

Pyrexia of unknown origin: a swollen gland and a glass of milk

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INTRODUCTION

Brucellosis is a disease which has rarely been seen in the UK since the pasteurization of milk. It often presents as a pyrexia of unknown origin and should be considered in the differential diagnosis. A case report is presented where the diagnosis was initially thought to be tuberculosis but months later was found to be brucellosis. The article then presents a summary of brucellosis and its management.

DISCUSSION

Brucellosis is a zoonotic disease caused by small aerobic, gram-negative bacilli. It is transmitted to humans from infected animals and

their dairy products. Since the pasteurization of milk and the introduction of eradication programmes the occurrence of brucellosis in developed countries is very rare. The overall incidence worldwide is 1 in 500 000, but is thought to be increasing (Madkour, 1995; Gotuzzo and Carillo, 1997).

Four different species exist; *Brucella melitensis* produces the most severe disease in South America, Europe and the Middle East. *B. abortus* is the commonest cause in America but produces a mild disease. *B. suis* and *B. canis* are less common.

The bacilli enter through the skin, inhalation of organisms or through the gut wall. They travel in the lymphatic

system before entering the blood, and finally localizing to the reticulo-endothelial system.

The clinical features are determined by the interaction between the host and bacteria. After an incubation period of 2–3 weeks brucellosis usually presents as a febrile illness with or without localization to a particular organ. Common symptoms include sweating, myalgia, headaches, lethargy, weight loss and abdominal pain. Clinically over 50% of patients have evidence of arthritis with spinal tenderness or other large joint involvement. One quarter of patients have hepatomegaly or splenomegaly, some with lymphadenopathy, most commonly tonsillitis or mesenteric adenitis.

It is thought that up to 95% of patients with brucellosis have microscopic granulomatous hepatitis which is mostly asymptomatic, producing a mildly raised aminotransferase level with a significant increase in alkaline phosphatase levels (Gotuzzo and Carillo, 1997; Yamada et al, 1999). A variety of skin lesions occur in 5–10% of patients (Berger et al, 1981). Other complications include pancytopenia, eye involvement and neurological disease, most commonly meningo-encephalitis and neuropsychiatric disorders. Rarely patients can suffer endocarditis and thyroiditis.

The diagnosis of brucellosis is usually made by the detection of raised brucella agglutinins (>1/160), combined with a positive blood or tissue culture, which may take up to 6 weeks to show a positive result. In diagnostically difficult cases bone marrow culture may be helpful.

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CASE REPORT

A 52-year-old construction manager had been working in Pakistan for 2 years. On return to the UK he presented to a maxillofacial surgeon with a swelling in his right submandibular gland. This and surrounding lymph nodes were removed. The histology of the lymph nodes showed numerous necrotizing granulomata with Langhans' giant cells. Ziehl-Neelsen stain was negative.

Chest X-ray was normal. However, a presumed diagnosis of tuberculosis was made and treatment commenced for 9 months with the conventional triple therapy of pyrazinamide and Rifinah (rifampicin plus isoniazid, Hoechst Marion Roussel, West Malling, Kent). He completed his course of therapy in Pakistan.

Four months after completion of the treatment, he became generally unwell and re-presented with pyrexia, night sweats and anorexia. Other than a maculopapular rash, the general examination was normal. Routine blood measurements were unremarkable except for an aspartate transaminase level of 60 IU/litre (normal 5–35 IU/litre). Thick and thin films were negative for malaria. Chest X-ray was again normal.

He remained pyrexial and had the following investigations: erythrocyte sedimentation rate was 30 mm/hour; autoantibody screen was negative; blood and stool culture were negative; serum angiotensin-converting enzyme level 40.9 U/litre (normal <36.6 U/litre); sputum acid-fast bacilli negative. Ultrasound of the abdomen showed slight splenomegaly; computed tomography scan of the thorax was normal; bone marrow and trephine showed reactive changes only, with no evidence of lymphoma. Liver biopsy showed one small caseating granuloma and reactive changes.

His temperature settled after 3 weeks and he was discharged, only to return 1 week later with further drenching night sweats and fever. Examination was again normal. His blood cultures on this occasion were positive for *Brucella melitensis*, with a serology of immunoglobulin G (IgG) titre of 1/80, IgM <1/80, direct agglutination test (DAT) 1/40.

Treatment with rifampicin 600 mg and doxycycline 200 mg daily was commenced, and over the next week he improved and his temperature settled. *Brucella* titres from his original admission showed DAT 1/160, IgG 1/80 and IgM 1/80. He completed 3 months treatment and his only complication was that of a reactive arthritis, principally of his knees, which was treated symptomatically.

Brucella organisms are intracellular and the most effective bactericidal antibiotics appear to be a combination of a tetracycline, such as doxycycline, and an aminoglycoside, for example streptomycin or gentamicin. Rifampicin and ciprofloxacin remain alternatives. Initial treatment should be for 1 month, followed by either a tetracycline with rifampicin, or co-trimoxazole, for a further 2 months (Madkour, 1995). This combination appears to reduce the relapse rate and chronicity of the disease. Clinical improvement should be seen within 14 days, and follow up is advised for 2 years.

CONCLUSION

This case highlights an unusual presentation of brucellosis, with swollen submandibular lymph nodes. The presumptive diagnosis of tuberculosis based on histology showing a necrotizing granulomata was later shown to be incorrect. However, partial treatment of brucellosis had occurred with the rifampicin in the anti-tuberculosis regimen. This would explain the subacute presentation and why the serology was not remarkable.

Pyrexia of unknown origin is a common problem in medicine and is often a diagnostic challenge. Despite brucellosis being uncommon in the UK, this

case is a reminder to consider it among the differential diagnosis, especially in those people who have travelled to less developed countries. **HM**

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