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KIKUCHI-FUJIMOTO DISEASE IN A YOUNG FEMALE: A CASE REPORT

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Abstract:
Kikuchi-Fujimoto Disease (KFD) is an uncommon, non-cancerous inflammatory condition of the lymph nodes that typically affects young women of Asian descent. It often manifests through vague clinical signs such as fever and swollen lymph nodes in the neck, which can easily be mistaken for more serious illnesses, including lymphoma or systemic lupus erythematosus (SLE). The difficulty in diagnosis is heightened by the lack of distinctive features on imaging studies, making histopathological examination via lymph node biopsy vital for establishing a definitive diagnosis and preventing incorrect treatment. This case involves a 25-year-old woman who experienced persistent fever and multiple painful cervical lymph nodes for two weeks. Blood tests indicated mild anemia and an increased erythrocyte sedimentation rate (ESR). Ultrasound revealed several solid, avascular nodules, and biopsy findings confirmed the presence of KFD. Treatment focused on symptom relief using non-steroidal anti-inflammatory drugs (NSAIDs), resulting in full recovery within a fortnight. Due to the disease's possible links with autoimmune conditions and its tendency to recur, ongoing monitoring of patients is essential. This case highlights the necessity of precise identification to avoid overtreatment and calls attention to the importance of further studies on KFD's underlying mechanisms, potential early diagnostic markers, and long-term patient outcomes to enhance clinical care.

Key words: Kikuchi-Fujimoto disease; lymphadenopathy; case report; autoimmune diseases; young women.

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INTRODUCTION

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare and unexplained condition that typically causes lymph node inflammation and tends to resolve on its own without aggressive treatment (Kikuchi, 1972; Saravanan et al., 2021; Soub et al., 2021). Kikuchi-Fujimoto disease is an uncommon, self-resolving illness that generally follows a mild course, frequently presenting with fever and localized swollen lymph nodes. While it is most often identified in Asian women, the condition can affect individuals of any gender equally (Bennett et al., 2016; Tsang J. K. et al., 1994). A viral origin has been proposed as a possible cause in the development of the disease, although the precise cause is still unknown. Management typically involves supportive care, as KFD usually resolves spontaneously within days to weeks without specific treatment. In rare instances, corticosteroids are prescribed for severe or persistent symptoms that do not respond to standard symptomatic therapy (Xu W. & Liu J., 2019).

Kikuchi-Fujimoto Disease (KFD), also known as histiocytic necrotizing lymphadenitis, is an uncommon, benign inflammatory condition that mainly involves the lymph nodes. Initially identified independently by Kikuchi and Fujimoto in Japan in the early 1970s, KFD has since been reported globally, though it remains a rare diagnosis. The disorder predominantly affects young adults, particularly females, with a greater incidence observed in Asian populations. Despite its infrequency,

KFD poses a diagnostic dilemma because its symptoms are nonspecific and can closely mimic other serious diseases such as lymphoma and systemic lupus erythematosus (SLE).

The etiology of KFD remains uncertain and is an area of active research. Several viral agents have been implicated as possible triggers, such as EBV, human herpesvirus 6 and 8, parvovirus B19, and CMV (Kerr, 2019; Moore et al., 2020; Münz, 2023; Tabibzadeh et al., 2020). However, no conclusive evidence has established a direct causal relationship between these viruses and KFD. Besides infectious triggers, autoimmune mechanisms have also been proposed. The frequent association of KFD with autoimmune diseases, particularly SLE, suggests that dysregulated immune responses play a critical role in its pathogenesis. This autoimmune hypothesis is supported by histopathological findings and immunophenotyping studies showing aberrant activation of T-cells and histiocytes.

Clinically, Kikuchi-Fujimoto disease usually manifests as painful swelling of the lymph nodes in the neck, often accompanied by systemic signs like elevated temperature, sweating at night, exhaustion, and unintended weight reduction. This lymph node swelling generally appears on one side and is focused in the back portion of the cervical area, though in some cases, the enlargement may be widespread. Other symptoms, including rash, arthralgia, and hepatosplenomegaly, are reported less frequently. Because these symptoms overlap with infectious, autoimmune, and malignant diseases, clinicians often face difficulty in establishing a timely and accurate diagnosis without histological confirmation.

Diagnosing Kikuchi-Fujimoto disease primarily depends on the histological analysis of a surgically removed lymph node. Key microscopic findings include areas of cell death within the paracortex containing extensive fragmented nuclear material, a predominance of histiocytes and plasmacytoid monocytes, and a notable lack of neutrophils and eosinophils. Immunohistochemical staining typically identifies histiocytes expressing CD68 and T cells positive for CD8. These distinguishing characteristics aid in differentiating KFD from conditions such as lymphoma, tuberculosis, and other inflammatory lymph node disorders. Since fine-needle aspiration biopsies frequently provide insufficient information, complete excision of the lymph node remains the preferred method to confirm the diagnosis.

The clinical course of KFD is generally self-limiting, with spontaneous resolution occurring within one to six months in most cases. Treatment is primarily supportive, aimed at relieving symptoms such as fever and pain. NSAIDs are frequently used to alleviate mild symptoms. For patients experiencing more intense or prolonged symptoms, treatment may involve corticosteroids or immunosuppressants, although a universally accepted therapy regimen has yet to be established. Careful and ongoing clinical monitoring is advised because of the possibility of relapse and the emergence of related autoimmune disorders.

Epidemiological studies indicate a higher incidence of KFD among young females, with a female-to-male ratio ranging from 3:1 to 4:1. The disease is most frequently diagnosed in individuals aged between 20 and 35 years. Nevertheless, cases have been reported across all age groups, including children and elderly patients. Geographic variation is also noted, with the highest prevalence reported in East Asia, especially Japan, Korea, and China, although the condition is increasingly recognized worldwide due to greater clinical awareness and improved diagnostic techniques.

Imaging techniques like ultrasound, CT scans, and MRI may offer helpful insights; however, they do not provide definitive or specific diagnostic information. Ultrasonography typically shows hypoechoic, well-defined lymph nodes with preserved fatty hilum. CT and MRI scans may reveal lymphadenopathy with characteristic features, but cannot definitively differentiate KFD from malignancies or infections. Thus, imaging primarily serves as a tool for assessing disease extent and guiding biopsy sites rather than for diagnosis.

The range of conditions to consider when diagnosing KFD is extensive, encompassing infectious lymph node inflammation, various lymphomas, tuberculosis, systemic lupus erythematosus (SLE), and other autoimmune disorders. The overlapping clinical and radiological features necessitate a high index of suspicion and histopathological confirmation to avoid misdiagnosis. Misidentification of KFD as lymphoma or other malignancies can lead to unnecessary aggressive treatments such as chemotherapy, underscoring the importance of accurate diagnosis.

Recent advances in immunopathology have shed light on the mechanisms underlying KFD. Studies reveal that apoptotic cell death, triggered by immune activation, contributes to the characteristic necrotizing lesions. The involvement of plasmacytoid dendritic cells and type I interferons suggests an aberrant antiviral immune response. However, the exact interplay of these immune components remains under investigation, with ongoing research focusing on elucidating molecular pathways and potential biomarkers.

While KFD is generally considered benign, its association with autoimmune diseases, especially SLE, warrants attention. Several cases have documented patients initially diagnosed with KFD who later developed SLE, indicating a possible continuum or shared pathogenic mechanism. This relationship highlights the need for long-term monitoring of KFD patients for the emergence of autoimmune disorders, which may alter clinical management and prognosis.

In brief, Kikuchi-Fujimoto Disease is an uncommon, self-resolving inflammation of the lymph nodes with an unknown cause, predominantly seen in young adults. Its symptoms and microscopic characteristics can be difficult to distinguish, frequently resembling more severe diseases like lymphoma or systemic lupus erythematosus. Despite its benign course, the potential for recurrence and association with autoimmune diseases necessitates careful follow-up. Increasing awareness, improving diagnostic accuracy, and understanding its pathogenesis are crucial for the appropriate management and prevention of misdiagnosis.

Kikuchi-Fujimoto Disease (KFD) is a rare, self-limiting condition characterized by necrotizing lymphadenitis predominantly affecting young adults, especially women in Asian populations. Despite its benign nature, KFD presents significant diagnostic challenges due to its nonspecific clinical presentation, which closely mimics serious diseases such as lymphoma, tuberculosis, and systemic lupus erythematosus (SLE). The limited awareness among clinicians and the rarity of the disease often lead to misdiagnosis and inappropriate treatment, underscoring the need for a better understanding of its etiology, clinical features, and diagnostic approaches.

Accurate diagnosis of KFD is urgent because misidentification can lead to unnecessary aggressive therapies, including chemotherapy or extensive antibiotic use, which increase patient morbidity and healthcare costs. Given that KFD can spontaneously resolve, early recognition would avoid overtreatment and psychological distress associated with misdiagnosis of malignancy. Furthermore, the potential link between KFD and autoimmune diseases such as SLE requires clinicians to maintain vigilance for disease progression or complications, necessitating long-term patient follow-up.

The scarcity of comprehensive epidemiological data on KFD, especially in non-Asian populations, and the lack of standardized treatment protocols emphasize the urgency to conduct research that elucidates the disease's pathophysiology and natural history. This will contribute to improved diagnostic accuracy, patient management, and the development of guidelines for monitoring autoimmune sequelae.

Several studies have described the clinical and histopathological characteristics of KFD. Tsang J. K. et al. (1994) analyzed 75 cases and highlighted the distinct histologic features differentiating KFD from malignant lymphadenopathies. Their work laid foundational knowledge for pathologists, but did

not extensively explore the immunological mechanisms behind the disease. Bosch A. et al. (2004) provided a comprehensive review emphasizing the enigmatic nature of KFD, its self-limiting course, and potential viral triggers, yet concluded that definitive causative agents remain unidentified.

More recent research by Kim K. S. et al. (2014) focused on pediatric versus adult presentations, revealing age-related differences in clinical manifestations and outcomes. Their findings underscored the need for tailored diagnostic and management approaches across age groups. Meanwhile, Sousa J. M. A. et al. (2010) presented case reports emphasizing the association of KFD with autoimmune diseases, suggesting a potential shared immunopathogenesis but highlighting the need for larger, longitudinal studies to validate this relationship.

Despite growing literature, significant gaps remain in understanding KFD's precise etiology and its immunopathological mechanisms. There is limited data on long-term outcomes and the progression from KFD to autoimmune disorders, particularly SLE. Moreover, the variability in clinical presentations across different ethnicities and age groups is insufficiently documented. This lack of standardized diagnostic criteria and treatment guidelines contributes to inconsistent patient management worldwide.

This study advances current knowledge by integrating clinical, histopathological, and immunological data from a documented case of KFD in a young Asian female, with a thorough review of diagnostic challenges and treatment outcomes. It uniquely emphasizes the importance of differential diagnosis and long-term surveillance for autoimmune conditions post-KFD. The case report format enriches existing literature by providing detailed clinical follow-up, thereby contributing valuable insight into disease prognosis and management.

The primary objective is to report and analyze a confirmed case of Kikuchi-Fujimoto Disease, detailing clinical presentation, diagnostic workup, and therapeutic management. Secondary aims include reviewing the literature to contextualize the disease within broader clinical practice, highlighting diagnostic pitfalls, and stressing the importance of long-term follow-up for autoimmune complications.

The findings provide clinicians with practical insights into recognizing and managing KFD, potentially reducing misdiagnosis and inappropriate treatments. The study reinforces the need for awareness of KFD's clinical spectrum and the role of lymph node biopsy in diagnosis. Additionally, it informs healthcare providers about the importance of monitoring for autoimmune diseases following KFD, thereby improving patient outcomes and guiding future research priorities.

METHOD

The method used in this case study was a descriptive clinical approach involving direct observation and comprehensive diagnostic evaluation of a patient presenting with lymphadenopathy. The diagnostic process included thorough clinical examination, routine laboratory tests, ultrasound imaging of the lymph nodes and thyroid, and lymph node biopsy for histopathological analysis to confirm the diagnosis of Kikuchi-Fujimoto Disease. Additional supportive investigations, such as antinuclear antibody (ANA) testing and chest X-ray, were performed to exclude other possible conditions. This approach focuses on collecting empirical data through physical examination, laboratory diagnostics, and imaging to describe the patient's clinical condition and assess the response to symptomatic treatment with non-steroidal anti-inflammatory drugs (NSAIDs).

Case report:

A 25-year-old female presented to us with multiple neck swellings, fever, of 14 days duration. The patient did not report any weight loss or prior history of tuberculosis, and had no other notable medical conditions. On physical examination, multiple tender and mobile lymph node swellings were found bilaterally in the cervical region, with no detectable lymphadenopathy elsewhere. Vital signs showed a blood pressure of 120/70 mm Hg and a pulse rate of 88 beats per minute.

Cardiovascular, respiratory, and neurological assessments were unremarkable. The abdomen was soft, with normal bowel sounds, and both skin and throat examinations were within normal limits. Routine blood tests, including hemoglobin, complete blood count, and peripheral smear, were all normal. Additionally, blood glucose, urea, creatinine, electrolytes (sodium, potassium, bicarbonate), as well as liver and kidney function tests, were within normal range.

Table 1. Laboratory Examination

TYPE OF EXAMINATION		RESULT
Hemoglobin	L	**10.8**
Hematocrit	L	**34.9**
Eritrosit		4.37
MCV		80
MCH	L	**25**
MCHC	L	**30.9**
Leukocytes		4.83
Diff Count		
Basofil		1
Eosinofil		1
Neutrofil		51
Lymphocyte		35
Monosite	H	**12**
Neutrophil/ Lymphocyte Ratio		1.5
Absolute Lymphocyte Count		1691
Platelet		360
ESR (Westergren)	H	**66**
CARBOHYDRATE		
Random Blood Glucose		85
AGD & ELECTROLYTES		
Sodium (Na)		135
Potassium (K)		3.7
Chloride (Cl)	H	108
Calcium Ion (Ca++)		1.27
LIVER FUNCTION		
AST		14
ALT		10
KIDNEY FUNCTION		
Ureum	L	13
Creatinine		0.70
eGFR		122

On thyroid ultrasound examination, multiple solid nodules with clear boundaries were found, with CDUS vascularization (-) in the right and left colli and the right supraclavicular area. There were no abnormalities in the right and left thyroid parenchyma.

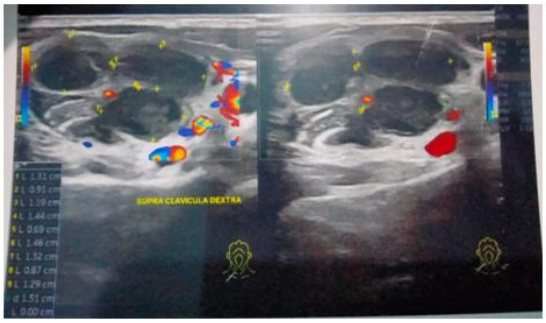


Figure 1. Ultrasound Right Supraclavicular

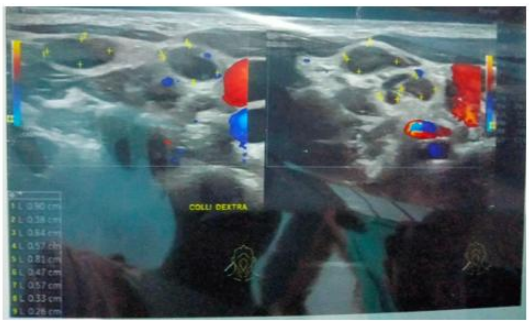


Figure 2. Ultrasound Right Colli

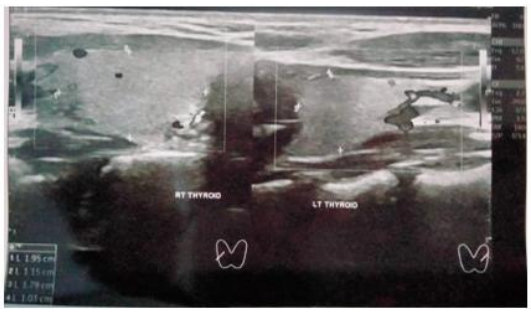


Figure 3. Ultrasound Right and Left Thyroid

Antinuclear antibody (ANA) was negative, chest X-ray was normal, lymph node biopsy was done, and the histological features suggested the diagnosis of Kikuchi-Fujimoto disease.

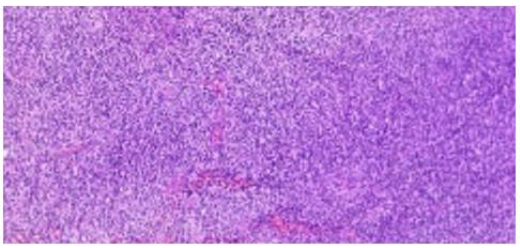


Figure 4. Histopathology of Kikuchi-Fujimoto disease. Several atypical nucleated cells were found

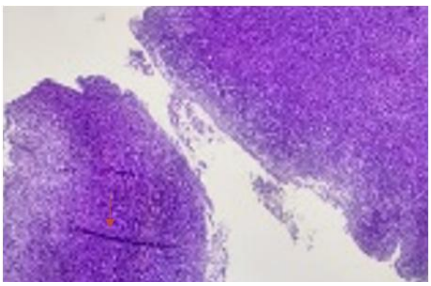


Figure 5. Large geographic areas of necrosis (Haematoxylin & Eosin, 40x). Fragment of incomplete lymph nodes with lymphoid follicles containing "Tangible Body Macrophages". Dilated sinuses containing lymphocytes and histiocytes

The Patient was treated symptomatically with non-steroidal anti-inflammatory drugs, and the lymph nodes regressed in two weeks.



Figure 6. Clinical nodules on colli after treatment were treated with non-steroidal anti-inflammatory drugs

RESULT AND DISCUSSION

Kikuchi-Fujimoto Disease is a benign condition that typically resolves on its own, so most patients require only supportive care. NSAIDs are commonly administered to reduce lymph node pain and fever. In more severe cases, corticosteroid therapy has been suggested (Jang K. et al., 2000). For patients experiencing persistent or intense symptoms, treatment may involve glucocorticoids or high-dose glucocorticoids combined with intravenous immunoglobulin (Lin M. S. et al., 2010).

Kikuchi-Fujimoto Disease predominantly affects young Asian females, most frequently occurring between the ages of 25 and 29, with the ratio of males to females ranging from 1:3 to 1:4 (Bosch A. et al., 2004). This patient is a young Asian woman who came with multiple lymph node tenderness and fever

Kikuchi's disease typically manifests as swollen lymph nodes in the neck region, which may be tender and often accompanied by fever and symptoms resembling an upper respiratory infection. Less frequently, patients may experience joint pain, skin eruptions, fatigue, and night sweats. Other reported signs include weight loss, diarrhea, loss of appetite, chills, nausea, vomiting, as well as chest and abdominal discomfort. Some cases have also shown enlargement of the liver and spleen. The precise cause of Kikuchi's disease remains unclear. Various viral agents—such as Epstein-Barr virus (EBV), HIV, Herpes simplex virus, dengue virus, HTLV-1, and Parvovirus B19—have been proposed, but none have been definitively linked to the disease. Additionally, bacterial pathogens like Toxoplasma, Yersinia enterocolitica, Bartonella, and Brucella have been considered. An autoimmune origin has also been suggested, given that Kikuchi's disease can occur alongside systemic lupus erythematosus (SLE). Although multiple reports indicate a possible connection between KFD and SLE, conclusive evidence is still lacking. Overall, the mechanisms driving the development of Kikuchi's disease are yet to be fully elucidated (Sousa J. M. A. et al., 2010).

Kikuchi-Fujimoto Disease is regarded as a self-resolving immune-related disorder triggered by virus-infected transformed lymphocytes. Additionally, the disease process may involve the activation of proliferating cytotoxic CD8+ T cells that induce programmed cell death (apoptosis) (Norris A. M. et al., 1996). The condition typically follows a mild course, resolving on its own within several weeks to months, with a low recurrence rate of about 3–4%. Nonetheless, extended monitoring is advised, particularly because of the potential for relapse and the suggested link between KFD and the development of autoimmune disorders such as systemic lupus erythematosus (Ramirez J. et al., 1999). The patient's symptoms improved after treatment with steroids, within two weeks.

The confirmation of Kikuchi-Fujimoto Disease (KFD) necessitates performing a lymph node biopsy coupled with immunohistochemical analysis. Patients diagnosed with KFD require prolonged monitoring to ensure complete remission and to identify any relapse promptly. A definitive diagnosis hinges on the histopathological examination of the lymph node, which also helps rule out more severe conditions such as lymphoma. The lymph node histology in KFD exhibits distinct patterns, setting it apart from lymphadenopathies caused by infections. Biopsy specimens typically show unevenly distributed paracortical regions of coagulative necrosis accompanied by nuclear debris, which disrupts the normal nodal structure. Additionally, there is a notable presence of immune cells, including myeloperoxidase-positive elements, CD68-positive and CD123-positive cells, plasmacytoid dendritic cells, and activated CD8+ T cells. When considering differential diagnoses, it is essential to distinguish KFD from lymphoma, tuberculous lymphadenitis, systemic lupus erythematosus, lymphogranuloma venereum, Kawasaki disease, metastatic cancers, infectious mononucleosis, toxoplasmosis, Yersinia infections, cat-scratch disease, and AIDS.

Lymph node enlargement occurs universally among patients, with approximately 90% showing involvement in the posterior cervical region, while generalized lymphadenopathy is seen in fewer than 22% of cases. The affected lymph nodes typically measure between 0.5 and 4.0 centimeters. Fever and painful, tender lymph nodes are frequent clinical features in those diagnosed with Kikuchi-Fujimoto Disease. Nearly 90% of patients experience a fever ranging from 38.6°C to 40.5°C, which persists for anywhere from one to seven weeks. Tenderness in the lymph nodes is reported in about 82% of cases. Additional clinical manifestations may include unintentional weight loss, nausea, vomiting, fatigue, headaches, night sweats, and symptoms resembling upper respiratory infection (Kim K. S. et al., 2014; Singh C. B. & Shermetaro, 2019).

Although Kikuchi's disease typically resolves on its own, ongoing monitoring for several years is important because a subset of patients may eventually develop systemic lupus erythematosus (SLE). This case report has certain limitations: the definitive diagnosis of KFD relies primarily on an excisional biopsy, an invasive procedure, and immunohistochemical testing was not conducted due to a lack of coverage by government insurance. Additionally, the brief duration of follow-up prevents us from determining whether the patient might develop SLE later on.

CONCLUSION

Kikuchi-Fujimoto Disease (KFD) is a rare and benign condition that predominantly affects young Asian women, characterized by variable clinical presentations that can mimic other diseases, making diagnosis challenging. Imaging findings in KFD are non-specific and therefore insufficient for definitive diagnosis. Consequently, lymph node biopsy remains essential to avoid misdiagnosis or missed diagnosis and to guide appropriate treatment. Given the potential for disease recurrence and the association with autoimmune disorders, long-term follow-up of patients is crucial. For future research, it is recommended that longitudinal studies be conducted to understand the natural history of KFD better, identify biomarkers for early diagnosis, and investigate the mechanisms linking KFD with autoimmune diseases, thereby improving patient management and outcomes.

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