Brucellosis disguised as infective endocarditis in the returning traveller

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This case report describes Brucellosis initially masquerading as endocarditis. We aim to increase awareness among physicians about the condition in order to aid early investigation and treatment of Brucellosis, which can prevent severe disability.

Case report

A 38-year-old South Asian man presented to accident and emergency with a 10-day history of fevers, rigors and headache; having returned from Pakistan three weeks prior to admission. He visited his family in the city of Peshawar and had spent a week living in a small rural village. He denied photophobia, rashes, neck stiffness and any contact with persons who have active tuberculosis. He had no significant medical history.

On examination his temperature was 39.2°C; with a sinus tachycardia at a regular rate of 120 beats per minute; and his blood pressure was 130/78. Physical examination revealed several splinter haemorrhages over his left ring finger, right index finger and right thumb. There was a systolic murmur heard over the pulmonary region.

On admission his C-reactive protein (CRP) was elevated at 26 mg/mL (reference range 0–8 mg/mL); white cell count and haemoglobin levels were normal. Alanine transaminase was mildly elevated at 76 IU/L (10–50 IU/L). Serial blood film examinations were negative for malaria and parasites. Urinanalyis and chest radiograph were unremarkable. Multiple blood cultures were taken from various peripheral sites. Trans-thoracic echocardiogram showed structurally normal valves with no vegetations. He was initially started on empirical antibiotics for infective endocarditis given the findings on examination. Three independent blood culture bottles yielded *Brucella melitensis* after three days.

On further directed questioning of the patient, he revealed he had consumed unpasteurized milk and dairy products while visiting family in the rural village outside Peshawar.

After discussion with microbiologists, he was commenced on a two-week course of intravenous gentamicin with a six-week course of oral rifampicin and doxycycline. The murmur heard was not present after two days of treatment and was felt to be a flow murmur secondary to the tachycardia. He was discharged one week later with a CRP of 6 mg/mL on parenteral antibiotics administered through the 'hospital at home' nursing team, having been afebrile for 72 hours.

The patient was reviewed in the infectious disease clinic two months after discharge; he remained asymptomatic and repeat blood cultures were negative having completed treatment.

Discussion

Brucellosis remains the commonest worldwide zoonotic infection with over 500,000 new cases being reported annually. The epidemiology of Brucellosis has rapidly evolved over the last decade; new endemics have emerged in Central Asia along with known areas of endemic infection (Middle East, Latin America, Western Asia and parts of Africa).[1] Brucellosis remains a major public health concern with delay in diagnosis leading to debilitating consequences.[2] With an ever increasing level of foreign travel and immigration it is important that physicians are alert to

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the possibility of encountering patients with a diagnosis of Brucellosis.

Human Brucellosis is primarily transmitted through the consumption of unpasteurised dairy products (such as raw milk, soft cheese, butter and ice cream) derived from infected animals. Brucella species are small Gram negative coccobacilli which are facultative intracellular pathogens in humans. The highest reservoirs of Brucellosis that cause human disease are found in sheep and goats.[3]

Brucellosis is a systemic infection, which can affect any organ and therefore can easily be mistaken for several infections that present with a non-specific picture such as typhoid and syphilis. Symptoms of Brucellosis include large joint arthralgia (73.7%), fever (72.2%) and fatigue (71.2%).[4] Clinical signs include fever (28.2%), haepatomegaly (20.6%) and peripheral arthritis (14.3%).[4] Suspicion should be raised when patients describe recent travel from an endemic area with consumption of dairy products. The incubation period for Brucellosis after infection is between 2–8 weeks and therefore may only present on returning home.

Others have reported focal manifestations of Brucellosis including spondylitis, epidydimo-orchitis, neurovascular manifestations (5%) (including meningitis and encephalitis) and cardiovascular manifestation (mainly in the form of endocarditis <2%).[4]

Case reports have shown delays of several months in the diagnosis of Brucellosis.[3] An article in 2010 suggests two main causes of this delay: firstly, the non-specific symptoms and signs of the disease and second the rarity of the condition, meaning physicians in the UK do not usually consider Brucellosis as a differential diagnosis.[5] This case report demonstrates the non-specific nature of this disease with a presentation of fever and a new murmur leading to an initial diagnosis of infective endocarditis. After subsequent blood cultures and a detailed history, the diagnosis of Brucellosis was identified.

Human Brucellosis is rarely fatal, but if not diagnosed and treated early, it may leave patients with severe disability. The overall mortality from Brucellosis is 5%, with endocarditis playing a major role.[2] Brucellosis is a notifiable disease in the UK and is subject to statutory disease control measure under the Health Protection Agency.

Investigations for Brucellosis should be ordered on all patients who have returned from travel in endemic areas, especially if they have consumed raw milk, meat and cheese. The most definitive test of diagnosing Brucellosis is blood culture. However positive results from blood culture may vary between 50 and 90%.[4] Other tests used to diagnose Brucellosis include the serum agglutination test.[4] Simple blood tests should be ordered looking for anaemia, leucopenia, thrombocytopenia, raised transaminases, raised CRP and erythrocyte sedimentation rate.

Brucellosis remains among the most common causes of laboratory associated infections, with articles reporting that 2% of all cases of Brucellosis are laboratory acquired.[6] A number of reports describe cases of laboratory-acquired Brucellosis (LAB) from various London and Canadian laboratories and provide recommendations as to managing staff with possible exposure to Brucellosis, as well as providing key recommendations in the prevention of LAB.[7,8]

From the clinical point of view, the most important recommendation suggests an increasing level of communication between clinical and laboratory staff to alert staff of specimens from high-risk patients.

There is no consensus over antibiotic regimen(s) that should be used in the treatment of Brucellosis; the UK has no national guidance. A recent meta-analysis of several trials comparing antibiotic combinations concluded that triple therapy using rifampicin, gentamicin and doxycycline is superior to dual therapies, with long duration of treatment (six weeks) offering an advantage over shorter treatments (30 days).[9] Other authors question the practicality of such a regimen suggesting that patient factors such as compliance, adherence and convenience are vital to consider. It is suggested that dual oral therapy may have a higher level of adherence compared with triple therapy (with an intramuscular aminoglycoside), and may therefore lead to improved overall outcome, which is crucial in treatments that may last for several weeks.[10]

References

1 Bruni M, Steffen R. Impact of travel-related health impairments. *J Travel Med* 1997;**4**:61–4
2 Franco MP, Mulder M, Gilman RH, *et al.* Human brucellosis. *Lancet Infect Dis* 2007;**7**:775–86

3 Memish ZA, Balkhy HH. Brucellosis and international travel. *J Travel Med* 2004;**11**:49–55
4 Buzgan T, Karahocagil MK, Irmak H, *et al.* Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. *Int J Infect Dis* 2010;**14**:e469–78
5 Ramin B, MacPherson P. Human brucellosis. *Br Med J* 2010;**341**:c4545
6 Fiori PL, Mastrandrea S, Rapelli P, *et al. Brucella abortus* infection acquired in microbiology laboratories. *J Clin Microbiol* 2000;**38**:2005–6
7 Reddy S, Manuel R, Sheridan E, *et al.* Brucellosis in the UK: a risk to laboratory workers? Recommendations for prevention and management of laboratory exposure. *J Clin Pathol* 2010;**63**:90–2
8 Robichaud S, Libman M, Behr M, *et al.* Prevention of laboratory-acquired brucellosis. *Clin Infect Dis* 2004;**38**: e119–22
9 Skalsky K, Yahav D, Bishara J, *et al.* Treatment of human brucellosis: systematic review and meta-analysis of randomised controlled trials. *Br Med J* 2008;**336**:701–4
10 Pappas G. Treatment of brucellosis: regimens containing aminoglycosides are most effective but difficult to implement in practice. *Br Med J* 2008;**336**:678–9