A Case Report on Kikuchi Disease

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ABSTRACT

Kikuchi-Fujimoto disease (KFD) is a rare benign (non-cancerous, non-malignant) and self-limited syndrome characterized by regional lymphadenopathy with tenderness, predominantly in the cervical region, which is usually accompanied by mild fever and night sweats. It is first described in Japan and reported in 1972 simultaneously by two pathologists named Kikuchi and Fujimoto. Symptoms include weight loss, vomiting, nausea and sore throat. It is an auto immune disorder. Its etiology is still unknown. It is diagnosed by obtaining a biopsy specimen from lymph node. There is no specific treatment for Kikuchi-Fujimoto disease, it can be only treated symptomatically and some surgical techniques may be followed if needed. We have highlighted an 18-year-old male patient who had bilateral multiple swelling of lymph node in the neck region and had complaint of fever since 4 months on and off. After the biopsy it was diagnosed as kikuchi disease.

Keywords: Kikuchi-Fujimoto disease, Non-malignant, Histiocytes, Lymphadenopathy

INTRODUCTION

Kikuchi-Fujimoto disease (KFD) is a rare benign (non-cancerous, non-malignant) and self-limited syndrome characterized by regional lymphadenopathy with tenderness, predominantly in the cervical region, which is usually accompanied by mild fever and night sweats. It is first described in Japan and reported in 1972 simultaneously by two pathologist named Kikuchi and Fujimoto [1]. KFD is a condition rarely associated with systemic lupus erythematosus (SLE), Polio myositis, lymphoma, scleroderma. Thyroiditis and Sjogren’s syndrome (an immune system disorder) are also associated with KFD [6]. Infectious agents such as Yersinia enterocolitica, Brucella, Bartonella henselae, Entamoeba Hisolytica, Mycobacterium szulgai and Toxoplasma gondii were implicated but subsequent studies failed to support these findings. Viruses such as Epstein-Barr virus, herpes virus, cytomegalo virus, parvovirus, paramyxovirus, parainfluenza virus, Rubella virus, Hepatitis-B, HIV, Human T-lymphotropic virus type-1 have all been suggested as possible aetiologies of KFD, but never demonstrated. Some authors...
mentioned that KFD may reflect a self-limited auto immune condition which is induced by virus-infected transformed lymphocytes. At clinical level KFD is almost similar to Systemic lupus Erythematous (SLE) (7).

**Etiology and Pathogenesis:**
The exact etiology of KFD is still unknown. However, role of viruses in the pathogenesis of Kikuchi’s disease is controversial and unremarked. Like SLE the lymphocytes and histiocytes in the patients of Kikuchi Disease show tubular reticular structures in their cytoplasm under electron microscopy. In genetically susceptible individuals, KFD may belong to exuberant T-cell mediated immune response which is provoked by variety of stimuli. Even though much studies have to be included regarding cell death in KFD, Ohshima and his associates has remarked apoptotic cell death might be involved in pathogenesis of KFD (8).

**Clinical Manifestations:**
The onset of Kikuchi’s disease is acute or subacute, which progress around a period of two to three weeks. Tender Cervical lymphadenopathy is the characteristic feature almost 56% - 98% of KFD which predominantly involves the posterior cervical triangle. Size of the enlarged lymph nodes varies from 0.5 cm to 4 cm. In rare cases, 1% - 22% generalized lymphadenopathy is also seen. At times, KFD more or less, rarely involves mediastinal, peritoneal or retroperitoneal regions of the body (9). In addition to lymphadenopathy, 30 to 50% of patients with KFD may have fever, usually low grade, associated with upper respiratory symptoms. Other symptoms which are associated include nausea, vomiting, sore throat and night sweats and leukopenia (seen in almost 50% of the cases) (9). Atypical lymphocytes in the peripheral blood have also been observed. Involvement of extra nodal sites is rare; however, skin, eye and bone marrow infection has also been reported (8). The affected lymph nodes showed the typical histology of HNL: irregular shaped "necrotic" foci with histiocytes engulfing apoptotic bodies intermingled with large sized blastic lymphocytes. These findings mimicked the partial involvement of large-cell lymphoma. However, the blastic cells were almost exclusively T cells, and numerous apoptotic bodies were present, which excluded the possibility of recurrence of diffuse large B-cell lymphoma (10).

**Diagnosis:**
Excisional biopsy of an enlarged lymph node is required for diagnosis of Kikuchi disease and immune chemistry findings helps to rule out alternative differential diagnosis. It shows histiocytes that are positive for myeloperoxidase, CD68, lysozyme, CD163 and CD4. It will also show T cells that are CD8 positive (11). Coagulative necrosis with ample karyorrhectic debris in paracortical areas of the involved lymph nodes is the characteristic histologic feature of KFD. Sometimes KFD express histiocytes resembling with signet-ring cells and can be confused with signet-ring carcinoma. However, metastatic adenocarcinoma contains cells with atypical nuclei and mucin debris instead of cellular debris (8). In paediatric populations, sources of benign lymphadenopathy such as pharyngitis, otitis media, upper respiratory infection should be considered. The absence of eosinophils, neutrophils and viral inclusions on histology also helps rule out infectious aetiology in Kikuchi disease (11). Lymphoma (non-Hodgkin’s lymphoma), tuberculosis, plasmacytoid T-cell leukaemia, Kawasaki’s disease, and myeloid tumour are included in the differential diagnosis of KFD (8).

**Imaging Findings:**
The most preferred method to examine cervical lymph node is USG. It is the best tool for children, to diagnose enlarged lymph nodes on the neck because it has no radiation hazards (6). Tsujikawa et al compared the size of lymph nodes and the
maximum standardized uptake value in 8 patients with KFD and 14 patients with non-Hodgkin lymphoma using 18F fluorodeoxyglucose positron emission tomography/computed tomography (12). Chest X-ray was unremarkable. As the presentation was suspicious of lymphoma, a CT (computerized tomography) scan of neck, chest, abdomen, and pelvis was performed. It revealed asymmetric lymphadenopathy in the neck involving lymph nodes within the right posterior triangle (size of 2.8 cm), right internal jugular chain (size of 1.5 cm), bilateral submental lymph nodes (size of 1.2 cm), and right supraclavicular chain (size of 2 cm) (7).

**Treatment:**
There is no specific treatment available for Kikuchi disease. It is typically a self-limiting disease, and spontaneous resolution occurs within one to four or one to six months. Treatment includes systematic supportive management with antipyretics, analgesics and anti-inflammatory therapies such as NSAIDs. The other treatments that have been successful include hydroxychloroquine, minocycline or intravenous immunoglobulins. For patients with co-diagnosis of Kikuchi disease and other autoimmune diseases (SLE being most common), the appropriate treatment for the secondary autoimmune disorder with agents such as corticosteroids and/or hydroxychloroquine is required (6, 11).

**Flow chart showing the treatment of Kikuchi-Fujimoto disease (KFD)**

NSAIDs: Non-Steroidal Anti-Inflammatory Drugs, SLE: Systemic Lupus Erythematosus, IL: Interleukin-1

Corticosteroids showed great benefit but only initially. If any patient has multiple recurrences of KFD, we can use anakinra, which is a recombinant human interleukin-1 (IL-1) receptor inhibitor. It blocks the downstream inflammatory actions of IL-1 alpha and IL-1beta. The human IL-1 inhibitors have a strong steroid-sparing effect. Therefore, we can use anakinra in case of treatment resistance or recurrent cases of KFD (13).

However, individuals with Kikuchi Fujimoto Disease should be examined systemically and they must be under regular follow-up in order to monitor the manifestations of SLE. The course of cervical lymphadenopathy is benign and resolves spontaneously. Very few cases have been reported as fatal. However, no standard or specific treatment of KFD has been recommended (8).
CASE PRESENTATION

An 18-year-old male patient was presented with chief complaints of fever on and off for 4 months, multiple bilateral swellings in neck (more on left side) for 1 month. He had no history of cough, breathlessness, chest pain, Headache, weight loss, pain abdomen, vomiting, Burning micturition. Patient was previously treated with antibiotics cefpodem, azithromyci and ofloxacin for 5 days.

The patient vital signs were found to be. BP: 120/80mmHg, Respiratory rate: 96/min, pulse rate: 96 beats per minute, Lungs: BAE+, no added sounds

Local Examination showed:

- Right upper jugular lymph node enlargement 0.5*0.5 cm, non tender, spherical in shape, skin over it normal.
- Left lower jugular cervical lymph node 1*1cm, non-tender spherical in shape.
- Left supraclavicular region 0.5*0.5cm enlarge lymph node, nontender, spherical in shape.

Laboratory findings of haemoglobin was 14 g/dl, R.B.C 4.85 million/ul, W.B.C 3,300 number/ul, Neutrophils 69%, Lymphocytes 25%, Eosinophils 01%, Monocytes 05%, platelet count 167000/Cumm. Hemogram showed mild leukopenia, with occasional reactive lymphocytes. Erythrocyte sedimentation rate was raised. Random plasma glucose was raised, it was 158mg/dl, serum creatinine was within normal limits (0.85 mg/dl). Serum total bilirubin 0.31mg/dl, serum direct bilirubin 0.13 mg/dl, serum alkaline phosphatase 266 U/L, S.G.P.T 36 U/L, S.G.O.T 31 U/L, serum proteins 8.0 gms/dl, serum albumin 4.5 gms/dl, Globulin 3.5 gms/dl, serum urea 14 mg/dl. PT with INR 14.6 seconds (within normal range). Urine examination revealed that total pus cells was 1-2, epithelial cells were occasional, R.B.C nil, urine is pale yellow in colour and has acidic in reaction. Ultra sound of whole abdomen, ECG and Chest X-ray was normal.

Ultra sound scan of neck revealed that right and left lobes of thyroid and isthmus were normal. Great vessels of neck are normal.

Right high cervical lymph nodes of size 10*5mm, 8*4mm. Multiple lymph nodes are noted in the left cervical region largest measuring 16*6mm. The lymph nodes are showing central necrosis.

Considering above findings of USG Neck, left cervical lymph node biopsy was performed and specimen was sent for histopathology and TB GeneXpert. The biopsy revealed features are consistent with Histiocytic necrotising lymphadenitis it is diagnosed as Kikuchi-Fujimoto Disease. TB GeneXpert was not detected.

Treatment:

Patient had history of usage of Antibiotics cepodoxime proxitil 200 mg, Azithromycin 500mg and ofloxacin for 5 days later only symptomatic treatment was given before and after biopsy, for fever paracetamol was given SOS after biopsy ibuprofen was prescribed for one week. After kikuchi was diagnosed nothing was prescribed except paracetamol for fever.

DISCUSSION

Kikuchi- Fujimoto disease (KFD) is a rare condition characterized by regional lymphadenopathy with tenderness, predominantly in the cervical region, which is accompanied by mild fever [1]. Some of the less common symptoms include weight loss, nausea, vomiting and sore throat. It is also known as histiocytic necrotizing lymphadenopathy [4]. The exact etiology of KFD is still unknown.

The onset of Kikuchi’s disease is acute or subacute, which progress around a period of two to three weeks. Tender Cervical lymphadenopathy is the characteristic feature. In addition to lymphadenopathy, 30 to 50% of patients with KFD may have fever (9). Excisional biopsy of an enlarged lymph node is required for diagnosis of Kikuchi disease.

We have highlighted an 18-year-old male patient who had bilateral multiple swelling of lymph node in the neck region and had complaint of fever since 4 months on and off. After the biopsy it was diagnosed as
kikuchi disease. Patient had history of usage of Antibiotics cepodoxime proxitin 200 mg, Azithromycin 500mg and Ofloxacin for 5 days later only symptomatic treatment for fever Paracetamol was given SOS after biopsy ibuprofen was prescribed for one week. After Kikuchi was diagnosed nothing was prescribed except Paracetamol for fever.

CONCLUSION
Kikuchi- Fujimoto disease (KFD) is a rare condition in which swelling of lymph nodes in the neck region is seen which is accompanied by mild fever. The exact cause of the disease is unknown. We have highlighted an 18-year-old male patient who had bilateral multiple swelling of lymph node in the neck region and had complaint of fever for 4 months on and off. After the biopsy it was diagnosed as kikuchi disease. The treatment was given symptomatically.

Declaration by Authors
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