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AN UNUSUAL CHALLENGING CASE OF CERVICAL LYMPHADENITIS -KIKUCHI FUJIMOTO DISEASE

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ABSTRACT

Introduction: Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a rare, benign, and self-limiting clinicopathological entity first described independently by Kikuchi and Fujimoto in Japan in 1972. It predominantly affects young women and is characterized by cervical lymphadenopathy, fever, and constitutional symptoms. Although the disease is generally self-limiting, its clinical presentation often mimics more serious conditions such as tuberculous lymphadenitis, lymphoma, metastatic lymphadenopathy, and systemic lupus erythematosus (SLE), leading to diagnostic challenges. Histopathological examination remains the cornerstone for establishing a definitive diagnosis.

Case Presentation: We report a rare case of Kikuchi-Fujimoto disease in a 20-year-old female with no significant past medical history who presented with acute onset painful left-sided cervical lymphadenopathy associated with malaise, intermittent fever reaching 100°F, and significant weight loss. Clinical examination revealed multiple enlarged cervical lymph nodes on the left side of the neck, with the largest node measuring approximately 2 × 3 cm. Fine-needle aspiration cytology suggested necrotizing lymphadenitis, demonstrating irregularly shaped pale areas composed predominantly of histiocytes and plasmacytoid dendritic cells with absence of neutrophils. In view of persistent cervical lymphadenopathy, the patient underwent excision biopsy under general anaesthesia. Intraoperatively, multiple enlarged lymph nodes involving cervical levels II, III, IV, and V were identified and excised. Histopathological examination revealed characteristic features of Kikuchi-Fujimoto disease, including patchy areas of necrosis with abundant karyorrhectic nuclear debris and absence of neutrophilic infiltration. Immunohistochemical analysis further confirmed the diagnosis. Following definitive diagnosis, the patient was treated with systemic corticosteroids and demonstrated a dramatic clinical improvement with complete resolution of symptoms.

Conclusion: Kikuchi-Fujimoto disease should be considered as an important differential diagnosis in young patients presenting with unilateral cervical lymphadenopathy accompanied by constitutional symptoms. Early recognition and histopathological confirmation are essential to avoid unnecessary investigations and inappropriate treatment. Furthermore, patients diagnosed with KFD should undergo long-term follow-up because of its documented association with systemic lupus erythematosus.

KEYWORDS: Kikuchi-Fujimoto disease; Histiocytic necrotizing lymphadenitis; Cervical lymphadenopathy; Cervical lymphadenitis; Excision biopsy; Systemic lupus erythematosus.

1. INTRODUCTION

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is an uncommon, benign, and usually self-limiting clinicopathological entity characterized by regional lymphadenopathy associated with fever and constitutional symptoms. First described independently by Kikuchi and Fujimoto in Japan in 1972, the disease has since been increasingly recognized worldwide.[1] Although initially believed to occur predominantly among Japanese women, subsequent reports have demonstrated its occurrence across diverse ethnic populations and geographical regions.[2] Nevertheless, young females of Asian ancestry continue to constitute the most commonly affected group.[3]

The exact etiology and pathogenesis of KFD remain poorly understood. Various infectious agents, including Epstein-Barr virus, human herpesvirus-6, human herpesvirus-8, parvovirus B19, cytomegalovirus, and Yersinia species, have been implicated as possible triggers; however, a definitive causal relationship has not yet been established.[4] In addition, several observations have suggested an autoimmune basis for the disease, particularly because of its close association with systemic lupus erythematosus (SLE).[5] It has been proposed that KFD may result from an exaggerated T-cell-mediated immune response occurring in genetically susceptible individuals following exposure to infectious or other unidentified antigenic stimuli.[6]

Clinically, KFD most commonly presents as tender unilateral cervical lymphadenopathy, often involving the posterior cervical chain. Fever is the second most frequent clinical manifestation and may be accompanied by constitutional symptoms such as malaise, fatigue, night sweats, anorexia, and weight loss.[7] Less frequently, patients may present with generalized lymphadenopathy, hepatosplenomegaly, skin manifestations, or extranodal involvement.[8] Because these clinical manifestations are nonspecific, the diagnosis is frequently challenging and often delayed.

One of the most important aspects of KFD is its ability to mimic several serious disorders. The differential diagnosis includes tuberculous lymphadenitis, malignant lymphoma, metastatic cervical lymphadenopathy, infectious mononucleosis, and autoimmune diseases, particularly SLE.[9] In countries where tuberculosis is endemic, such as India,

patients with cervical lymphadenopathy are frequently presumed to have tuberculous lymphadenitis, leading to unnecessary investigations or empiric treatment.[10] Likewise, the constitutional symptoms and histopathological features of KFD may closely resemble lymphoma, resulting in considerable diagnostic confusion and patient anxiety.[11]

Although routine laboratory investigations are often nonspecific, leukopenia, elevated erythrocyte sedimentation rate, and mildly deranged liver function tests may occasionally be observed.[12] Fine-needle aspiration cytology may provide preliminary diagnostic clues; however, its sensitivity is limited because cytological findings can overlap with those of other benign and malignant conditions.[13] Consequently, excisional lymph node biopsy remains the gold standard for establishing a definitive diagnosis. Histopathological examination typically reveals patchy or confluent areas of necrosis containing abundant karyorrhectic nuclear debris surrounded by crescentic histiocytes and plasmacytoid dendritic cells, with a characteristic absence of neutrophils and eosinophils.[14] Immunohistochemical analysis may further aid in differentiating KFD from malignant lymphoproliferative disorders.[15]

KFD generally follows a benign and self-limiting course, with spontaneous resolution occurring within one to six months in most patients. Supportive treatment with analgesics and antipyretics is usually adequate, whereas corticosteroids, hydroxychloroquine, or other immunomodulatory agents may be considered in patients with severe, recurrent, or extranodal disease.[16] Despite its favorable prognosis, long-term follow-up is recommended because recurrence may occur and an association with subsequent development of SLE has been well documented.[17]

We herein report an unusual and diagnostically challenging case of Kikuchi-Fujimoto disease in a young female presenting with unilateral cervical lymphadenitis and constitutional symptoms, emphasizing the importance of considering this rare entity in the differential diagnosis of cervical lymphadenopathy.

CASE PRESENTATION

A 20-year-old female with no significant past medical history presented to the outpatient department of R. L. Jalappa Hospital and Research Centre (RLJH) with complaints of acute onset painful swelling on the left side of the neck associated with tenderness, malaise, intermittent fever reaching up to 100°F, and unintentional weight loss. There was no history suggestive of tuberculosis, recent upper respiratory tract infection, exposure to tuberculosis, or any known autoimmune disorder.

On physical examination, multiple enlarged cervical lymph nodes were palpable on the left side of the neck involving cervical levels II, III, IV, and V. The lymph nodes were tender, discrete, and mobile, with the largest node measuring approximately 2 × 3 cm in size. The overlying skin appeared normal, and no evidence of hepatosplenomegaly or generalized lymphadenopathy was noted.

Fine-needle aspiration cytology (FNAC) of the cervical lymph node was performed as part of the initial diagnostic workup. Cytological examination revealed irregularly shaped pale areas composed predominantly of histiocytes, plasmacytoid dendritic cells, and eosinophils, with an absence of neutrophils, findings suggestive of necrotizing lymphadenitis.

Figure 1: Gross specimen showing excised left cervical lymph nodes following excision biopsy.

In view of the persistent cervical lymphadenopathy and to establish a definitive diagnosis, the patient was planned for excision biopsy under general anaesthesia. Intraoperatively, multiple enlarged lymph nodes were identified in the left cervical region involving levels II, III, IV, and V. The largest lymph node measured approximately 2 × 3 cm. Complete excision of the involved lymph nodes was performed, and the specimens were sent for histopathological examination and immunohistochemical (IHC) analysis. Adequate haemostasis was achieved, a surgical drain was placed, and the wound was closed in two layers.

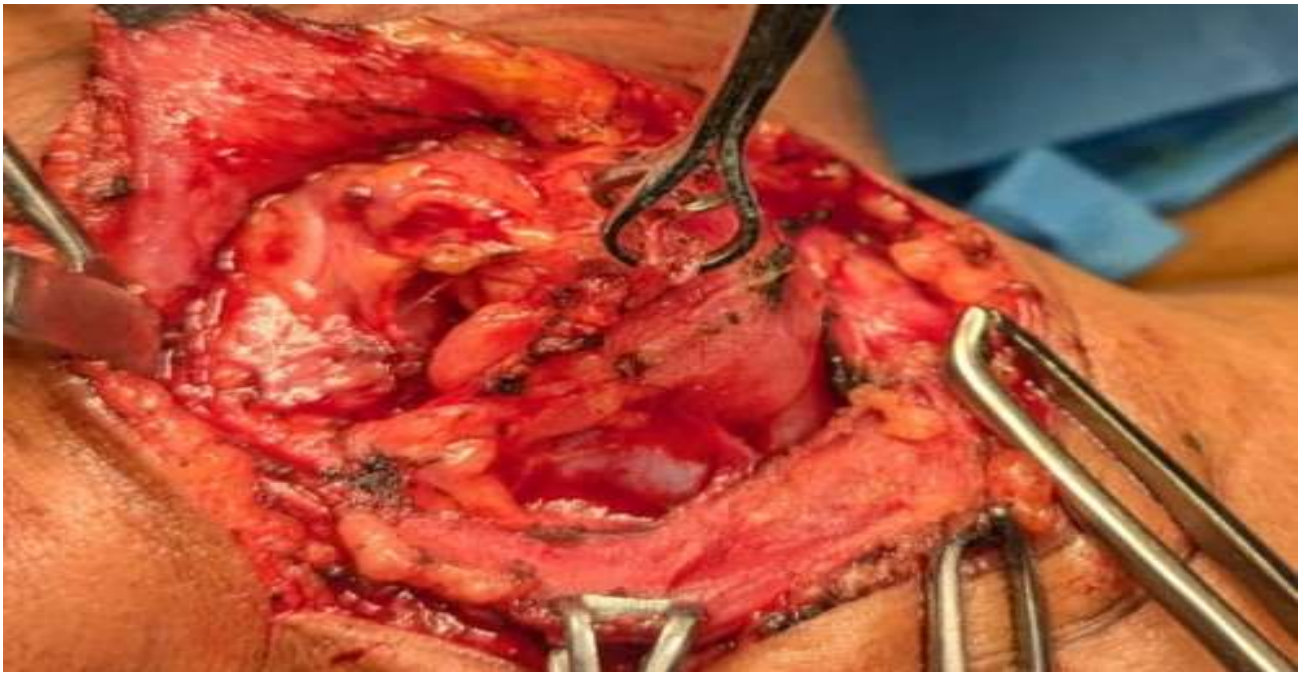
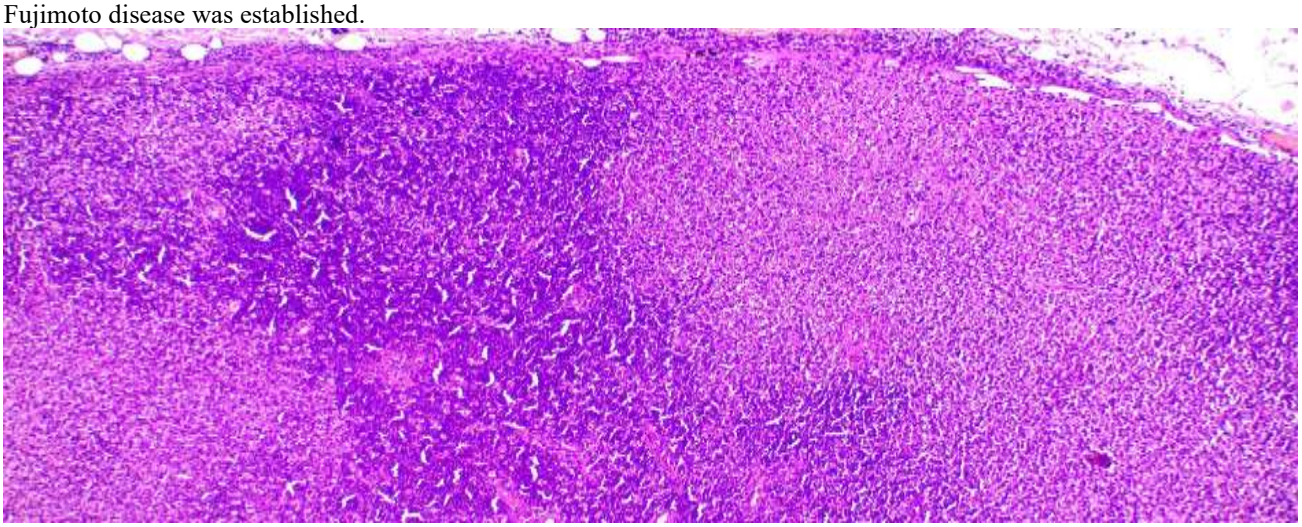


Figure 2: Intraoperative photograph showing enlarged cervical lymph nodes during excision biopsy.
Histopathological examination demonstrated characteristic features of Kikuchi-Fujimoto disease, including patchy areas of necrosis containing abundant karyorrhectic nuclear debris. Immunohistochemical analysis further supported the diagnosis. Based on the combined clinicopathological and immunohistochemical findings, a final diagnosis of Kikuchi-Fujimoto disease was established.



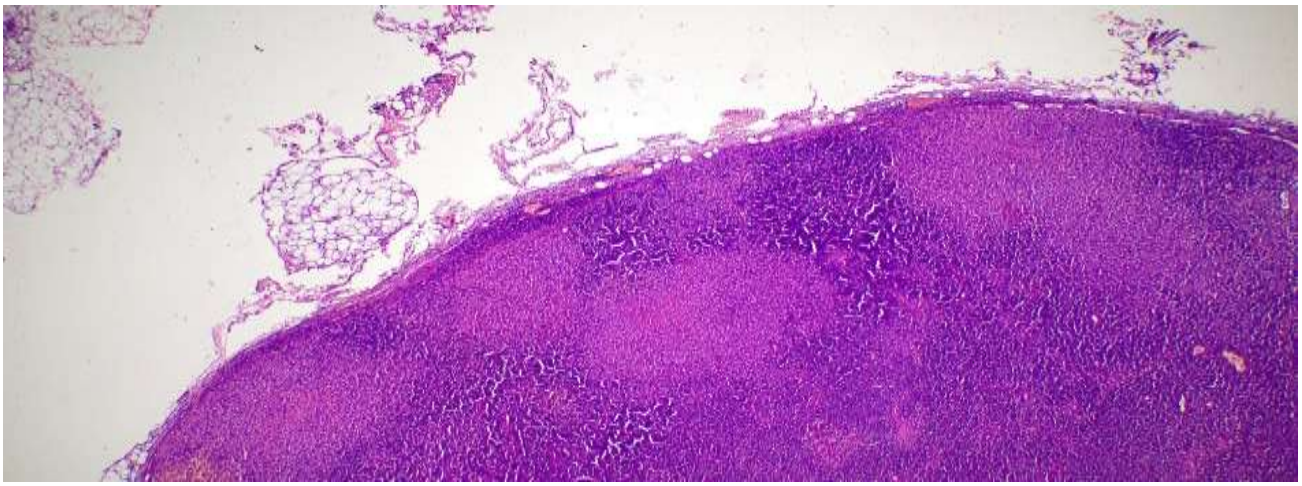


Figure 3: Microscopic section showing necrotizing lymphadenitis with patchy necrosis and abundant karyorrhectic nuclear debris, consistent with Kikuchi-Fujimoto disease.

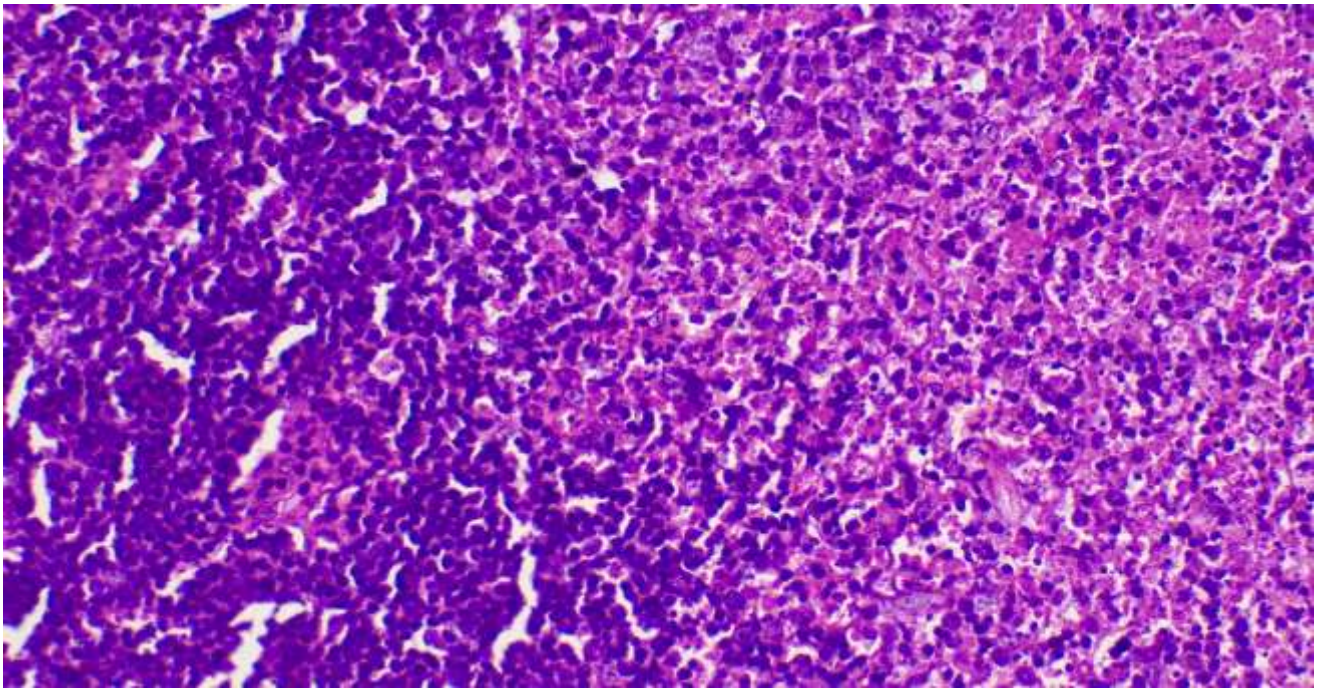


Figure 4: High-power microscopic view showing histiocytic proliferation with karyorrhectic debris and absence of neutrophilic infiltration. Following confirmation of the diagnosis, the patient was treated with systemic corticosteroids, resulting in a dramatic clinical improvement with significant resolution of symptoms and cervical lymphadenopathy during follow-up.

DISCUSSION

Kikuchi-Fujimoto disease (KFD) is an uncommon, benign, and self-limiting cause of cervical lymphadenopathy that predominantly affects young women and often presents a significant diagnostic challenge because of its nonspecific clinical manifestations.[1] Since its first description, increasing awareness of this entity has led to more frequent recognition worldwide; however, it continues to remain underdiagnosed in routine clinical practice.[2]

The present case involved a 20-year-old female presenting with unilateral cervical lymphadenopathy associated with fever, malaise, and weight loss. This clinical presentation is consistent with the typical demographic and symptom profile reported in the literature, wherein young females constitute the majority of affected individuals.[3] Histopathologically, KFD is characterized by necrotizing lymphadenitis with abundant karyorrhectic debris and a conspicuous absence of neutrophils, findings that were also observed in our patient.[4]

The exact etiology of KFD remains unclear, although infectious and autoimmune mechanisms have been proposed.[5] An exaggerated T-cell-mediated immune response triggered by viral or other antigenic stimuli has been suggested as the most plausible pathogenic mechanism.[6] The constitutional symptoms observed in our patient, including fever, malaise, and weight loss, have been frequently described in previously reported cases and may reflect the underlying inflammatory process.[7]

A major challenge in the management of patients with KFD lies in differentiating it from other causes of cervical lymphadenopathy. In a large analysis of 244 patients, Kucukardali et al. reported cervical lymphadenopathy as the most common clinical manifestation, emphasizing that KFD should always be considered in the differential diagnosis of persistent cervical lymphadenopathy in young adults.[8] In regions where tuberculosis is highly prevalent, such as India, KFD may easily be mistaken for tuberculous lymphadenitis, leading to unnecessary investigations and treatment.[9]

In the present case, FNAC provided initial evidence suggestive of necrotizing lymphadenitis; however, definitive diagnosis was established only after excisional biopsy and immunohistochemical analysis. Hassan et al. highlighted the important role of immunohistochemistry in distinguishing KFD from lymphoma and other malignant conditions, thereby avoiding inappropriate therapeutic interventions.[10] Similarly, Kim et al. reported that clinicopathological correlation remains essential because laboratory findings are often nonspecific.[11]

Dumas et al., in their retrospective analysis of 91 cases, demonstrated that although KFD generally follows a benign course, accurate diagnosis is essential because of its close resemblance to malignant and autoimmune disorders.[12] Histopathological examination remains the gold standard for diagnosis and typically reveals patchy necrosis, abundant apoptotic debris, histiocytic proliferation, and absence of neutrophilic infiltrate, features that were observed in our patient.[13]

Recent evidence from a case series by Deb et al. further emphasized the heterogeneous clinical presentation of KFD and reiterated the importance of maintaining a high index of suspicion in young patients presenting with cervical lymphadenopathy and constitutional symptoms.[14] Furthermore, Cheng et al. demonstrated that careful histopathological assessment is crucial in differentiating KFD from lymphoma, as both entities may exhibit overlapping clinical features.[15]

The management of KFD is predominantly supportive because the disease is generally self-limiting. Nevertheless, corticosteroid therapy may be beneficial in patients with severe, persistent, or symptomatic disease.[16] In the present case, systemic corticosteroid administration resulted in a dramatic clinical response, with significant improvement in symptoms and regression of lymphadenopathy.

Although the prognosis of KFD is usually excellent, recurrence has been reported and an association with systemic lupus erythematosus has been increasingly recognized. Therefore, long-term clinical follow-up is recommended to monitor for

disease recurrence and the possible development of autoimmune disorders.[17]

CONCLUSION

Kikuchi-Fujimoto disease is an uncommon, benign, and self-limiting cause of cervical lymphadenopathy that predominantly affects young adults, particularly females. Despite its favorable prognosis, the disease continues to pose a significant diagnostic challenge because of its nonspecific clinical presentation and its close resemblance to more common and potentially serious conditions such as tuberculous lymphadenitis, lymphoma, metastatic cervical lymphadenopathy, and systemic lupus erythematosus. Consequently, a high index of clinical suspicion is essential, especially in young patients presenting with unilateral cervical lymphadenopathy accompanied by constitutional symptoms.

The present case highlights the importance of considering Kikuchi-Fujimoto disease as a differential diagnosis in patients with persistent cervical lymphadenitis. Although fine-needle aspiration cytology may provide preliminary diagnostic clues, excisional lymph node biopsy with histopathological examination remains the gold standard for definitive diagnosis. The characteristic histopathological findings, supported by immunohistochemical analysis, are invaluable in distinguishing KFD from malignant and infectious causes of lymphadenopathy, thereby preventing unnecessary investigations and inappropriate therapeutic interventions.

Furthermore, this case demonstrates the excellent response of symptomatic Kikuchi-Fujimoto disease to systemic corticosteroid therapy, resulting in marked clinical improvement. Given the documented association of KFD with systemic lupus erythematosus and the possibility of disease recurrence, long-term follow-up is strongly recommended. Increased awareness among clinicians, surgeons, and pathologists regarding this rare entity can facilitate early diagnosis, ensure appropriate management, and improve patient outcomes while avoiding overtreatment.

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