Brucellosis in a Sickle Cell Patient with Hyposplenia

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ABSTRACT

Sickle cell disease patients are prone to infection and overwhelming sepsis because an immune-deficient state arises from asplenia (autosplenectomy/surgical splenectomy) and functional hyposplenism. The common pathogen encountered in sepsis with asplenic/hyposplenism patients is encapsulated organism, gram-negative bacilli, but in developing countries like India, there are many possibilities of infection by an uncommon organism that make it difficult to diagnose. Here, we have described a case of sickle cell disease presented with persistent fever and later, found to have an atrophic spleen with involvement of respiratory system and osteoarticular system. After extensive workup, he was diagnosed to be brucellosis. So, unusual infectious causes be kept as a differential diagnosis in a susceptible host while dealing with persistent symptoms. Uncommon infections like Brucella need to be studied in hyposplenism patients as data are lacking.

INTRODUCTION

Sickle cell anemia is a genetically transmitted disease in which infection is a significant cause of mortality apart from other complications like vaso-occlusive crisis and acute chest syndrome. Sickle cell disease patients are susceptible to infection because of autosplenectomy, surgical splenectomy, or hyposplenism.1,2

Brucellosis is an underreported zoonotic disease across the world, including in India. The clinical manifestation ranges from mild flu-like febrile illness to severe life-threatening organ involvement.3 Brucellosis is a very uncommon infection in sickle cell disease patients with or without hyposplenia. There are very few studies of brucellosis in India.4

CASE DESCRIPTION

A 22-year-old young male patient presented to us with complaints of intermittent high-grade fever, back pain, shoulder pain, and pain in the bilateral lower chest for 2 weeks. He did not give any history of cough, dysuria, skin lesion, gastrointestinal symptom, or joint swelling. He had similar episodes of fever 1 month back that resolved with a short course of antibiotics. The patient was a known case of sickle cell disease with a history of blood transfusion a few years back, and he was on hydroxyurea for 3 years. He had a history of cat bites over the dorsum of his right hand 1 year back without any sequelae.

There was only pallor on examination, and the rest of the general physical examination was unremarkable. Pulse rate—112/minute, blood pressure—108/66 mm Hg, respiratory rate—20/minute, temperature—101°F. Systemic examination revealed hepatomegaly.

Routine investigation showed hemoglobin—9.5 gm/dL, leukocytosis (16000/cumm), monocytes (14%, 2350/cumm), indirect hyperbilirubinemia (1.49 mg/dL), transaminitis (aspartate transaminase—166 U/L, alanine aminotransferase—154 U/L). The kidney function test was normal. Routine urine microscopy was normal. ESR (90 mm at 1 hour) and C-reactive protein (CRP) (104.2 mg/dL) were high.

X-ray showed right lower zone increased bronchovascular marking with subtle haziness. He was managed empirically with piperacillin/tazobactam, vancomycin, azithromycin, and other supportive treatment. Serology for malaria, dengue, scrub typhus, hepatitis (A, B, C, and E), and human immunodeficiency virus were negative. COVID-19 reverse transcription polymerase chain reaction was negative. Later blood serology for leptospira—in immunoglobulin (Ig) M and IgG (immunochromatography) came positive. Blood and urine cultures were sterile. Peripheral smear showed granules with leukocytosis. Serum procalcitonin was normal. Antibiotics were changed to meropenem and doxycycline on day 6 as he was still symptomatic.

On further workup, the whole abdomen sonography revealed hepatomegaly (20 cm) and an atrophic spleen (6.6 cm). High-resolution computed tomography (HRCT) chest showed bilateral basal opacification predominantly in the right with ill-defined lytic-sclerotic lesions in D5, D6, and D8 vertebrae (Fig. 1). Bronchoalveolar lavage (BAL) was done and the sample was negative for gram stain, fungal KPotassium hydroxide test, Acid-Fast Bacilli Smear, and Cartridge based nucleic acid amplification test. BAL sample showed no growth for bacteria, fungi, or mycobacteria (liquid culture). Toxoplasma serology (IgM, IgG) was negative. Serum galactomannan and Mantoux tests were negative. He was still febrile even after day 15 of antibiotics. Repeated blood cultures did not show any growth. Gentamycin was added considering the organism associated with asplenia/functional hyposplenism.

Later, Brucella IgM (13.8 U/mL) by enzyme-linked immunosorbent assay, normal (<12 U/mL) came positive whereas Brucella IgG was 0.63 U/mL (negative, normal <12 U/mL). So, the diagnosis was finalized as sickle cell disease with functional hyposplenism with brucellosis (pneumonia and vertebral osteomyelitis). After 8 days, the patient became afebrile and was later discharged. On follow-up, the patient was afebrile with complete normalization of blood parameters, including inflammatory markers (ESR, CRP) except anemia.

DISCUSSION

Brucellosis is a major underdiagnosed and underreported disease of livestock as well as humans and is endemic in Asia. The prevalence of brucellosis varies from <0.01 to >200 per 100,000 across the world. In India also, the prevalence varies from 0.8 to 26.6%.5 The average prevalence of high-risk groups, for example, veterinarians, meat handlers, and abattoir workers, is around 11%. The prevalence varies from 0.8 to 26.6% in India.4

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Fig. 1: HRCT chest showing consolidation in the right lower zone of the lung
prevalence in clinically suspected hospitalized patients was 7%. Causative agents of brucellosis are Brucella abortus (cattle), Brucella melitensis (small ruminant), Brucella suis (swine), Brucella canis (dogs), and Brucella ovis (sheep). Transmission is mainly by direct/indirect contact with infected animals or through the consumption of animal products (cattle, sheep, pigs, and dogs). However, transmission by a cat is unclear. In developing countries, contact and exposure to livestock are obscurely high. In our case, the cat might be a suspect of disease transmission.

Clinical features of brucellosis range from undifferentiated febrile illness to life-threatening organ involvement lasting a few days to 1 year. Nonspecific symptoms may be muscle pain, sweating, and arthralgia. Common complications reported are hepatitis (45%), osteoarthritis (22%), respiratory involvement mainly pneumonia (13%), cardiovascular system (9%), central nervous system (5%), and orchitis/epididymitis (9%).

Our case had persistent fever involving the respiratory system, hepatobiliary, and osteoarticular system.

Abnormal laboratory parameters reported in the literature are leucocytosis (24.1%), anemia (23.9%), thrombocytopenia (15.8%), and pancytopenia (13.2%). The gold standard test for diagnosis is blood culture, but it only has a sensitivity of 48.3%. So, where blood culture is negative with a high index of suspicion, the serological test may be applied for early disease detection.

Hyposplenism is an acquired disorder of functional impairment of the spleen seen in hematological disease, hemoglobinopathies, and immunological diseases. The encapsulated organism like Streptococcus, Neisseria, and H. influenzae are major pathogens for bloodstream infection in these patients. Other less common pathogens are gram-negative bacilli, Capnocytophaga, Bartonella, malaria, and Babesia. The work-up for all tropical infection, including tuberculosis, were negative in our case. However, leptospiral serology was positive, which may be fortuitously positive as our country is endemic. Again, the prolonged fever with pneumonia, skeletal involvement with serological evidence, and response to doxycycline plus aminoglycosides, all favor the diagnosis of brucellosis.

**CONCLUSION**

Brucellosis in sickle cell disease with altered splenic function has not been reported in the literature. Are sickle cell diseases with/without functional spleen more prone to brucellosis? Also, is hydroxyurea responsible for increased predisposition to infection? So further research is required to address these questions. The unusual cause of febrile illness should be kept in the etiological checklist while dealing with undifferentiated prolonged febrile patients.

**Declaration**
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

**REFERENCES**