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KIKUCHI-FUJIMOTO DISEASE- A COMMON BUT RARELY DIAGNOSED DISEASE- CASE REPORT AND REVIEW OF LITERATURE

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ABSTRACT

Kikuchi fujimoto disease is a self limiting lymphadenitis of unknown aetiology which mostly involves cervical lymph nodes and rarely needs steroid for treatment. Most of the time, this disease is misdiagnosed as tuberculosis, lymphoma, SLE etc. So awareness of this disease among clinician and pathologist can avoid misdiagnosis and inappropriate treatment. We hereby report this disease in a 29 year old female who was referred with tender cervical lymph node on the left side and fever for 3 months. Patient had been misdiagnosed as tubercular lymphadenitis and was given anti tubercular therapy for 2 months. Since there was no response, patient was referred to us. We performed FNAC & biopsy of the lymph node and histopathology report showed features suggestive of kikuchi fujimoto disease. Patient was started on prednisolone of 1mg/kg for 2 months and then tapered for another 6 month following which the patient became asymptomatic with non palpable lymphnodes.

KEYWORDS- Kikuchi Fujimoto disease, lymphadenitis, Anti Tubercular Therapy, Prednisolone.

CASE REPORT

29 year old married female, belonging to high socio economic status was referred to us with complaints of swelling on left side of neck, low grade fever, loss of appetite and loss of weight for 3 months.

On detail history: Patient initially developed a small swelling on left side of neck which enlarged within one week, located 6cm below the left ear. The swelling was painful and she also developed fever at the same time which was low grade with evening rise of temperature. She also had decreased appetite. For these problems the patient sought medical consultation elsewhere. An FNAC initially done showed reactive Lymph adenitis. She was given Antibiotics for 10 days, but she didn't get any symptomatic relieve. Based on her clinical profile she was treated with empirical anti tubercular therapy (ATT) of cat 1. Even after 2 months of ATT, the patient didn't get any relief, her swelling and fever was same as earlier and she lost 4 kg weight in 2 months. With this clinical course patient was referred to the Department of respiratory medicine, velammal medical college hospital and research institute, a tertiary health care in Madurai, Tamil Nadu for further evaluation.

Patient did not have any significant past medical and surgical history. She was not a known case of diabetes, hypertension or allergy. She is teacher in 12 std school by occupation. She didn't have any significant relevant family history.

On examination: she was afebrile, with no pallor, cyanosis, clubbing and no other significant finding on general examination. Neck examination: there were two lymph nodes below the left ear just medial to the sternocleidomastoid muscle, One node was 3x3 cm and another one 1.5x1 cm. Both nodes were mobile, firm and slightly tender. There were no other significant peripheral lymph nodes palpable.

ENT examination- no significant abnormal finding. Other systemic examination like respiratory system, cardiovascular system, abdominal system, nervous system, were normal.

Investigation- Routine blood investigation like TLC, DLC, RBS, SGPT, SGPT, Urea and Creatinine were normal. ESR was 80 mm/l by westergren method. HIV, HBsAg, ANA, Anti dsDNA antibody, RA factor, ANCA were normal. Radiological examination like Chest X-ray, CT Scan thorax and ultrasonogram of abdomen was normal.

Fine needle aspiration cytology was performed and reported as 'Reactive lymphoid hyperplasia and histiocytic hyperplasia showing significant hemophagocytosis' (Fig 1).

Lymph node biopsy was also done at our institute. Microscopic examination revealed a fragmented section of lymph node showing distorted nodal architecture. Large areas of necrosis with paucity of acute inflammatory cells like neutrophils and eosinophils were seen.

On higher magnification, numerous nuclear debris were seen in the necrotic area and numerous neutrophils were showing hemophagocytosis. Azzopardi phenomenon and haematoxylin bodies were not observed (Fig 2). Based on these findings a diagnosis of Kikuchi Fujimoto disease was given.

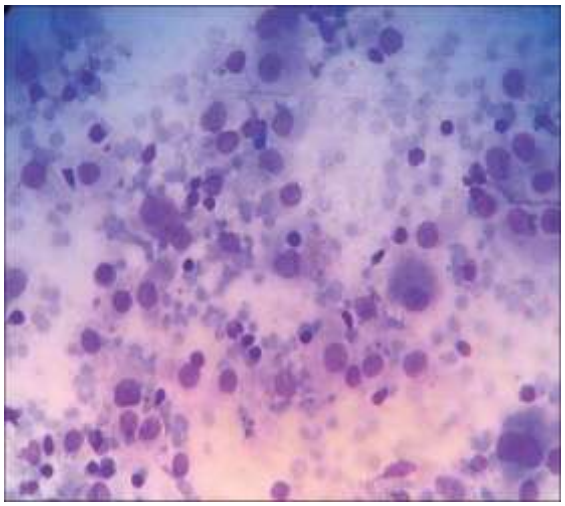

Fig 1: High power magnification showing numerous histiocytes showing hemophagocytosis. No granulomas or atypical cells seen (H&E x100).

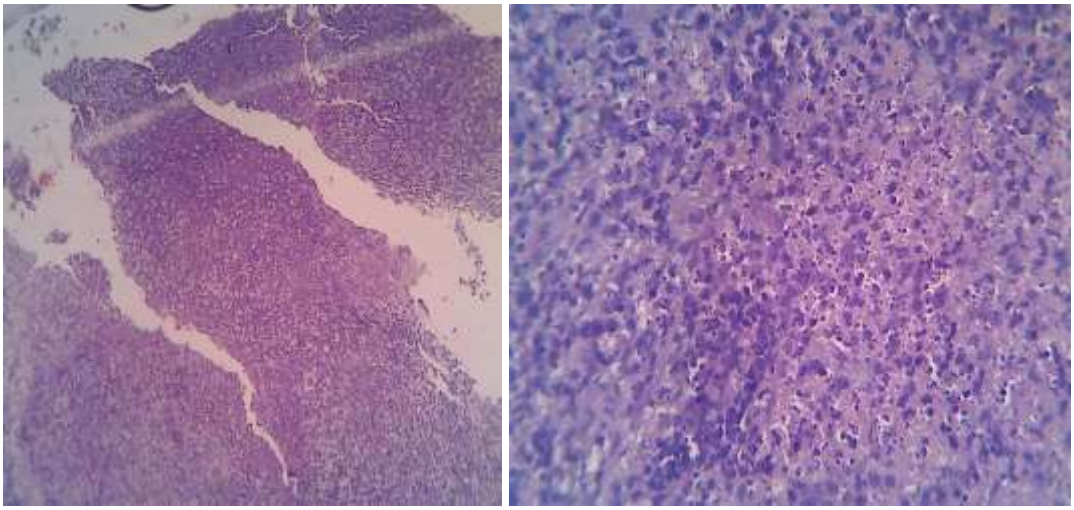

Fig 2a: Low power image showing fragmented lymphnode showing distorted nodal architecture. (H&E x200). Fig 2b: Higher magnification showing reactive lymphoid cells with areas of necrosis, necrotic debris, histiocytic proliferation showing hemophagocytosis and paucity of acute inflammatory cells (H&E X100).

Patient was started steroid of Prednisolone 1mg/kg for 8 weeks and then tapered for another 6 months. After one month of steroid therapy, patient became asymptomatic and there was significant reduction in the size of the lymphnode. After 2 months of steroid therapy, the

lymph nodes became non palpable and she gained 2 kg weight. Further follow up didn't show any recurrence of disease.

Discussion and review of literature

Kikuchi-Fujimoto disease (KFD) was first described independently by Kikuchi and Fujimoto in Japan in 1972.[1] It is also known as Kikuchi disease, necrotizing lymphadenitis, histiocytic necrotizing lymphadenitis, Kikuchi necrotizing lymphadenitis, sub acute necrotizing lymphadenitis and phagocytic necrotizing lymphadenitis. Earlier it was thought that is more common in female, but now studies show almost equal incidence in adults (M: F=1:1)[2], commonly in the 3rd decade. In children, the disease is more common in males (M: F=1.8:1).[3]

KFD usually presents as tender and painful cervical lymphadenopathy with fever. The onset is usually acute or subacute. The common location of the lymphadenopathy is the neck, however, rarely it can affect other locations like the axilla, mediastinum and retroperitoneum. In mediatinum, it can mimic thymoma or lymphoma. Piotr Błasiak et al[4] reported a case of 37-year-old female who had an oval tumour sized 6.5 × 4.7 × 5.3 cm with smooth contours in the upper front mediastinum in thorax CT scan which was suggestive of thymoma radiologically, later on she underwent excision biopsy and histopathology was suggestive of KFD. The etiology of KFD is complex and still is not clear but most likely cause of KFD is infectious or autoimmune. Some authors suggest that KFD may be an autoimmune disease that is triggered by a viral infection like Epstein-Barr virus (EBV), human immunodeficiency virus (HIV- 1), parvovirus B19, human T-cell lymphotropic virus (HTLV-1), human herpes viruses (HHV6, HHV-7, HHV-8), among these EBV is most common.[3,5]

Kuo[5] proposed a histopathological classification of KFD that includes 3 forms: proliferative, necrotic (most common) and xanthomatous (least common). The proliferative form can closely mimic lymphoma, whereas the necrotic form frequently mimics SLE lymphadenitis and infectious process like tuberculosis.

The important differential diagnosis of KFD includes Tuberculosis, Hodgkin's and non-Hodgkin's lymphoma, myeloid leukemia, lupus lymphadenitis, herpes simplex, Kawasaki's disease, and even metastatic carcinoma.[6]

In our country where Tuberculosis is more prevalent, KFD can mimic clinically, radiologically and pathologically tuberculosis. Many cases of KFD have been initially misdiagnosed as tuberculosis and treated with antituberculous medications.[7]

KFD can resemble SLE and also may occur in patients with pre-existing SLE, or simultaneously with SLE or evolve into SLE.[8]

Diego F Baenas et al[9] reported a case of a 27-year-old female, who had cervical lymphadenopathy and skin lesion. After detailed work up patient was found to have KFD by histopathology and SLE by SLE diagnostic criteria.

KFD may precede or follows other autoimmune disease like SLE, Sjogrens etc.

Jun Zhang et al[10] reported a 17-year-old girl pathologically diagnosed as KFD who suffered recurrence of KFD and developed into Sjogren's syndrome (SS) after four years of follow up. Gómez-Mariscal M et al[11] reported a case of Recurrent Bilateral Anterior Uveitis and cervical lymphadenopathy in a 31 year old female. Histopathology from lymph nodes proved KFD.

Associations: KFD is usually associated with autoimmune disease like autoimmune thyroiditis[12], myasthenia gravis[13], recurrent aseptic meningitis.[14]

Other disease like scarring alopecia[15], acute disseminated encephalomyelitis (ADEM)[16] etc have also reported to be associated with KFD.

Complications: Neuromyelitis optica spectrum disorder[17], SLE and Lupus Nephritis, Aseptic meningitis[18], encephalitis, peripheral neuropathy etc.

Jasti DB et al[19] reported a 15yr old female who had brainstem encephalitis with secondary blepharospasm in a diagnosed case of KFD.

Other complications: Disseminated intravascular coagulation (DIC)[20] caused death of a patient with KFD.

Diagnosis is confirmed by *Immunohistochemical profile*. The histiocytes of KFD express lysozyme, myeloperoxidase (MPO) and CD68. Plasmacytoid dendritic cells (plasmacytoid monocytes) are positive for CD123, CD303, CD68, HLA-DR, CD4 and CD74.

Clinical course and management. KFD is typically a self-limiting disease, which usually resolves within 1 to 4 months with recurrence rate of 3-13%[2], only symptomatic treatment like NSAID should be used.

Corticosteroids have been used in severe, relapse and recurrent cases and found to be effective.[3]

In cases with multiple recurrence of KFD other drugs like hydroxychloroquine has been used. Miri Hyun et al[21] used HCQ in his patient of 25 year old female, who had 4th time recurrence of biopsy proven KFD and in whom other therapy like NSAID and steroid was given in earlier episodes. Patient responded well with 4 month of HCQ of 3mg/kg/day.

M. Noursadeghi et al[22] used intravenous immunoglobulin in an 35-yr-old woman who had rapidly worsening lymphadenopathy causing impending airway obstruction, dysphagia to solids and periorbital oedema. Biopsy had confirmed KFD. Pulse high dose methylprednisolone and thalidomide had been ineffective.

CONCLUSION

KFD is rare, self-limiting and under-diagnosed disease of adults 20-30 years. It is mostly misdiagnosed as tuberculosis and lymphoma so awareness of this disorder by clinicians and pathologists is crucial to avoid misdiagnosis and inappropriate treatment. When treated appropriately it has excellent prognosis. The diagnosis is made only by identifying characteristic pathologic features from involved tissue.

A hyper-immune reaction of immune cells to EBV is most probably involved in the pathogenesis of KFD. Treatment is mostly symptomatic and sometime corticosteroids.

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