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Case Report

An interesting case of pyrexia of unknown origin

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ABSTRACT

Pyrexia of unknown origin (PUO) is defined as fever≥101°F on at least two occasions, illness duration of ≥3 weeks. Brucellosis is a bacterial infection caused by brucella species that includes *Brucella canis*, *Brucella abortus*, *Brucella melitensis*, and *Brucella suis*. They are gram-negative coccobacilli. They are non-motile, non-spore-forming, and facultative intracellular organisms. Kikuchi disease is a benign self-limiting disease, also referred to as histiocytic necrotizing lymphadenitis. Kikuchi disease mainly affects young women and usually presents as fever, lymphadenopathy and leucopenia. The manifestations are similar to brucellosis. Both coexist in a patient, which can be challenging for the treating physician. Here, we presented a case of brucellosis with coexisting Kikuchi disease.

Keywords: Kikuchi, Brucellosis, Pyrexia of unknown origin

INTRODUCTION

Pyrexia of unknown origin (PUO) is defined as fever ≥101°F on at least two occasions, Illness duration of ≥3 weeks, No known immune-compromised state, diagnosis that remains uncertain after a thorough history-taking, physical examination, and the following obligatory investigations: determination of ESR and CRP level, platelet count, leukocyte count, measurement of levels of hemoglobin, electrolytes, creatinine, total protein, alkaline phosphatase, SGOT, SGPT, lactate dehydrogenase, creatine kinase, ferritin, antinuclear antibodies, and rheumatoid factor, protein electrophoresis, urinalysis, blood cultures, urine culture, chest X-ray, abdominal ultrasonography, and TST or IGRA.[1]

Bacterial infections are common around the world. They typically present with fever, malaise, lymphadenopathy, and weakness to fatal conditions like septicemia. The standard and most widely accepted as well as used classification is by Grams' staining. Grams' staining divides them into gram-positive and gram-negative cocci or bacilli, depending upon their shapes. Brucellosis is a bacterial infection caused by brucella species that includes *Brucella canis*, *Brucella abortus*, *Brucella melitensis*, and *Brucella suis*. They are gram-negative coccobacilli.[2] They are non-motile, non-spore-forming, and facultative intracellular organisms.

Brucellosis presents as muscle pain and night sweats, like other febrile illnesses. It usually presents as a chronic disease. Severe manifestations like bacteremia, anemia, splenomegaly, and leucopenia may be seen. The most common organism causing human infections is *B. melitensis*.[3]

Kikuchi disease is a benign self-limiting disease, also referred to as histiocytic necrotizing lymphadenitis. Kikuchi disease mainly affects young women and usually presents as fever, lymphadenopathy, and leucopenia.[4] The manifestations are similar to brucellosis. Both coexist in a patient, which can be challenging for the treating physician.

Here, we presented a case of brucellosis with coexisting Kikuchi disease.

CASE REPORT

A 25-year-old patient presented with a fever of ≥38.3°C (≥101°F) for three weeks. We probed her history and discovered that she had a recurrent fever for five months. She complained of weight loss, easy fatiguability, myalgia, and arthralgia. She also admitted having seizure disorder and was on antiseizure medication oxcarbazepine 300 mg for five years. She also had a positive history of bilateral cervical lymphadenopathy of level II, III, and IV nodes; no medical attention was sought. She had no history of diabetes mellitus and hypertension. We diagnosed PUO from the patient's history and initial clinical examination. Vitals and other systemic examinations were normal. Local examination of the axilla and neck revealed significant lymphadenopathy.

All routine blood investigations, including liver and renal function tests, failed to show abnormalities. To rule out tuberculosis tuberculin skin test and interferon gamma release assay (IGRA) was done and found to be normal. Anti-nuclear antibody (ANA) and rheumatoid factor (RF) were also negative. Urinalysis and culture and sensitivity of urine and blood failed to reveal any growth. All the above investigations help us rule out some important causes of PUO. The patient was subjected to a lymph node biopsy, which revealed histopathological findings suggestive of Kikuchi disease.

Microscopic image showing necrosis, pale histiocytes and abundant karyorrhectic debris with characteristic absence of neutrophils.

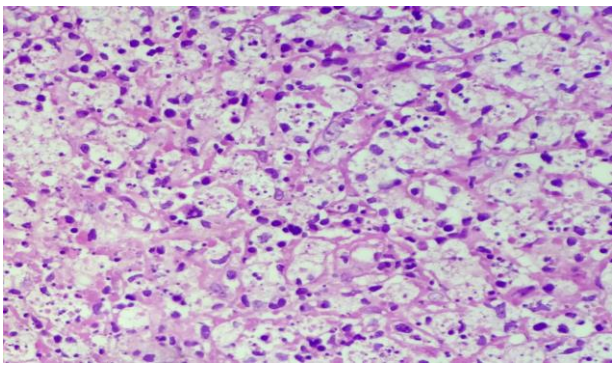

Figure 1: Kikuchi disease.

The patient's blood sample also yielded a positive result for IgM titers with a value of 21.6 NTU (normal <9 NTU) for brucella. IgG titers for brucella were found to be normal, ruling out chronic infection of Brucellosis. With this, we diagnosed the patient as having Kikuchi disease with co-existent brucellosis.

DISCUSSION

Kikuchi disease is a benign self-limiting disease of lymph nodes. In countries like India, any case presenting with fever and lymphadenopathy, generally tuberculosis is considered as the aetiology because of its endemicity.[5]

The histopathological hallmark of Kikuchi disease is necrotizing lymphadenitis. The lymph nodes most commonly involved are of cervial area.[6] Kikuchi disease can predispose to various infections during illness.[7] One of the infections that mimic Kikuchi disease in many aspects is brucellosis. The manifestations of fever, lymphadenopathy, and leucopenia are common in both conditions. Despite similarities, the etiological factors are quite different. Brucellosis is a bacterial infection caused by brucella species of bacteria. Brucellosis is usually acquired by drinking unpasteurized milk. The organisms associated with brucellosis are *Brucella melitensis*, *Brucella abortus*, and *Brucella canis*. The most common organism associated with human infection is *Brucella melitensis*.

Brucellosis is rare in places that follow proper hygienic practices. It can be seen in patients who are not aware of good hygiene. Brucellosis presents as a mild illness in most cases. The infection has a chronic and indolent course.

Sometimes severe manifestations like bacteremia, which is specifically referred to as melitococccemia, may be present. Brucellosis being a gram-negative coccobacillary infection, can also predispose to sepsis. In our scenario patient had a 5-month history of recurrent febrile illness that was found to be Kikuchi disease which in turn predisposed to brucellosis. The laboratory tests established the development of brucellosis, followed by Kikuchi disease.

A negative IgG with a positive IgM for brucella antibody showed that the onset of brucella infection was much later than Kikuchi disease; this also clarified our dilemma between the start of Kikuchi disease and brucellosis. Brucellosis is one of the commonly co-existent conditions with Kikuchi disease.[8] Kikuchi disease usually does not require any treatment, because it is a self-limiting condition. But in certain cases, steroids can be started when the effects are debilitating.[9] This duo has already been reported in the literature. The incidence of Kikuchi disease itself is rare, and such a co-existent duo will be pretty uncommon. The prevalence of brucellosis varies, ranging from 0.8-26% in various parts of India.[10]

CONCLUSION

PUO is the entity one could think of with such a presentation. The hallmark feature of PUO is an unexplained illness with a similar presentation for at least a month. To label a patient with PUO, the physician has to evaluate and rule out all possible causes of such presentation. The lab findings and lymph node biopsy, which nailed the diagnosis of Kikuchi disease with co-existent brucellosis. Knowledge regarding this presentation is essential for physicians to aid in optimistic

healthcare services. A good understanding and awareness regarding such scenarios will prevent further dilemmas in treating patients with deceiving manifestations.

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