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CASE REPORT

A Case of Recurrent Kikuchi-Fujimoto Disease

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Abstract

Kikuchi-Fujimoto disease or necrotising histiocytic lymphadenitis is a rare non-malignant immune mediated condition that presents with cervical lymphadenopathy, upper respiratory tract symptoms, low grade fever, night sweats and weight loss in young females. Although mostly self-resolving after months of onset, recurrences have been reported increasingly, with certain specific factors predicting frequent relapse. It closely mimics lymphoproliferative disorders and has been reported as a harbinger of autoimmune diseases like SLE. Here we describe a case of a young female with past history of KD who presented with painful cervical lymphadenopathy, fever, cough, along with leukopenia and splenomegaly with node biopsy revealing KD, who was treated with a prolonged course of steroids for the relapsing disease.

Keywords:

- Kikuchi- Fujimoto Disease
- Necrotising Histiocytic Lymphadenitis

Introduction

Kikuchi Fujimoto disease is a rare, benign, usually self-resolving syndrome that presents in adolescents or young adults with acute or sub-acute onset localised tender lymphadenopathy, night sweats and low-grade fever. KFD is known to have a worldwide distribution with a higher prevalence among Japanese and other Asiatic people [1,4-7] and generally has a female preponderance (4:1) [18,21]. The exact etiopathogenesis seems unclear but it has been proposed to be caused by virally induced immune response of T cells and tissue histiocytes. Other less common presentations of the disease include generalised lymphadenopathy, leukopenia, FUO, nausea, vomiting, sore throat [1,4,8,10] and rarely skin, eye, bone marrow and liver involvement [22-24].

It needs to be differentiated from infective causes of cervical lymphadenopathy and can be mistaken for malignancy or lymphoma. KD can also evolve into SLE and has association with other autoimmune diseases. Though usually self-resolving within a period of 4 to 6 months with a low recurrence rate [1,4,17-19,34,35] recent studies [36-38] have reported increasing rate of

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recurrence. Most patients require supportive treatment measures, however for those with frequent flares and a bulky disease corticosteroid treatment is warranted.[41]

Case Report

18-year-old female diagnosed as a case of Kikuchi Disease in the past, was admitted with 1week history of fever, cough, and painful swelling in the neck. On examination patient was febrile (temperature 100.8), had pallor and left sided cervical lymphadenopathy in the posterior triangle, which was 2 cms in the largest dimension and tender and firm on palpation, along with moderate splenomegaly, and no other abnormalities. Past history of the patient was significant for an acute pharyngitis like illness in 2017 and Fever with cervical lymphadenopathy and splenomegaly with nodal biopsy features of KD in 2016.

Laboratory investigations followed over a week revealed the following findings:

Table 1: Hemogram

Hb	TLC	N	L	M	Platelets	MCV	MCH	ESR
4.9	2.8	32.14	53.4	14.2	121	77.2	19.6	64 mm/hr.
5.1	2.2	50.2	40.2	10.1	144	76.7	19.8	
6.8	3.4	76.4	20.2	3.60	247	77.6	22.4	

Table 2/3: Biochemistry:

Urea (mmol/L)	Creatinine (mmol/L)	Na+ (mEq/dL)	K+ (mEq/dL)	Ferritin (mg/dL)
30	0.90	144	4.13	<10.0
24	0.82	141	3.9	

Bilirubin (mg/dl)	AST (U/L)	ALT (U/L)	ALP (U/L)	TP (g/dl)	Alb (g/dl)
0.9	37	20	100	7.3	3.4
0.9	38	17	105	7.0	3.3

Blood and Urine cultures: sterile.
ANA: negative (titre: 9.88) USG Abdomen: Splenomegaly (15 cms).

USG Abdomen: Splenomegaly (15 cms).

Lymph Node (Cervical) Biopsy: Widespread necrotic areas with abundant karyorrhectic debris and fibrin deposition with evidence of patchy collection of mononuclear cells comprising od lymphocytes, macrophages and few scattered plasma cells (suggestive of Kikuchi necrotising lymphadenitis).

Labs revealed severe iron deficiency anaemia with pancytopenia with a low ANC and high ESR, however cultures were sterile. The patient was managed with broad spectrum iv antibiotics and two units of blood transfusion, and was planned for an excision biopsy of the lymph node. In view of suspected relapse of the Kikuchi Disease, the patient was also started on steroids (30 mg per day of prednisolone). Biopsy revealed features consistent with Kikuchi Fujimoto disease, and was negative for AFB stain. The was dramatic improvement in symptoms with resolution of fever, cough and tenderness over one week of admission in the hospital, and was subsequently discharged on oral steroids with tapering regimen over the next 3 weeks.

Discussion

Kikuchi-Fujimoto disease is a rare, benign and self-limited syndrome characterized by regional lymphadenopathy with tenderness, predominantly in the cervical region, and usually accompanied by mild fever, night sweats and weight loss. Initially described in Japan, KFD was first reported in 1972 almost simultaneously by Kikuchi [1] and by Fujimoto *et al*. [2] as a lymphadenitis with focal proliferation of reticular cells accompanied by numerous histiocytes and extensive nuclear debris [3]. KFD is known to have a worldwide distribution with a higher prevalence among Japanese and other Asiatic people [3-7]. It is scarcely known in the Western hemisphere. A recent series from Taiwan of 61 patients with KFD revealed a mean age of 21 years [8]. In general, a female preponderance has been reported (female/male ratio, 4:1) [9-11].

The aetiology of KFD is unknown. Certain causative organisms have been proposed. These include Epstein-Barr virus, human T-cell leukaemia virus type 1, human herpesvirus type 6, B19 parvovirus, cytomegalovirus, *Brucella*, *Yersinia enterocolitica*, and parainfluenza virus [12-14]. An autoimmune mechanism has also been proposed because KFD is seen in conjunction with SLE. One theory involves molecular mimicry [15]. Another theory regarding autoimmunity is that apoptotic cells are the source of the autoantigens of SLE. In patients with defective clearance of these cells (i.e., complement deficiency), these cells may become a nidus for autoimmune disease[16.] The onset of KFD is acute or subacute, over a period of 2 to 3 weeks with cervical lymphadenopathy seen in 56% to 98% of cases, more commonly consisting of tender lymph nodes involving the posterior cervical triangle (88.5%), generally unilateral (88.5%). Lymph node size ranges from 0.5 to 4 cm (93.4%), and occasionally, lymph nodes are larger than 6 cm. Painful lymphadenopathy is seen in up to 59% of patients. Generalized lymphadenopathy has been reported in 1% to 22% of cases. [1,4,8, 17-19]. In addition to lymphadenopathy, 30% to 50% of patients with KFD might have fever, usually low-grade, associated with upper respiratory symptoms. Less frequent symptoms include weight loss, nausea, vomiting, sore throat, and night sweats [1,4,8,20,21].

Laboratory studies in some patients show anaemia and a slight elevation of the erythrocyte sedimentation rate. Mild leukopenia has been observed in 25% to 58% of patients, whereas leucocytosis is found in 2% to 5% of cases. About 25% to 31% of patients have atypical peripheral blood lymphocytes, [1,4,8,17-19] which supports the speculated viral cause. Involvement of extra nodal sites by KFD is uncommon, but skin and bone marrow involvement and liver dysfunction have been reported [21-24]. A few patients have had generalized lymphadenopathy and hepatosplenomegaly as the initial manifestations of KFD. It has been reported rarely in HIV-positive patients [25,26] and in association with the human T-cell leukaemia/lymphoma (lymphotropic) virus type 1 (HTLV-1). A recent article from Thailand suggested an association between Mycobacterium szulgai lymphadenitis and KFD [27]. Also, SLE has been found to develop in some patients thought to have true KFD, the

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diagnosis of KFD can precede, postdate, or coincide with the diagnosis of SLE [28].

Diagnosis of KFD is generally on the basis of an excisional biopsy of affected lymph nodes. This disorder does not have a characteristic appearance on ultrasonographic or computed tomographic (CT) examination The characteristic histopathologic findings of KFD include irregular paracortical areas of coagulative necrosis with abundant karyorrhectic debris, which can distort the nodal architecture, and large numbers of different types of histiocytes at the margin of the necrotic areas. The immunophenotype of KFD typically consists of a predominance of T cells, with very few B cells. There is a predominance of CD8+ cells over CD4+ cells, along with a decreased ratio in the affected areas of the lymph node. Striking plasmacytoid monocytes also are positive for cutaneous lymphocyte-associated antigen and CD68 but not for MPO [29].

The histologic differential diagnosis of KFD includes mainly reactive lesions such as lymphadenitis associated with SLE, lymphadenitis associated with herpes simplex and other microorganisms, non-Hodgkin lymphoma, plasmacytoid T-cell leukaemia, Kawasaki disease, nodal colonization by acute myeloid leukaemia, and even metastatic adenocarcinoma [30].

KFD typically is self-limited, and lasts 1 to 4 months. A low, but possible, recurrence rate of 3% to 4% has been reported [1,4,17-19,31,32]. Recent studies [33,34,35] have reported increasing rate of recurrence. In a study [36] the KD recurrence rate was 11.3% in all patients and 13.2% in children under 18 years of age. More extra nodal symptoms, lymphopenia, and a longer duration for lymphocyte count recovery were significantly associated with KD recurrence [37].

There is no specific treatment for patients with KFD. Since, the disease is self-limited, only symptomatic treatment measures to relieve distressing local and systemic complaints should be used (analgesics, antipyretics, and rest). On the basis of some pathogenetic and immunologic considerations, it is argued that, some patients with KFD with a more severe clinical course or with relapsing signs and symptoms could benefit temporarily from corticosteroids as other authors have pointed out [38].

Conclusion

Kikuchi Fujimoto Disease is a very rare, benign usually self-resolving disease that affects young females causing regional cervical lymphadenopathy, fever and other rare extra nodal features. Frequent recurrences of the disease are being reported which need glucocorticoid treatment. It is important to recognise the disease as it can be mistaken for lymphoma or adenocarcinoma and other infections, and such patients need to be evaluated and followed to rule out concomitant SLE.

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