

Kikuchi Disease "A Lupus Mimicker": A Case Report

Aliya Juma Alsaadi^{1*}, Saud Al Hashmi¹ and Nabila Al-Julandani²

¹Dermatology Department, Armed Forces Hospital, Muscat, Oman

²Histopathology Department, Armed Forces Hospital, Muscat, Oman

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*Corresponding author: dr.aliya334@gmail.com

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Abstract

Kikuchi disease, also called, Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis, is a rare self-limiting illness with an unknown etiology and pathogenesis. It is predominantly seen among young females. The cardinal clinical features include fever and cervical lymphadenopathy. Skin eruptions have also been reported. In Oman, two cases have been reported to date, one in 2005 and one in 2020, with only one case exhibiting skin manifestations. There is a paucity of disease in our country and worldwide. In this case report, we discuss the diagnosis of Kikuchi disease in a previously healthy 17-year-old Omani female who presented with fever, cervical lymphadenopathy, and malar rash. The clinical picture in this case resembled that of SLE. Due to the rarity of Kikuchi disease, particularly in our region, it is crucial to consider it as a differential diagnosis when a patient exhibits the aforementioned symptoms to prevent misdiagnosis and inappropriate treatment, as it can easily be misdiagnosed as SLE.

Keywords: Histiocytic Necrotizing Lymphadenitis; Lymphadenopathy; Oman.

Introduction

Kikuchi disease, or Kikuchi Fujimoto disease (KFD), is an uncommon benign illness first described by Japanese pathologists in 1972.^{1,2} The exact etiology is unknown, but viral and autoimmune causes have been suggested. It predominantly affects young adults of Asian ethnicity although cases have been reported worldwide.³ The typical clinical presentation includes fever and cervical lymphadenopathy, with the skin the most affected extranodal organ, although such cases are rare. The clinical and laboratory findings of KFD can resemble SLE. As the disease is self-limiting, there is no specific treatment. Supportive therapy is typically employed, and corticosteroids may be initiated in severe cases.⁴

Case Report

A 17-year-old female with no significant medical history presented to the A&E with a high-grade fever, skin eruption lasting nearly one month, associated with weight loss of approximately 3 kg, malaise, arthralgia, and progressive swelling on the left side of her neck. Despite multiple courses of broad-spectrum antibiotics, there was no clinical improvement. The patient was admitted for further evaluation of her febrile illness.

On examination, the patient appeared sick, with fever and tachycardic. Physical examination revealed multiple palpable cervical lymph nodes on the left-side, tender to touch. The largest swelling measured approximately 2 × 3 cm at level 3. There was an erythematous, non-blanching, non-scaly maculopapular eruption on the face, particularly affecting the malar area [Figure 1 a]. Multiple non-pruritic, non-blanchable pinpoint erythematous macular eruptions were also observed on the forearms and lower extremities [Figure 1 b] with extending to the palms and soles [Figure

1 c]. No hepatosplenomegaly or neurological deficits were detected. The rest of her systemic examination was unremarkable.

Laboratory studies showed the following results: Hb 8.5 g/dL, WBC count $1.99 \times 10^9/L$, platelets count is 568×10^9 , INR 1.12, PT 12.8 s, APTT normal range, Ferritin 571 ug/L, lactate dehydrogenase 515 U/L, C-reactive protein 37 mg/L, ALT 66 U/L, AST 107 U/L, Hepatitis B surface antigen and hepatitis C antibodies were negative, C3 2.24 g/l, C4 0.41 g/l. Antinuclear antibodies (ANA) were detected with a titer of 1/640 and a speckled pattern. Anti-dsDNA and ENA resulted negative. Blood, urine analysis, and cultures were negative. Throat swab, COVID-19 rapid antigen test, and Quantiferon test (Interferon-Gamma Release Assay) were all negative. HIV and syphilis test were negative., EBV serology showed positive IgG and EBNA, but negative IgM. Other viral and bacterial serological tests yielded negative results.

Imaging studies were done, including an echocardiogram and chest X-ray, which were both normal. A pan CT scan was performed due to suspicion of lymphoproliferative disease. The scan showed multiple enhancing lymph nodes in the left submandibular, left upper, mid, deep cervical, and posterior cervical regions. Some of these lymph nodes showed central necrosis. Bilateral axillary lymph nodes were small and non-necrotic. No lymphadenopathy was found in the abdomen and pelvis.

To rule out other potential causes, excisional lymph node biopsy and skin biopsy were performed. The lymph node biopsy showed extensive necrosis composed of histiocytes, plasmacytoid dendritic cells, and abundant karyorrhectic debris. No neutrophils or plasma cells were seen. No atypical lymphoid infiltration or granuloma were seen. Immunohistochemistry revealed that the mononuclear cell infiltrate consisted of predominantly CD68-positive histiocytes and CD3-positive T cells. The histiocytes exhibited myeloperoxidase positivity, and the T cells were mostly CD8-positive with a smaller number of CD4-positive cells. EBER in situ hybridization showed negative staining for EBV.

A skin biopsy was performed, revealing vacuolar interface changes and scattered necrotic keratinocytes. In the papillary and reticular dermis, there was perivascular and interstitial lymphohistiocytic infiltration with prominent karyorrhexis. No neutrophils, eosinophils, or plasma cells were seen [Figure 2]. Ziehl-Neelsen (ZN) staining was negative for acid-fast bacilli (AFB). Immunohistochemistry showed perivascular and interstitial infiltration of CD68-positive histiocytes as the predominant inflammatory cells [Figure 3 a] along with a higher number of CD8-positive cytotoxic T-lymphocytes are predominant cells of the lymphocytes compared to few CD4 cells [Figure 3 b].

Considering the patient's age, gender, clinical presentation, and the histopathological findings of the skin and lymph nodes, a diagnosis of KFD with skin involvement was made. The patient was started on oral prednisolone at 1 mg/kg. After 1–3 weeks of treatment, the fever resolved, lymphadenopathy improved to a non-palpable state, and the skin rash improved.



Figure 1: (a) Dusky to erythematous papules coalescing into a plaque over the malar area and dorsal nose. Petechiae and purpura on both forearms and (b) shins with involvement of the palm and (c) soles.

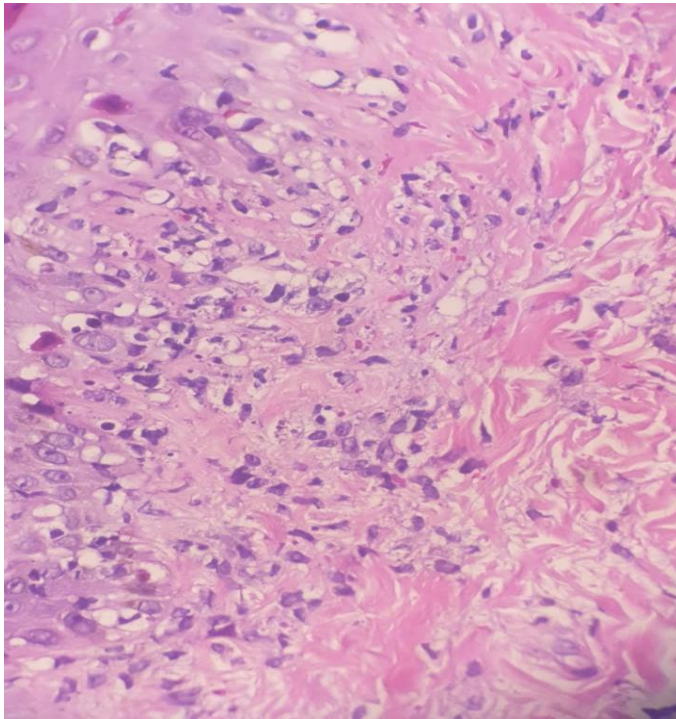


Figure 2: Skin biopsy show papillary and reticular lymphohistiocytic infiltration, interface dermatitis, and karyorrhexis. H&E staining, magnification = 40 \times .

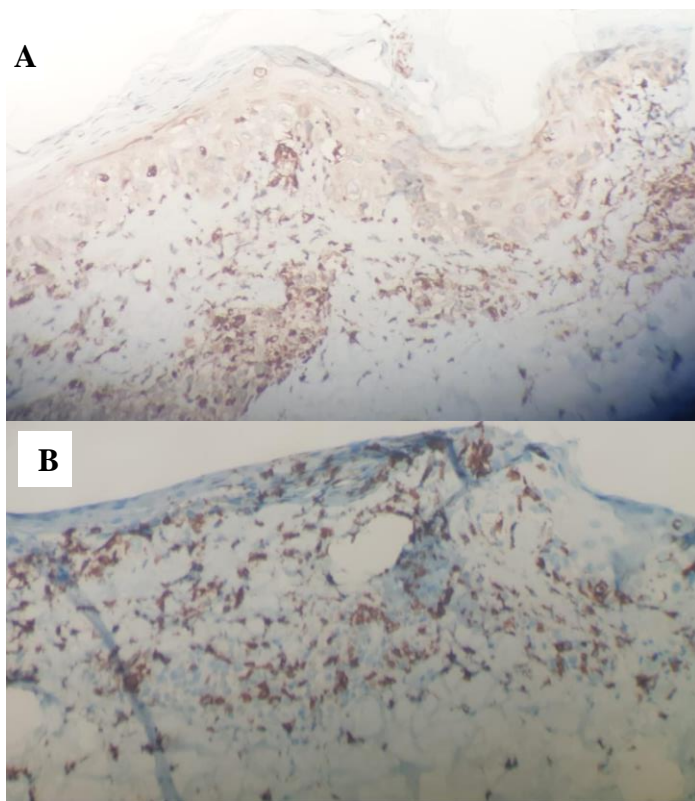


Figure 3: Immunohistochemistry (a) CD68 shows that histiocytes are the predominant inflammatory cells. (b) CD8 positive cytotoxic T lymphocytes are the predominant cells of the lymphocytes. Magnification = 40 ×.

Discussion

KFD is a rare condition with unclear etiology and pathophysiology. Two theories have been proposed regarding the cause of KFD: infectious and autoimmune. Various bacterial and viral agents have been identified as potential triggers. Additionally, an association between KFD and autoimmune diseases, particularly systemic lupus erythematosus (SLE), has been observed.³ The exact relationship between SLE and KFD is not fully understood.⁵ Both disease predominantly affect young women, and they share several clinical characteristics.⁶

Our patient had common symptoms and laboratory findings of SLE, such as fever, malaise, weight loss, arthralgia, malar rash, cervical lymphadenopathy, anemia, leukopenia, and positive ANA.

Our patient presented with a high platelet count, which gradually reduced to the normal range after starting oral prednisolone. In a recent study looking at blood changes in 367 patients with KFD, 282 (77%) had CBC data; of these, anemia (22%) was the most common abnormality, followed by lymphopenia (17%), neutropenia (11%), atypical lymphocytes (9%), and thrombocytopenia (8%) but the increased cell count were relatively rare.⁷ A case was reported in Turkey for a female patient diagnosed with KFD who suddenly had deranged Hb and raised D-dimer, activated partial thromboplastin time, prothrombin time, and international normalized ratio with decreased fibrinogen and developed disseminated intravascular coagulopathy (DIC).⁸

Several studies have reported cases of KFD associated with SLE. Some patients were diagnosed with SLE following the diagnosis of KFD, while others had a prior diagnosis of SLE. Kuckardali et al. reported 28 cases of SLE-associated KFD that satisfied the diagnostic criteria for SLE in a study encompassing 244 patients; of those, 18

cases had both KFD and SLE, while six cases had SLE diagnosed after KFD, and four cases had a prior diagnosis of SLE.⁹ Santana et al. reported 35 cases of SLE-associated KFD, in which 14 patients were diagnosed with SLE following KFD.¹⁰ Patra et al. reported a case of a woman who developed SLE after two years of KFD.¹¹ In 4 cases, KFD was identified before the diagnosis of SLE, according to Goldblatt et al.¹² therefore, a close follow-up is recommended to detect the evolution of SLE.

In Oman, where our patient was from, only two cases of Kikuchi disease have been reported, with skin manifestations observed in one case.^{13,14} In Saudi Arabia, 15 cases were reported as KFD in one report.¹⁵ with another reporting five 5 cases.¹⁶ There have been 14 cases documented in Qatar, three of which had cutaneous symptoms.¹⁷ There is limited data on whether these reported cases of KFD had a previous diagnosis of SLE or they developed SLE later.

Skin manifestations in KFD are non-specific and have been described in 40% of cases¹⁸ and may resemble lupus eruption. In our patient, skin eruption preceded the appearance of lymphadenopathy and improved after initiating treatment with oral prednisolone. Histopathological criteria, including the presence of karyorrhexis and the absence of neutrophils as major criteria, have been proposed to diagnose KFD with skin involvement. Minor criteria included the presence of interface dermatitis, presence of inflammatory cell infiltration in the reticular dermis or subcutaneous fat tissue.¹⁹ Our patient met all the major and minor criteria supporting the diagnosis of KFD.

Histopathological findings of cutaneous lesions in KFD can resemble those seen in SLE, such as interface dermatitis, dermal mucin deposition, and panniculitis.²⁰ However, plasma cells, which are commonly observed in SLE, are usually absent in KFD.¹⁹

A definitive diagnosis of KFD can be made based on the histopathological findings from the lymph node biopsy, ruling out other possible causes. The histopathological features that can support SLE are an increased number of plasma cells, hematoxylin bodies, DNA deposits in the vascular walls, neutrophilic infiltration, and varying degrees of coagulative necrosis with the Azzopardi phenomenon. In contrast, the absence of hematoxylin bodies and neutrophils indicates KFD rather than SLE.²⁰

As KFD is a self-limiting disease, no specific treatment is required, and the condition usually resolves within 1–6 months. Treatment is generally symptomatic treatment with analgesics and antipyretics. However, severe cases may benefit from a course of corticosteroids.⁴

Conclusion

Our case highlights the importance of considering KFD as a rare entity when evaluating patients with clinical features and laboratory findings that mimic SLE. The similarities between KFD and SLE in terms of clinical presentation and laboratory results make it challenging to differentiate between the two conditions without a biopsy. It is crucial to perform a histopathological examination, such as lymph node biopsy, to confirm the diagnosis and exclude other potential causes. Proper diagnosis is essential to avoid inappropriate treatment and to ensure appropriate long-term follow-up, considering the possibility of the evolution of SLE.

Disclosure

The authors declared no conflicts of interest. Written consent was obtained from the patient.

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