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Diagnostic Challenges and Scientific Management of Suspected Recurrent Kikuchi-Fujimoto Disease: A Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 26-year-old
Final Diagnosis: Kikuchi-Fujimoto disease
Symptoms: Fever •fatigue • cough • sputum production
Clinical Procedure: —
Specialty: Immunology

Objective: Rare disease

Background: Kikuchi-Fujimoto disease is a rare, benign, and self-limiting disease typically characterized by persistent fever and lymphadenopathy. The clinical manifestations are nonspecific, and consensus diagnostic criteria are currently unavailable; therefore, it is easily misdiagnosed as lymphoma, tuberculosis, or autoimmune diseases. Definite diagnoses rely on lymph node biopsy results. Recurrence of Kikuchi-Fujimoto disease is not uncommon, with recurrence rates varying across different age groups, ranging from 3% to 42.4%. Most patients have a favorable prognosis, while some progress to autoimmune diseases during follow-up.

Case Report: A 26-year-old man presented with a history of recurrent fever with lymphadenopathy and positive autoantibodies. He received empirical treatment for an upper respiratory tract infection in the early stage; finally, Kikuchi-Fujimoto disease was confirmed by lymph node biopsy. Given the patient's similar clinical symptoms without prior pathological confirmation 2 years ago, we presumed that the current episode was a recurrence of Kikuchi-Fujimoto disease.

Conclusions: The case exemplifies the diagnostic challenges of Kikuchi-Fujimoto disease. It is easily neglected by clinicians due to insufficient awareness of the disease, and Kikuchi-Fujimoto disease should be included in the differential diagnosis of fever of unknown origin. Choosing appropriate diagnostic modalities is crucial for establishing a timely and definitive diagnosis. Although the recurrence in this case was presumed, recurrence does occur with a certain incidence in Kikuchi-Fujimoto disease; therefore, long-term follow-up observation is necessary for Kikuchi-Fujimoto disease, especially for patients with positive autoantibodies.

Keywords: Kikuchi-Fujimoto Disease • Lymphadenopathy • Recurrence

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Introduction

Kikuchi-Fujimoto disease, also known as histiocytic necrotizing lymphadenitis, was first described by Kikuchi and Fujimoto in 1972 [1]. It is a benign, self-limiting disease characterized by necrotizing lymph node lesions with high misdiagnosis rates due to nonspecific clinical manifestations. It is easily misdiagnosed as lymphoma, tuberculous lymphadenitis, and autoimmune diseases. Although generally benign, recurrence [2-4]and mortality [5,6]rates associated with Kikuchi-Fujimoto disease vary across studies. Associations between Kikuchi-Fujimoto disease and systemic autoimmune disorders have been reported. Autoimmune disorders can precede Kikuchi-Fujimoto disease [7], occur concurrently [8,9], or develop afterward [10,11]. According to Baenas et al, Kikuchi-Fujimoto disease precedes SLE in 30% of cases, coexists with SLE in 47%, and follows SLE in 23% [12]. At diagnosis, some Kikuchi-Fujimoto disease patients test positive for multiple autoantibodies, including ANA, anti-dsDNA, anti-SSA, and anti-RO. Notably, some patients who are initially negative for autoantibodies at Kikuchi-Fujimoto disease diagnosis later progress to autoimmune disorders [13]. Here, we present a case of suspected recurrent Kikuchi-Fujimoto disease without prior pathological confirmation, and Kikuchi-Fujimoto disease was diagnosed by lymph node biopsy in the current episode, which was initially misdiagnosed as an upper respiratory tract infection. The purpose of this report is to improve clinicians' understanding of the disease, highlight the importance of Kikuchi-Fujimoto disease in the differential diagnosis of fever of unknown origin, especially in patients with painful lymphadenopathy and ineffective antibiotic treatment, and emphasize the necessity of long-term follow-up considering the risk of recurrence and progression to autoimmune diseases.

Case Report

A 26-year-old man was admitted for fever, fatigue, cough, and sputum production for 6 days, with peak temperature reaching 39.5°C prior to admission. The patient reported a history of hospitalization for persistent fever and painful cervical lymphadenopathy 2 years ago. As no other characteristic symptoms were present, a definitive diagnosis was not established at the first hospital. Subsequently, he was referred to a higher-level hospital due to persistent fever of unknown origin. The patient received empirical treatment without undergoing lymph node biopsy, including antibiotics and nonsteroidal anti-inflammatory drugs but the details of the treatment were not available. After treatment, he achieved clinical remission with no sequelae.

The patient had a smoking history of over 1 year, with a daily consumption of 7 cigarettes, no alcohol consumption, no drug exposure, and no tuberculosis contact. Physical examination on admission revealed enlargement and tenderness of the right cervical lymph nodes, but no other obvious abnormalities were found. A complete blood count performed before admission showed leukopenia, lymphopenia, neutropenia, eosinopenia, and thrombocytopenia. **Table 1** summarizes the patient's laboratory results after hospitalization, along with reference ranges. Pathogen testing was negative for influenza virus, adenovirus, SARS-CoV-2, mycoplasma pneumoniae, cytomegalovirus, and Epstein-Barr virus. Given the patient's respiratory symptoms, the patient received empirical treatment for an upper respiratory tract infection in the early stage, the detailed medication information was as follows, ibuprofen as needed, levofloxacin injection, 0.5 g qd for 7 days, and dexamethasone sodium phosphate injection, 10 mg qd for 2 days. The treatment showed minimal efficacy, and the patient continued to experience persistent fever. The normal inflammatory marker was inconsistent with the presenting symptoms, which indicated the definitive diagnosis remained unclear. Further diagnostic tests were implemented to rule out atypical pathogens, autoimmune diseases, including *Brucella* antibody, blood cultures and rheumatologic and immunologic markers. Examination results indicated that *Brucella* antibody and blood culture were negative, as were anti-nuclear antibody (ANA, granular pattern, 1: 80) and anti-SSA was positive. Rheumatoid factor, anti-CCP, anti-U1RNP/Anti-ENA, anti-Sm, anti-SSB, anti-Scl-70, anti-Jo-1, anti-rRNP, and anti-double-stranded DNA. Although ANA and anti-SSA were positive, the patient had no symptoms related to autoimmune diseases. Because lymphadenopathy with tenderness was the predominant symptom in this patient, lymph node ultrasonography and excisional biopsy were performed to rule out lymph node malignancies and other conditions. Ultrasound of the lymph nodes revealed multiple enlarged lymph nodes in the right cervical region, and the largest was 1.6 cm×0.8 cm. The result of cervical lymph node biopsy indicated focal apoptotic necrosis in the paracortical area, accompanied by crescent-shaped histiocytes containing abundant karyorrhectic debris, without neutrophil infiltration (**Figure 1**), consistent with Kikuchi-Fujimoto disease. After partial resection of the lymph node, the patient had persistent low-grade fever and received clinical remission finally without specific treatment. Given the patient's similar clinical presentation 2 years ago, we speculate that the current episode was likely a recurrence of Kikuchi-Fujimoto disease, but the conclusion is limited due to the lack of prior pathology confirmation.

Discussion

Kikuchi-Fujimoto disease is a benign, self-limiting disorder of unknown etiology. Most cases have favorable outcomes, while a minority progress to severe complications such as

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Table 1. Laboratory data of patient on admission and prior to discharge.

Variables	On admission	Prior to discharge	Reference range
White blood cell count (×10^9/L)	2.39	4.38	4-10
Neutrophil (×10^9/L)	1.47	2.25	2-7
Lymphocyte (×10^9/L)	0.61	1.51	0.8-4
Eosinophil (×10^9/L)	0	0.05	0.5-5
Hypersensitive C-reactive protein (mg/L)	3.8	0.1	0-5
Procalcitonin (ng/mL)	0.035		0-0.05
Red blood cell sedimentation rate (mm/h)	17	11	0-15
Alanine aminotransferase, ALT (U/L)	20.5		5-40
Aspartate aminotransferase, AST (U/L)	21.3		8-40
Creatinine (μmol/L)	78		44-97
Rheumatologic and immunologic markers			
Rheumatoid factor (IU/mL)	5.71		0-18
Anti-CCP (RU/ml)	3.35		0-20
Anti-U1RNP/Anti-ENA	Negative		Negative
Anti-Sm	Negative		Negative
Anti-SSA	Positive		Negative
Anti-SSB	Negative		Negative
Anti-Scl-70	Negative		Negative
Anti-Jo-1	Negative		Negative
Anti-rRNP	Negative		Negative
Anti-double-stranded DNA	Negative		Negative
Anti-nuclear antibody	Nuclear granular pattern (1: 80)		<1: 80

Anti- CCP, anti-cyclic citrullinated peptide antibody; Anti-U1RNP, anti-U1 ribonucleoprotein antibody; Anti-ENA, anti-extractable nuclear antigen antibody; Anti-Sm, anti-Smith antibody; Anti-SSA, anti-Sjögren syndrome antigen A antibody; Anti-SSB, anti-Sjögren syndrome antigen B antibody; Anti-Scl-70, anti-scleroderma 70 antibody; Anti-rRNP, anti-ribosomal ribonucleoprotein antibody.

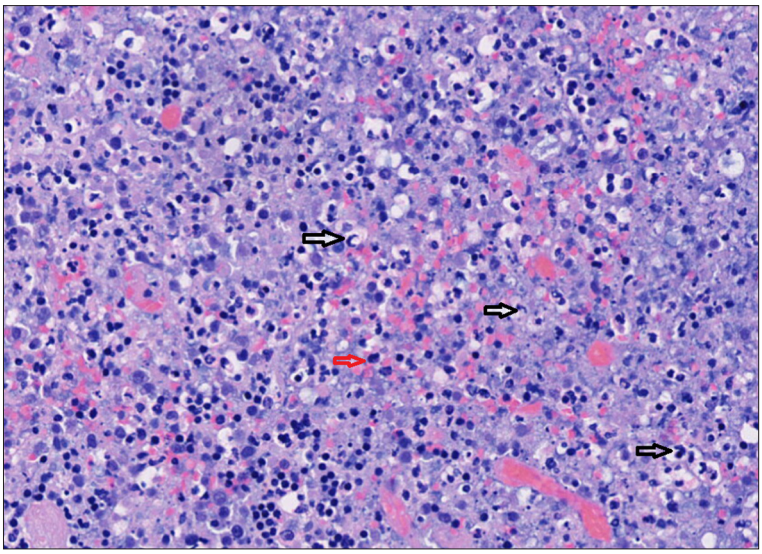

Figure 1. Lymph node biopsy pathology. HE (high-power lens), Lymph node staining revealed features consistent with histiocytic necrotizing lymphadenitis. Focal apoptotic necrosis was observed in the paracortical area, accompanied by crescent-shaped histiocytes (black open arrow) containing abundant karyorrhectic debris (red open arrow), with no neutrophil infiltration.

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hemophagocytic syndrome [14]. Previous studies have indicated that this disease predominantly affects young Asian females [15, 16], especially those under 30 years old. The sex distribution varies by age stratification, and multiple studies have suggested that males account for a higher proportion of cases among patients under 15 years old, whereas females predominate in those over 15 years old [16, 17]. Symptoms of Kikuchi-Fujimoto disease are nonspecific, including unexplained fever accompanied by painful lymphadenopathy. Nevertheless, headache, fatigue, arthralgia, myalgia, rash, weight loss, and abdominal pain are relatively uncommon. Abnormal blood cell counts are the most common laboratory abnormality. According to a report on changes in blood and bone marrow cells of Kikuchi-Fujimoto disease patients, anemia (22%) was the most common abnormality, followed by lymphopenia (17%), neutropenia (11%), atypical lymphocytes (9%), and thrombocytopenia (8%) [17]. Given the uncertain etiology and pathogenesis, as well as the lack of specificity in clinical features, no consensus diagnostic criteria are currently available. As a result, Kikuchi-Fujimoto disease is frequently misdiagnosed as other conditions such as lymphoma, tuberculosis, neck abscess or SLE. The disease is susceptible to underdiagnosis due to the following factors, such as insufficient understanding of Kikuchi-Fujimoto disease among clinicians and pathologists, lack of targeted examination, and delayed assessment of antibiotic ineffectiveness. Definitive diagnosis requires lymph node biopsy, with characteristic histopathology including paracortical lesions with variable necrosis, crescent-shaped histiocytes containing abundant karyorrhectic debris, predominance of CD8+ T cells, and marked absence of neutrophils [18-20].

In this case, a 26-year-old man presented with persistent fever, fatigue, and painful cervical lymphadenopathy and abnormal blood cell counts, but the inflammation markers were normal, including hypersensitive C-reactive protein and procalcitonin. Given the patient's clinical manifestations, hematological disorders and infectious diseases were among the most likely initial considerations. The patient experienced similar symptoms 2 years ago, but no lymph node biopsy was performed due to the clinicians' unawareness of Kikuchi-Fujimoto disease. Although the patient achieved clinical remission, the true etiology remained unclear, reflecting the difficulty of diagnosing Kikuchi-Fujimoto disease. The definite diagnosis was confirmed by lymph node biopsy in current episode. This case report may enhance clinician awareness of this disease and indicates that Kikuchi-Fujimoto disease should be included in the differential diagnosis of fever of unknown origin. Choosing appropriate diagnostic modalities is crucial for establishing a timely and definitive diagnosis. Timely diagnosis can avoid unnecessary treatments and alleviate patient anxiety.

Recurrence in Kikuchi-Fujimoto disease is not uncommon, with rates ranging from 3% to 42.4% across age groups [2-4]. A multicenter retrospective study in children reported a 14.8% recurrence rate; high-risk factors for recurrence included age ≤6 years, CRP >16 mg/L, peripheral blood CD4+ T cells <30%, ferritin >150 μg/L, and platelets ≤200×10^9/L [21]. Recurrence risk in adult is associated with extranodal manifestations, positive ANA, significant leukopenia, and low C4 levels [14,22,23]. Our patient reported a prior hospitalization for unexplained fever with lymphadenopathy 2 years ago, which resolved with empiric treatment but remained undiagnosed. By comparing the current clinical symptoms with previous manifestations, we speculate that the previous episode was also Kikuchi-Fujimoto disease, but this cannot be confirmed due to the absence of lymph node biopsy results. Although the recurrence in this case is presumed, the risk of recurrence is elevated in individuals with specific characteristics. Although the patient had no evidence of extranodal disease, the presence of positive ANA and anti-SSA antibodies, severe leukopenia, and a previous similar episode indicated a high risk of recurrence. Therefore, close follow-up and observation are recommended.

The relationship between Kikuchi-Fujimoto disease and autoimmune diseases is particularly close, especially with SLE. A study reported that the rate of developing into autoimmune diseases after Kikuchi-Fujimoto disease diagnosis was 2.7% (13/480), and patients with Kikuchi-Fujimoto disease recurrence, extranodal symptoms, or anti-nuclear antibody (ANA) positivity were more likely to develop into systemic autoimmune disorders [24]. Although the result was limited by the small sample size, its clinical significance in predicting the progression to autoimmune diseases deserves attention. Our patient had positive ANA and anti-SSA antibodies, had a suspected history of recurrence, and had a high risk of progressing to autoimmune diseases. Kikuchi-Fujimoto disease patients with positive specific autoantibodies should be closely monitored to facilitate timely detection of the onset and progression of rheumatic or autoimmune diseases.

This case report highlights the difficulty of diagnosing Kikuchi-Fujimoto disease and emphasizes the importance of follow-up for such patients. Several limitations must be acknowledged. First, this is a report of a single case, which limits the applicability of our findings to a broader patient population. Second, recurrence was suspected based on the prior clinical presentation, without pathological confirmation by lymph node biopsy. Finally, owing to the absence of long-term follow-up results, the relationship with autoimmune diseases can only be deduced from available literature.

Conclusions

The case report describes the entire diagnostic process of this case, and highlights that Kikuchi-Fujimoto disease should be

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considered in the differential diagnosis of fever of unknown origin, especially in patients with painful lymphadenopathy and ineffective antibiotic treatment. When conventional tests fail to yield a diagnosis, the direction of diagnostic reasoning should be revised. Improving the clinicians' understanding of the disease is important to accurately identifying Kikuchi-Fujimoto disease, and could avoid misdiagnosis and ensure that patients accept appropriate treatment and scientific management. Given the possibility of recurrence and its association with autoimmune diseases, long-term follow-up is recommended to monitor for potential disease progression.

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Department and Institution Where Work Was Done

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Patient Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

References:

1. Fujimoto Y, Kozima Y, Yamaguchi K. Cervical subacute necrotizing lymphadenitis: A new clinicopathologic entity. Naika. 1972;20:920-27
2. Lin YC, Huang HH, Nong BR, et al. Pediatric Kikuchi-Fujimoto disease: A clinicopathologic study and the therapeutic effects of hydroxychloroquine. J Microbiol Immunol Infect. 2019;52:395-401
3. Yoo IH, Na H, Bae EY, et al. Recurrent lymphadenopathy in children with Kikuchi-Fujimoto disease. Eur J Pediatr. 2014;173:1193-99
4. Lou D, Song Y. Clinical features of histiocytic necrotizing lymphadenitis in children. Eur J Pediatr. 2024;183:1333-39
5. Barbat B, Jhaj R, Khurram D. Fatality in Kikuchi-Fujimoto disease: A rare phenomenon. World J Clin Cases. 2017;5:35-39
6. Sharma V, Rankin R. Fatal Kikuchi-like lymphadenitis associated with connective tissue disease: A report of two cases and review of the literature. Springerplus. 2015;4:167
7. Al Barazanjy HA, Alabdullah AR, Shabbir A, et al. A case report of lupus cerebritis in a female with preceding Kikuchi-Fujimoto disease. Cureus. 2025;17:e82594
8. Nijim K, Dockerwolcke K, Da'meh A, et al. Systemic Lupus Erythematosus Developing In A Young African Female Patient With Kikuchi-Fujimoto disease. Cureus. 2025;17:e88381
9. Yousefi M, Rukerd MRZ, Binafar H, et al. The co-occurrence of Kikuchi-Fujimoto disease and systemic lupus erythematosus: A case report. J Med Case Rep. 2023;17:448
10. Coccia C, Lepri G, Levani J, et al. Rare in the rare: Kikuchi-Fujimoto disease associated with connective tissue disorders. A report of our experience. Reumatismo. 2025;77:1853
11. Takahashi K, Okura Y, Shimomura M, et al. Development of Sjögren's syndrome following Kikuchi-Fujimoto disease – A sibling case. Pediatr Int. 2023;65(1):e15524
12. Baenas DF, Diehl FA, Haye Salinas MJ, et al. Kikuchi-Fujimoto disease and systemic lupus erythematosus. Int Med Case Rep J. 2016;9:163-67
13. Zhang D, Su GX, Wu FQ, et al. [Clinical features and prognosis of 118 children with histiocytic necrotizing lymphadenitis]. Zhonghua Er Ke Za Zhi. 2023;61:533-37 [in Chinese]
14. Shen Z, Ling J, Zhu X, et al. Macrophage activation syndrome in children with Kikuchi-Fujimoto disease. Pediatr Rheumatol Online J. 2023;21:10
15. Ruaro B, Sulli A, Alessandri E, et al. Kikuchi-Fujimoto's disease associated with systemic lupus erythematous: Difficult case report and literature review. Lupus. 2014;23:939-44
16. Liu J, Zheng Q, Shi L, et al. A retrospective study of 134 patients with cervical region Kikuchi-Fujimoto disease. Laryngoscope Investigaive Otolaryngology. 2023;8:865-69
17. Yu SC, Huang HH, Chen CN, et al. Blood cell and marrow changes in patients with Kikuchi disease. Haematologica. 2022;107:1981-85
18. Thongsuksai P, Kayasut K. Histiocytic necrotizing lymphadenitis (Kikuchi's disease): Clinicopathologic characteristics of 23 cases and literature review. J Med Assoc Thai. 1999;82:812-18
19. Hon JD, Vergara-Lluri ME, Siddiqi I, et al. Kikuchi-Fujimoto disease involving retroperitoneal lymph nodes: An uncommon presentation. Hematol Rep. 2021;13:9001
20. Mahajan VK, Sharma V, Sharma N, Rani R. Kikuchi-Fujimoto disease: A comprehensive review. World J Clin Cases. 2023;11:3664-79
21. Xie YP, Xu YW, Li Y. Recurrence of histiocytic necrotizing lymphadenitis in children: A 10-year multicenter retrospective study. J Inflamm Res. 2025;18:4307-18
22. Nishimura MF, Sakao C, Kurokawa Y, Nishimura Y. Kikuchi-Fujimoto disease: Investigating comprehensive clinicopathological features and risk factors for recurrence. Histopathology. 2025;87:68-80
23. Zhang X, Jin X, Zhang X, Shen Y. Clinical features and recurrence predictors of histiocytic necrotizing lymphadenitis in Chinese children. Pediatric Rheumatology. 2024;22:61
24. Jung HJ, Lee IJ, Yoon SH. Risk assessment of recurrence and autoimmune disorders in Kikuchi disease. Risk Manag Health Policy. 2020;13:1687-93

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