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Management challenges of kikuchi-fujimoto disease mimicking tuberculosis lymphadenitis: an evidence-based case report

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ABSTRACT

A 27-year-old man presented with a tender left inguinal mass, fever, productive cough, anorexia, and weight loss. Laboratory findings showed leukocytosis, lymphocytopenia, and elevated ESR. Chest X-ray suggested pulmonary tuberculosis; however, GeneXpert and HIV tests were negative. Due to suspected tuberculosis lymphadenitis, empirical antibiotics were administered and an excisional biopsy was performed. Histopathological examination revealed necrotizing histiocytic lymphadenitis consistent with Kikuchi–Fujimoto Disease which is rare but an important differential diagnosis. An evidence-based review was conducted to compare supportive management with aggressive pharmacological therapy in Kikuchi–Fujimoto Disease initially suspected as tuberculosis lymphadenitis. Of 152 identified records, eight case-based studies met inclusion criteria after systematic screening and critical appraisal using the Joanna Briggs Institute tool. Empirical anti-tuberculosis therapy in Kikuchi–Fujimoto Disease may delay appropriate management due to lack of clinical improvement. Early tuberculosis testing and histopathological confirmation are essential to avoid misdiagnosis and unnecessary exposure to potentially toxic anti-tuberculosis therapy. Excisional biopsy is crucial for definitive diagnosis. Kikuchi–Fujimoto Disease generally responds well to supportive treatment with NSAIDs or corticosteroids, and empirical anti-tuberculosis therapy should be avoided without histopathological confirmation.

INTRODUCTION

Patient presenting with an inguinal mass, fever, productive cough, and weight loss are frequently diagnosed with infectious lymphadenopathy most commonly tuberculosis lymphadenitis. This often leads to misdiagnosis and inappropriate therapy. Kikuchi-Fujimoto Disease (KFD) is a differential diagnosis that is rarely considered due to its low prevalence. Furthermore, KFD is a pathological diagnosis that can only be confirmed through histopathological examination, a facility typically available only in referral hospitals. KFD is a rare necrotizing lymphadenitis with an unclear etiology. Its primary diagnosis is retrospective, based on the histopathological characteristics of the affected lymph nodes, while treatment remains largely empirical. Interestingly, KFD and Systemic Lupus Erythematosus (SLE) share a complex relationship; SLE may precede KFD or develop subsequently. KFD is also frequently misdiagnosed as malignant lymphoma in its acute or subacute forms or may remain undiagnosed altogether due to its rarity, clinical similarities with other common conditions, and a lack of awareness among clinicians.

A 27-year-old male presented with a mass in the left inguinal region, with no discharge or pus and no other palpable masses elsewhere. The patient reported a low-grade intermittent fever over the past week, which had become high-grade in recent days, a productive cough for one week, and systemic symptoms including loss of appetite and weight loss.

General physical examination revealed a patient with poor nutritional status; notably, there was no butterfly rash, oral candidiasis, or adventitious breath sounds. Local status examination showed an enlarged left inguinal lymph node measuring 3×2×1 cm, which was mobile, firm, well-defined, warm to the touch, and tender on palpation. There was no erythema or fluctuation, and no lymphadenopathy was found in other anatomical sites.

Laboratory investigations revealed leukocytosis rising to 15.348/µL, lymphocytopenia 20%, and an elevated erythrocyte sedimentation rate (ESR) at 31 mm/hour.

The patient was initially diagnosed with inguinal lymphadenitis with suspected pulmonary tuberculosis. Initial treatment included injectable empirical antibiotics (ceftriaxone and metronidazole) and other symptomatic medications.

Chest X-ray showed findings consistent with pulmonary tuberculosis. Musculoskeletal ultrasound revealed multiple enlarged lymph nodes in both right and left inguinal regions, with the largest lymph node measuring approximately 2.52×1.48 cm on the left side. There was no evidence of bowel herniation in either inguinal region. The patient was referred to a pulmonologist for preoperative clearance. Both The GeneXpert and HIV test showed negative results.

Despite these findings, an excisional biopsy was perfomed in a negative-pressure room because the patient was suspected of having tuberculosis lymphadenitis. After surgery, the patient was planned to be admitted to an isolation room, similar to standard management for tuberculosis patients, until the histopathological examination results became available.

The post-excisional biopsy showed from macroscopic examination revealed an irregularly shaped tissue measuring 3×2×1.5 cm, weighing 7 grams, with a gray color and a rubbery to firm consistency. The cut surface was whitish with brownish speckled areas, and three tissue cassettes were prepared. Microscopic examination showed lymphoid tissue composed of lymphoid follicular hyperplasia, consisting of both large and small follicles with prominent germinal centers. Foci of necrosis containing abundant apoptotic debris were identified. The stroma appeared hyperemic and was accompanied by hemorrhage.

Based on these findings, the histopathological features were consistent with Kikuchi Necrotizing Histiocytic Lymphadenitis or Kikuchi-Fujimoto Disease (KFD). The patient's symptoms improved four days after hospitalization with injectable NSAID therapy for pain control. He was subsequently discharged with supportive analgesic medications and oral cefixime for five days. On follow-up, his symptoms had completely resolved within one week.

RESEARCH METHODS

This evidence-based case report was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The clinical question addressed whether, in patients with KFD initially suspected of having tuberculosis lymphadenitis, supportive management is associated with favorable clinical outcomes compared with aggressive pharmacological treatment. Specifically, the review evaluated the effectiveness of supportive therapy and/or empirical antibiotic treatment versus aggressive pharmacological interventions, including anti-tuberculosis therapy (ATT) and systemic corticosteroids, in patients with histopathologically confirmed KFD who were initially managed as cases of tuberculosis lymphadenitis.

A comprehensive literature search was performed independently by three authors on January 13, 2026, across four electronic databases: PubMed, the Cochrane Library, Google Scholar, and Scopus. The search strategy incorporated the keywords "Kikuchi-Fujimoto Disease," "histiocytic necrotizing lymphadenitis," "inguinal lymphadenopathy," and "tuberculous lymphadenitis," together with relevant Medical Subject Headings (MeSH) terms and their synonyms. Where available, database-specific filters and advanced search functions were applied to optimize the sensitivity and specificity of the search strategy. The complete search terms and the number of records retrieved from each database are presented in Tables 1 and 2.

Table 1. Clinical Question

Population	Intervention	Comparison	Outcome
Patients with Kikuchi-Fujimoto Disease confirmed by histopathology, intially suspected to have tuberculosis lymphadenitis	Empirical antibiotic and/or supportive management (NSAID, acetaminophen, etc.) followed by biopsy	Aggressive pharmacological therapy, including anti-tuberculosis therapy, and/or systemic corticosteroid followed by biopsy	Favorable clininal outcomes

Table 2. Literature Searching

Database	Keywords	Results	Selected Articles
Pubmed	((Kikuchi-Fujimoto Disease OR KFD OR histiocytic necrotizing lymphadenitis OR kikuchi lymphadenitis) AND (inguinal lymphadenopathy OR tuberculous lymphadenitis OR tuberculous adenitis OR TBLN)) Filters: in the last 5 years	33	12
Cochrane	((Kikuchi-Fujimoto Disease):ti,ab,kw OR (KFD):ti,ab,kw OR (histiocytic necrotizing lymphadenitis):ti,ab,kw OR (kikuchi lymphadenitis):ti,ab,kw) AND ((inguinal lymphadenopathy):ti,ab,kw OR (tuberculous lymphadenitis):ti,ab,kw OR (tuberculous adenitis):ti,ab,kw OR (TBLN):ti,ab,kw)	1	0
Scopus	(TITLE-ABS-KEY (Kikuchi-Fujimoto Disease) OR TITLE-ABS-KEY (KFD) OR TITLE-ABS-KEY (histiocytic necrotizing lymphadenitis) OR TITLE-ABS-KEY (kikuchi lymphadenitis) AND TITLE-ABS-KEY (inguinal lymphadenopathy) OR TITLE-ABS-KEY (tuberculous lymphadenitis) OR TITLE-ABS-KEY (tuberculous adenitis) OR TITLE-ABS-KEY (TBLN)) AND PUBYEAR > 2020 AND PUBYEAR < 2027	41	8
Google scholar	(Kikuchi-Fujimoto Disease OR KFD OR histiocytic necrotizing lymphadenitis OR kikuchi lymphadenitis) AND (inguinal lymphadenopathy OR tuberculous lymphadenitis OR tuberculous adenitis OR TBLN))) Custom range 2021-2026	116	2

Studies were screened rigorously according to predefined inclusion and exclusion criteria. The inclusion criteria were: (1) studies involving patients who initially presented with suspected tuberculosis lymphadenitis but were subsequently diagnosed with KFD based on biopsy findings; (2) patients with a

confirmed diagnosis of KFD established through histopathological examination; (3) studies reporting clinical presentation, diagnostic evaluation, management, and patient outcomes; (4) observational studies, including case series, and case reports; and (5) studies published within the last five years. The exclusion criteria were: (1) review articles, systematic reviews, and literature reviews; and (2) grey literature, conference abstracts without full-text availability, expert opinions, editorials, and commentaries.

The study selection process was summarized using a PRISMA flow diagram (Figure 1). A total of 152 records were identified through searches of PubMed, the Cochrane Library, and Google Scholar. Following title and abstract screening, 131 records were excluded. Full-text assessment was subsequently conducted on the remaining articles, resulting in the exclusion of 13 studies due to ineligible population characteristics, outcomes, or insufficient diagnostic confirmation of KFD. Eight studies met the eligibility criteria and were included in the qualitative synthesis. Given that the available evidence was limited to case reports and small case series, data extraction and quality assessment were independently conducted by three authors using the Joanna Briggs Institute (JBI) Critical Appraisal Tool for Case Reports (Table 3). The detailed literature search and study selection process are presented in Figure 1.

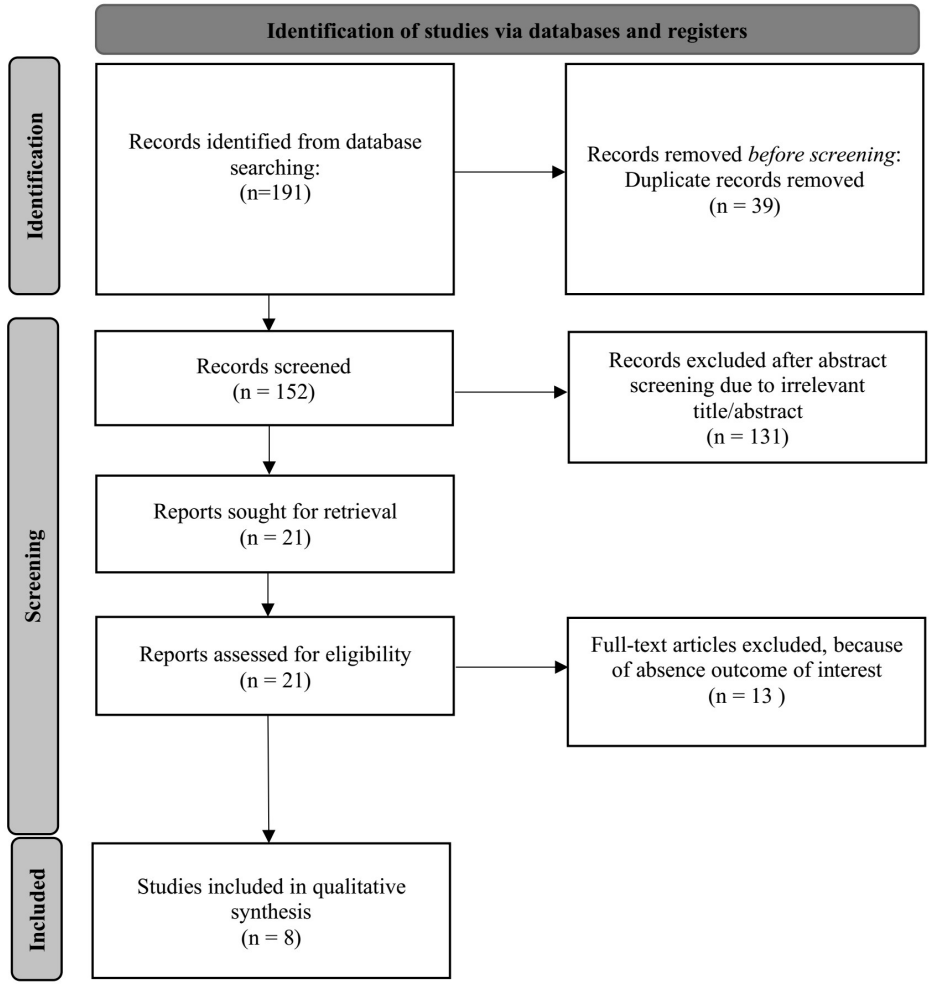

Figure 1. Flow Chart of Search Strategy

Table 3. Critical Appraisal of Eight Studies Based on Criteria by JBI Critical Appraisal Checklist for Case Reports

No	Checklist	Author							
		Sahoo, et al.	**Kedar, et al.**	**Tewoldemedhin, et al.**	**Hoan, et al.**	**Sharath, et al.**	**Daoo, et al.**	**Sarfraz, et al.**	**Buch, et al.**
1	Were patient's demographic characteristics clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Was the patient's history clearly described and presented as a timeline?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3	Was the current clinical condition of the patient on presentation clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4	Were diagnostic tests or assessment methods and the results clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5	Was the intervention(s) or treatment procedure(s) clearly described?	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	Unclear
6	Was the post-intervention clinical condition clearly described?	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes
7	Were adverse events (harms) or unanticipated events identified and described?	Yes	No	No	No	No	No	No	No
8	Does the case report provide takeaway lessons?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Overall appraisal	Include	Include	Include	Include	Include	Include	Include	Include

Based on the literature search, eight articles met the eligibility criteria, all of which are case reports. The characteristics of each study are presented in Table 4.

Table 4. Summary of Studies Included

Author (Year)	Clinical Presentation	Additional Symptoms	Therapy	Results
Sahoo, et al. (2025)	A 36-year-old woman with cervical and submandibular lymphadenopathy.	NR	Initiation of empirical antibiotics and empirical ATT for 3 weeks after inconclusive FNAC, followed with excisional biopsy cervical lymph node and corticosteroid for 7 days.	Persistence of the swelling and distressing dyspeptic symptoms after antibiotic and empirical ATT. Vitals return to stable and regression of lymph node size after excisional biopsy followed by corticosteroid.
Kedar, et al. (2024)	A 22-year-old male with multiple cervical, occipital, axillary, and inguinal lymphadenopathy.	Fever, dry cough, loss of appetite, multiple joint pains, and weight loss.	Self medication with antipyretic and analgesic, followed by excisional biopsy cervical lymph node, oral NSAID, and oral glucocorticoid.	Vitals return to stable and regression of lymph node size.
Tewoldemedhin, et al. (2023)	A 29-year-old male with multiple cervical lymphadenopathy with history of left cervical lymph node Mycobacterium tuberculosis infection.	Otalgia with ear fullness, erythematous rash, fever, night sweats, malaise, loss of appetite, multiple joint pains, and weight loss.	Initiation of empirical antibiotics, followed by excisional biopsy cervical lymph node and supportive therapy for 3 weeks.	Vitals return to stable and regression of lymph node size with complete resolution at 3 weeks.
Hoan, et al. (2021)	A 25-year-old woman with multiple cervical lymphadenopathy.	Fever.	Percutaneous ultrasound-guided biopsy followed with NSAID for 2 weeks.	Vitals return to stable and regression of lymph node size with complete resolution at 2 weeks.
Sharath, et al. (2023)	A 16-year-old male with multiple cervical lymphadenopathy.	Fever, night sweats, and weight loss	Initiation of empirical antibiotics for two weeks and ATT for three weeks, followed by excisional biopsy cervical lymph node and supportive therapy.	Vitals return to stable and regression of lymph node size with complete resolution at 4 months.

Table 4. Summary of Studies Included

Author (Year)	Clinical Presentation	Additional Symptoms	Therapy	Results
Daoo, et al. (2025)	A 6-year-old boy with multiple cervical, axilla, and inguinal lymphadenopathy with a history of recurrent tonsillitis and allergic symptoms.	Fever.	Biopsy from axillary lymph followed with prednisolone for 5 days. Acyclovir intravenous with iron supplements for two weeks. ATT for six weeks.	No clinical improvement was observed after treatment, leading to cessation of the drugs. KFD was diagnosed after the treatments failed to resolve the patient's vital signs and lymph node enlargement.
Sarfraz, et al. (2025)	A 25-year-old male with multiple cervical lymphadenopathy.	Fever and malaise.	Initiation of empirical antibiotics for two weeks, followed with excisional biopsy and paracetamol for 1 week.	Vitals return to stable and regression of lymph node size with complete resolution at 4 months.
Buch, et al. (2025)	A 7-year-old male with multiple cervical, axilla, and inguinal lymphadenopathy.	Fever, malaise, and weight loss	Initiation of empirical antibiotics, followed with higher injectable antibiotics, then axilla excisional biopsy.	Vitals return to stable and regression of lymph node size with complete resolution at 1 month.

Description: ATT=anti tuberculosis therapy, FNAC=Fine needle aspiration cytology, KFD=Kikuchi-Fujimoto Disease, LOS=Length of stay, NSAID=Nonsteroidal Anti-Inflammatory Drugs, NR=not reported

RESULTS AND DISCUSSION

Based on the included studies, the clinical presentation of KFD is typically nonspecific. The most common features are fever, lymphadenopathy, and constitutional symptoms.[1,2] The diagnosis of tuberculosis lymphadenitis was initially considered in our patient because several clinical and radiological findings were highly suggestive of tuberculosis. In our case, the patient presented with a low-grade intermittent fever for one week, accompanied by productive cough, decreased appetite, and weight loss. Physical examination revealed left inguinal lymphadenopathy. These manifestations are commonly reported in both pulmonary and extrapulmonary tuberculosis, frequently overlap with the clinical presentation of KFD. Up to 90% of patients with KFD experience fever lasting between one and seven weeks, and approximately 82% present with tender lymph nodes. Other reported symptoms include weight loss, nausea, vomiting, generalized weakness, headache, night sweats, and upper respiratory tract symptoms. Lymphadenopathy occurs in nearly 100% of patients; in up to 90% of cases, it involves the posterior cervical region. Generalized lymphadenopathy is seen in less than 22% of cases.[3,4] Our case is unique because lymphadenopathy was localized exclusively to the inguinal region, with symptoms mimicking tuberculosis disease. Inguinal involvement is uncommon both for KFD and for tuberculosis lymphadenitis, making the diagnostic process particularly challenging. Laboratory findings in KFD are also nonspecific including anemia, leukopenia or leukocytosis, thrombocytopenia, elevated liver enzymes, increased lactate dehydrogenase (LDH), and elevated erythrocyte sedimentation rate (ESR).[4,5] In our patient, laboratory evaluation demonstrated leukocytosis, lymphocytopenia, and elevated ESR. Chest X-ray revealed findings pulmonary tuberculosis and a negative GeneXpert result. However, the possibility of tuberculosis lymphadenitis should not be ruled out because the diagnostic performance of GeneXpert in tuberculosis lymphadenitis remains suboptimal, particulary in extrapulmonary disease, where the bacillary burden is often low (paucibacillary disease). A study evaluated the performance of Xpert for TB lymphadenitis, the overall sensitivity is 48.7% (36/74). The sensitivity and specificity with tissue specimen were 39.6% (95% CI 26.8 – 54.0) and 100% (95% CI 80.8 – 100), respectively.[6] Therefore, a negative GeneXpert does not definitively rule out tuberculous lymphadenitis when clinical and radiological findings remain highly suggestive of tuberculosis.

Availability bias may contribute to misdiagnosis, especially when physicians frequently encounter diseases with overlapping clinical features.[5] Therefore, in cases of chronic lymphadenopathy, excisional biopsy with histopathological examination is essential to exclude infectious and malignant causes and to establish a definitive diagnosis of KFD.[5,7] In the present case, histopathological examination of the excised inguinal lymph node revealed lymphoid follicular hyperplasia with follicles of varying sizes containing prominent germinal centers. Multiple necrotic foci with abundant apoptotic debris were identified, accompanied by hyperemic stroma and focal hemorraghe. No evidence of malignancy was observed. These findings were consistent with Kikuchi necrotizing histiocytic lymphadenitis and provided definitive confirmation of the diagnosis.

The histopathological findings observed in our patient correspond well with the characteristic features of KFD described in the literature. KFD is typically characterized by patchy paracortical caogulative necrosis with abundant karyorrhectic debris, distortion of the normal nodal architecture and infiltration by histiocytes and active T lymphocytes. Crescent shaped histiocytes and macrophages with foamy cytoplasm are commonly observed, whereas neutrophils are characteristically absent. These microscopic findings are particularly valuable in distinguishing KFD from the other causes of necrotizing lymphadenitis. Unlike tuberculosis lymphadenitis, KFD lacks granulomatous inflammation, Langhans giant cells, caseous necrosis, and acid-fast bacilli. Likewise, the absence of malignant cells excluded lymphoma, while the absence of hematoxylin bodies and plasma cell-rich infiltrates argued against systemic lupus erythematosus-associated lymphadenitis. Taken together, the histopathological findings strongly supported the diagnosis of Kikuchi-Fujimoto Disease in this patient despite the initial clinical suspicion of tuberculosis.[7,8]

Although no specific radiological features can definitively diagnose KFD, imaging studies provide supportive information. Chest radiography is routinely performed in patients presenting with fever and unexplained lymphadenopathy. Computed tomography (CT) or magnetic resonance imaging

(MRI) findings are generally nonspecific and may resemble malignant lymphoma or other forms of lymphadenitis, thus necessitating histopathological confirmation.[1,7]

Given the limited evidence and the absence of standardized guidelines for KFD treatment, we suggest that patients initially suspected of having tuberculous lymphadenopathy should undergo appropriate tuberculosis testing before initiating aggressive therapy, including extensive laboratory and radiological investigations. A major clinical dilemma arises when tuberculosis tests are negative, yet radiological findings suggest pulmonary tuberculosis, particularly in patients with atypical symptoms. Determining the appropriate timing for escalation to aggressive treatment in such cases remains challenging. In tuberculosis-endemic countries, empirical treatment for extrapulmonary tuberculosis is often initiated based solely on clinical suspicion. Early histopathological examination is crucial to prevent misdiagnosis and avoid unnecessary exposure to potentially toxic anti-tuberculosis therapy.[5]

In our patient, excisional biopsy was performed in a negative-pressure operating room, and definitive therapy was deferred until histopathological confirmation was obtained. Close clinical monitoring was maintained. One week after excisional biopsy, combined with supportive care and empirical oral cefixime therapy, the patient's symptoms completely resolved. Management of KFD primarily focuses on symptomatic treatment and supportive care. Antibiotics are generally ineffective but may be administered empirically to prevent or treat secondary bacterial infections.[7,8] Systemic corticosteroids are indicated in patients with prolonged fever, persistent symptoms lasting more than two weeks, or recurrent disease. In mild cases, non-steroidal anti-inflammatory drugs (NSAIDs) are usually sufficient to control fever and lymph node tenderness, as demonstrated in our patient.

The limitations of this study include the lack of high-level evidence beyond case reports, reflecting the rarity of KFD. Furthermore, variations in supportive and aggressive treatment strategies across the literature may contribute to differences in reported clinical outcomes.

CONCLUSION

Kikuchi–Fujimoto Disease (KFD) is a rare, benign, and usually self-limiting necrotizing lymphadenitis that predominantly affects young individuals, particularly those of Asian descent, and commonly presents with fever and cervical lymphadenopathy. Because its clinical and imaging features are nonspecific, it may mimic tuberculosis, malignancy, or autoimmune disease, and misdiagnosis can occur. Excisional lymph node biopsy is generally regarded as the most reliable means of establishing the diagnosis, as fine-needle aspiration cytology is often inconclusive. In tuberculosis-endemic settings, suggestive clinical and radiological findings may understandably prompt consideration of empirical anti-tuberculosis therapy; however, initiating such treatment before histopathological confirmation may be less than ideal, as it carries the risk of delaying an accurate diagnosis and exposing patients to unnecessary medication. Where feasible, histopathological confirmation should therefore be pursued before committing to empirical therapy. It should be acknowledged that current evidence on KFD is largely derived from case reports and small case series, which limits the strength of any firm recommendations. Within these constraints, available data nevertheless suggest that KFD often follows a benign course requiring mainly supportive management, with NSAIDs or corticosteroids reported to provide symptomatic relief and generally favorable outcomes.

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