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A CASE REPORT OF KIKUCHI DISEASE RELAPSE IN A YOUNG ADULT

General Medicine

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ABSTRACT

Kikuchi-Fujimoto Disease (KFD) is a rare, benign and self-limited condition affecting lymph nodes predominantly, although extra lymph nodal manifestations are seen. The first case was reported in 1972 almost simultaneously by Kikuchi and Fujimoto et al. Prevalence is more common in the Asian population, affecting females more than males. The cause of the disease is unknown but thought to be due to autoimmunity triggered by an external stimulus. Few cases are associated with infectious agents like CMV, EBV, Histoplasmosis, and toxoplasmosis. Most commonly associated with tuberculosis, SLE and lymphoma. Cases are managed conservatively, and severe cases & relapses with corticosteroids. Relapse rates are at 3 to 4 per cent in adults. Here we discuss a case of an 18-year-old male with complaints of swelling in the right arm, fever, loss of appetite and generalized weakness with a known diagnosed case of KFD four months back and TB one year back, and on further investigations of normocytic anaemia, predominant lymphocyte leucocytosis, raised ESR (50mm). CRP was normal. Chest X-ray suggests fibrotic changes (old TB) in the middle zone of the right lung. USG of right arm swelling suggests multiple necrotic lymph nodes with loss of hilum. USG abdomen and pelvis showed splenomegaly of 14.8 cm. sputum for AFB, and the CBNAAT result was negative. On Mantoux, no induration is seen. ANA was positive with homogenous nucleoli (1:80). Complement levels c3 were normal, and c4 was low (7), thought TB lymphadenitis, on biopsy, showed findings suggestive of KFD. The patient was further managed with a short course of corticosteroids and antibiotics and is under observation.

KEYWORDS

Kikuchi Fujimoto Disease, SLE, Tuberculosis

INTRODUCTION

Kikuchi-Fujimoto Disease (KFD), also known as histiocytic necrotizing lymphadenopathy, is a benign condition of lymph nodes[1]. It is a rare condition with a prevalence in Asian countries[1,2]. Patients are usually young and are seen more commonly in females with a ratio of 3-4:1[2,3]. In children, female to male is 1:1.9, with a preference for boys[3]. This is a self-limited condition and clinically presents with lymphadenopathy (predominantly cervical), fever, fatigue, and night sweats[4]. The cause is unknown, and various genetic, autoimmune and infectious aetiologies have been proposed. An external stimulus is thought to trigger the autoimmune process[6]. Infectious agents, especially of viral origin such as Human Herpes Virus (HHV) 6 & 8, Epstein Bar Virus (EBV), Human Immunodeficiency Virus (HIV), Parvo Virus B19, Torque Teno Virus/Torque Teno like Mini Virus (TTV/TTMV). TTV closely resembles the circovirus, which is known to cause necrotizing lymphadenitis in pigs. In a few cases of KFD, successful amplification and DNA sequencing of TTV/TTMV were done[4].

KFD uncommonly also occurs in extranodal locations like skin (manifesting as nodules, rashes, erythema multiforme, erythematous papules, indurated erythematous lesions, and erythematous maculopapular lesions), bone marrow, and liver[5]. The differential diagnosis for this presentation includes infectious diseases like tertiary syphilis, gonococcus, cat scratch disease, viral diseases like CMV, disseminated HIV, EBV, and fungal diseases like histoplasmosis or toxoplasmosis. KFD closely mimics mycobacterial infections such as disseminated tuberculosis, lepromatous leprosy, and atypical mycobacterial infections. Autoimmune conditions mimicking KFD are SLE (most common) and Graves' disease[6]. Laboratory tests are usually within normal limits, and they may present with normocytic normochromic anaemia and elevated CRP & ESR levels. Few cases were reported with leukopenia and the presence of atypical lymphocytes[3]. As SLE is more commonly observed in cases of KFD, it is mandatory to evaluate for the same, including antibiotics for antiphospholipid syndrome, rheumatoid factor, and complement levels. Definitive diagnosis is by a histopathological study from the biopsy of the lymph nodes. Classical findings include necrotic tissue with abundant karyorrhectic nuclear debris[7]. As such, there is no effective treatment for a diagnosed case of KFD. It is benign and self-limited and resolves in 1-4 months. Treatment is mainly symptomatic with rest, analgesics, antipyretics, and antibiotics. Steroids play a role in patients with severe disease (pulmonary oedema, encephalitis) and relapsing disease. The relapse rate is 3-4 per cent in adults[7]. Here, we present a case of an 18-year-old male with recurrent lymphadenopathy and a history of tuberculosis, and KFD was evaluated and further confirmed on biopsy as KFD and managed accordingly.

CASE REPORT

An 18-year-old male presented to OPD with complaints of swelling over the right arm (medial and lower part) for five days which was painful and aggravated with movements. Associated with continuous high-grade fever, loss of appetite, arthralgia, weakness and non-productive cough for the past three days. No history of evening rise in temperature, weight loss, vomiting, diarrhoea, neck stiffness, and skin lesions. History of tuberculosis one year back used Antituberculous treatment for six months. Sputum for acid-fast bacilli was negative after the completion of treatment. Four months back, he presented with a history of swelling in the left groin for six days, insidious in onset, gradually progressive and tender. It was associated with low-grade fever and generalized weakness. There is no history of easy fatiguability, weight loss, evening rise of temperature, or loss of appetite. On local examination, 3*1.5 cm in size, local rise of temperature is present, tender and no superficial discolouration seen. Routine investigations showed leucocytosis, HIV 1&2 is NR. USG suggested enlarged lymph nodes, the largest measuring 3.4*1.5 cm with a central hypoechoic area (necrosis) with no evidence of any collection in the subcutaneous or intermuscular planes. An excisional lymph node biopsy was done, and the report showed irregular, pale areas composed of histiocytes, plasmacytoid dendritic cells, eosinophilic granular material and abundant karyorrhectic debris surrounding the area of necrosis (Figure1). The above features are suggestive of Kikuchi-Fujimoto disease. He was managed conservatively with antibiotics (3rd generation cephalosporins), antipyretics and other supportive care. He responded well and got discharged. The patient has no history of bronchial asthma, epilepsy, hypothyroid or hyperthyroid, or cardiac disorders. The patient is not using any medications.

On local examination, swelling of 1.5*2cms, with the local rise of temperature felt and tenderness, is present. No cutaneous markers of tuberculosis were seen. Labs suggest normocytic anaemia, lymphocyte-predominant leucocytosis, and raised ESR (50mm). CRP was normal. Chest X-ray suggests fibrotic changes (old TB) in the middle zone of the right lung. USG abdomen and pelvis showed splenomegaly of 14.8 cm. USG of right arm swelling suggests multiple

necrotic lymph nodes with loss of hilum. On biopsy, it showed findings suggestive of KFD. Sputum for AFB and the CBNAAT result were negative. On Mantoux, no induration is seen. ANA was positive with homogenous nucleoli (1:80). Complement levels c3 were normal, and c4 was low (7mg/dl). ANA profile was negative for antibodies (Table1). As the patient did not have any clinical features of other autoimmune conditions, he was observed and managed conservatively with a short course of corticosteroids, antibiotics, antipyretics and other supportive care. The patient is under observation for symptoms of autoimmune conditions or relapse of the same.

Table1. Lab Parameters

Laboratory tests	Observed values
Hb	11.2 gm%
TLC	11600/cmm (Lymphocytes 48%)
ESR	50mm/hr
CRP	Normal
RA	Negative
Viral Markers • HIV1,2 • HBsAg	• Non-Reactive • Non-Reactive
CBNAAT	Negative
Mantoux	No induration after 48 hours
ANA Hep-2	Positive (1:80) Nucleoli homogenous
ANA Profile - Immunoblot	Negative for antibodies
C3	124 mg/dl (WNL)
C4	7mg/dl (Low)

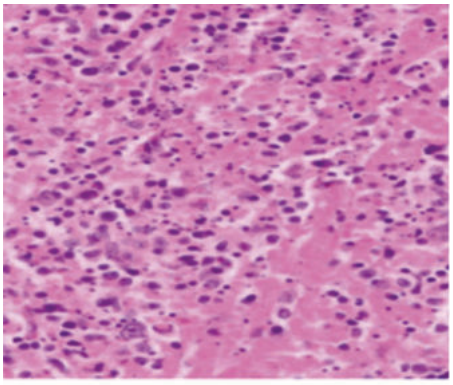

Figure1. Lymph node biopsy showing apoptosis with histiocytes

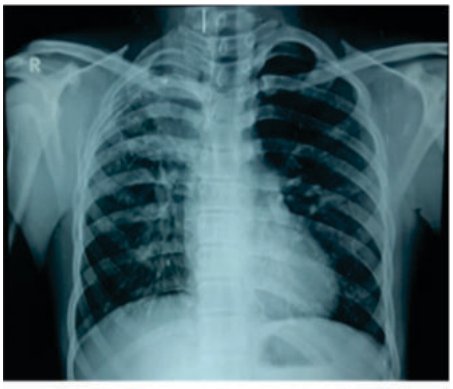

Figure2. Chest X-ray showing right middle zone fibrotic changes

DISCUSSION

Kikuchi disease is a self-limited condition that causes tender lymphadenopathy, mostly in the cervical region and is more commonly seen in females of 20 to 40 years of age and are of Southeast Asian region[8,10]. The sex ratio in the paediatric age group is reversed, predominantly for boys. The clinical symptoms include fever, fatigue, generalized body aches, arthralgias, hepatosplenomegaly, and weight loss apart from tender lymphadenopathy[9]. The cause of this disease is thought to be due to an exaggerated T-cell mediated immune response to an external stimulus. In a case study of 244 cases of KFD, it showed that fever (35%), fatigue (7%), joint pains (7%), lymphadenopathy (100%), high ESR (40%), anaemia (23%), leukopenia (43%) was seen[4]. Our patient had a high-grade fever, lymphadenopathy, high ESR, normocytic normochromic anaemia and splenomegaly. ANA was positive, and low c4 levels were seen.

Baenas et al. noted the patterns of association between SLE and KFD, where the KFD was present earlier than the onset of SLE in 30%, simultaneous occurrence in 47% of cases, and SLE before KFD in 23% of cases[10].

Goldblatt et al. reported 4 cases who developed SLE after KFD in 4 to 13 months after diagnosis[10].

Although an association is seen between KFD and SLE, the diagnosis of SLE cannot be made as our patient did not meet the criteria to diagnose SLE. At the time of the first admission, KFD diagnosis was done and managed conservatively. After the relapse, the patient was managed with a short course of corticosteroids, antibiotics, antipyretics, and analgesics.

Sing et al. reported an increase in relapse rates in diagnosed cases of KFD with ANA positivity. Fever, fatigue, extranodal involvement and positive ANA fluorescence as predictive factors for relapse[10].

The patient is symptom-free and is under close observation for any clinical features of associated conditions like SLE, Graves' disease, and lymphoma.

CONCLUSION

To conclude, it is beneficial to include KFD in cases of young individuals presenting with lymphadenopathy. As the disease has associations with various other infections and autoimmune conditions, it is mandatory to evaluate further and manage the case accordingly to prevent complications, as relapses are common, as in the patient.

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