Case Report

An Unusual Cause of Non-Resolving Pneumonia—Brucellosis

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Abstract

A 76-year-old male, cotton mill worker by occupation, "never smoker", reported to us with complaints of fever, dry cough, breathlessness, loss of weight and loss of appetite of one month duration. He had no other co-morbid illness. He was evaluated elsewhere and on the basis of clinical presentation and chest radiographic findings, he was started on Category I therapy under Directly Observed Treatment, short-course (DOTS) for possibile miliary tuberculosis (TB). After three weeks of anti-TB treatment, patient came to our department with increasing breathlessness, persistent fever and cough. Physical examination revealed fever, low oxygen saturation on pulse oximetry, bilateral crepitations in the chest and hepatomegaly. High resolution computed tomography (HRCT) of the chest showed bilateral nodular opacities with few reticular shadows involving all the lobes Serological testing for rickettsia and dengue was negative. Fibreoptic bronchoscopy was performed and testing of bronchial washings for bacteria, fungi, *Mycobacterium tuberculosis* were all negative. He gave history of consuming raw milk for many years. Liver biopsy showed granulomatous hepatitis. Standard agglutination test for *Brucella* antibody was positive, and the patient was treated with oral rifampicin and doxycycline for six weeks. Patient had clinical improvement within two weeks of therapy. A repeat chest radiograph and CT at four weeks showed near total resolution of the shadows. We document this case with miliary pattern as an uncommon manifestation of brucellosis. The present case highlights the fact that, in endemic areas, brucellosis should be considered in the differential diagnosis of pulmonary diseases, especially when there is a history of consumption of raw milk.
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Key words: Brucellosis, Pneumonia, Non-Resolving, Miliary pattern

Introduction

Not all miliary opacities on a chest radiograph are due to tuberculosis (TB). Brucellosis is an important zoonotic disease and remains a worldwide public health problem. This is a multi-system infection that may present with a wide range of clinical presentation, organ system involvement and complications. Presentation with a miliary pattern is a rare manifestation of brucellosis. We report the case of a 76-year-old male who presented with prolonged fever, miliary pattern on the chest radiograph in whom the diagnosis of brucellosis was confirmed as the aetiological cause.

Case Report

A 76-year-old-male, a cotton mill worker by occupation presented with complaints of one month of fever, dry cough, breathlessness, loss of weight and loss of appetite. Patient was a never smoker and had no co-morbid illness. He was evaluated elsewhere and on the basis of clinical presentation and chest radiograph (Figure 1) started on Category I therapy under Directly Observed Treatment, short-course (DOTS) for possibile miliary TB. Three weeks after taking anti-TB treatment, patient came to our department with increased breathlessness, persistent fever and cough.

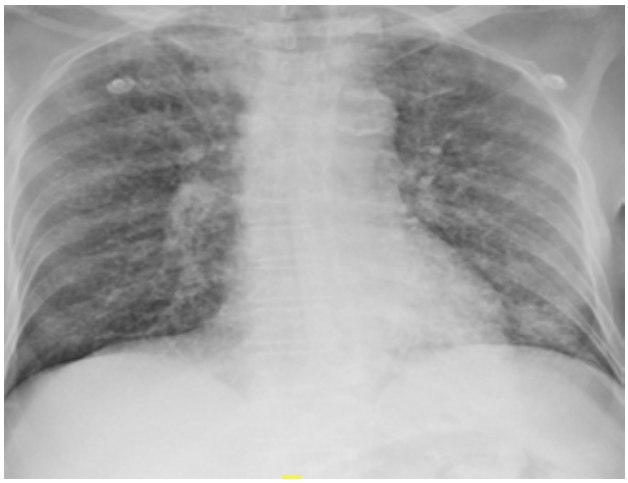

Figure 1. Chest radiograph (postero-anterior view) at admission showing bilateral nodular infiltrates involving all zones.

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On examination, he was febrile and had low oxygen saturation on pulse oximetry. Respiratory system examination revealed bilateral crepitations. Abdominal examination showed hepatomegaly. He was evaluated for persistent fever. Sputum cultures for pyogenic organisms were contaminated. Sputum testing for for acid-fast bacilli (AFB) was negative. High resolution computed tomography (HRCT) of the chest showed bilateral nodular opacities with few reticular shadows involving all the lobes (Figure 2). Blood culture was contaminated. Serological testing for rickettsia, dengue was negative. Urinalysis and culture were sterile. Fibreoptic bronchoscopy, testing of bronchial washings for bacteria, fungi, catridge-based nucleic acid amplification test (CBNAAT) for TB and mycobacterial culture were all negative.

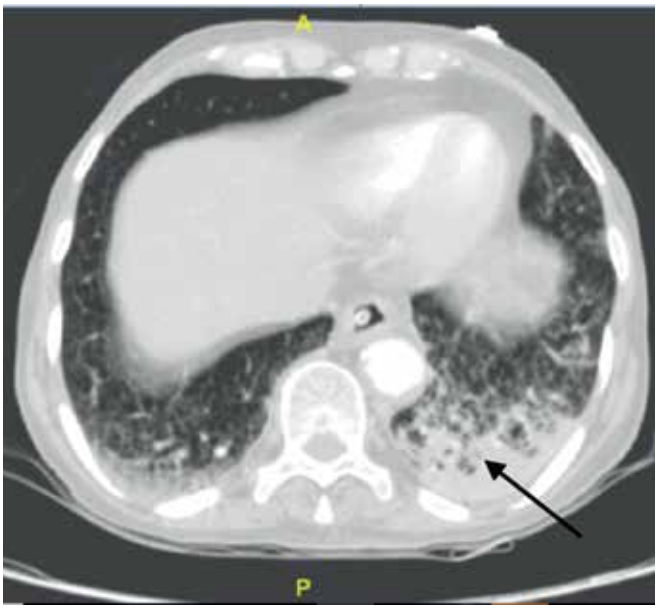

Figure 2. Computed tomography of the chest (lower cuts) showing consolidation involving bilateral lower lobes with few nodular lesions.

Upon revisiting the history, he gave history of consuming raw (unpastuerised) milk for many years. Liver biopsy showed granulomatous hepatitis. As the patient had completed one month of Category I DOTS treatment, during the evaluation period with no clinical or radiological improvement, other causes of granulomatous hepatitis were considered. In view of history of consuming unpasteurised milk, brucellosis was considered. Standard agglutination test for *Brucella* antibody was positive. A diagnosis of brucellosis was made and the patient was prescribed oral rifampicin 600mg once-a-day along with oral doxycycline 100mg twice-a-day for six consecutive weeks. Patient had clinical improvement within two weeks of therapy. A repeat chest radiograph and CT at four weeks showed near total resolution of the shadows (Figure 3 and 4)

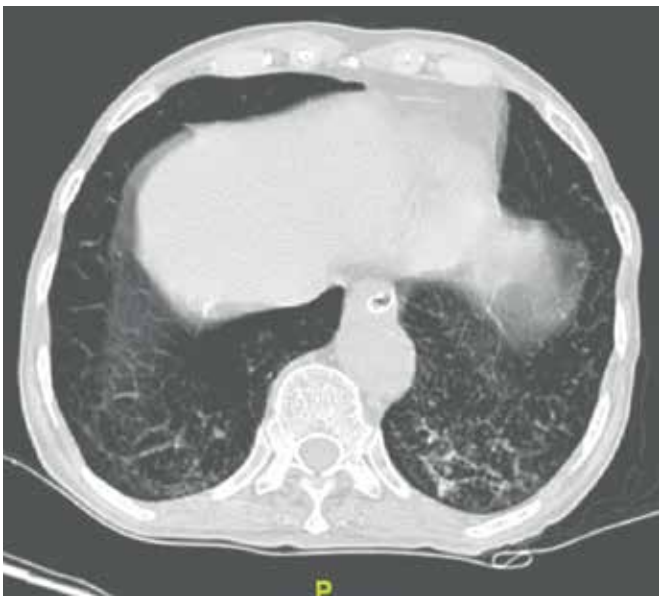

Figure 3. Computed tomography of the chest (lower cuts) showing near total resolution of the consolidation post–treatment.

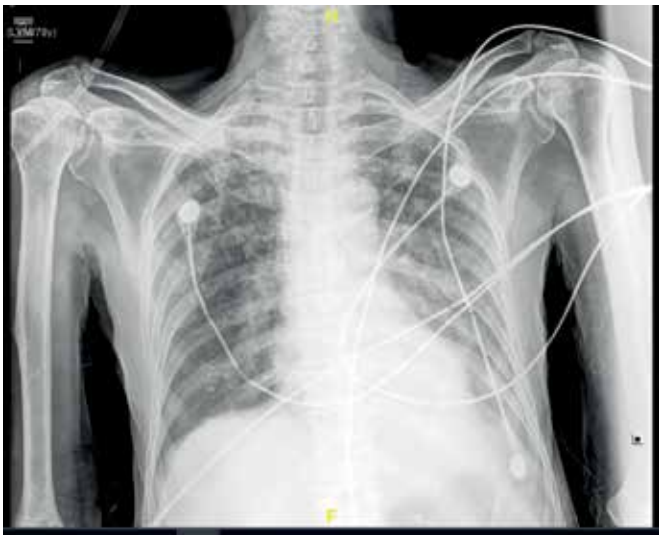

Figure 4. Chest radiograph (anterio-posterior view) showing near total resolution of the opacities.

Discussion

Brucellosis is primarily a zoonotic disease with occasional human transmission caused by organisms belonging to genus *Brucella* which is a Gram-negative, non-sporeforming, facultative intracellular bacteria. Human diseases are predominantly caused by *B. abortus* and *B. melitensis*. The disease is endemic in the Mediterranean regions, India, Mexico, Middle and South American countries. Primary human infection

occurs through consumption of non-pasteurised milk or milk products from infected goats, sheep or cows, the consumption of contaminated meat or by direct contact with infected animals. Accidental laboratory ingestion or inhalation has also been implicated. Though the disease spreads from animals to human, a few reports of human to human transmission has also been reported.[1]

In India the true incidence of human brucellosis is unknown. Studies based on sero-prevalence suggest incidence between 0.9% – 18.1%, with higher risk in veterinarians and farm attenders.[2-4] However, this incidence could be much higher as brucellosis is often misdiagnosed.[2-4] Population at risk include people involved in rearing of farm animals, slaughter house workers, veterinarians and laboratory personnel.[3]

The clinical manifestation of human *Brucella* infection is variable. The most common presentation is fever and *Brucella* is one of the common cause for pyrexia of unknown origin (PUO). Other symptoms include fatigue, malaise, headaches, myalgia, arthralgia and weight loss. Clinical features include lymphadenopathy, hepatosplenomegaly, haematological manifestations like anaemia, leucopaenia, neutropaenia, thrombocytopaenia and infective endocarditis.[2]

Pulmonary involvement of brucellosis occurs due to inhalation of infected aerosol or as a part of septicaemia. Clinical presentation include fever, cough with expectoration and flu like symptoms. The symptoms may be mistaken for acute bronchitis or bronchopneumonia. Radiological lesions include reticulonodular infiltration, diffuse ground-glass opacity, lung abscess, hilar lymphadenopathy and pleural effusion.[5,6] Miliary mottling and pneumothorax have also been reported. Occasionally chest radiograph may be normal.[7] Pleural effusion in brucellosis is similar to tubercular effusion with protein rich, lymphocyte predominance and elevated adenosine deaminase.[8] Brucellosis can also cause haemorrhagic pleural effusion.[9]

Diagnosis of brucellosis is by isolation of the organism from clinical samples, serological tests for identification of *Brucella* antigen and antibodies. Isolation of *Brucella* from blood culture is the definitive evidence of infection. However, it may not be positive in all cases. Prior antibiotic usage can result in negative cultures. Bone marrow cultures, widely considered as gold standard, are also not always positive. Antigen detection by enzyme linked immunosorbent assay (ELISA), polymerse chain reaction for genomic identification have also been tried. Antibody detection is perhaps the most widely used method for the diagnosis of *Brucella* infection.[3] In our patient, diagnosis was established by the standard agglutination test. Also the blood culture in our patient was contaminated. For the diagnosis of *Brucella* by blood culture, sub-cultures need to be done for atleast four weeks. In our case following contamination, the blood culture was discarded. Sputum cultures for brucellosis has only been rarely positive. In a multi-centric study involving 37 patients with respiratory involvement, none of them had positive *Brucella* on sputum cultures.[10]

Appropriate antibiotics for the treatment of brucellosis include a combination of tetracyclines, rifampicin and aminoglycosides. Combination treatment include administration of oral doxycycline (200mg/day) and rifampicin (600mg/day) for six weeks; or oral doxycycline (200mg/day), rifampicin (600mg/day) for six weeks with intramuscular streptomycin (1g/day) for the first two weeks. A six week therapy is usually sufficient. Some authors advice treatment up to eight weeks for disseminated brucellosis. In children, combination of rifampicin with cotrimoxazole or gentamicin is adviced. The use of quinolones is beneficial in the setting of drug resistance.[7,11,12]

There is no vaccine available for the prevention of human brucellosis. Brucellosis can be controlled by vaccination of livestock. People should be advised regarding boiling of milk and consumption of pasteurised milk.

In conclusion, pulmonary involvement is rare in the course of brucellosis. However, due to misdiagnosis the incidence could be higher than estimated. In endemic regions, brucellosis should be considered as a causative agent in patients with pulmonary symptoms. Because of the difficulty in the diagnosis, a prompt and careful history will help us in diagnosing brucellosis early.

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