Case Report

Kikuchi's Disease

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Abstract

Kikuchi's disease, also known as histiocytic necrotizing lymphadenitis, is a rare entity with classic clinical findings of cervical lymphadenopathy and fever. Although Kikuchi's disease does predominantly affect young women, it can appear at all ages; irrespective of gender. The rarity of the disease has led us to report this case. The clinical features and diagnosis have been discussed with review of literatures about this uncommon entity. Our patient, a young female of 20 years presented in a rural tertiary care hospital with features of upper respiratory tract infection and discrete lymphadenopathy on the left cervical region; fine-needle aspiration cytology revealed the diagnosis of Kikuchi's disease. She received a course of antibiotics and showed complete recovery over a month. Last follow-up about 3 years later till writing this report she was found normal. The cause of Kikuchi's disease is unknown, although infectious and autoimmune etiologies have been proposed. The disease usually runs a benign course with complete recovery. While rare, Kikuchi's disease should remain in the differential diagnosis during evaluating a patient having lymphadenopathy. Its initial clinical appearance is commonly similar to that of a lymphoma, and it can be pathologically misdiagnosed as such. Despite the fact that Kikuchi's disease is benign, an accurate diagnosis is important because misdiagnosis might lead to unnecessary surgery and/or chemotherapy.

Keywords: *Kikuchi's disease, Kikuchi-Fujimoto disease, Histiocytic necrotizing lymphadenitis.*

Introduction

Kikuchi's disease, also called histiocytic necrotizing lymphadenitis or Kikuchi-Fujimoto disease is an uncommon, idiopathic, generally self-limited cause of lymphadenitis[1]. Kikuchi first described the disease in 1972 in Japan. Fujimoto and colleagues independently described Kikuchi's disease in the same year. Although uncommon, Kikuchi's disease has been reported recently throughout the world and in all races[2]. Most cases have been reported from East Asia, with fewer cases from Europe and North America. It is possible that Kikuchi disease has been under-diagnosed and therefore under-reported. Kikuchi disease occurs in a wide age range of patients (2-75 years), but it typically affects young adults (mean age, 20-30 years). Women are affected more frequently then men[3]. The cause of Kikuchi disease is unknown, although infectious and autoimmune etiologies have been proposed. Features that support a role for an infectious agent include the generally self-limited course of the disease and its

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frequent association with symptoms similar to those of upper respiratory tract infections (URTIs)[4]. Several authors have reported an association between Kikuchi disease and Systemic lupus erythematosus (SLE). Systemic lupus erythematosus can follow or coexist with Kikuchi's disease[5,6]. However the association of Kikuchi disease with SLE, if any, remains unclear.

The most common clinical manifestation of Kikuchi disease is relatively acute onset cervical lymphadenopathy and a flu-like prodrome, with or without systemic signs and symptoms[7-10]. The nodes are usually described as painless or mildly tender. The nodes that are usually firm and mobile tend to be 2-3 cm in diameter, although masses of multiple nodes may reach 6 cm. In patients with Kikuchi disease, diagnostic laboratory and radiologic test findings are nonspecific. Although results of fine-needle aspiration cytology (FNAC) may be suggestive[11,12], the diagnosis of Kikuchi disease is confirmed by excisional lymph node biopsy. Treatment of Kikuchi disease is generally supportive. Although many treatment regimens have been recommended, there has not been any established therapy for this disease. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used to alleviate lymph node tenderness and fever. However those with prolonged or severe symptoms or with concomitant systemic lupus erythematosus or other autoimmune processes may respond well to glucocorticoids and/or hydroxychloroquine[13]. Kikuchi disease almost always runs a benign course and resolves by several weeks to months[14-16]. Disease recurrence is unusual, and fatalities are rare, although they have been reported[1]. Lymphadenopathy most often resolves over several weeks to 6 months, although the disease occasionally persists longer. Approximately 3% of patients develop a recurrence, usually in 6 to 12 years[17].

Case report

A young female, college student of 20 years, presented at the outpatient department of Medicine of Khwaja Yunus Ali Medical College and Hospital on 3rd January 2011 with the complaints of pyrexia, dry cough, sore throat, malaise, pruritus, and mild burning pain upper abdomen for six days. She also noticed small discrete lumps on the left side of the neck for more than one month duration. There was no history of arthralgia, skin rash, hemoptysis, night sweats or weight loss. No past history of tuberculosis or any significant illness. On examination pulse was 104/min, oral temperature: 99.8^{o}F, respiratory rate: 20/min, BP: 110/70 mmHg, weight: 59 kg, and height: 155 cm. There was no anemia, jaundice, dehydration, edema, skin eruptions, koilonychia, or clubbing. Physical examination of the neck revealed multiple discrete lymphadenopathy on the left cervical region. The lymph nodes were firm, mobile, mildly tender and about 3-4 cm in diameter size. Examination of the throat revealed mild enlargement of the left tonsil which was congested. Her abdomen was soft, with mild epigastric tenderness on deep palpation. There was no clinical evidence of organomegaly or ascites. Her bowel sounds were audible. Chest examination was clinically normal. Examination of the precordium revealed nothing significant. Other systems were found normal on clinical examination.

The laboratory analysis demonstrated a normal complete blood cell count (total white blood cell count: 7.60 x 10^9/L with a differential count of 65% neutrophils, 26% lymphocytes, 05% eosinophils and 4% monocytes; platelet count: 311 x 10^9/L and hemoglobin: 11gm/dL) normal erythrocyte sedimentation rate (14 mm in 1st hour), and normal chest radiograph; abdominal ultrasound was unremarkable. Her routine urine examination, liver function tests, serum creatinine and blood urea levels were also normal. C-reactive protein level was normal. Results of autoimmune antibody studies, including rheumatoid factor (RF) and antinuclear factor (ANF) studies were negative. She was started with a 7 days course of oral erythromycin and paracetamol. However omeprazole was also prescribed. Tuberculin (Mantoux) test was negative (2 mm induration size after 72 hours). Later fine needle aspiration cytology (FNAC) was done which reported features highly suggestive of acute necrotizing lymphadenitis (Kikuchi's disease). Her fever, sore throat and pain abdomen subsided within several days, but lymph node regression took about a month. As per last follow up on 6th Nov 2013, she was found to be in good health.

Discussion

The etiology of Kikuchi's disease is not entirely known. Features that support a role for an infectious agent include upper respiratory tract infections and several viral infections caused by cytomegalovirus, Epstein-Barr virus, human herpes virus, varicella-zoster virus, parainfluenza virus, parvovirus B19 and paramyxovirus[2,18]. These, however were discredited by George[19] et al. Some case reports have linked Kikuchi's

disease to systemic lupus erythematosus (SLE) as well; as patients who attributed their symptoms to Kikuchi's disease went on to develop SLE[20]. The clinical presentation of Kikuchi's disease is very similar to malignant lymphoma, tuberculosis, and systemic lupus erythematosus [9,21-23].

Symptoms of Kikuchi's disease can be very distressing to the patient, especially the lingering fever and lymphadenopathy. It is important for clinicians and pathologists to be aware of this possibility, especially when dealing with young female patient with fever and cervical lymphadenopathy.

A definitive diagnosis of Kikuchi disease can be made only by tissue evaluation. Diagnosis of Kikuchi's disease is confirmed by lymph node histology, which reveals paracortical foci of necrosis and a histiocytic infiltrate. It is possible to use fine needle aspiration cytology (FNAC) to confirm the diagnosis of Kikuchi's disease, but the focal involvement can be completely missed. Cytologic examination by fine needle aspiration cytology (FNAC) can suggest the diagnosis of Kikuchi's disease, when supported by typical clinical findings[11,12] but excisional biopsy of an involved lymph node is needed to confirm the diagnosis in doubtful cases[2].

The pathologic hallmark of Kikuchi's disease is the presence of an enlarged lymph node with paracortical necrotic foci, which are devoid of neutrophils and surrounded by plasmacytoid monocytes, immunoblasts and crescentic histiocytes[2]. Pathologists are likely to report the result as "suggestive of" Kikuchi's disease. It is therefore advisable to confirm the diagnosis of Kikuchi's disease by excisional biopsy in doubtful cases[2].

While rare, Kikuchi's disease should remain in the differential diagnosis during evaluating a patient having cervical lymphadenopathy. Other causes are lymphomas, tuberculosis (TB), infectious mononucleosis, SLE, syphilis, toxoplasmosis, sarcoidosis, and adenocarcinomas. Hence, differentiating Kikuchi's disease from common lymphadenopathic conditions is extremely vital.

Conclusion

However, despite the fact that Kikuchi's disease is benign, an accurate diagnosis is important because misdiagnosis might lead to unnecessary surgery and/or chemotherapy. Early recognition of Kikuchi's disease will minimize potentially harmful and unnecessary evaluations and thus prevent misdiagnosis and inappropriate treatment. We can thereby avoid laborious investigations for infectious and lymphoproliferative disorders.

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