Case Report

Kikuchi-Fujimoto Disease: A Diagnostic Challenge in Histiocytic Necrotizing Lymphadenitis

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Abstract

Kikuchi-Fujimoto disease (KFD) is a rare, self-limiting lymphadenitis characterized by fever and cervical lymphadenopathy. Its etiology is unclear but is linked to immune responses to viral or bacterial infections. Diagnosis relies on histopathological examination due to similarities with tuberculosis, lymphoma, and systemic lupus erythematosus (SLE). This case report highlights a 39-year-old woman initially misdiagnosed with tuberculosis, later confirmed to have KFD. Awareness and accurate differential diagnosis are crucial for appropriate management and avoiding unnecessary treatment.

Key words: *Kikuchi-Fujimoto Disease, Necrotizing Lymphadenitis, Lymphoma, Tuberculosis, Diagnostic Challenge.*

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Introduction

Kikuchi-Fujimoto disease (KFD), formally termed histiocytic necrotizing lymphadenitis, is an uncommon inflammatory disorder that predominantly targets the lymph nodes. First recognized in Japan in 1972 by Masahiro Kikuchi and Y. Fujimoto, this condition is self-limiting and distinct in its pathological characteristics.[1,2] This disease typically presents with fever, lymphadenopathy (often cervical 80%), and constitutional symptoms such as fatigue and night sweats.[3] Although its exact etiology remains unclear, it is widely believed to involve immune-mediated mechanisms triggered by infections, particularly viral agents like Epstein-Barr virus (EBV) and human herpesvirus 6 (HHV-6).[1]

KFD predominantly affects young adults, with an average onset between the ages of 20 and 30. It is more commonly found in women, occurring at a ratio of 3:1 compared to men. This gender disparity is hypothesized to happen because women are more likely to develop autoimmune conditions, their hormones can affect how the immune system works, and they may carry certain genes that make them more prone to the disease.[3, 4] KFD was first found in East Asian countries like Japan, Korea, and Taiwan, where it is still more common. However, it is now known to occur in many parts of the world. Cases have been reported in different regions, showing that the disease can affect people of various backgrounds and is not limited to any one ethnicity or environment.[6,7] Diagnosis relies on histopathological examination of lymph node biopsies, revealing characteristic findings of necrotizing lymphadenitis with histiocytes and plasmacytoid dendritic cells but no neutrophilic infiltration. The disease is often mistaken for lymphoma, systemic lupus erythematosus (SLE), or other infectious causes due to overlapping clinical and histological features.[5,8] Raising awareness of this disorder is crucial for reducing the misdiagnosis and promoting appropriate treatment strategies.

Case summary

A 39-year-old female housewife presented to Khwaja Yunus Ali Medical College, Bangladesh, a tertiary-level hospital with a 10-days history of gastrointestinal symptoms, including severe nausea, occasional vomiting, loss of appetite, and generalized abdominal discomfort. She reported the presence of a noticeable swelling on the left side of her neck, which had been aspirated and cytologically evaluated. The cytological examination findings indicated chronic inflammation, with no evidence of granulomatous inflammation, multinucleated giant cells, or caseous necrosis.

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Despite the absence of definitive cytological evidence suggestive of tuberculosis, the patient was empirically started on a Category I (CAT-I) anti-tuberculosis therapy regimen 14 days prior to admission. She denied classical systemic symptoms of tuberculosis such as fever, night sweats, and unintentional weight loss, and had no known history of close contact with individuals diagnosed with tuberculosis.

Upon clinical examination, a solitary, non-tender, firm supraclavicular lymph node was palpated on the left side. Ultrasonography of the neck region revealed no evidence of necrosis or fluid collection within the lymph node. Considering the findings, a lymph node biopsy was performed for definitive diagnosis.

Histopathological examination of the biopsy specimen revealed a necrotizing lesion (Figure 1) consistent with Kikuchi-Fujimoto disease (histiocytic necrotizing lymphadenitis), a rare and self-limiting inflammatory condition often mistaken for tuberculosis or lymphoma in its early presentation. This finding led to a reassessment of the initial empiric anti-tuberculosis treatment, emphasizing the importance of histopathological confirmation in cases with atypical presentations.

Table I: Laboratory data

Variable	Result	Reference range
Hemoglobin (g/dl)	11.6	11.5 - 16
Platelet count (c/mm)	265	150 - 450
White blood cell count (c/mm)	4.49	4-11
Neutrophil (%)	78.2	40 - 75
PCV(%)	34.8	6 - 46
Erythrocyte sedimentation rate (mm/hr)	64	0 - 20
Serum bilirubin (µmol/L)	11.74 (4.37)	2 - 21
SGPT(U/L)	148 (10)	<35
AST(U/L)	415	<35
ALP(U/L)	64 (45)	20 - 130
Prothrombin time (second)	13.10	9 - 13
D - dimer (mg/L)	2.20	<0.5
CRP (mg/L)	48	10 - 20
ANA (AU/ml)	17.13	Negative: <40.0 AU/ml
Serum creatinine (µmol/L)	54.63	45 - 96

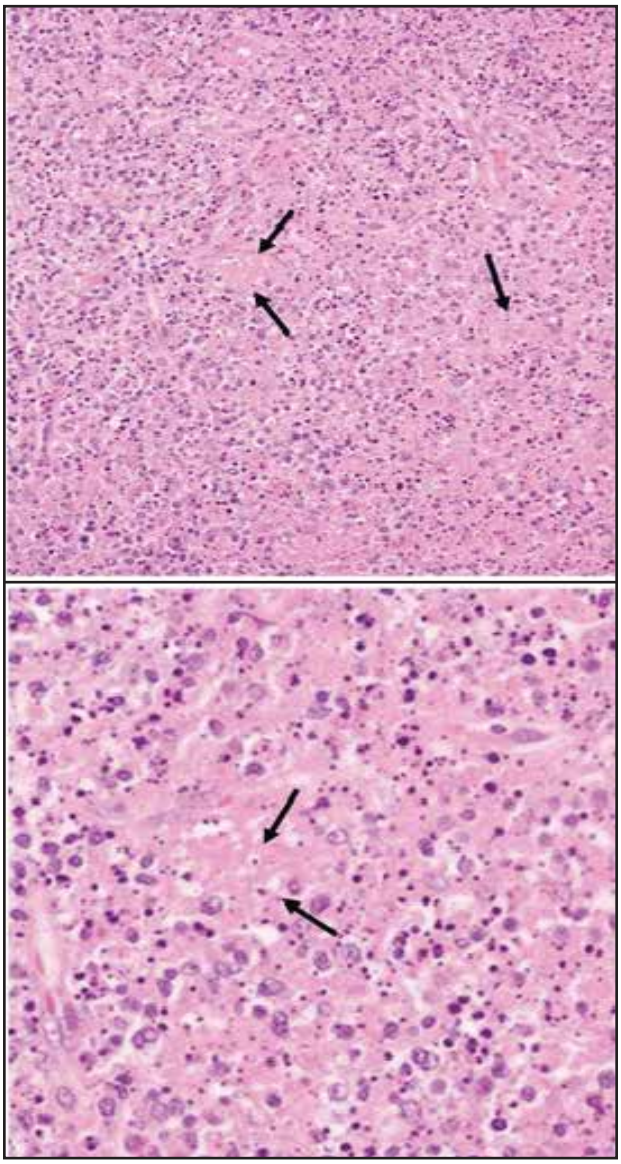

Figure 1: The lymph node biopsy shows regions of tissue necrosis, an increased presence of pale histiocytes, a higher number of apoptotic cells, along with cellular fragments and nuclear debris.

Discussion

The exact cause of KFD is still unclear, but this disease may be connected to infections and how the immune system reacts. It is believed to happen when the body's defense system responds too strongly to certain bacteria, viruses, or other triggers. Potential yet unidentified causative agents of this disease may include bacterial pathogens such as Brucella and Yersinia enterocolitica. Additionally, viral organisms including Epstein-Barr virus, human herpesvirus, cytomegalovirus, parvovirus B19, and HIV have been considered as possible contributing factors. Furthermore, Toxoplasma gondii and various fungal species may also serve as potential etiological agents.[3-5]

KFD may be influenced by genetic and autoimmune factors.[9] Some studies suggest a possible link between KFD and SLE,

though this link remains uncertain.[10] Specific genes, particularly Human Leukocyte Antigen (HLA) class II alleles, appear more frequently in KFD patients, especially among Asians. Scientists suggest that substances from infections or damaged cells could activate the immune system, causing inflammation in affected tissues.[11]

Case reports indicate that KFD may be associated with various pathological conditions, including neurological, cardiac, pulmonary, renal, hematological disorders, and malignancies.[12-18] Additionally, foreign bodies such as breast implants and pacemakers have been suggested as potential contributing factors.[19]

KFD, initially prevalent in Japan and East Asia, is now recognized worldwide, including in Bangladesh.[20] Though it mainly affects young adults, cases have been reported across all age groups, including children.[21] Unilateral cervical lymphadenopathy is a key feature, with possible involvement of axillary and mediastinal lymph nodes. Additionally, cases of parotid enlargement and inguinal lymphadenopathy have been reported.[22] Common symptoms include unexplained fever and night sweats.[23] Our patient presented with less common symptoms such as nausea, vomiting, anorexia, and abdominal discomfort. Routine laboratory tests aren't very useful for diagnosing KFD, except erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in some cases. Fine-needle aspiration cytology (FNAC) has limited diagnostic value. KFD diagnosis is confirmed through lymph node biopsy, revealing necrotic nodules and proliferating immune cells. KFD is frequently misdiagnosed as lymphoma, tuberculosis, systemic lupus erythematosus (SLE), or metastatic adenocarcinoma due to overlapping clinical features. To rule out these conditions, clinicians may conduct targeted investigations—such as tests for tuberculosis, viral infections (including EBV, CMV, and HIV), and autoimmune markers—based on clinical presentation and local disease patterns. Therefore, clinicians should consider KFD in patients presenting with unexplained lymphadenopathy. The disease is self-limiting, resolving within one to four months, with symptomatic treatment.

Medical treatment

Supportive medical care is generally sufficient for managing KFD. In mild and early cases, non-steroidal anti-inflammatory drugs (NSAIDs) are administered to alleviate fever and tenderness in the lymph nodes. For severe extra-nodal or generalized KFD, corticosteroids such as prednisolone are commonly used.[24, 25] Jang et al. suggest that corticosteroids may also be beneficial in less severe cases when symptoms persist for more than two weeks despite NSAIDs treatment. These steroids can prompt faster recovery and prevent disease recurrence. Some cases where patients do not respond to steroids, alternative treatments such as hydroxychloroquine and intravenous immunoglobulin may be considered.[26-28]

Conclusion

While Kikuchi disease is generally benign and resolves spontaneously within a few weeks to months, it is clinically significant due to its potential for misdiagnosis and association with autoimmune conditions like SLE. Understanding its clinical presentation, pathogenesis, and differential diagnoses is crucial for accurate recognition and management of this condition.

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