Brucellosis-induced autoimmune haemolytic anaemia (AIHA)

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SUMMARY

Brucellosis is a rare zoonotic infection caused by small, fastidious Gram-negative coccobacilli of the genus *Brucella* that may be associated with haemolytic complications including thrombotic microangiopathy and haemolytic anaemia. We describe a patient with culture confirmed brucellosis who presented with malaise, high grade fever, hepatosplenomegaly and Coombs-positive autoimmune haemolytic anaemia. The patient was successfully treated with combination of doxycycline and rifampicin with no further episodes of relapses or haemolysis. Although rare, the possibility of brucellosis should always be kept in mind in patients with risk factors who present with haemolysis and endemic area.

INTRODUCTION

Brucellosis is a rare zoonotic infection transmitted by ingestion of infected meat or dairy products, direct contact with an infected animal or inhalation of aerosols. The true incidence of human brucellosis is unknown for most countries. Worldwide, the incidence in endemic disease areas varies widely, from < 0.01 to 200 per 100,000 population.[1] Brucellosis may involve any organ system, the most common complication is osteoarticular involvement.[2] It might also involve the haematological, the nervous, genitourinary, dermatological or the respiratory system. Mild anaemia and leukopaenia have been frequently associated with acute brucellosis, but pancytopaenia, thrombocytopaenia, and haemolysis are less frequently seen.[3] Clinical presentations are non-specific with fever being the commonest presenting symptoms. Physical examination is usually normal, although hepatomegaly, splenomegaly, or lymphadenopathy may occur. Autoimmune haemolytic anaemia (AIHA) is a rare clinical presentation of this disease. In this report, we describe a patient with brucellosis who presented with Coombs-positive AIHA.

CASE REPORT

A previously healthy 31-year-old female of Malay descent, presented with 1 week history of high grade fever and malaise. She had no joint pain, no respiratory, gastrointestinal or genitourinary tract symptoms. There was no recent travel or significant family history. Her husband reared cattle in their backyard farm of their village house. However patient denied direct contact with cattle nor ingestion of unpasteurised milk. Her husband and other family members were otherwise well.

Clinical examination revealed pallor, jaundice and hepatosplenomegaly, but no lymphadenopathy. Examination of the cardiovascular, respiratory and neurological systems were unremarkable.

Blood investigations revealed normochromic normocytic anaemia with raised indirect bilirubin, high lactate dehydrogenase, reticulocytosis and positive direct Coombs test suggestive of immune haemolysis.

Other blood investigations including renal profile and coagulation profile were normal. Anti-nuclear antibody (ANA), Glucose-6-phosphate dehydrogenase deficiency (G6PD) and infective screen including HIV, Hepatitis B and Hepatitis C was negative.

Peripheral blood smear showed moderate anisopoikilocytosis with polychromatic cells and microspherocytes. Tear drop cells and multiple fragmented red blood cells were also noted. The changes in the red cells morphology were suggestive of haemolysis. There were also leukocytosis with neutrophilia and hypersegmented neutrophils suggestive of bacterial infection. Ultrasound of the hepatobiliary system confirmed hepatosplenomegaly with no other significant findings. Patient was empirically started on intravenous ceftriaxone 2g daily for broad-spectrum coverage of unknown source of sepsis. In view of ongoing immune haemolysis, she was started on oral prednisolone 1mg/kg/day which was subsequently tapered down within 2 weeks. She required 1 pint packed cell transfusion due to symptomatic anaemia. Haemoglobin on discharge was 9g/dL. *Brucella melitensis* was isolated from her blood cultures which was susceptible to doxycycline, rifampicin and gentamicin. She was treated with oral doxycycline 100mg BD and oral rifampicin 15mg/kg/day for total duration of 6 weeks. We did not test her husband and other family members as they were asymptomatic. Patient was followed up in our clinic for 18 months. Her haemoglobin on follow up was 10.6g/dL, LDH, bilirubin and reticulocytes count normalised. Repeated Coombs Test was negative.

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Table I: Blood investigations

	Results	Normal range
Haemoglobin (g/dl)	7.1	11.5-17
Mean cell volume (fL)	87	80-100
Mean cell haemoglobin (pg)	31.3	27-32
White blood cells (109/L)	9.9	4-10
Neutrophils (%)	76	40-75
Platelet count (109/L)	217	150-500
Bilirubin (umol/L)	47.6	5-21
Indirect bilirubin (umol/L)	27.8	< 18
ALT (U/L)	49	< 45
ALP (U/L)	48	30-120
LDH (U/L)	947	140-280
Reticulocytes (%)	15.6	0.5-2.5
ESR (mm/hr)	> 120	<12
CRP (mg/L)	26.63	5-40
ANA / Anti-dsDNA	Negative	
G6PD screening	Normal	
Direct Coombs	Positive	
HIV / Hepatitis B / Hepaitis C	Negative	

DISCUSSION

Diagnosis of brucellosis is based on the demographic and epidemiologic characteristics of the disease, as well as the presence of symptoms, results of serological tests and isolation of the microorganism from the blood or bone marrow[4]. This patient had an important risk factor as she had cattle in her backyard farm and the diagnosis was confirmed based on blood culture and is the first case reported at our centre.

Haematologic complications in brucellosis are common and can be multifactorial. Anaemia in brucellosis is common, but the aetiology of anaemia may vary. In general, the anaemia is mild, transient, and related to bone marrow suppression due to high affinity of brucellosis to the reticuloendothelial system. Microangiopathic and autoimmune haemolytic anaemia are other rare but can be severe. The pathogenesis of Brucella-induced haemolysis has not been clearly understood, but it seems to be multifactorial. Several possible mechanisms have been suggested for the haemolysis caused by brucellosis, such as releasing of endotoxins, and formation of immune complexes in the circulation.

There is high mortality rate in AIHA patients with severe haemolysis, hence early recognition and immediate treatment is imperative. Brucellosis is hard to eradicate due to its ability to evade the systemic immune response and its propensity for relapse, even when treated adequately. Durga et al., described a 18 year old female with similar presentation of AIHA with positive blood culture for Brucella and successfully with prednisolone.[2] Similarly Eskazan AE et al., described two patients who responded well to prednisolone.[3] Cases refractory to corticosteroids are typically treated with invasive procedures such as splenectomy, and rituximab may be considered in selected patients. Bourantas LK et al., describe a 79 year old patient with Brucella induced AIHA refractory to corticosteroids but responded to rituximab.[5]

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