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Kikuchi's Lymphadenitis from a Surgical Perspective: A Case Report and Literature Review

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Abstract

Kikuchi-Fujimoto Disease (KFD) typically presents as cervical lymphadenopathy in young healthy women. Cervical lymph node involvement has been found in almost all of the previous studies, axillary lymph node involvement, however, was reported only in one out of eight cases reported from Nepal. In the 11 cases reported from India, all of them involved the cervical lymph nodes. In a retrospective study of 195 patients by Cheng et al., only 2.6% only had involvement of axillary lymph nodes.

Here we report a case of a 21-year-old male who presented with fever and right-sided axillary lymphadenopathy. Furthermore, in contrast to the typical presentation, the patient had a normal Erythrocyte sedimentation rate, thrombocytopenia and tested negative for EBV.

Keywords: Kikuchi-Fujimoto; Lymphadenitis; Immune response; *Yersinia*; Tuberculous

Abbreviations: KFD: Kikuchi Fujimoto Disease; EBV: Epstein Barr Virus; HIV: Human Immunodeficiency Virus; SLE: Systemic Lupus Erythematosus

Introduction

KFD, also known as histiocytic necrotizing lymphadenitis, is so named because Kikuchi and Fujimoto were the first scientists to describe it in Japan in 1972 [1]. It's a rare and self-limited syndrome characterized mostly with tender cervical lymphadenopathy, usually in a young, previously healthy woman. While the pathogenesis of Kikuchi disease is unknown, the clinical presentation, course, and histologic changes suggest an immune response of T cells and histiocytes to an infectious agent. Numerous inciting agents have been proposed, including Epstein Barr Virus (EBV), Human Herpesvirus 6, Human Herpesvirus 8, Human Immunodeficiency Virus (HIV), parvovirus B19, paramyxoviruses, parainfluenza virus, *Yersinia enterocolitica*, and Toxoplasma [2].

The diagnosis of Kikuchi disease relies on histology and microscopic examination of the lymph node, which is usually characterized by paracortical necrosis and infiltration of *histiocytes*. Here we present a case of a 21-year-old male with an atypical presentation of Kikuchi's disease who initially presented with a history of fever and a right-sided axillary lump.

Case Report

21-year old male not a known case of any medical illness who presented to the emergency department with a 3-week history of fever and a 2-week history of a right-sided axillary lump, review of other symptoms was otherwise negative including weight loss, headache, cough, abdominal pain, nausea, vomiting, diarrhea, joint pain and skin rash. He denied recent illness, sick contacts, recent travel and exposure to animals or unusual bites. The patient was diagnosed as a case of lymphadenitis in another hospital and was managed conservatively by antibiotics with no improvement. Upon presentation to our hospital the patient had a documented fever of 38.5°C. Physical exam was notable only for right oval-shaped axillary swelling almost 2.5 × 2 cm in size with red overlying skin and minimal tenderness on deep palpation left axillary, cervical, supraclavicular and inguinal lymph were not palpable. Among the multitude of tests that were carried out, white cell count was 3.04 × 109/L with 49% neutrophils, 42.6% lymphocytes, 7.5% monocytes, 0.2% eosinophils, 0.1% basophils and a platelet count of 123 × 109/L, Hemoglobin of 13.4 g/dL and a C-reactive protein of 6.4 mg/L. The patient was admitted under the care of internal medicine department with an impression of fever for further evaluation to rule out immunological disease and was started on ceftriaxone 2 g IV. Upon other investigations Blood and urine cultures showed no growth, Erythrocyte Sedimentation Rate was 20.0 mm/hr, Complements C3, C4, Anti-double stranded DNA (ds-DNA) and Anti-Smith were within the normal range, furthermore the EBV DNA, PCR and serum IGG and IGM were not detected. Ultrasound study of the axilla was done and it revealed few variable-sized lymph nodes' largest one was 4.1 × 2.4 suggesting a picture of right axillary lymphadenopathy (Figure 1), chest x-ray showed no pulmonary infiltrations, pneumonic consolidation bronchiectasis changes or mass lesions.

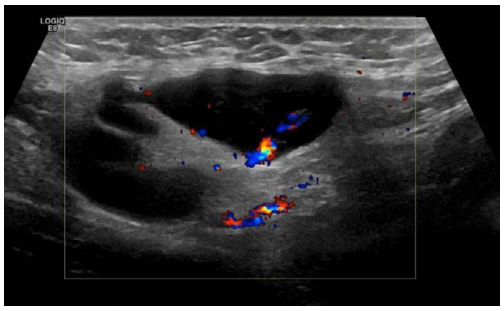

Figure 1: Spindle shaped large single right axillary lymph node with echogenic fatty hilum, hypervascular with thickened cortex measuring around 4 × 2 cm, no cystic or necrotic changes seen.

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During his hospital stay the patient continued to have fluctuating temperatures ranging from 37°C-38.8°C, White cell count continue to fluctuate as well with the lowest reading of 1.76 × 109/L. In regards to the laboratory abnormalities; antibiotic was changed to Tazocin 4.5 g, 6th hourly and the patient was kept on IV paracetamol regularly. On the 7th day of admission, general surgery team was consulted as the clinical presentations were considered to be suggestive of lymphoma. After the first week of admission, the patient settled down clinically, no spikes of fever were documented in the previous 24 hours and the patient completed 5 days of Tazocin so the decision was made by both teams to peruse the surgical intervention on an elective basis. After 14 days of the initial presentation, the patient underwent excisional biopsy of right axillary lymph nodes under general anesthesia. Microscopic examination of the samples showed a reactive lymph node containing sheets of histiocytes, focal areas of necrosis with karyorrhectic material (Figures 2-5). No evidence of malignancy was noted. Features of consistent necrotizing histiocytic lymphadenitis (Kikuchi's lymphadenitis) was concluded.

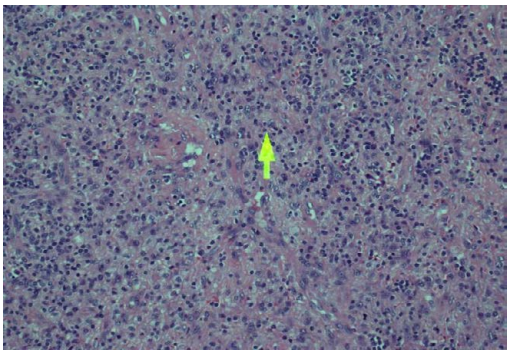

Figure 2: Sheets of histiocytes with chronic inflammatory cells low power view.

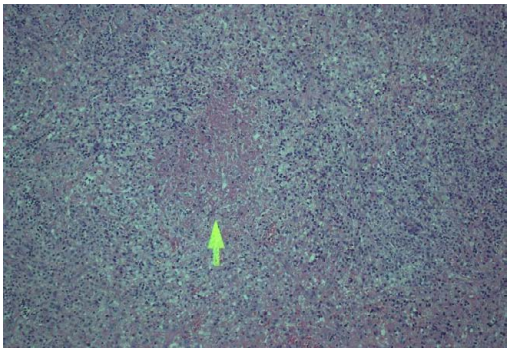

Figure 3: Sheets of histocytes with chronic inflammatory cells low power view.

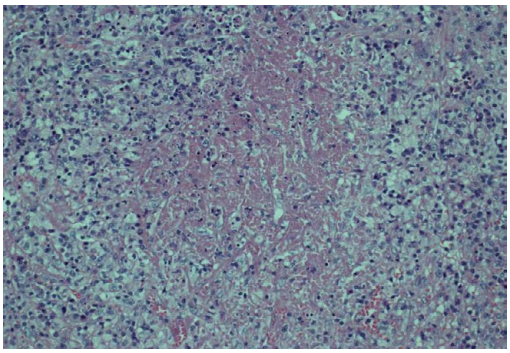

Figure 4: Hyper view of the necrotic area.

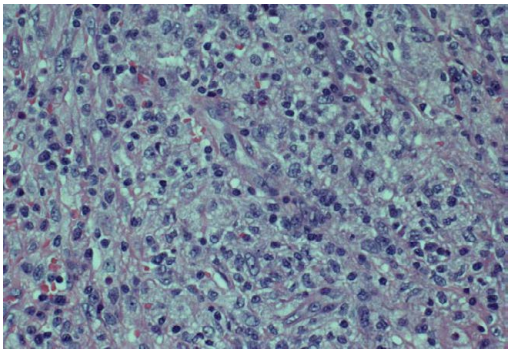

Figure 5: Low power view of histiocytes with chronic inflammatory cells.

Discussion

Kikuchi-Fujimoto Disease (KFD) was first reported in 1972 in Japan by Kikuchi and Fujimoto in two concurrent but separate case reports. It is an extremely rare disease, described as a lymphohistiocytic necrotizing lyphadenitis with "focal proliferation of reticular cells accompanied by numerous histiocytes and extensive nuclear debris" [3]. The aetiology of KFD is not well established. There is a hypothesis postulating that KFD develops as an immune response of T cells and histiocytes to a "provoking agent" [4].

A multitude of infectious agents have been implicated, including Ebstein Barr virus [5], *Yersinia enterocolitica*, parainfluenza, toxoplasma, parvovirus, and other paramyxoviruses [4]. An association between KFD and Herpesvirus 7 has also been proposed [6]. A meta-analysis found that KFD was not more associated with EBV than normal controls, while HHV was more likely to have an association, although not well established by the small sample size [7]. Epidemiologically, KFD presents in young adults with a mean age of 21 years according to a case series of 61 cases [8], and 25 years according to a case series of 244 cases, with 70% of patients younger than 30 years old [9]. Most commonly, KFD presents in females [10] in a case series of 244 cases, 77% of cases were female and 33% male [9]. Other sources report the ratio of 4:1 female to males [11]. There are multiple KFD cases reported worldwide, affecting individuals of many ethnic origins, but it is known to most commonly affect individuals of Asian origin. [12] Most of the cases were reported in Taiwan (36%), USA (6.6%), and Spain (6.3%) [9].

KFD's archetypal presentation is tender cervical lymphadenopathy with fever [13]. KFD has a characteristic tendency towards the posterior cervical nodes, observed in 83% of reported cases in a case review of 96 cases [14], and 88.5% in a review of 61 reported cases. Fever is one of the primary symptoms in 30%-50% of patients with KFD [13], followed by fatigue (7%) and joint pain (7%) [9]. The most common findings in KFD were reported to be lymphandenomegaly (100%), erythematous rashes (10%), hepatosplenomegaly (3%), leukopenia (43%), high ESR (40%) and anaemia (23%) [9].

There are only a few reports of KFD presenting as axillary lymphadenopathy. One reported case was an Indian woman in her 20's presenting with a solitary left axillary lump with systemic symptoms; fever, chills, loss of appetite, and generalized weakness [15]. Another reported case was that of a 56-year-old Greek male who presented with a nodal growth in the axilla and was otherwise asymptomatic [16]. Furthermore, there was a reported case of combined intra-mammary and axillary lymphadenopathy in a 30-year-old female [17].

The differential diagnosis for lymphadenopathy with a similar clinical presentation to KFD can include malignant lymphoma, sarcoidosis, SLE, tuberculosis, and HIV, other atypical forms of infection and some rare malignancies [4].

The definitive diagnosis of KFD is made through lymph node excisional biopsy and histological examination [18]. This disease has most commonly been misdiagnosed as malignant lymphoma [13]. A study showed that out of 108 lymph node biopsies of KFD reviewed, 30% were initially diagnosed as lymphomas [19]. Kikuchi-Fujimoto Disease (KFD) does not have an established treatment. Treatment offered is commonly supportive with analgesics (NSAIDs) and antipyretics to alleviate lymph node tenderness and pyrexia [19]. When symptoms are bothersome and uncontrolled there has been some reported improvement with using glucocorticoids [20]. KFD is usually benign and self-limiting with an acute or sub-acute onset, usually resolving in a span between 1 and 4 months [15]. The reported mortality rate is 2.1% [9]. A low recurrence rate has been reported in 3%-4% of cases [12]. It has been suggested that patients with KFD require a full workup and regular follow up lasting for a few years, as some go on to develop Systemic Lupus Erythematosus (SLE) [8].

Conclusion

Although Kikuchi-Fujimoto disease is known to be self-limiting with a mostly benign course, it can often imitate other conditions such as tuberculous lymphadenitis and malignant lymphoma. Thus, it is necessary for physicians to keep KFD in their list of differential diagnoses, as its treatment drastically differs from that of other conditions that present with lymphadenopathy. It is important in all cases presenting with lymphadenopathy to correlate clinical, radiological and histopathological findings in order to arrive in diagnosis with certainty prior to pursuing definitive treatment. Early recognition and diagnosis of the disease are can potentially minimize harmful and unnecessary investigations and treatments. Furthermore, leukopenia is present in a patient with lymphadenopathy; this can be a helpful indicator for the physician to suspect KFD.

In a patient diagnosed with KFD, it is important for the treating physician to ensure follow-up for the patient due to the possibility, albeit not common, of KFD recurrence or progression to SLE.

Conflict of Interest

We declare that there is no conflict of interest regarding the publication of this paper.

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