Case Report

Unveiling Kikuchi-fujimoto disease in systemic lupus erythematosus: Case report and comprehensive review of literature

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ABSTRACT

Kikuchi-Fujimoto disease (KFD) also referred to as histiocytic necrotizing lymphadenitis is an uncommon, non-malignant condition with unknown etiology. The diagnosis of KFD was hampered by the similarity to lymphoma, viral infections, and other autoimmune diseases. We present a 43-year-old female with a history of systemic lupus erythematosus (SLE) with a history of low-grade fever for 10 days, associated with chills, rigors, and pain over the posterior aspect of the neck with swelling. An excisional biopsy of the cervical lymph node confirmed the diagnosis of KFD. KFD should be considered in patients with SLE who presented with cervical lymphadenopathy and systemic symptoms. KFD is often confused with malignancy/tubercular lymphoma which requires costly diagnostic techniques and medications, but KFD is a self-limited condition.

Key words: Cervical lymphadenopathy, Glucocorticoids, Histopathology, Hydroxychloroquine, Kikuchi-Fujimoto disease, Systemic lupus erythematosus

Kikuchi-Fujimoto disease (KFD), also known as Kikuchi histiocytic necrotizing lymphadenitis, was initially documented in 1972 by Japanese researchers Seishi Kikuchi and Y. Fujimoto, who presented their findings independently in the same year [1]. KFD is an uncommon, non-malignant condition that resolves on its own and its cause is unclear. KFD exhibits a worldwide distribution, with a comparatively elevated occurrence among Asian and Japanese populations. Initial accounts indicated a female-to-male ratio of 4:1; however, newer research indicates that the ratio is considerably closer to 1:1 [2]. KFD often manifests as the enlargement of lymph nodes in the neck region accompanied by an elevated body temperature. The cause of KFD is still unknown; however, its clinical symptoms and histological abnormalities suggest that it involves a response from T-cells and histiocytes to an infectious pathogen. The diagnosis of KFD was hampered by the similarity to lymphoma, viral infections, and other autoimmune illnesses [2].

KFD is often misdiagnosed and underdiagnosed condition due to its rarity and its resemblance to other conditions, such as tuberculosis (TB) and malignancy, which results in inappropriate management. The coexistence of KFD with systemic lupus erythematosus (SLE) is notable because both conditions share immunological and inflammatory mechanisms, yet overlap is relatively rare. Reporting such cases contributes to medical literature which, in turn, helps clinicians to consider Kikuchi as a potential differential diagnosis when encountering cases of cervical lymphadenopathy. This case study examines a 43-year-old woman who has a confirmed diagnosis of SLE and is experiencing fever and swollen lymph nodes.

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CASE REPORT

A 43-year-old female with a history of SLE presented to the outpatient department with a 10-day history of low-grade fever, chills, rigor, generalized weakness, painful swallowing, and pain over the posterior aspect of the neck with swelling. The swelling had been progressively increasing over the past 3 months. She also reported decreased appetite, undocumented weight loss, and irregular menstrual cycles. She had a history of pulmonary TB treated 20 years ago and denied any substance abuse.

On examination, the patient was conscious and oriented. Her vital signs were as follows: Blood pressure 130/90 mmHg, pulse rate 112 beats/min, temperature 102.5°F, respiratory rate 20 breaths/min, and room air saturation 98%. Her body mass index was 21 kg/m^2. The general examination was unremarkable except for cervical lymphadenopathy. Local examination of the posterior

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cervical region revealed bilateral multiple cervical lymph node enlargements, with the largest measuring 1.3 cm. The nodes were nodular, firm, warm, and tender without ulceration or pus discharge.

The laboratory investigations of the patient are shown in Table 1. The baseline blood reports indicated anemia, leukopenia, and raised inflammatory markers. A computed tomography scan of the neck showed multiple enlarged bilateral cervical lymph nodes suggestive of an infectious etiology, primarily TB. However, sputum acid-fast bacteria, culture and sensitivity, and Mantoux tests were negative. Other infections such as hepatitis and HIV were suspected and immuno-serology was done which was negative, hence it is excluded.

An excisional biopsy of the affected lymph node was performed. Histopathology revealed lymph nodes with effaced architecture, extensive areas of geographic necrosis, karyorrhectic debris, histiocytes, and lymphocytes. Neutrophils were scarce, and no granulomas or atypia were observed. These findings confirmed the diagnosis of Kikuchi Fujimoto lymphadenitis.

The patient was admitted and managed conservatively with glucocorticoid therapy and hydroxychloroquine (HCQ). She also received antibiotics (injection sulbactam cefoperazone, tablet azithromycin), antipyretics, and analgesics for 3 days. The patient responded well to the treatment, and her symptoms resolved. On the 4th day of hospitalization, she was discharged with counseling that KFL is a self-limiting condition and advised to follow-up after 1 month. At the 1-month follow-up, the patient's neck swelling and fever had completely resolved.

DISCUSSION

The KFD exhibits a greater incidence in Asia and West Europe. This geographic preponderance may be attributed to the occurrence of certain human leukocyte antigen (HLA) alleles, including HLA Class II alleles, HLA-DPA1, and HLA-DPB1, in these populations [3]. The research found that the average age of individuals with KFD was 32.7 ± 8.8 years, which is consistent with our own study [4]. Prior research has demonstrated that the occurrence of KFD is higher among females, with a ratio of 4:1 (female: Male). However, new investigations have indicated that the incidence is really much closer to 1:1, suggesting that the previous findings may have exaggerated the increase in cases. The precise occurrence and frequency of this disorder within the general population have not yet been ascertained [5,6].

Table 1: Initial laboratory investigations of the patient

Laboratory parameters	Patients value	Normal range
Hemoglobin (g/dL)	7.3	12–15
PCV (%)	26	36–46
TC (cells/mm^3)	3400	4000–11000
Platelets (L/mm^3)	1.72	1.5–4.0
MCV (fL)	72.3	80.0–100.0
MCH (pg)	24	27.0–32.0
MCHC (g/dL)	26.8	30.0–35.0
Total bilirubin (mg/dL)	0.4	0.3–1.2
SGOT (U/L)	34	Upto 31
SGPT (U/L)	46	Upto 34
ALP (U/L)	141	42–98
ESR (mm/h)	96	0–20
CRP (mg/dL)	80	<6
Uric acid (mg/dL)	2.5	3.0–6.0

PCV: Packed cell volume, TC: Total count of white blood cells, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic-pyruvic transaminase, ALP: Alkaline phosphatase, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein

KFD is an uncommon condition that leads to lymphadenopathy, which is the enlargement of lymph nodes. It is characterized by the presence of benign necrotizing lymphadenitis, which is the inflammation and death of lymph node tissue. Due to its similarities with other causes of lymphadenopathy, such as TB and lymphoma, KFD is sometimes misdiagnosed. Despite being first reported in 1972, KFD has been a challenge to doctors due to its infrequency and ambiguous clinical presentation, often resulting in many cases of underdiagnosis [7]. Research found that 40% of patients were incorrectly classified as lymphoma [8]. Our study found that it was misdiagnosed as TB, which raises issues regarding the costly treatment of a minor, self-limiting infection.

The precise etiopathogenesis of KFD is not well understood and continues to be a topic of debate. Nevertheless, KFD can be linked to the expansion of CD8+ T cells caused by either autoimmune or infection. Multiple studies have indicated that viruses such as Epstein-Barr virus may have the ability to contribute to certain conditions [3,9]. Research and case studies have shown a strong correlation between KFD and autoimmune conditions such as SLE. SLE has been diagnosed before, subsequent to, or simultaneously with KFD. When diagnosing KFD, it is essential to assess patients for SLE and to regularly monitor them to prevent the development or advancement of SLE [10,11]. The patient in our research had previously been diagnosed with SLE at the age of 20 and was receiving steroid treatment.

Several investigations have indicated that the most common clinical characteristic of KFD is the presence of unilateral cervical lymphadenopathy, which affects the lymph nodes located in the posterior triangle in 56–98% of cases [2]. The dimensions of impacted lymph nodes often vary between 0.5 and 4 cm, with rare instances where they surpass 6 cm. In addition, 30–50% of patients exhibit a little increase in body temperature and experience symptoms related to the upper respiratory system [1,12]. The patient displayed a mild fever and swelling of the lymph nodes on the left side of the neck, measuring 1.3 cm, which is in line with these observations. Approximately 40% of patients have skin involvement, which can range from a non-specific rash to lupus-like characteristics. Infrequently reported symptoms include nausea, vomiting, night sweats, arthralgia, weight loss, sore throat, weariness, and rash. KFD predominantly presents in lymph nodes, with cutaneous involvement being the most prevalent extranodal location. Occasionally, it can also impact organs such as bone marrow and liver [12-14]. The

laboratory results in KFD are not specific and may show signs of anemia, thrombocytopenia, increased liver enzymes, raised levels of lactate dehydrogenase, and an elevated erythrocyte sedimentation rate (ESR) [4]. Imaging scans commonly reveal enlarged lymph nodes, which might offer supportive evidence but not a conclusive diagnosis. The diagnosis of KFD is determined by histopathologic examination of the afflicted lymph nodes. Some characteristic findings include follicular hyperplasia, larger paracortical regions, well-defined necrotic patches, and necrotic foci. Performing fine needle aspiration or biopsy is essential to definitively establish the diagnosis [4]. The patient's laboratory findings revealed the presence of anemia, leukopenia, elevated levels of C-reactive protein, and an increased ESR. The patient's diagnosis was verified following the histology report.

KFD is a self-limiting condition that usually disappears after a few months under conservative management, but there is currently no established medication that is successful. Analgesics, antipyretics, and non-steroidal anti-inflammatory drugs can provide symptomatic relief for lymphadenopathy and associated symptoms. If patients experience severe or persistent symptoms, they may be treated with glucocorticosteroids and intravenous immunoglobin [10,12]. In our investigation, the patient exhibited a broad range of symptoms. Given her previously diagnosed case of SLE, she was treated symptomatically using antipyretics and glucocorticoid treatment.

CONCLUSION

KFD should be considered in patients with SLE who present with cervical lymphadenopathy and systemic symptoms. This case emphasizes the importance of histopathological examination for accurate diagnosis, differentiating KFD from conditions, such as TB and lymphoma. Conservative management with glucocorticoids and HCQ proved effective in this patient, leading to symptom resolution. Increased awareness and recognition of KFD in clinical practice are essential for timely and appropriate management, especially in patients with underlying autoimmune conditions.

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