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Challenges in diagnosis: A case of Kikuchi-Fujimoto disease presenting with lymphadenopathy

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Abstract

Background: Kikuchi-Fujimoto disease (KFD) is a non-malignant and self-limiting condition, characterized by localized swelling of the cervical lymph nodes. It is typically accompanied by a mild increase in body temperature and excessive sweating during the night.

Case Presentation: This case report presents a case of a 45-year-old male presented with a history of moderate, episodic fever with chills, body aches, fatigue, and myalgia for 6 weeks. The fever was unchanged in intensity. The patient denied respiratory or gastrointestinal symptoms, maintained a normal appetite, and did not experience weight loss. Notably, there were no exacerbating factors, and symptoms were relieved by medication. His medical history included smoking 20 cigarettes daily for 20 years, with no known chronic conditions or significant family history apart from maternal diabetes and hypertension.

Physical examination revealed stable vital signs and multiple mobile, non-tender lymph nodes in the left lower cervical region. Imaging, including chest X-ray, abdominal ultrasound, and CT scan, indicated multiple enlarged lymph nodes and suspicious findings in the duodenum and liver. Esophagogastroduodenoscopy revealed grade B esophagitis, erosive antral gastritis, and mild duodenitis, with biopsies indicating reactive lymphadenitis consistent with KFD.

The diagnosis of KFD was confirmed through lymph node biopsy, showing characteristic histopathological features and negative special stains for microorganisms. The patient was managed with prednisolone and fluconazole for esophageal candidiasis. Follow-up revealed resolution of fever and lymphadenopathy, with the patient being clinically stable.

Conclusion: This case highlights the clinical presentation, diagnostic challenges, and effective management of Kikuchi-Fujimoto Disease in a middle-aged male. This emphasizes the need to consider KFD in the differential diagnosis of prolonged fever and lymphadenopathy, especially when systemic symptoms and positive markers for infections or autoimmune diseases are absent.

Keywords: Kikuchi-Fujimoto disease; Esophagogastroduodenoscopy; Necrotizing lymphadenitis; Lymphadenopathy

1. Introduction

Kikuchi-Fujimoto disease is a benign and self-limiting condition characterized by tender regional lymphadenopathy, most commonly occurring in the cervical area (1, 2). Despite its unclear origins, the disease typically resolves on its own. (1) It is typically accompanied by night sweats and mild fever (3). Kikuchi-Fujimoto disease (KFD) was first documented in Japan in 1972 when it was independently discovered by Fujimoto et al and Kikuchi et al (4). It was then identified as

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lymphadenitis characterized by the proliferation of reticular cells, as well as the presence of a significant number of nuclear debris and histiocytes (5).

KFD is a very uncommon condition that is found all over the world, but it is more commonly seen in Japanese and other Asian individuals (6). The disease is rarely seen in children, with most cases occurring in young adults below thirty years (7). The literature has highlighted a higher number of cases among females, with a ratio of four females to one male (8). It appears that recent reports suggest that the previous emphasis on the higher number of females may have been exaggerated and that the actual ratio is now believed to be closer to an equal split between females and males (9). Typically, the disease follows a mild and temporary course, characterized by swelling of the lymph nodes in the neck (most common) (10). Occasionally, there may be additional symptoms like, night sweats, fatigue, nausea, and weight loss (10). Typically, KFD is diagnosed by performing an excisional lymph node biopsy and analyzing the tissue under a microscope (9). There are several conditions that share similar characteristics with KFD, such as autoimmune conditions, inflammatory disorders, lymphoma, and infectious causes like tuberculosis infection (11). It is crucial to keep KFD in mind when dealing with persistent lymphadenopathy and to distinguish it from these other conditions (12). Treatment typically involves addressing symptoms through the use of antipyretics, non-steroidal anti-inflammatory drugs, or, in rare cases, steroids. KFD typically involves spontaneous recovery within a period of 1–4 months (12).

2. Case Presentation

A 45-year-old not diabetic, non-hypertensive Indian male presented to the hospital with a history of moderate fever, characterized by chills and body aches, persisting for six weeks. The fever was episodic, fluctuated in intensity, and remained unchanged throughout its course. He experienced fatigue and myalgia but denied any respiratory or gastrointestinal symptoms, such as cough, vomiting, diarrhea, abdominal pain, or dysuria. His appetite remained normal, and there was no weight loss. Additionally, there were no factors noted that exacerbated his disease, and his symptoms were relieved by medication.

The patient had a past medical history of smoking 20 cigarettes on a daily basis for the past 20 years. He did not consume alcohol and had no known chronic medical conditions. His mother had a history of diabetes and hypertension. He reported no recent travel or animal contact and worked as a cook. Six weeks of daily fever accompanied by progressive fatigue and muscular pains prompted him to seek medical advice privately, where he received antibiotics (levofloxacin and then Augmentin) without improvement.

On physical examination, the patient was alert, conscious, and oriented, with stable vital signs. His cardiovascular and chest examinations were normal. Abdominal examination revealed a soft abdomen with no tenderness. Additionally, palpation revealed multiple mobile, non-tender lymph nodes, approximately 1 cm in size, in the left lower cervical region.

Laboratory investigations revealed a sodium level of 131 mmol/L, creatinine of 85.7 micromol/L, urea of 5.6 mmol/L, potassium of 3.9 mmol/L, and creatine kinase of 389.7 iu/ml. His lactic acid level was 7.7 - 1.97, white blood cell count was 3.5 x10^9/L, hemoglobin was 133 g/L, and platelets were 241 x10^9/L. C-reactive protein was elevated at 85.5 mg/L. Malaria and Mycobacterium PCR tests were negative, urinalysis was normal, and complement C3 was within normal limits. An autoimmune workup returned negative results. Chest X-ray and abdominal ultrasound were unremarkable.

Echocardiography showed preserved left ventricular systolic function with an ejection fraction of 60%, normal cardiac valve morphology, and no evidence of vegetation. A CT scan of the abdomen revealed multiple enlarged lymph nodes in conglomeration along the hepatic artery and between the aorta and IVC at the level of the renal hilum. Suspicious mural thickening of the third part of the duodenum and a small hypodense lesion located in the liver's left lobe were also noted.

Esophagogastroduodenoscopy findings included grade B esophagitis with various white patches indicative of candida, erosive antral gastritis, and mild erythematous duodenitis. Biopsies were taken from the esophagus, stomach, and duodenum. Pathology reports indicated reactive lymphadenitis consistent with Kikuchi-Fujimoto disease, with special stains for microorganisms being negative.

The patient was prescribed prednisolone and fluconazole for esophageal candidiasis. On follow-up, he was afebrile, clinically stable, and exhibited no lymphadenopathy. The differential diagnosis of Kikuchi-Fujimoto disease was considered, ruling out systemic lupus erythematosus, disseminated tuberculosis, lymphoma, sarcoidosis, and viral lymphadenitis based on clinical findings, negative antibody tests, and histopathology results.

3. Discussion

KFD is a very uncommon disease that causes cervical lymphadenitis, and it was first identified in 1972 (2). Although there have been reports of the cases across the world, they are common in Asian countries. (13). Previous beliefs about KFD indicated a higher occurrence in females, but recent reviews indicate a nearly equal ratio between females and males (14). The exact cause of KFD remains unclear, but some studies suggest that an Epstein-Barr virus infection may be a contributing factor (15). Several viruses, including human herpesvirus 6, Parvovirus B19, HIV, HSV, HHV 8, and HHV 7 have been suggested as possible triggers, although a definitive link has not been proven (16). Autoimmunity might be a factor in the development of KFD due to its similarities to SLE lymphadenitis on a histopathologic level (17).

Typical symptoms of KFD include fever and swollen lymph nodes in the neck. Additionally, patients may encounter constitutional symptoms like fatigue, night sweats, and weight loss. Our patient was admitted to the hospital with a six-week history of moderate, episodic fever. There was no associated history of weight loss. The diagnosis of KFD is determined following the completion of a lymph node biopsy and the histological examination of the tissue (18). KFD is characterized histopathologically by paracortical and cortical proliferation of histiocytes and coagulative necrosis (12). Scattered nuclear debris may also be observed, which is a histologic finding that can also be associated with lymphoma (19). Neutrophil absence is a common feature of KFD (19). The definitive diagnosis of KFD in our patient was confirmed through lymph node biopsy, showing reactive lymphadenitis with special stains negative for microorganisms, consistent with KFD's characteristic histopathology.

In cases, where ultrasound-guided core needle biopsy cannot provide a diagnosis for our patient, it is still considered more accurate compared to fine needle aspiration. Consequently, it is recommended as the primary diagnostic method for KFD when it is suspected (18). Core needle biopsy takes less time and is a noninvasive procedure compared to open excisional biopsy (18). It may also be a more cost-effective option, as it doesn't typically require monitored anesthesia care or the use of an operating room (18). It is highly recommended to prioritize lymph node biopsy over other diagnostic methods in order to obtain a prompt and conclusive diagnosis.

At the moment, there are no clear standard management protocols for KFD (20). Typically, the most common initial approach for KFD is supportive care with NSAIDs and corticosteroids (21). This is so because KFD frequently goes away on its own in one to four months (22). Our patient responded well to prednisolone and fluconazole, with resolution of fever and lymphadenopathy on follow-up.

Doctors have also found that corticosteroids and hydroxychloroquine can effectively treat patients with severe, persistent symptoms. Usually, they try using one medication first before combining them (23).In another case report, following the two courses of prednisone, the patient was prescribed hydroxychloroquine as a single treatment option (3). In that case report , this decision was made in response to the patient's recurring symptoms and the adverse effects experienced from the steroids (3). However, in out case no adverse effects were noted from steroids. Some other case reports have discussed the potential use of hydroxychloroquine in situations where steroids are ineffective or when there are recurring symptoms of KFD (24-26). Long-term use of hydroxychloroquine can lead to the development of retinopathy. Therefore, it is recommended that individuals who are expected to undergo long-term hydroxychloroquine therapy should have an initial eye examination shortly after starting the medication, followed by a follow-up examination after 5 years of treatment (3).However, hydroxychloroquine was not prescribed in our case.

4. Conclusion

This case of a 45-year-old Indian male with Kikuchi-Fujimoto Disease (KFD) underscores the critical role of considering KFD in the differential diagnosis for persistent lymphadenopathy and fever. Although the patient exhibited classic KFD symptoms, the ineffectiveness of antibiotics highlights the limitations of empirical treatment and emphasizes the need for definitive diagnosis through histopathology and biopsies. This case further emphasizes the potential for misdiagnosis and unnecessary interventions. Early and accurate diagnosis can prevent ineffective antibiotic use and potential complications from prolonged steroid therapy. The swift recovery achieved through targeted treatment with prednisolone for KFD and fluconazole for esophageal candidiasis demonstrates the value of a specific approach. In conclusion, heightened clinician awareness of KFD is paramount for accurate diagnosis and optimal patient management. A strong suspicion for KFD, coupled with appropriate diagnostic strategies, can prevent unnecessary interventions and facilitate a quicker path to recovery.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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