

## Kikuchi-Fujimoto Syndrome: A Rare Entity to Consider

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### ABSTRACT

**Introduction:** Kikuchi-Fujimoto disease (KFD) is a rare, benign, necrotizing lymphadenitis of unknown aetiology with good prognosis. It is characterized by cervical lymphadenopathy, nocturnal diaphoresis and fever. Surgical excision of the adenopathy, histopathological study and immunophenotyping are crucial for diagnosis.

**Patients and methods:** This paper describes five patients with three different histological subtypes of KFD, including an atypical presentation masquerading as pyelonephritis and two other cases where physicians mistakenly started chemotherapy. In one other case cytomegalovirus was identified as the responsible aetiological agent, while in the remaining patient, KFD evolved into an autoimmune condition.

**Discussion:** KFD, although rare, may mimic infectious, autoimmune and neoplastic diseases. It also poses a risk for the subsequent development of an autoimmune disorder.

### LEARNING POINTS

- Kikuchi-Fujimoto disease (KFD), although rare, should be included in the differential diagnosis of patients with cervical lymphadenopathy and fever of unknown origin.
- Early recognition of KFD may minimize the use of unnecessary aggressive examinations and therapies.
- The course of KFD in most patients is self-limiting, but there is a risk of progression to an autoimmune syndrome.

### KEYWORDS

Kikuchi-Fujimoto disease, lymphadenitis, fever of unknown origin, rare disease

### INTRODUCTION

Kikuchi-Fujimoto disease (KFD) is a rare, benign, necrotizing lymphadenitis of unknown aetiology, with fever and preferential involvement of the cervical region<sup>[1]</sup>. This self-limiting condition may, due to its similarity, be confused with tuberculosis, systemic lupus erythematosus and haematological malignancies<sup>[2,3]</sup>. Thus, surgical excision of the affected adenopathy, histological study and immunophenotyping are vital for establishing the correct diagnosis<sup>[3]</sup>.

No aetiological factors have been identified, but it is thought that this syndrome results from an immune response by CD8+ T-lymphocytes and histiocytes to an infectious insult<sup>[1-3]</sup>. The main aetiological cause is assumed to be viral<sup>[3]</sup>.

KFD, similarly to diseases such as systemic lupus erythematosus or other autoimmune conditions, is primarily found in young women. However, there are reports of affected male patients, as well as individuals aged between 6 and 80 years<sup>[3]</sup>.

The most frequent signs and symptoms are cervical and localized lymphadenopathies, fever, rash, arthritis, fatigue and hepatosplenomegaly. Other uncommon symptoms are night sweats, nausea, vomiting, diarrhoea, neck stiffness, weight loss and more extensive lymph node involvement<sup>[3,4]</sup>.

The literature describes cases of KFD associated with pathologies such as Still's disease, B-cell lymphoma and cryptogenic pneumonia. The risk of it developing into an autoimmune condition is higher in adults, and patients with late-onset systemic lupus erythematosus have been reported<sup>[3]</sup>.

Surgical excisional biopsy is vital, as there are no radiological or ultrasound characteristics to establish the diagnosis<sup>[2,3]</sup>. The disease has three histological subtypes: proliferative, necrotizing and xanthomatous. The last subtype, unlike the previous two which depict disease progression, is a distinct histological variant of undetermined aetiology<sup>[2,3]</sup>.

## CASE DESCRIPTION

### Case 1

A 72-year-old female patient with haematuria, dysuria and pollakiuria was admitted with pyelonephritis. A thoracic and abdominal CT scan revealed accidental thoracic and abdominal adenopathy. Laparoscopic excision of the hepatic ganglia revealed non-necrotizing granulomatous lymphadenitis.

### Case 2

A 19-year-old man presented with odynophagia, fever, rash, asthenia, anorexia and weight loss. Hepatomegaly, right cervical adenomegaly and neurological worsening were documented. The patient underwent a cycle of chemotherapy due to high suspicion of a lymphoproliferative syndrome with central nervous system involvement. Subsequently, excisional biopsy of the cervical adenomegaly confirmed necrotizing lymphadenitis.

### Case 3

A 58-year-old woman was admitted with to a 2-month history of myalgia, asthenia, weight loss, nocturnal diaphoresis, dyspnoea and non-productive cough. In light of clinical worsening, and the development of unilateral pleural effusion and bilateral axillary adenomegaly, the patient started a chemotherapy regimen due to suspicion of lymphoma. A biopsy of the axillary adenomegaly later confirmed follicular hyperplasia.

### Case 4

A 58-year-old man was admitted for painful adenomegaly measuring 3 cm in diameter in the right inguinal region, associated with fever. A thoracic-abdominopelvic CT scan showed contrast uptake only in the enlarged gland proximal to the right external femoral vessels. Serology was positive for HBsAg, IgG CMV and IgM CMV. Excisional biopsy later confirmed necrotizing lymphadenitis.

### Case 5

A 31-year-old female patient with KFD, which had been histologically confirmed 3 years previously, developed scaly erythematous skin lesions on the face and scalp. A skin biopsy revealed discoid lupus erythematosus.

## DISCUSSION

Despite the good prognosis of this clinical entity, patients with a fever of undetermined aetiology with associated lymphadenopathies should undergo surgical biopsy<sup>[3]</sup>. Two of the described patients mistakenly underwent chemotherapy due to high suspicion of lymphoma<sup>[3]</sup>. KFD can be even more challenging to diagnose when there is ganglion involvement not localized to the cervical region. Cases of acute abdomen resulting from this pathology have been described, and its presentation as pyelonephritis, as described above, is unprecedented<sup>[1]</sup>. To date, no therapeutic guidelines has been established for KFD. Patients with classic symptoms respond favourably to non-steroidal anti-inflammatory drugs. However, patients with atypical and refractory symptoms may require corticosteroid therapy<sup>[3]</sup>. There are reports of patients receiving intravenous immunoglobulin, hydroxychloroquine or combination therapy<sup>[3]</sup>.

Most cases of KFD are self-limiting, but some patients may experience relapse. The recurrence rate is less than 7%, and it is assumed that patients with asthenia, non-localized ganglion involvement and persistent symptomatology are at higher risk of relapse.

There are no standardized methods for managing this condition. Therefore, patients with KFD should be followed up due to the risk of recurrence and also the high probability of the development of autoimmune conditions such as systemic lupus erythematosus<sup>[3,4]</sup>.

In general, KFS should be considered in the differential diagnosis of patients with cervical lymphadenopathy and fever of unknown origin, as its early recognition can minimize the use of aggressive tests and therapies, and iatrogenesis<sup>[2-5]</sup>.

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