Presentation of necrotizing lymphadenitis of the Kikuchi–Fujimoto type in an adolescent male systemic lupus erythematosus - case report

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ABSTRACT

Background: Kikuchi–Fujimoto disease (KFD) has been reported more frequently in Asian countries. Its clinical course is usually transient, with spontaneous resolution within 1 to 4 months.

Case Presentation: An 18-year-old male with a history of febrile seizures in childhood presented with 1 month of persistent fever, malaise, rash, and generalized painful lymphadenopathy. On admission, he was tachycardic, febrile, and exhibited significant pancytopenia. Infectious studies were negative, while acute-phase reactants were elevated. Computed tomography imaging revealed systemic lymphadenopathy and hepatosplenomegaly. A lymph node biopsy was performed, demonstrating necrotizing lymphadenitis consistent with KFD. Only after histopathologic confirmation and due to the known association with systemic lupus erythematosus (SLE), immunologic testing was expanded, revealing elevated anti–double-stranded DNA antibodies and positive European Alliance of Associations for Rheumatology/American College of Rheumatology criteria, confirming KFD secondary to lupus. Immunosuppressive therapy was initiated, resulting in clinical and hematologic improvement, and the patient was discharged with follow-up in Rheumatology.

Conclusion: The coexistence of KFD and SLE should be considered in patients presenting with fever, lymphadenopathy, and pancytopenia. Diagnosis relies on histopathologic evaluation to differentiate it from hematologic, infectious, or autoimmune etiologies. Early identification is essential, as KFD is self-limited, whereas SLE requires prompt immunosuppressive therapy.

Keywords: Pancytopenia, lymphadenopathy, systemic lupus erythematosus, Kikuchi–Fujimoto, fever of unknown origin.

Type of Article: CASE REPORT **Specialty:** Rheumatology

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Introduction

Kikuchi–Fujimoto disease (KFD) is a rare, self-limited condition of uncertain etiology, characterized mainly by persistent lymphadenopathy with or without systemic symptoms. It commonly presents with firm cervical lymph nodes and intermittent fever, although some patients may develop weight loss, splenomegaly, leukopenia, and elevated inflammatory markers. Diagnosis relies on histopathological confirmation, as its clinical features frequently mimic malignant lymphoma or other infectious and autoimmune disorders, contributing to diagnostic delay. Management is empirical and focused on symptomatic relief [1]. This review summarizes the key diagnostic challenges of KFD, including its infrequent recognition and its presentation in male patients.

Why this case matters

This case is clinically relevant for several reasons. First, KFD is a rare and underdiagnosed entity whose clinical presentation may mimic high-impact conditions such as lymphoma, tuberculous lymphadenitis, or systemic autoimmune diseases, frequently leading to diagnostic delays and unnecessary interventions. The presence of prolonged fever, generalized lymphadenopathy, constitutional symptoms, and pancytopenia in a young patient represents a significant diagnostic challenge and necessitates a broad and systematic diagnostic approach.

Second, this case is particularly noteworthy because it involves a male patient, as both KFD and systemic lupus erythematosus (SLE) show a clear female predominance. The coexistence of these two entities in male patients is

uncommon and sparsely reported in the literature, highlighting the need to maintain a high index of suspicion even in atypical populations.

Furthermore, KFD may precede, coexist with, or represent the initial clinical manifestation of SLE, as observed in this patient. Early recognition of this association is essential, since KFD is typically a self-limited condition, whereas SLE requires timely immunosuppressive treatment to prevent organ damage and long-term complications. In this context, excisional lymph node biopsy was crucial to establish the correct diagnosis and to exclude malignant or infectious processes.

Finally, the limited number of reported cases of KFD associated with SLE in Latin America and Mexico confers additional value to this report, as it contributes to expanding regional knowledge of this entity, raises awareness among clinicians regarding its early recognition, and reinforces the importance of including it in the differential diagnosis of young patients presenting with fever of unknown origin and lymphadenopathy.

Case Description

An 18-year-old male with no relevant allergic history presented to the emergency department. He reported a family history of rheumatoid arthritis and vitiligo on his maternal side. He denied exposure to relevant zoonoses. His personal history included multiple hospitalizations during childhood for febrile seizures (Referred to as generalized tonic-clonic seizures lasting 4 minutes, without available imaging studies), currently without treatment, with the last episode documented 7 years prior.

He arrived with a 1-month history of persistent evening-predominant fever reaching temperatures up to 39°C, with mild response to antipyretics, accompanied by malaise, asthenia, adynamia, myalgias, arthralgias, a non-pruritic rash on the trunk and upper extremities (Figure 1), and generalized lymphadenopathy, which is painful, firm, unilateral, and approximately 2 cm on palpation, predominantly in the cervical region associated with pharyngitis. He also reported unintentional weight loss and night sweats. On admission, vital signs showed tachycardia (125 bpm) and fever (38.8°C).

Initial laboratory studies revealed significant pancytopenia: normocytic normochromic anemia (Hb 8 g/dl; MCV 86 fl; MCH 30 pg) with features of an anemic syndrome; leukopenia of 1,500 cells/mm³ with absolute neutropenia of 480 cells/mm³; and thrombocytopenia of 115,000 platelets/mm³. Renal function was preserved (urea 30 mg/dl, creatinine 0.7 mg/dl). Liver function tests were normal. The direct Coombs test was negative. Peripheral blood smear showed no abnormalities. Iron studies revealed no deficiency (Serum iron: 100 mg/dl, transferrin saturation of 30%, total iron binding capacity of 321 mg/dl). Serologies for Human immunodeficiency virus, Hepatitis B virus, Hepatitis C virus dengue, Rose Bengal test, sepsis panel, throat culture, procalcitonin, heterophile antibodies, cytomegalovirus, and cultures—all negative. Acute-phase reactants were elevated: ESR 58 mm/h, CRP 384 mg/l, and ferritin 753 ng/ml.

Chest, abdominal, and pelvic computed tomography (CT) imaging demonstrated multiple axillary, mesenteric, retroperitoneal, pelvic, and inguinal lymph nodes, as well as hepatosplenomegaly (Figure 2). Based on these findings, a diagnosis of fever of unknown origin was established, and the corresponding workup was initiated.

Given the presence of febrile neutropenia, empiric antimicrobial therapy was started with trimethoprim–sulfamethoxazole 160/800 mg every 72 hours, fluconazole 200 mg daily, and acyclovir 400 mg every 12 hours.

A transthoracic echocardiogram was performed due to the presence of a systolic murmur at the mitral area, showing no vegetations; a hyperdynamic heart with Left ventricular ejection fraction of 64% was observed. The murmur was attributed to the anemic syndrome.

Rheumatologic evaluation showed positive antinuclear antibodies by immunofluorescence at a titer of 1:1,280 with a homogeneous pattern, normal complement levels, and negative antiphospholipid antibodies, rheumatoid factor, and anti-Smith antibodies. Due to significant osteomuscular symptoms, CPK, aldolase, and anti-U1-RNP antibodies were obtained, all of which were negative.

An inguinal lymph node biopsy was performed due to initial suspicion of hematologic disease (lymphoma) or tuberculous lymphadenitis (Figure 3). Histopathology revealed chronic necrotizing lymphadenitis with areas of immunoblastic atypia. Zones of necrosis were observed

CUTANEOUS MANIFESTATIONS

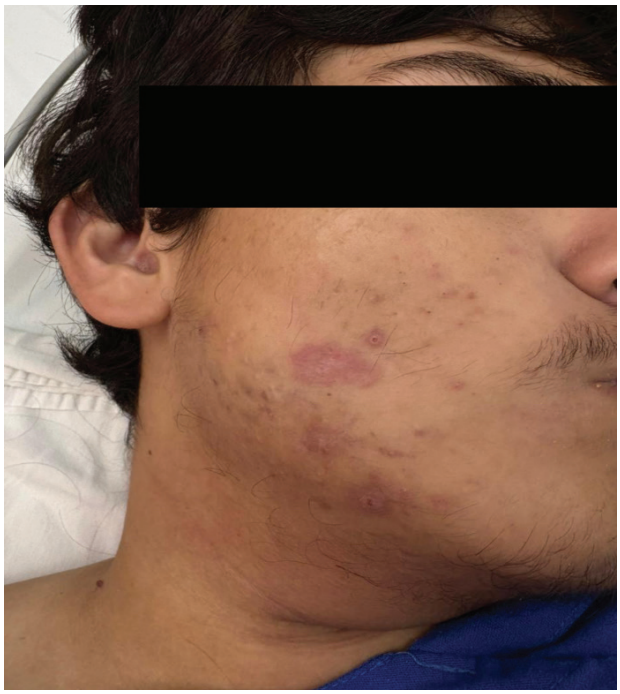

Figure 1. *Erythematous plaque on the right cheek region, with a slightly raised surface and no visible desquamative changes.*

ABDOMINOPELVIC CT SCAN

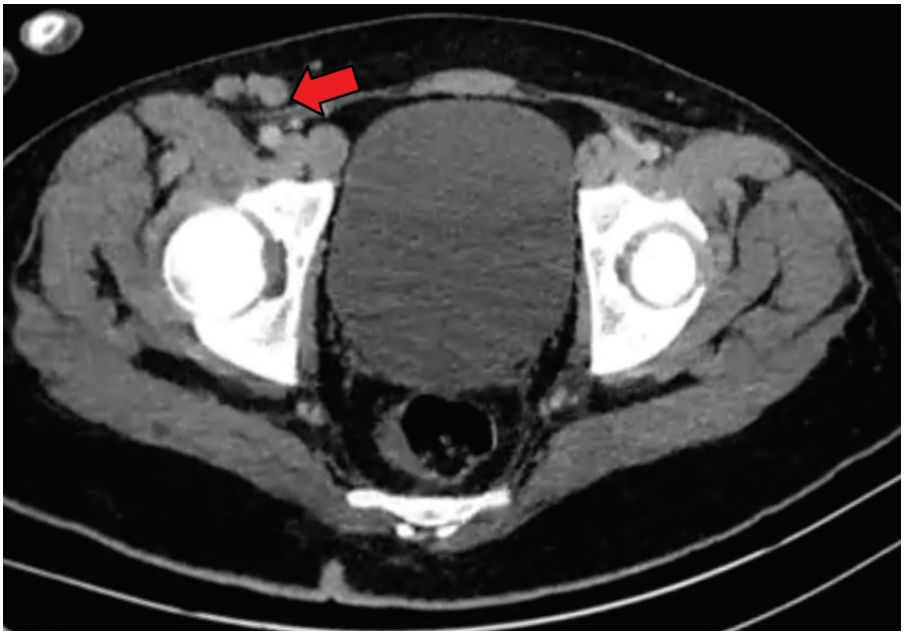

Figure 2. *Lymph node chains. Multiple mesenteric, retroperitoneal, pelvic, and inguinal lymphadenopathies* ***(red arrow)****, measuring up to 18 mm.*

INGUINAL LYMPH NODE BIOPSY

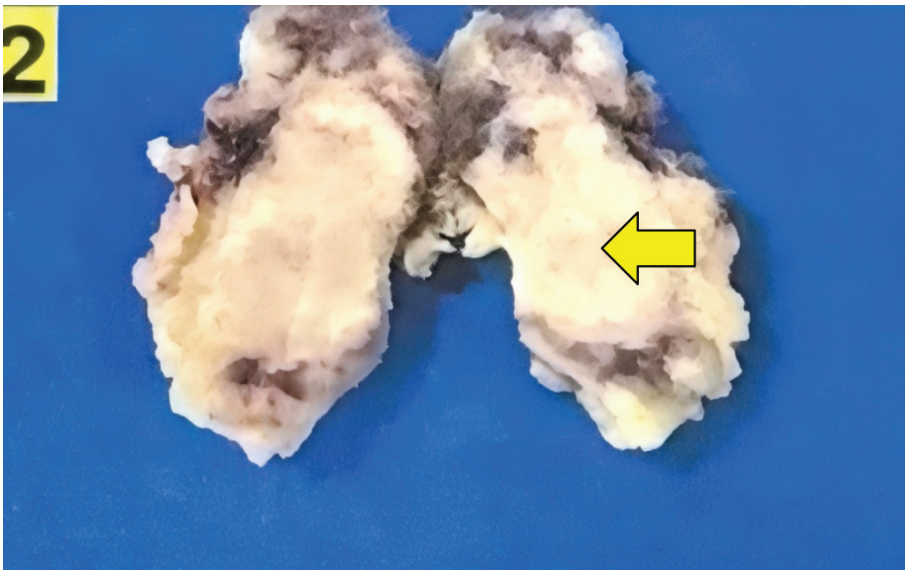

Figure 3. *Close-up view of the cut surface of the largest lymph node, showing whitish areas (****necrosis[a]*** ***yellow arrow****) and regions of congestion.*

with dense inflammatory infiltrates, abundant histiocytes exhibiting phagocytosis of cellular debris and erythrocytes, absence of neutrophils, and no evidence of fungi, parasites, intranuclear inclusions, or overt malignancy (Figures 4 and 5).

These findings supported the diagnosis of necrotizing lymphadenitis consistent KFD. Due to its frequent association with SLE, the immunologic profile was expanded, revealing elevated double-stranded DNA antibodies (800 IU/ml).

Clinical reevaluation identified lupus stigmata, and the score on the European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) classification criteria reached 20 points: fever (2 points), alopecia (2 points), thrombocytopenia (4 points), positive anti-dsDNA antibodies (6 points) and arthritis (6 points), considering that ≥ 10 points is classifying for lupus, the diagnosis of KFD secondary to SLE is established.

Following EULAR recommendations for the treatment of SLE, corticosteroid treatment was initiated due

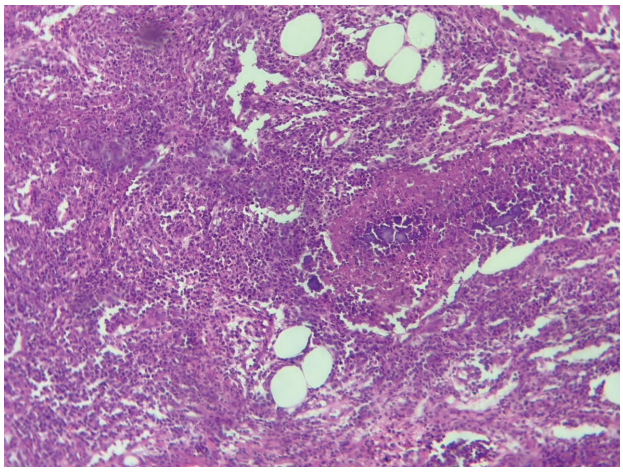

Figure 4. *A granular necrotic area with abundant karyorrhexis is observed, intermingled with a dense infiltrate of histiocytes and small lymphocytes.*

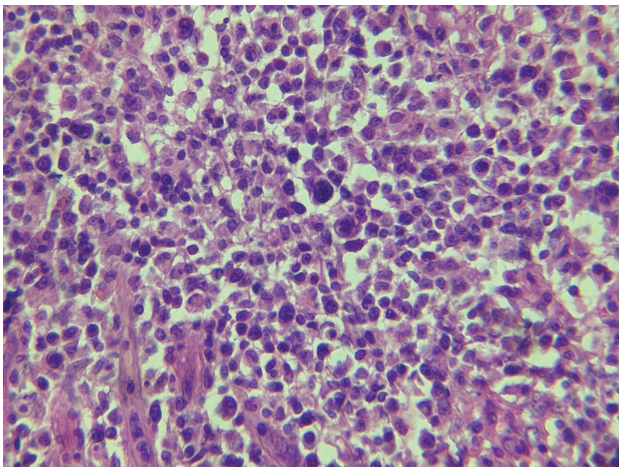

Figure 5. *Numerous histiocytes with broad, pale cytoplasm—several displaying plasmacytoid morphology—are identified, intimately mixed with small lymphocytes and abundant nuclear debris.*

to the severity of the clinical presentation and pancytopenia. Methylprednisolone 1,000 mg/day was administered, along with steroid-sparing therapy using hydroxychloroquine 200 mg/day and azathioprine 50 mg/day. The patient showed significant clinical improvement from the second day of treatment, with progressive normalization of all three hematological cell lines (Hb increased from 8 to 10 g/dl; leukopenia from 1,448 to 5,960 cells/mm³; and thrombocytopenia from 62,000 to 152,000 platelets/mm³). Treatment was initiated with corticosteroids due to the severity of the presentation and pancytopenia, administering prednisone 100 mg/day, along with steroid-sparing therapy using hydroxychloroquine 200 mg/day and azathioprine 50 mg/day. The patient showed significant clinical improvement beginning on the second day of treatment, with progressive normalization of all three hematologic cell lines.

The patient improved and was discharged with scheduled rheumatological follow-up, and was prescribed medical management with prednisone (40 mg/day) for 2 weeks, after which the dose was reduced (5 mg/day). In addition, treatment with hydroxychloroquine plus azathioprine was continued.

Discussion

A male patient in his second decade of life presented with persistent fever refractory to antipyretics and generalized lymphadenopathy. Given the criteria for fever of unknown origin in an immunocompetent patient [2], extensive laboratory and imaging studies were performed, all of which were negative for infectious etiologies. CT confirmed systemic lymphadenopathy, raising suspicion for lymphoma or tuberculous lymphadenitis, prompting a lymph node biopsy. Histopathology established the diagnosis of KFD.

KFD, first described in 1972 and also known as necrotizing histiocytic lymphadenitis [1], typically presents with fever of unknown origin and small-volume lymphadenopathy, generally <1 cm, helping distinguish it from hematologic malignancies [3]. Although most frequently reported in Asian populations [4], cases have also been described in Latin America, with scarce reports in Mexico. It predominantly affects individuals <40 years and is more common in females [5].

Its etiology remains unclear, with a leading hypothesis supporting a viral–autoimmune mechanism. Although multiple infectious and noninfectious triggers have been proposed, none show definitive causality. In contrast, strong associations with autoimmune diseases—particularly SLE, Sjögren syndrome, and autoimmune thyroiditis—have been documented. In this patient, KFD may represent an early manifestation of SLE. Genetic susceptibility has been suggested through shared HLA genotypes (HLA-Cw7, HLA-B25), and periodontal infections have been proposed as possible factors [1].

Clinically, KFD presents heterogeneously. Cervical lymphadenopathy occurs in 55%-99% of cases, although up to half may show generalized involvement. Systemic manifestations include fever, weight loss, arthritis, leukopenia, and cutaneous lesions, reported in up to 40% [6]. This variability underscores its importance in the differential diagnosis of febrile lymphadenopathy in young individuals.

Diagnosis is challenging due to overlap with malignant lymphoma and SLE. Laboratory and imaging findings are nonspecific; thus, excisional lymph node biopsy remains the diagnostic gold standard. Histology reveals necrosis with karyorrhexis, prominent histiocytic infiltrates, and absence of neutrophils, features essential for differentiating KFD from other clinically similar disorders [7].

Comprehensive evaluation is required to rule out infectious, neoplastic, and hematologic causes, including toxoplasmosis, cytomegalovirus, head and neck malignancies,

Castleman disease, tuberculous lymphadenitis, and hemophagocytic lymphohistiocytosis [3].

Symptomatic or persistent cases may require systemic therapy with corticosteroids, Nonsteroidal anti-inflammatory drugs, antipyretics, or antimalarials. When associated with SLE, treatment must address lupus activity with corticosteroids and hydroxychloroquine, reserving additional immunosuppression for severe or refractory cases [8].

Although the coexistence of KFD and autoimmune diseases—particularly SLE—has been described, it remains uncommon [9]. Its identification in a male patient is notable given the female predominance in SLE. Using the 2019 EULAR/ACR criteria, which have high sensitivity and specificity [10], the patient reached a score of 20, confirming concomitant KFD and SLE.

KFD typically resolves spontaneously within 1–4 months, making observation the most common management approach [11]. Although generally benign, recurrences occur in up to 11.3% of cases, and rare complications such as cardiac tamponade, pleural effusion, and polyarteritis nodosa have been reported [1].

Reviewing similar published cases provides relevant comparisons and strengthens diagnostic suspicion, reinforcing the need to include KFD in the differential diagnosis of febrile lymphadenopathy.

Conclusion

The coexistence of KFD and SLE should be considered in patients with persistent fever, generalized lymphadenopathy, and pancytopenia. This association represents a diagnostic challenge, particularly in low-prevalence regions and in male patients. Histopathological evaluation is essential to distinguish KFD from hematologic, infectious, or autoimmune conditions with similar features. Early recognition is crucial, as KFD is typically self-limited, whereas SLE requires timely immunosuppressive therapy to prevent complications. A comprehensive and prompt diagnostic approach can significantly influence patient outcomes.

What is new?

- The association between KFD and SLE may occur even in male patients, despite the higher prevalence of SLE in females; thus, the diagnosis should not be excluded based on sex.
- Histopathological examination is essential to differentiate KFD from other causes, such as lymphoma, tuberculosis, or lupus lymphadenitis, enabling accurate and timely diagnosis.
- Early recognition of the KFD–SLE association is critical, since KFD is typically self-limited, whereas SLE requires urgent immunosuppressive therapy to prevent complications and improve prognosis.

List of Abbreviations

ACR	American College of Rheumatology
ANA	Antinuclear antibodies
anti-dsDNA	Anti–double-stranded DNA antibodies
CMV	Cytomegalovirus
CRP	C-reactive protein
CT	Computed tomography
EULAR	European Alliance of Associations for Rheumatology
ESR	Erythrocyte sedimentation rate
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
KFD	Kikuchi–Fujimoto disease
LVEF	Left ventricular ejection fraction
NSAIDs	Nonsteroidal anti-inflammatory drugs
SLE	Systemic lupus erythematosus

Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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Consent for publication

Written informed consent was obtained from the patient for the publication of this case, including clinical information and accompanying images.

Ethical approval

Ethical approval was not required for this case report in accordance with institutional policies; however, all applicable ethical standards and guidelines for research involving human subjects were fully adhered to.

Author contributions

All authors participated in the preparation of the manuscript and approved the final version.

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Summary of the case

Item	Details
Age/sex	18-year-old male
Presentation	One-month history of persistent fever, malaise, asthenia, myalgias, arthralgias, non-pruritic rash, painful generalized lymphadenopathy (predominantly cervical), pharyngitis, weight loss, and night sweats
Key findings	Pancytopenia (Hb 8 g/dl, leukocytes 1,500/mm³ with neutropenia, platelets 115,000/mm³); elevated inflammatory markers (ESR 58 mm/h, CRP 384 mg/l, ferritin 753 ng/ml); CT scan showing generalized lymphadenopathy and hepatosplenomegaly; ANA 1:1,280 (homogeneous pattern); elevated anti–dsDNA antibodies
Diagnostic workup	Extensive infectious and hematologic evaluation negative; excisional inguinal lymph node biopsy showing necrotizing histiocytic lymphadenitis without neutrophils or malignancy, consistent with KFD
Diagnosis	KFD associated with SLE (EULAR/ACR 2019 score: 20 points)
Management	High-dose corticosteroids (prednisone 100 mg/day), hydroxychloroquine 200 mg/day, and azathioprine 50 mg/day
Outcome	Rapid clinical improvement with resolution of fever and symptoms; progressive normalization of hematologic parameters; discharged with outpatient rheumatology follow-up