



A Rare Case of Pyrexia of Unknown Origin (PUO) Secondary to Brucellosis Associated with Kikuchi's Lymphadenitis

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ABSTRACT

Pyrexia of unknown origin (PUO) is a challenging medical problem, which acts as a burden to the patient and the family especially in resource-limited countries like India. Brucellosis is a highly contagious zoonotic infection which spreads through the consumption of unpasteurized milk and undercooked meat. Lymphadenopathy can be the presenting feature for brucellosis but it can also be secondary to other systemic diseases. Here we report a rare case of a young female with PUO secondary to brucellosis that had persistent fever and lymphadenopathy even after adequate treatment and on subsequent investigations was found to have Kikuchi's lymphadenitis.

Keywords: Kikuchi's lymphadenitis, Brucellosis

INTRODUCTION

Pyrexia of unknown origin (PUO) in any age group poses a significant burden emotionally and economically. Due to the many infectious diseases in India, it is a tedious and expensive dilemma. The earlier definition of PUO by Petersdorf and Beeson required admission for a prolonged period and had many subdivided groups making it cumbersome [1]. Thus PUO is now defined as fever $>38.3^{\circ}\text{C}$ (101°F) on at least two occasions with illness duration of ≥ 3 weeks with no known immune-compromised state in whom the diagnosis remains uncertain after a thorough history-taking, physical examination, and the following investigations. Investigations include erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, histogram with differential count, electrolytes, creatinine, total protein, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatine kinase, ferritin, antinuclear antibodies, and rheumatoid factor which included protein electrophoresis, urinalysis, blood cultures ($n=3$), urine culture, chest x-ray, abdominal ultrasonography, and tuberculin skin test (TST) [1]. Despite adequate investigations and observation, some cases remain undiagnosed. Here we report a rare case of PUO that was later diagnosed with Brucellosis with Kikuchi's lymphadenitis.

Case History

A 16-year-old female with no addictions presented with complaints of high-grade intermittent fever with chills, decreased appetite and generalized body ache for 25 days. There was no history of diarrhea, vomiting, constipation, cough, dyspnea, chest pain, backache, headache, neck stiffness, seizure, rash, hair loss, weight loss, ulcers, and joint pains. She was investigated multiple times and had taken anti-malarial, cefixime, and amoxicillin with clavulanic acid. The patient on detailed history evaluation gave a history of cattle exposure. On examination, she was febrile with tachycardia and had non-tender, non-matted, firm cervical level II and apical and anterior axillary lymphadenopathy of $1\text{ cm} \times 1\text{ cm}$ size, with discrete margins. The lymph nodes were not fixed to the underlying structures. Systemic examination only showed non-tender hepatomegaly 2 cm below the costal margin which was soft in consistency, rest all systemic examination was normal.

Investigations showed a normal histogram, procalcitonin, RFT, LFT with negative Widal and blood culture. Only ESR (102 mg/dl) and CRP (77 mg/dl) were elevated. The abdominal sonography showed the presence of mesenteric lymph nodes in the right iliac fossa and paraumbilical region. The sonography of the neck was suggestive of multiple lymph nodes the largest measuring $1.5\text{ cm} \times 0.34\text{ cm}$ with no evidence of central necrotic core. CT abdomen showed

non-specific mesenteric and paraumbilical lymphadenopathy with changes of inflammation. Epstein Barr virus and *Brucella* titers were done which showed *Brucella abortus* to be positive with titers of 1: 320. The area being non-endemic with a history of cattle exposure, the patient was diagnosed with brucellosis. Thus the patient was started on doxycycline with amikacin. The patient was then afebrile for 36 hours and was given discharge. The doxycycline was to be continued for 6 weeks and injectable amikacin for 2 weeks. The patient was afebrile for 10 days following which she again developed fever spikes of 104°F. The total counts had decreased to 1800 with persistence of anemia and elevated ESR. The lymph nodes had increased in the size. A lymph node excision biopsy showed partial effacement of lymphoid architecture with focal and diffuse necrotizing lesions with fibrin deposits suggestive of Kikuchi's lymphadenitis. BACTEC for TB from the biopsy was negative. The patient was started on steroids for the Kikuchi's disease following which she made a complete recovery.

DISCUSSION

In resource-poor countries, like India located in the tuberculosis-endemic zone, all cases of lymphadenopathy are traditionally considered as a tuberculous etiology [2]. Extrapulmonary TB and lymphoma could be quite similar in clinical presentation and radiological findings and have been reported to cause difficulty in diagnosis [3]. Thus, in this case, extra-pulmonary TB versus lymphoma was the primary concern. But with the history of living near cattle and having unpasteurized milk made *Brucella* a likely possibility. After adequately treating the brucellosis the patient had initially improved and then had a recurrence of fever spikes with persistent cervical lymphadenopathy. Now the diagnosis was narrowed down to tuberculous lymphadenitis or low-grade lymphoma. And thus an immediate lymph node excision biopsy was done, which was suggestive of Kikuchi's lymphadenitis.

Kikuchi's disease is a rare disease whose etiology is not completely understood yet various infectious and autoimmune causes have been stated. It is proposed that the disease is a non-specific hyper-immune reaction to an infectious, chemical, physical and neoplastic agent. The features that support a role for an infectious agent include the association of EBV, herpes, CMV, paramyxovirus, parvovirus. SLE has also been found before and after diagnosis of Kikuchi's lymphadenopathy [4]. A study in India of patients with Kikuchi's lymphadenitis showed that the most common symptom was painless lymphadenopathy (74%). The less common symptoms were painful lymphadenopathy, fever, chills, anorexia, joint pain and skin rashes. The cervical lymph nodes were most commonly involved [5]. The diagnostic dilemma in such cases is that hemogram only reveals raised ESR, and atypical lymphocytes are seen in 25 to 31% of patients, CRP may be raised [6]. Diagnostic yield of fine needle aspiration of cytology is only 56%, in most cases, the report is reactive hyperplasia of lymph nodes [7]. Hence, only excision biopsy of lymph nodes is the confirmatory test. Wheeler reported a case showing *Brucella* to be a differential of Kikuchi's lymphadenopathy [8]. The association of *Brucella* and Kikuchi's lymphadenitis has been noted in one study where Kikuchi's lymphadenitis followed brucellosis after 3 months. This lead to the suggestion that the initial infection of *Brucella* causes an autoimmune reaction, which results in Kikuchi's necrotizing lymphadenitis [9]. Kikuchi's lymphadenitis does not require treatment most of the times, as it is a self-limiting condition. But in certain cases when the effects are debilitating, steroids can be started as in this case [8].

CONCLUSION

Both brucellosis and Kikuchi's disease may coexist together. One of the important differential diagnoses of cervical lymphadenopathy remains Kikuchi's disease. Persistent fever spikes should always direct the physician to investigate further in spite of a confirmed etiology.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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