Kikuchi-Fujimoto disease: A study of Four cases

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ABSTRACT

Kikuchi-Fujimoto disease (KFD) manifests in most cases as unilateral cervical lymphadenomegaly with or without accompanying fever. The disease is rare and mainly affects young women and has a self-limited course. KFD should be included in the differential diagnosis of suspected cases of viral infections, tuberculosis, reactive lymphadenitis, systemic lupus erythematosus and metastatic diseases. It can be histologically confused with lymphoma. The disease is benign and self-limiting and an excisional biopsy of an affected lymph node is often necessary for diagnosis. There is no specific therapy. This study reports four cases of female patients with KFD who were attended at Yashoda hospital, Malakpet. A review of the literature was carried out with a systematic search on this topic with the aim of informing physicians about this entity that is manifested by cervical masses and fever. Fourth case was interesting because of its association with autoimmune disease (SLE-systemic lupus erythematosus.).

Keywords: Kikuchi disease, histiocytic necrotizing lymphadenitis, lymphatic diseases, neck, lymph nodes.

INTRODUCTION

Cervical lymphadenomegaly is a frequent clinical sign and may correspond to a series of diseases that require diverse work-ups and therapies. Kikuchi-Fujimoto disease (KFD) is a form of histiocytic necrotizing lymphadenitis first described in Japan in 1972, almost simultaneously by Kikuchi and Fujimoto.[1-3] They studied patients treated for lymphoma who evolved surprisingly well showing much faster recovery than expected. In fact, these patients did not have lymphoma but a condition that has been called Kikuchi-Fujimoto disease since its initial description.[4]

KFD mainly affects young women of Asian origin (the female-to-male ratio of occurrence is 4:1).[1,5,6] Clinically, KFD manifests as cervical (usually unilateral) lymphadenopathy with fever and is frequently associated with other nonspecific symptoms.[5,7] Laboratory test results are almost always unchanged, except for erythrocyte sedimentation rate and C-reactive protein levels.[3,7]

An excisional biopsy from an affected lymph node is often necessary for diagnosis.[5] The disease is benign and self-limiting.[3,6,7] Rheumatological diseases such as SLE and Sjögren's syndrome may be associated with KFD and therefore, investigations for the presence of these diseases and patient follow-up are necessary.[8] More than 85% patients present with cervical lymphadenopathy, less commonly axillary lymph nodes are involved. The etiology of Kikuchi-Fujimoto disease is uncertain and speculations exist regarding relationships with previous viral infections or autoimmune processes.[1-3]

CASE REPORTS

Case 1

A 24-year-old female came to the outpatient department with complaints of a cervical mass on the left side of her neck which had existed for a month and was associated with fever. The mass showed fast growth and was mildly painful. The patient did not report any other complaints.

An excisional biopsy was performed on the lymph node and the histopathological diagnosis determined was KFD (Figure:1)

The patient was followed up on an outpatient basis after associated SLE had been ruled out.

Case 2

A 16-year-old girl sought medical care with complaints of bilateral cervical lymphadenopathy, The patient did not have any other associated complaints. Routine investigations documented: ESR-41 mm in 1st hour, chest x-ray was found to be normal.

An excisional biopsy was performed on right cervical lymph node and histopathological analysis revealed this to be a case of KFD (Figure:2)

The patient progressed well but presented with high fever on the fifth postoperative day. This was not correlated with any infectious symptoms and regressed spontaneously. Remission from the cervical lymphadenopathy was achieved slowly after the fever. Associated rheumatological diseases were ruled out.

Case 3

A 21-year-old woman sought medical care because of a two-month history of multiple right posterior cervical lymphadenopathy associated with eight days of fever. A chest x-ray and Mantoux test were normal. USG guided FNAC was done, it revealed only necrosis. (Figure: 3)

An excisional biopsy was performed on one of the lymph nodes and the histopathological analysis revealed KFD. (Figure:4)

The patient was followed up on an outpatient basis and showed spontaneous remission of lymphadenopathy.

Case 4

A 39-year-old female came with complaints of fever, arthralgia and left axillary lymphadenopathy since 6 months. Routine investigations documented: Hb-10 g/dl, TLC-9900, Platelets-3.48. ESR-66 in 1st hour and raised liver enzymes .

CT chest showed interstitial pulmonary fibrosis changes. FNAC and excision biopsy were performed and showed reactive lymph node features in FNAC. Histopathological examination

revealed necrotizing lymphadenitis with occasional neutrophils (Figure:5). Therefore differential diagnosis was given as 1) Auto immune etiology 2) Kikuchi disease. Further tests were advised. Serological tests for RA factor and ANA were normal but Anti RNP antibodies and Anti smith antibodies were positive. Finally based on clinical details, serology and histopathology SLE lymphadenitis was diagnosed.

*Special stain AFB -noncontributory in all cases.

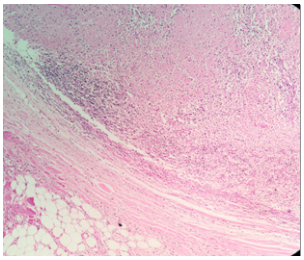

Figure 1-Hematoxyllin and eosin stained section show lymphnode with capsule and extensive necrosis .

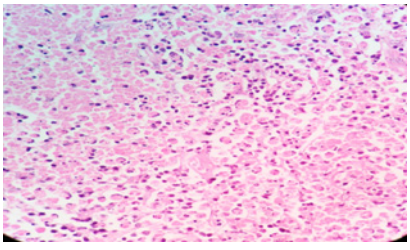

Figure 2-Hematoxyllin and eosin stained section show abundant appoptotic debris, histiocytes and some with cresentric morphology.

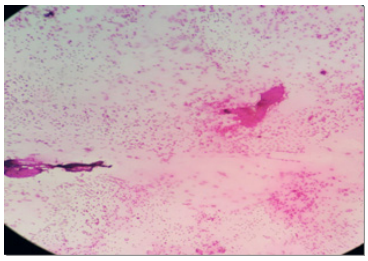

Figure 3: H&E stained FNAC smears showing only necrosis-10x

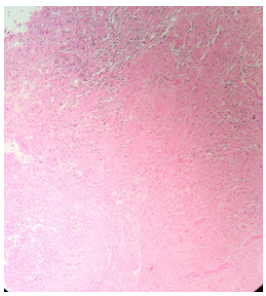

Figure 4

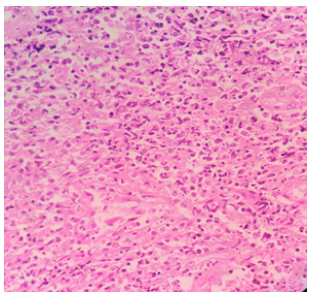

Figure 5

Figure 4& 5: H&E showing necrotic areas with histiocytes and occasional neutrophil-40x

DISCUSSION

This disorder is therefore frequently under diagnosed. Many cases are given a presumptive diagnosis of viral infections, especially among young patients with little swelling of the lymph nodes or pain. KFD has no pathognomonic clinical signs or symptoms and a definitive diagnosis can only be made histologically using lymph node biopsy tissue.[1,4]

However, the axillary, intraparotid, mesenteric, thoracic and inguinal chains may also be involved.[6,7] The lymph nodes are mainly small (less than 3 cm), mobile and painless.[3,6,7]

KFDis most commonly seen in young adults and in women. The main clinical manifestation of KFD is lymphadenomegaly which is cervical in 70% to 98% of cases and generally occurs in the jugular lymph nodes and posterior cervical chain.[7,10]

Fever (usually high) is the first symptom in 30% to 50% of the cases; weight loss is observed in 10% and shivering in 4%.[7,9,12,13]

On FNAC, the overall picture is of reactive lymphoid aspirate.There can be frank necrosis of numerous nuclear apoptotic debris along with histiocytes engulfing the debris. Cresent shaped histiocytes can also be observed. Granulomas should be ruled out. Neutrophils and eosinophils are absent.

Histopathalogy of KFD: The lymph node architecture is partially maintained. The tissue necrosis is represented by isolated apoptotic cells, numerous histiocytes engulfing the cellular debris, some with cresentric morphology. Distinctive feature of this lesion is consistent absence of neutrophils and

eosinophils. There is usually a degree of perilymphadenitis seen.[11]

The etiology of KFD is unknown. A viral infection is suggested by the clinical and histological features and various viruses including EBV virus, CMV and Parvovirus B19. [14-16]

Early apoptosis leads to extensive cell death in KFD, CD8 T lymphocytes are predominant Cells that undergo apoptosis. Ohshima et al have also noted that serum concentration of interleukin-6, Interferon and FAS-L are increased in acute phase of KFD. [17]

Deep lymph nodes are very rarely involved . Other less common manifestations are myalgia, sore throat, skin rashes. Leucopenia, mild lymphocytosis and atypical lymphocytes may be seen in 3% of cases. Elevation of LDH may occur in some cases, but returns to normal level in few days. Most patients recover within 1-2 months without any treatment. [17]

Four subtypes recognized : Lympho histiocytic type, phagocytic type, necrotic type, foamy cell type. Most common type is lymhohistiocytic type.

Differential diagnosis of necrotising lymphadenopathies are tuberculosis, lupus erythematosus, and lymphoma. [18]

CONCLUSION

Final diagnosis of Kikuchi disease is mainly based on histopatholog . All physicians should be aware that Kikuchi disease has a self limited course and inform the patients about the spontaneous remission of disease and regular follow up of the patients because of its association with other autoimmune diseases like SLE.

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