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Case Report

Kikuchi-Fujimoto disease: a two-case series of necrotizing histiocytic lymphadenitis mimicking other pathologies: a care compliant case report

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ABSTRACT

Kikuchi-Fujimoto disease (KFD) is a rare, benign, and self-limiting cause of cervical lymphadenitis. It is often misdiagnosed as tuberculosis or lymphoma. A histopathological examination is crucial for a definitive diagnosis. We report two female patients with cervical lymphadenopathy. Case 1: A 67-year-old woman had a 3-week history of painful swelling in her right neck. Imaging and FNAC did not provide clear results. An excision biopsy showed necrotizing histiocytic lymphadenitis. Case 2: A 29-year-old woman had a 1-month history of painless swelling in her right neck and evening fever. Histopathology after an excision biopsy confirmed KFD. Both patients received conservative management with symptom relief and showed complete recovery. KFD should be included in the differential diagnosis of persistent cervical lymphadenopathy, especially in women, to prevent unnecessary treatment with antibiotics or cancer therapies.

Keywords: Kikuchi-Fujimoto disease, Cervical lymphadenopathy, Necrotizing histiocytic lymphadenitis, Case report

INTRODUCTION

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare, self-limiting cause of swollen lymph nodes. It was first described in Japan in 1972 by Kikuchi and independently, by Fujimoto and their teams.[1,2] Although it was initially thought to be confined to East Asia, KFD has since been reported worldwide with cases have documented in Europe, North America, the Middle East, and South Asia.[3,4] Despite its presence in many regions, it remains a rare diagnosis in most clinical settings, often leading to misdiagnosis or delayed recognition.

In terms of demographics, KFD affects people of various ages, from young children to older adults. However, it is most commonly found in young women, with a female-to-male ratio of up to 4:1.[3,5] The average age of onset is typically between 20 and 30 years.[3] The exact cause is still unknown, proposed mechanisms include an autoimmune response triggered by viral or other infections.[3,4,6] Viruses like Epstein-Barr virus (EBV), cytomegalovirus (CMV), human herpesvirus-6, and parvovirus B19 have been linked to KFD in different studies, but no single pathogen has been consistently identified.[3,4]

The autoimmune theory is backed by the presence of activated cytotoxic T lymphocytes and apoptotic cellular debris in affected lymph nodes as well as occasional links to systemic lupus erythematosus (SLE) and other connective tissue diseases.[4-6] Clinically, KFD usually appears as acute or subacute unilateral cervical lymphadenopathy, particularly the posterior cervical nodes. This may occur with or without symptoms, such as

fever, night sweats, fatigue, rash, or arthralgia.[5-7] In some cases, the Lymphadenopathy is painless, while in others, it can be tender and associated with constitutional symptoms. Laboratory tests are non-specific and may show leukopenia, mild granulocytopenia, and elevated levels of markers like the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), or the lactate dehydrogenase (LDH).[4-6] Imaging techniques such as ultrasound, CT, or MRI can reveal enlarged lymph nodes but cannot reliably distinguish KFD from other causes of lymphadenopathy.[8] The gold standard for diagnosis is still histopathological examination.

Characteristic features include patchy paracortical necrosis, karyorrhectic debris, an abundance of crescent-shaped histiocytes, and an absence of neutrophils. These findings help differentiate KFD from other conditions such as tuberculous lymphadenitis (granulomas with caseation and acid-fast bacilli), lymphoma (monomorphic atypical lymphoid proliferation), and SLE-associated lymphadenitis (haematoxylin bodies, plasma cells).[6,7] KFD is generally benign and resolves spontaneously within 1 to 4 months in most cases.[3-9] Treatment is mostly supportive, with non-steroidal anti-inflammatory drugs (NSAIDs) or antipyretics for symptomatic relief. Corticosteroids are reserved for severe, persistent, or extra-nodal disease.[9] Recurrence is rare but has occurred in up to 3% of patients.[10]

We report two cases of KFD, one in a young woman and another in an elderly woman. Both presented with cervical lymphadenopathy but differed in symptom profiles. These cases highlight the clinical variability of KFD and underscore the importance of histopathological confirmation to avoid unnecessary treatments for infections or malignant conditions.

CASE REPORT

Case 1

Patient information

A 67-year-old woman presented with swelling over the right side of her neck for three weeks. Initially 2×2 cm, it progressed to 5×5 cm. The pain was dull and intermittent, with no factors making it worse or better. She had no fever, cough, trouble swallowing, weight loss, or loss of appetite. She managed hypothyroidism with levothyroxine.

Clinical findings

She had several matted lymph nodes in the right posterior triangle. The largest measured 3×3 cm and was tender, firm, without any local rise in temperature.

Diagnostic assessment

Ultrasound: Showed bilateral posterior triangle lymphadenopathy, greater on the right than the left.

FNAC: Indicated features suggestive of Rosai–Dorfman disease; differential diagnosis included toxoplasmosis.

Excision biopsy (21/10/2023): Found matted lymph nodes with caseating material at levels IV and V.

Histopathology: Showed acute suppurative lymphadenitis; TB PCR was negative.

PET-CT: Revealed metabolically active cervical nodes on both sides.

IGRA: Negative; CRP: 19.48 mg/L; Serum ACE: 19.68 U/L; Toxoplasma IgG: Negative.

Immunohistochemistry: Positive for CD5, CD3 (T cells), CD68 (histiocytes), CD20, and CD79a (B cells); no Hodgkin cells present.

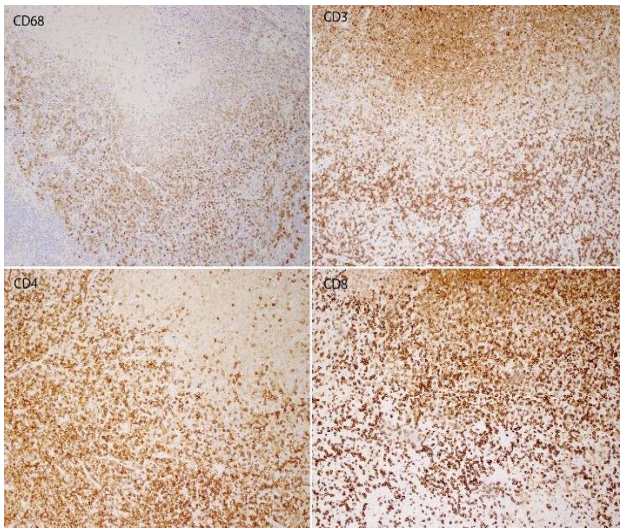

Figure 1: Immunohistochemistry shows a predominance of CD3/CD5-positive T cells with CD8 dominance and abundant CD68-positive histiocytes. Scattered B cells are present, and CD15/CD30 are negative, supporting a diagnosis of necrotizing histiocytic lymphadenitis (Kikuchi–Fujimoto disease).

Therapeutic intervention and outcome

She was managed conservatively with NSAIDs, with no antibiotics or corticosteroids. Her symptoms resolved over eight weeks, and there was no recurrence at the three-month mark.

Case 2

Patient information

A 29-year-old woman presented with a one-month history of swelling on the right side of her neck. It started at 2×2 cm and enlarging to 4×4 cm, and was painless. She experienced evening fevers for 15 days, with no cough,

dysphagia, weight loss, or TB exposure. She had no other health issues.

Clinical findings

She had several matted lymph nodes in the right posterior triangle, with the largest being 3×3 cm. They were firm and non-tender, with no local temperature rise.

Diagnostic assessment

Ultrasound: Showed enlarged nodes in the right posterior triangle, levels I and II.

Excision biopsy (13/03/2023): Found multiple matted nodes in the posterior triangle and one in the anterior triangle.

GeneXpert MTB/RIF: Negative; AFB culture: Negative.

Histopathology: Showed partial loss of nodal architecture, aggregates of histiocytes, karyorrhectic debris, and patchy necrosis, which was diagnostic of KFD.

Therapeutic intervention and outcome

She was treated conservatively with NSAIDs and fully recovered in six weeks, with no recurrence at follow-up.

Table 1: Clinical course and management of two patients with Kikuchi-Fujimoto disease according to care guidelines.

Parameter	Case 1 (67F)	Case 2 (29F)
Onset and initial symptoms	Painful right neck swelling × 3 weeks	Painless right neck swelling × 1 month; evening fever × 15 days
Past medical history	Hypothyroidism on levothyroxine	None
Physical examination	Multiple matted lymph nodes, right posterior triangle; largest 3×3 cm; firm, tender	Multiple matted lymph nodes, right posterior ± anterior triangle; largest 3×3 cm; firm, non-tender
Ultrasound	Bilateral posterior triangle lymphadenopathy (R>L)	Enlarged nodes in right posterior and anterior triangle
PET-CT	Metabolically active bilateral cervical nodes	Not performed
FNAC	Suggestive of Rosai–Dorfman disease	Not performed
TB PCR / GeneXpert	Negative	Negative
Histopathology	Necrotizing histiocytic lymphadenitis	Necrotizing histiocytic lymphadenitis
Immunohistochemistry	Positive for T- and B-cell markers, histiocytes; no hodgkin cells	Not performed
Management	NSAIDS, supportive care	NSAIDS, supportive care
Outcome	Complete resolution at 8 weeks; no recurrence at 3 months	Complete resolution at 6 weeks; no recurrence at 3 months

Table 2: Chronological timeline of clinical events for both cases.

Date duration	Case 1 events	Case 2 events
Week 0	Onset of painful right neck swelling (2×2 cm, enlarging)	Onset of painless right neck swelling (2×2 cm, enlarging)
Week 3	Ultrasonography: bilateral posterior triangle lymphadenopathy (R>L); FNAC inconclusive	Evening fevers begin
Week 4	Excision biopsy performed (levels iv and v nodes)	Ultrasonography: enlarged nodes in right posterior and anterior triangle
Week 4.5	Histopathology: necrotizing histiocytic lymphadenitis; IHC confirming KFD; TB PCR negative	Excision biopsy performed; histopathology: necrotizing histiocytic lymphadenitis; TB PCR negative
Week 4–12	Supportive management with NSAIDS; gradual resolution; complete recovery at 8 weeks	Supportive management with NSAIDS; complete recovery at 6 weeks
3-month follow-up	No recurrence	No recurrence

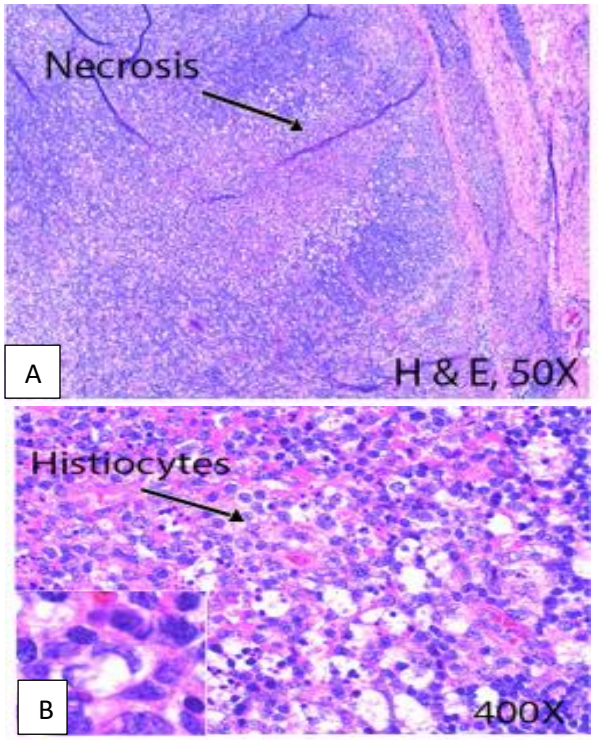

Figure 2: Histopathological features of Kikuchi–Fujimoto disease: (A) low-power photomicrograph showing areas of paracortical necrosis within the lymph node (H and E ×50), (b) high-power view highlighting numerous histiocytes with crescent-shaped nuclei and karyorrhectic debris, typical of necrotizing histiocytic lymphadenitis (H and e ×400).

DISCUSSION

KFD is a rare and benign cause of cervical lymphadenopathy that typically follows a self-limiting course, with spontaneous resolution occurring over weeks to a few months. Although it predominantly affects young women, KFD can also occur in older adults, as demonstrated in our first case, indicating that age should not exclude this diagnosis. The clinical presentation is variable and may include painful or painless lymph node enlargement, with or without systemic symptoms such as fever, which often leads to diagnostic confusion.

Histopathological investigation is crucial for differentiating KFD from other significant etiologies of cervical lymphadenopathy. Tuberculous lymphadenitis is marked by granuloma formation accompanied by caseation and acid-fast bacilli, whereas lymphoma is characterized by abnormal lymphoid growth and architectural distortion. Ultrasonography or computed tomography can help narrow down the differential diagnosis. Lymph nodes in KFD are commonly smaller, less rounded, and usually don't have core necrosis. However, these findings are not specific and cannot replace a tissue diagnosis.[8] Management is supportive. NSAIDs and antipyretics are sufficient for most patients. Corticosteroids may be employed in particular situations, such as patients displaying severe symptoms, a prolonged or recurrent treatment regimen, or extranodal involvement; however, their use is generally restricted to refractory cases. The prognosis is very good overall, with a low chance of the disease coming back (about 3-4%) and few long-term problems. It is very important to get an early and correct diagnosis so that unnecessary tests and treatments that could be dangerous or not right do not happen.[9] Recurrence is uncommon but has been documented in a limited number of patients.[10] Both patients in our series showed complete clinical recovery with conservative therapy alone and experienced no recurrence during follow-up, highlighting the benign nature and favourable prognosis of Kikuchi–Fujimoto disease when appropriately identified.

CONCLUSION

KFD should be considered in the differential diagnosis of persistent cervical lymphadenopathy, especially in women. Increased awareness among clinicians can help avoid unnecessary antimicrobial or cancer treatments.

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