Case Report

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A Rare Case of Kikuchi-Fujimoto Disease Associated with Sjögren's Syndrome in a Young Male without Classical Sicca Symptoms

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Running Title Kikuchi-Fujimoto Disease Associated with Sjögren's Syndrome

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ABSTRACT

Kikuchi-Fujimoto disease (KFD) is a rare, self-limiting condition characterized by fever and lymphadenopathy. Its association with Sjögren's syndrome (SS) is exceedingly rare, particularly in the absence of classical sicca symptoms. This case report describes a young male with KFD and SS, highlighting the diagnostic challenges and the importance of a multidisciplinary approach in atypical presentations.

A 21-year-old male presented with a 20–25-day history of intermittent high-grade fever, chills, generalized weakness, and severe epigastric pain. Initial investigations suggested enteric fever, but the recurrent symptoms prompted further evaluation. Imaging revealed widespread lymphadenopathy, and histopathological examination confirmed the diagnosis of KFD. Serologic testing revealed SS despite the absence of dry eyes or mouth. The patient was managed symptomatically, and his condition improved with supportive care.

This case highlights the importance of considering rare autoimmune etiologies in young patients with persistent febrile illnesses and atypical systemic features. The concurrent diagnosis of KFD and SS without classical sicca symptoms adds to the limited literature on this rare association. A multidisciplinary approach, including histopathological and serological testing, is crucial for accurate diagnosis and management. Further research is needed to better understand the pathogenesis and autoimmune associations of KFD.

Introduction

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare, self-limiting condition characterized by fever and lymphadenopathy. First described in 1972 by Kikuchi and Fujimoto, it predominantly affects young women in their 20s and 30s, with a slight female predominance. The exact etiology of KFD remains unknown, but viral infections such as Epstein-Barr virus (EBV) and human herpesvirus-6 (HHV-6) have been implicated as potential triggers. Interestingly, some studies suggest that KFD may represent an exaggerated immune response to viral antigens, leading to histiocytic infiltration and necrosis in lymph nodes [1,2].

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Sjögren's syndrome (SS), on the other hand, is a chronic autoimmune disorder characterized by lymphocytic infiltration of exocrine glands, leading to sicca symptoms such as dry eyes and dry mouth. SS primarily affects middle-aged women, with a female-to-male ratio of 9:1. While SS is often associated with other autoimmune conditions like rheumatoid arthritis and systemic lupus erythematosus (SLE), its association with KFD is exceptionally rare [3,4].

The co-occurrence of KFD and SS is exceedingly rare, with only a handful of cases reported in the literature. This case is particularly unique because it involves a young male without classical sicca symptoms, which is highly unusual for SS. This case report aims to contribute to the limited literature on this rare association and highlight the diagnostic challenges in patients with atypical presentations.

Case Presentation

A 21-year-old male presented with a 20–25-day history of intermittent high-grade fever and chills, accompanied by dry cough, joint pain, generalized weakness, and headaches for one week. He denied any history of dry eyes, dry mouth, or other sicca symptoms, making the diagnosis of SS particularly challenging. There was no significant family history of autoimmune disease, and the patient had no prior medical conditions. He reported prior treatment at another hospital, where he was diagnosed with clinical enteric fever based on an elevated C-reactive protein (CRP) level of 78 mg/L. Despite initial improvement with intravenous antibiotics and antipyretics, his fever recurred within a week of discharge, accompanied by chills and vomiting.

On admission to our hospital, the patient had a temperature of 100.1°F, a pulse rate of 120 bpm, blood pressure of 110/76 mmHg, and a respiratory rate of 22 breaths per minute. Physical examination revealed severe tenderness in the epigastric region but no significant findings in other systemic examinations. There was no palpable lymphadenopathy, hepatosplenomegaly, or skin rash, which initially made the diagnosis of KFD less obvious.

In laboratory finding we found: Procalcitonin: 1.42 ng/mL, Calcium: 7.7 mg/dL, CRP: 247.8 mg/L, Lactate Dehydrogenase (LDH): 472 U/L, Ferritin: 788 ng/mL, Complete blood picture (CBP): Within normal limits, Serum creatinine: Normal, Liver function tests: Normal, Renal function tests: Normal, Viral serologies (EBV, HHV-6, HIV): Negative

The imaging taken include: - Abdominal ultrasound: No abnormalities.

And Contrast-enhanced CT scan: Multiple small-to-medium-sized cervical, thoracic, and abdominal

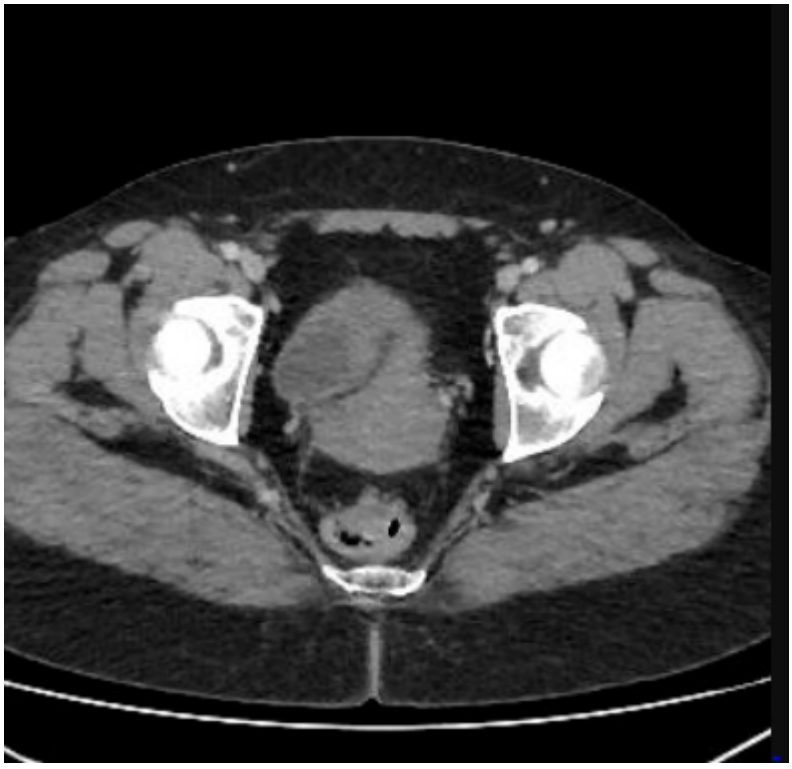

Fig. 1. Contrast-enhanced CT scan

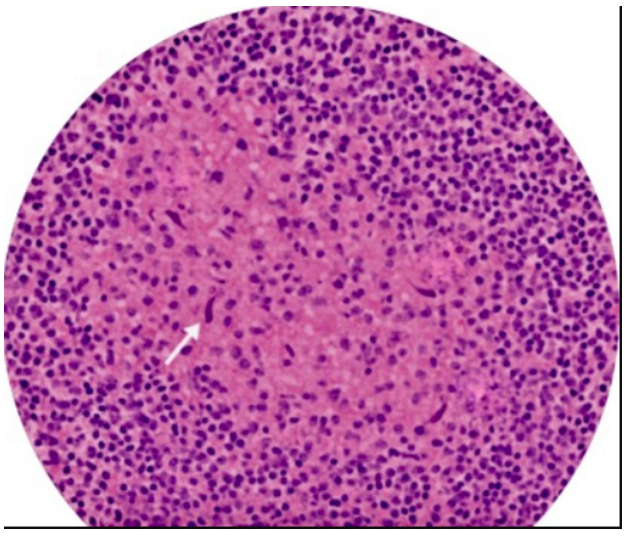

Fig. 2. Cervical lymph node biopsy

lymphadenopathy. The largest lymph node measured 1.5 cm in diameter and showed no evidence of necrosis or calcification, which initially raised the possibility of lymphoma or tuberculosis. (Figure 1)

Cervical lymph node biopsy revealed widespread necrosis with characteristic crescent-shaped histiocytes, confirming KFD [Figure 2]. Immunohistochemistry showed a predominance of CD68+ histiocytes and CD8+ T cells, consistent with the diagnosis of KFD. The absence of granulomas or malignant cells ruled out tuberculosis and lymphoma, respectively.

In serologic testing: - Antinuclear antibody (ANA): Strongly positive with a speckled pattern.

- ANA blot: Significant correlation with SS and weak association with systemic lupus erythematosus (SLE). Additional testing revealed positive anti-Ro/SSA and anti-La/SSB antibodies, further supporting the diagnosis of SS.

The patient was initially managed symptomatically with antipyretics and intravenous proton pump inhibitors (PPIs) for fever and epigastric pain, respectively. Following the diagnosis of KFD associated with SS, treatment shifted to supportive care, as KFD is self-limiting. The patient was started on hydroxychloroquine (200 mg twice daily) for SS, and his symptoms gradually improved over the next four weeks.

Week 1: Fever resolved, and inflammatory markers (CRP, LDH) began to decline.

Week 4: Complete resolution of symptoms, and repeat imaging showed a significant reduction in lymphadenopathy.

Month 3: The patient remained asymptomatic, and serologic testing showed a decrease in ANA titers.

Learning Points

1. Rare Association of KFD and SS: This case highlights the rare co-occurrence of Kikuchi-Fujimoto disease (KFD) and Sjögren's syndrome (SS) in a young male without classical sicca symptoms. It underscores the importance of considering autoimmune etiologies in patients with persistent fever and lymphadenopathy, even in the absence of typical symptoms.

2. Diagnostic Challenges: The case demonstrates the diagnostic challenges of KFD, which can mimic infectious or malignant conditions. A multidisciplinary approach, including histopathology and serologic testing, is crucial for the accurate diagnosis and management of rare autoimmune conditions like KFD and SS.

3. Clinical Implications: Early recognition of autoimmune associations in KFD is essential for long-term management. This case emphasizes the need for clinicians to maintain a high index of suspicion for rare autoimmune conditions in patients with atypical presentations, ensuring timely and appropriate treatment.

Discussion

Kikuchi-Fujimoto disease (KFD) is a rare, self-

limiting condition that primarily presents with fever, lymphadenopathy, and elevated inflammatory markers [1]. Despite its characteristic features, it can mimic other diseases, including infectious mononucleosis, tuberculosis, and systemic autoimmune disorders, due to overlapping symptoms. The diagnosis of KFD is often challenging, particularly in the absence of classical features, and requires a high index of suspicion [2].

The association between KFD and autoimmune diseases, particularly systemic lupus erythematosus (SLE), has been well documented in the literature. However, the co-occurrence of KFD and Sjögren's syndrome (SS) is much rarer, with only a few reported cases [5]. This case adds to the limited literature on this rare association and highlights the importance of considering autoimmune diseases in patients with atypical presentations of KFD.

The exact pathophysiology of KFD remains unclear, but several hypotheses have been proposed. Viral infections, such as Epstein-Barr virus (EBV) and human herpesvirus-6 (HHV-6), have been implicated as potential triggers, leading to an aberrant immune response in genetically susceptible individuals. In this case, the patient's strong positive antinuclear antibody (ANA) with a speckled pattern and significant correlation with SS on ANA blot testing support the diagnosis of an underlying autoimmune disorder [4,5].

This case underscores the importance of a multidisciplinary approach in the diagnosis and management of KFD, particularly when associated with autoimmune diseases. Early recognition of autoimmune associations is crucial for long-term management and prevention of complications.

Conclusion

This case highlights the importance of considering rare conditions like Kikuchi-Fujimoto disease (KFD) in the differential diagnosis of fever and prolonged lymphadenopathy, especially when the presentation is atypical for common infectious or autoimmune etiologies. The concurrent diagnosis of Sjögren's syndrome, without the typical sicca symptoms, adds a unique aspect to this case and underscores the need for a broad diagnostic approach in patients with persistent systemic symptoms.

Although KFD is self-limiting and typically resolves without specific treatment, the recognition of associated autoimmune conditions such as SS is crucial for long-term management. This case also highlights the need for further research into the pathogenesis and autoimmune associations of KFD to improve diagnostic accuracy and treatment strategies.

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Ethical Considerations

Compliance with ethical guidelines

This case report was conducted in compliance with ethical guidelines. Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

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Conflict of Interests

The authors declare no conflicts of interest related to this manuscript.

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