifth day, he started to refer arthralgia on his left hip and knee which were swollen and reddened. He was submitted to an US of his left knee and right shoulder and MRI of the hip that showed non-specific inflammatory signs on all three joints, with moderate volume of liquid on the subacromial bursa. He was then submitted to a fine needle aspiration and purulent liquid was drained. No agent was isolated.

The microbiological studies performed on the ascitic fluid and blood revealed the presence of Gram-negative coccobacilli (figure 1) that were identified by agglutination with anti-Brucella-specific serum. Serological tests were also performed. Rose Bengal and Huddleson were both positive. We achieved a positive result for immunoglobulin (Ig)M anti-Brucella and negative for IgG antibodies by ELISA.

There was no evidence of other kind of focal involvement or complications. He was submitted to a transthoracic echocardiography, a CT scan of the head, cervical spine, thorax, abdomen and pelvis.

TREATMENT

The antibiotic therapy was subsequently changed to Doxycycline and Rifampin with evident clinical efficacy after the first few days.

OUTCOME AND FOLLOW-UP

The laboratory evolution was slow, but favourable. He was discharged after 4 weeks and went on to continue the antibiotic scheme for a total of 8 weeks.

He is currently under evaluation for orthotopic liver transplantation. At the moment of hospital discharge, he was a Child Pugh C (10 points), MELD 16. He was still jaundiced (bilirubin—4 mg/dl), but without encephalopathy or ascites.

DISCUSSION

Brucellosis is one of the most widespread zoonotic infections worldwide, especially in endemic areas, with *Brucella melitensis* being the most common agent.¹⁸ Acute brucellosis usually causes a flu-like syndrome, but can involve any organ system.⁷

SBP is a frequent complication of cirrhosis, with most common agents being the Gram-negative bacteria *Escherichia coli* and *Klebsiella pneumoniae*.¹⁹ Apart from these, there are a few agents that are considered to have an aetiological role in a small number

of cases; in this group, *Yersinia enterocolitica*, *Listeria monocytogenes* and *Brucella melitensis* are included.^{20 21}

SBP is a severe infection that carries a dismal prognosis with a short-term mortality risk between 10% and 33% (with or without albumin),²² which increases without effective antimicrobial therapy. The diagnosis of brucellosis is not straightforward. One should be aware of the possibility of brucellosis, especially in a patient who has recently been on an endemic region and who presents with suggestive symptoms as is the case of arthralgia of large joints, even without obvious contact with animals or without ingestion of unpasteurised milk.

The pathogenesis of *Brucella* peritonitis is not clear, it has been advocated that it may occur via haematogeneous spread or simply by intestinal bacterial translocation like in SBP by the other, more frequent, agents.

The diagnosis can be made by serology and confirmed by culture and PCR either with blood or with ascitic fluid¹² as in our case.

Specific antibiotic therapy should be prompt initiated with a combination regimen and kept for a prolonged duration,²³ depending on the presence of focal disease and severe complications, which should be systematically ruled out by means of imaging examination.

There are no recommendations on the duration of treatment in SBP caused by *Brucella* sp., but it is accepted to keep the combination regimen (usually doxycycline and streptomycin or rifampin)²⁴ for at least 6 weeks or as dictated by the clinical course, especially in the presence of complications.

Learning points

- ▶ Different spontaneous bacterial peritonitis (SBP) aetiologies should be considered in international migrants.
- ▶ Brucellosis is a potentially fatal, but treatable, disease.
- ▶ Brucellosis is to be suspected in a cirrhotic patient with SBP, suggestive epidemiology, articular involvement and poor response to conventional empiric antimicrobial therapy.
- ▶ Effective antimicrobial combination regimen should be kept for at least a 6-week period.
- ▶ Severe, but treatable, complications (spondylitis and endocarditis) should be systematically ruled out.

Figure 1 Colonies growing on blood agar culture medium.

Contributors AOF and RTM were directly involved in the patient care and the manuscript writing. LNM was involved the microbiology diagnostic and in the making of the manuscript. JV was involved in manuscript writing.

Competing interests None.

Patient consent Obtained.

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