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KEY WORDS: Kikuchi –Fujimoto Disease, Histiocytic Necrotizing Lymphadenitis, KFD.

HISTIOCYTIC NECROTISING LYMPHADENITIS- KIKUCHI DISEASE -AN OVERVIEW

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ABSTRACT

Histiocytic Necrotizing Lymphadenitis or Kikuchi-Fujimoto disease is an uncommon, self-limited condition characterized by cervical lymphadenopathy with associated fever and systemic symptoms. In this article we describe a series of 5 cases of Kikuchi Disease along with a review of the Literature. In our study 4 patients were women and one was a male patient and all presented with painless cervical lymphadenopathy of varying sizes.

INTRODUCTION :

KFD is a rare benign, uncommon, self-limited condition with focal proliferation of histiocytic cells and abundant karyorrhectic debris. It is a rare cause of lymphadenopathy and frequently associated with fever and other systemic symptoms. The exact etiology of Kikuchi's Disease is still unknown. No specific laboratory tests contribute to the diagnosis. Diagnosis requires histopathologic examination and exclusion of other factors by ancillary studies. Involved lymph nodes demonstrate paracortical areas of apoptotic necrosis with abundant karyorrhectic debris and a proliferation of histiocytes, plasmacytoid dendritic cells, and $CD8^+$ T cells in the absence of neutrophils. Non-Hodgkin lymphoma and Systemic Lupus Erythematosus and Tuberculosis should be ruled out before diagnosis of Kikuchi-Fujimoto disease, given the overlapped clinical and histologic features as well as the different therapeutic approaches. Treatment involves supportive measures, and the symptoms usually resolve spontaneously within 4 months.

CLINICAL PICTURE:

In this article we describe a series of 5 cases of Kikuchi Disease along with a review of the Literature. In our study 4 patients were women and one was a male patient and all presented with painless cervical lymphadenopathy of varying sizes ranging from 2cm*4cm with mild fever. All our patients presented with one or two weeks history of fever, generalised myalgia and cervical lymphadenopathy. Routine blood investigations were normal. Electrocardiogram and chest radiographs were normal. FNAC showed features of Reactive Lymphadenitis and the patients were started on broad spectrum antibiotics with no improvement. Computerised tomography demonstrated generalised lymphadenopathy .Subsequently all underwent Lymph Node Biopsy which revealed para-cortical necrosis and zonal histiocytic proliferation suggestive of Necrotising Histiocytic Lymphadenitis / Kikuchi Disease. All patients were treated with Analgesics and supportive medication and improved clinically in 3 months with resolution of the lymphadenitis.

FIGURE 1-3: CLINICAL PICTURE OF PATIENTS WITH CERVICAL LYMPAHDENOPATHY

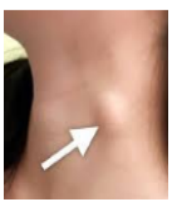


FIGURE 1

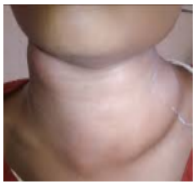


FIGURE 2

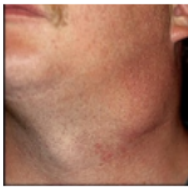


FIGURE 3

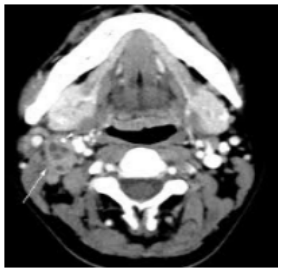


FIGURE 4: CT SCAN NECK SHOWING CERVICAL LYMPHADENOPATHY

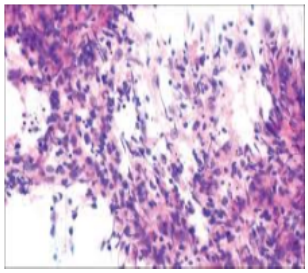


FIGURE 5: FNAC PICTURE OF NECK NODE

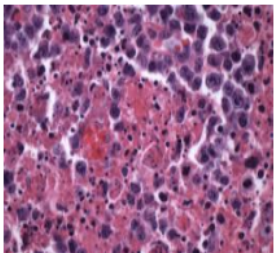


FIGURE 6: PLASMOCYTOID MONOCYTES, PARA-CORTICAL NECROSIS AND ZONAL HISTIOCYTIC PROLIFERATION

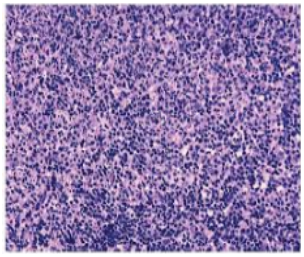


FIGURE 7 : KARYORRHECTIC DEBRIS AND NECROSIS SURROUNDED BY CRESENTERIC HISTIOCYTES .

DISCUSSION:

Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis, was first described in 1972 simultaneously by Kikuchi and Fujimoto and colleagues as a lymphadenitis with focal proliferation of histiocytic cells and abundant karyorrhectic debris. It is a rare cause of lymphadenopathy, commonly seen in individuals of Asian descent and rarely in other regions of the world and frequently associated with fever and sometimes, other systemic symptoms. The disease, most often occurs in young adults below 40 and seldom in children. At first, little female predominance was considered, but the recent literature shows a male to female ratio 1:1.

The exact etiology of Kikuchi's Disease is still unknown. The recent literature is inclined to viral or autoimmune causes. However, role of viruses (Epstein-Barr virus and others) in the pathogenesis of Kikuchi's Disease is controversial and unremarked. On the other hand, Unger and coworkers are in favor of viral etiology as Kikuchi disease manifests certain viral features ie, atypical lymphocytosis, certain histologic features, flulike respiratory prodrome and no response to antibiotic therapy.

Like systemic lupus erythematosus (SLE), lymphocytes and

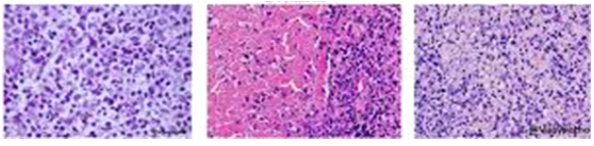
histiocytes in the patients with Kikuchi's Disease show tubular reticular structures in their cytoplasm on electron microscopy. It has been opinioned that in genetically susceptible individuals, Kikuchi disease may belong to exuberant T-cell mediated immune response provoked by variety of stimuli. Ohshima and his associates remarked apoptotic cell death might be involved in the pathogenesis of Kikuchi disease.

Kikuchi's Disease starts as an acute or sub-acute condition, developing over two to three week period. Tender cervical lymphadenopathy is the characteristic feature (56%–98%) of KFD, predominantly involving the posterior cervical triangle. Size of the enlarged lymph nodes ranges from 0.5 cm to 4 cm (occasionally 6 cm). 59% patients represent painful lymphadenopathy and 1%–22% patients undergo generalized lymphadenopathy with rare involvement of mediastinal, peritoneal or retroperitoneal regions of the body.Fever (30%–50%) associated with upper respiratory symptoms, sore throat, night sweats, weight loss, headache, rash, nausea, vomiting, and leukopenia (about 50%) are the other manifestations of the disease. Atypical lymphocytes have been reported in the peripheral blood film of patients with Kikuchi disease. Extranodal involvement is rare; however, skin, eye and bone marrow affection has been reported

In patients with Kikuchi Fujimoto Disease, an excisional biopsy of the involved lymph nodes is the investigation of choice. Coagulative necrosis with ample karyorrhetic debris in paracortical areas of the involved lymph nodes is the characteristic histologic feature. Other baseline investigations are reported unaffected. Nevertheless, laboratory results in some patients have reported anemia, little rise in ESR and even leukopenia. One third individuals with Kikuchi disease have shown atypical lymphocytes in their peripheral blood films predominantly, T-cells (CD8+ T-cells) with absent neutrophils and scarce plasma cells.

It is necessary to bear in mind the differential diagnosis of Kikuchi disease viz. Lymphoma (non-Hodgkin's lymphoma), Tuberculosis, Systemic Lupus Erythematosis, plasmacytoid T-cell leukemia, Kawasaki's disease, and myeloid tumor since the treatment differs dramatically.

THREE HISTOLOGICAL PHASES OF KIKUCHI DISEASE



Proliferative Stage Expresses Various Histiocytes, Plasmacytoid Monocytes And Lymphoid Cells Containing Karyorrhetic Nuclear Fragments, And Eosinophilic Apoptotic Debris	Necrotizing Stage Shows A Degree Of Coagulative Necrosis	Xanthomatous Stage Predominantly Stuffed With Foamy Histiocytes.

FIGURE -8

Kikuchi Fujimoto Disease (histiocytic necrotizing lymhadenitis) is a self-limiting condition that resolves spontaneously within 1 to 4 months of period. However, studies reveal recurrence of the disease in 3%–4% of the patients. Additionally, Systemic Lupus Erythymatosis may happen to occur some years later. No hereditary risk has been documented in Kikuchi disease. Most of the time symptomatic relief is offered for the local and systemic complains of the disease. Lymph node tenderness and fever is treated with analgesics, antipyretics, and NSAIDs. Sometimes, but rarely, steroids can be used temporarily, especially in severe extranodal involvement or generalized clinical course. An excision biopsy of the enlarged lymph nodes is mandatory to confirm the diagnosis. 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 Kikuchi disease has been recommended.

CONCLUSION

Kikuchi Fujimoto Disease is an idiopathic, extremely rare, more or less worldwide, and often under-diagnosed condition commonly involving the posterior cervical lymph nodes. Kikuchi's disease seems to be more prevalent in Japanese and Asian individuals and has an excellent prognosis with little risk of fatality. Histopathologic features support its cause being viral. Early recognition of Kikuchi's Disease is of prime importance to avoid extensive and expensive investigations related to malignant lymphoma and other related disorders. In order to avoid misdiagnosis, awareness of this disease is necessary for the clinician as well as for the pathologist and Kikuchi disease should be considered in young patients with nodal biopsy showing necrosis and karyorrhexis.

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