

Kikuchi–Fujimoto Disease in a Woman with axillary lymphadenopathy, a rare site of presentation: Case Report and Review of the Literature.

Jasmine Khanna

Corresponding Author: Jasmine Khanna

Abstract: Kikuchi–Fujimoto disease (KFD) is a rare, benign, generally self-limiting disease that has higher prevalence in Asian people with a few cases reported in European countries¹. It generally affects young females and characterized by cervical lymphadenopathy². Here, we present a case of a 25-year-old woman who was extensively examined for right axillary lymphadenopathy associated with fever, night sweats, fatigue, and weight loss. She was diagnosed as having the KFD only after an excision biopsy of the largest right axillary lymph node and was then managed symptomatically with NSAIDs. We finally highlight that it is noteworthy to consider KFD as differential diagnosis of lymphadenopathy since a misdiagnosis of lymphoma, tuberculosis and metastasis is actually feasible and an early biopsy has to be taken into account for confirming diagnosis and helping in the timely and appropriate management.

Date of Submission: 26-08-2019

Date of Acceptance: 10-09-2019

I. Introduction

Kikuchi–Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is a rare, benign and generally self-limiting disease that is over expressed in Asian people,

Although a worldwide distribution has been reported. The disease usually affects young females during the third decade of life and frequently manifests as an acute or subacute form with painful posterior cervical lymphadenopathy and systemic

Symptoms like fever, fatigue, and headache³. Its etiology is still unknown, and differential diagnosis includes a spectrum of infectious diseases as well as connective tissue disorders and lymphoproliferative diseases. Here, we describe a case of a 25 years old female who presented with fever and right axillary lymphadenopathy along with night sweats and weight loss who was finally diagnosed as having KFD by histological examination of the largest right axillary lymph node.

II. Case Presentation

A 66-year-old female patient was admitted to our Surgery Unit on 17 June, 2019 with a two-month history of low grade fever, malaise, fatigue, night sweats, gradual decrease in appetite, and body weight loss of 4 kilograms. She also complained of on and off pain in right axillary lymph nodes for the past 1 month. Her clinical history was unremarkable except for hypothyroidism diagnosed in 2016 for which she took medication for six months and then stopped herself. She had no past history of tuberculosis or contact with it. On admission, her heart rate was 90 bpm, blood pressure was 110/60 mmHg, respiratory rate was 16 breaths/minute, and body temperature was 37.5°C. Physical examination revealed multiple right nontender and painful right axillary lymph nodes. There was no

hepatosplenomegaly or other clinically appreciable lymphadenopathy elsewhere. Examination of respiratory and other systems was normal. Laboratory analysis showed slight increase in C-reactive protein, (LDH), and erythrocyte sedimentation rate (ESR) values that were, respectively, of 20 mg/L (n.v. < 2.9), 705 UI/L

(n.v. < 450), and 54 mm/h. , thyroid hormones and neoplastic markers were all within the normal range. Antinuclear antibody, anti ds-DNA, and rheumatoid factor were negative; HIV, cytomegalovirus IgM, herpes virus IgM, Epstein–Barr

virus IgM, Brucella, and Toxoplasma were all negative. Chest X-ray was unremarkable. Ultrasonography revealed multiple, round to oval shaped hypoechoic masses suggestive of lymph nodes in right axillary region, few of these masses had central echogenic hilum. The largest lymph node measured 3.5* 2.3 cm. Impression on USG was right sided axillary lymphadenopathy with few lymph nodes showing necrosis. Because of a dilemma in clinical diagnosis and the persistence of symptoms, an excision biopsy of the largest right axillary lymph node was performed. Histological examinations showed paracortical necrotic foci

with the presence of small to large lymphocytes in addition to numerous histiocytes expressing CD68 and MPO and abundant apoptotic nuclear debris. No polymorphonuclear neutrophils and no caseous necrosis were observed (**Figures 1 and 2**). On the basis of these morphological and immunophenotype findings, a diagnosis of Kikuchi–Fujimoto disease was made. Patient was treated symptomatically with NSAIDs and at two-month follow-up, malaise, fatigue, and appetite were improved; she denied fever and night sweats, and ultrasonography showed a decrease in the size of right axillary lymph nodes. ESR, CRP, and LDH were also restored at normal range. At six-month follow-up, the patient was free Of symptoms, and right axillary lymph nodes were no more detectable on ultrasonography.

III. Discussion

KFD is a benign disease more prevalent in Asian populations that affects young adults predominantly females. Patients with KFD commonly present with nonspecific , signs and symptoms mainly characterized by enlargement of unilateral cervical lymph nodes and fever **although in our case it was axillary lymph node which is very rare**. Less common symptoms are weakness, night sweats, anorexia, weight loss, arthralgia, or cutaneous manifestations [1, 9]. An involvement of other lymph nodes has been described, and extranodal manifestations affecting skin, eye, bone marrow, or liver as well as disseminated disease with fatal outcome have been reported in a very few cases [10–13].

Etiopathogenesis of KFD is still unknown. An autoimmune contribution to the pathogenesis has been suggested, and lymphocyte-infecting viruses have been postulated to have a causative role, even though there is not convincing evidence so far. Bacteria and parasites have also been implicated in the pathogenesis with controversial results [14, 15].

There are no specific laboratory analyses or instrumental examination that can suggest a diagnosis of KFD. Leukopenia with sometimes atypical peripheral blood lymphocytes and anemia is noted in few cases [16, 17]. An increase in LDH and alanine aminotransferase has been sometimes documented. Imaging findings are usually nonspecific and can mimic not only lymphoma but also various nodal diseases with necrosis. Ultrasounds, CT scan, and magnetic resonance in many case showed particular signs with a distinctive lymphadenopathy pattern consisting of many small clustered lymph nodes [9, 18, 19]; however, these observations must be interpreted cautiously. Fine-needle aspiration cytology

(FNAC) has been performed in some cases, but it has limited diagnostic potential with an overall diagnostic accuracy for KFD estimated at about 56% [20–22]. Therefore, biopsy is the only way to have a correct diagnosis of KFD. In this report, we described a case of a 25 year old female with right axillary lymphadenopathy accompanied by fever who also complained of fatigue, night sweats, and body weight loss. No variations in laboratory analyses were observed, except of slight ESR, CRP, and LDH elevation. Extensive breast examination was done and was normal. A differential diagnosis including viral and bacterial diseases, lymphoma, as well as systemic lupus erythematosus was also considered, but microbiological analysis and autoimmunity examination were all negative.

Ultrasound revealed only right axillary lymphadenopathy along with few lymph nodes showing necrosis. FNAC report revealed atypical lymphoid hyperplasia. To rule out the suspected diagnosis of lymphoproliferative disease, and before starting any specific therapy, we decided to perform a biopsy of the largest right axillary lymph node. Unexpectedly, the histological examination excluded a diagnosis of lymphoproliferative disease and showed typical features of KFD, that is, necrotic paracortical foci formed by different cellular types, predominantly histiocytes

and small or large lymphocytes with absence of neutrophils and granulomatous reaction at the margin of the necrotic areas. The histopathological diagnosis was also confirmed by the immunophenotype of KFD that typically consists of a predominance of T cells and relatively few B cells and NK cells and histiocytes expressing histiocyte-associated antigens, myeloperoxidase and CD68. Usually, NSAIDs or corticosteroids in case of persistent or more severe symptoms. Therapy with colchicine has also been reported in some cases [1]. In our case, we decided to start therapy with NSAIDs after the histological results because of persistence of fever, fatigue, and night sweats. After one week of therapy, the patient denied fever, and malaise and night sweats were improved. At six-month follow-up, the patient was free of all symptoms. **In conclusion, an original feature of this case report was the diagnosis of KFD in young female with a rare site of presentation.**

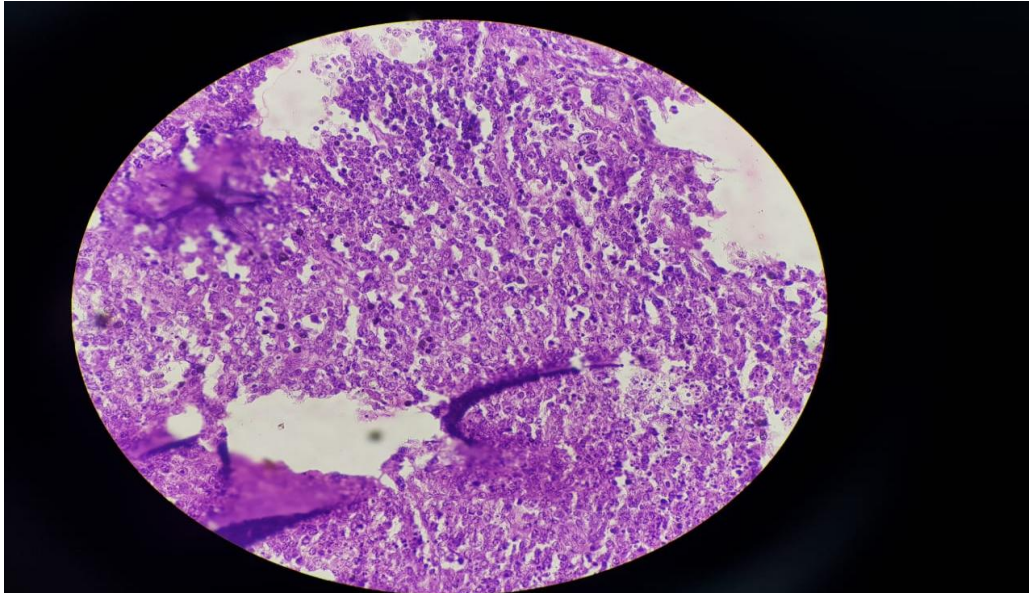
Since a misdiagnosis of lymphoma is actually feasible, we highlight that if one patient presents with lymphnode enlargement eventually associated with other nonspecific signs and symptoms, an early biopsy has to be taken into account for confirming diagnosis and helping in the timely and appropriate management. Finally, we speculate that KFD may be underdiagnosed in clinical practice as Infectious disease. Hence, the recognition of KFD is important to avoid misdiagnosis.

Conflicts of Interest

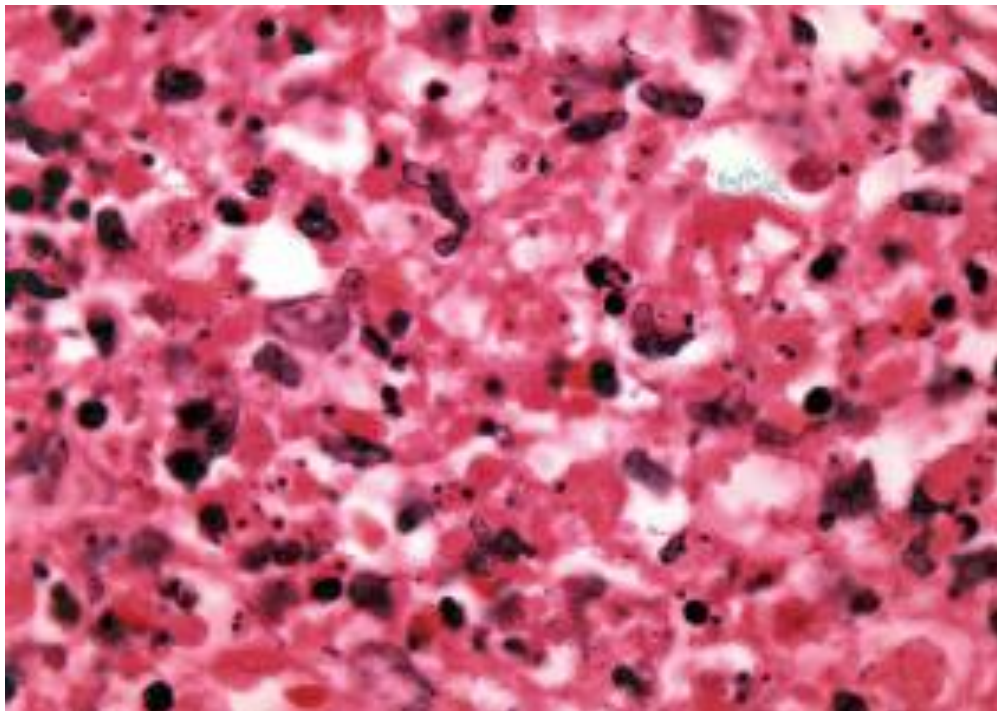
The authors declare that there are no conflicts of interest regarding the publication of this article.

References

- [1]. D. Deaver, P. Horna, H. Cualing, and L. Sokol, "Pathogenesis, diagnosis, and management of Kikuchi-Fujimoto disease," *Cancer Control*, vol. 21, no. 4, pp. 313–321, 2014.
- [2]. A. Biggio, A. Lai, G. Demontis, S. Cossu, L. Canu, and E. Proto, "Kikuchi-Fujimoto disease with lateral neck localisation: a case report," *Acta Otorhinolaryngologica Italica*, vol. 23, no. 4, pp. 322–325, 2003.
- [3]. S. Pallotti, A. Gasbarrone, and S. Giuliano, "Necrotising histiocytic lymphadenitis in a patient with hypothyroidism. Aetiopathogenesis and description of a rare clinical case," *Minerva Endocrinologica*, vol. 28, no. 3, pp. 255–257, 2003.
- [4]. C. Vergara, A. Pilato, M. Novelli, A. Inverso, and D. Fico, "Una rara causa di linfadenopatia: malattia di Kikuchi-Fujimoto," *Recenti Progressi in Medicina*, vol. 103, no. 6, pp. 239–241, 2012.
- [5]. F. Prignano, A. M. D'Erme, F. Zanieri, D. Bonciani, and T. Lotti, "Why is Kikuchi-Fujimoto disease misleading?," *International Journal of Dermatology*, vol. 51, no. 5, pp. 564–567, 2012.
- [6]. S. Guerriero, E. Ruggeri, D. Piscitelli, and L. Pomes, "Kikuchi-Fujimoto disease: a rare case of orbital involvement," *Orbit*, vol. 31, no. 6, pp. 420–422, 2012.
- [7]. B. Ruaro, A. Sulli, E. Alessandri, G. Fraternali-Orcioni, and M. Cutolo, "Kikuchi-Fujimoto's disease associated with systemic lupus erythematosus: diXcult case report and literature review," *Lupus*, vol. 23, no. 9, pp. 939–944, 2014.
- [8]. M. L. Fiorella, M. Gelardi, A. Marzullo, E. Sabattini, and R. Fiorella, "Kikuchi-Fujimoto disease: an uncommon cause of neck swelling," *European Archives of Oto-Rhino-Laryngology*, vol. 274, no. 3, pp. 1761–1764, 2017.
- [9]. X. Bosch, A. Guilabert, R. Miquel, and E. Campo, "Enigmatic Kikuchi-Fujimoto disease: a comprehensive review," *American Journal of Clinical Pathology*, vol. 122, no. 1, pp. 141–152, 2004.
- [10]. U. Mahadeva, T. Allport, B. Bain, and W. K. Chan, "Haemophagocytic syndrome and histiocytic necrotising lymphadenitis (Kikuchi's disease)," *Journal of Clinical Pathology*, vol. 53, no. 8, pp. 636–638, 2000.
- [11]. E. Uslu, S. Gurbuz, A. Erden et al., "Disseminated intravascular coagulopathy caused by Kikuchi-Fujimoto disease resulting in death: ?rst case report in Turkey," *International Medical Case Reports Journal*, vol. 7, pp. 19–22, 2014.
- [12]. Y. Kucukardali, E. Solmazgul, E. Kunter, O. Oncul, S. Yildirim, and M. Kaplan, "Kikuchi-Fujimoto disease: analysis of 244 cases," *Clinical Rheumatology*, vol. 26, no. 1, pp. 50–54, 2007.
- [13]. A. Seno, R. Torigoe, K. Shimoe, J. Tada, J. Arata, and M. Suwaki, "Kikuchi's disease (histiocytic necrotizing lymphadenitis) with cutaneous involvement," *Journal of the American Academy of Dermatology*, vol. 30, no. 3, pp. 504–506, 1994.
- [14]. X. Bosch and A. Guilabert, "Kikuchi-Fujimoto disease," *Orphanet Journal of Rare Diseases*, vol. 1, no. 1, p. 18, 2006.
- [15]. Y. Chong and C. S. Kang, "Causative agents of Kikuchi-Fujimoto disease (histiocytic necrotizing lymphadenitis): a meta-analysis," *International Journal of Pediatric Otorhinolaryngology*, vol. 78, no. 11, pp. 1890–1897, 2014.
- [16]. Y. W. Lin, H. Horiuchi, I. Ueda, and M. Nambu, "Recurrent hemophagocytic lymphohistiocytosis accompanied by Kikuchi's disease," *Leukemia and Lymphoma*, vol. 48, no. 12, pp. 2447–2451, 2007.
- [17]. C. Y. Cheng, W. H. Sheng, Y. C. Lo et al., "Clinical presentations, laboratory results and outcomes of patients with Kikuchi's disease: emphasis on the association between recurrent Kikuchi's disease and autoimmune diseases," *Journal of Microbiology, Immunology and Infection*, vol. 43, no. 5, pp. 366–371, 2010.
- [18]. M. J. Bennie, K. M. Bowles, and S. C. Rankin, "Necrotizing cervical lymphadenopathy caused by Kikuchi-Fujimoto disease," *British Journal of Radiology*, vol. 76, no. 909, pp. 656–658, 2003.
- [19]. S. Y. Kwon, T. K. Kim, Y. S. Kim, K. Y. Lee, N. J. Lee, and H. Y. Seol, "CT ?ndings in Kikuchi disease: analysis of 96cases," *American Journal of Neuroradiology (AJNR)*, vol. 25, no. 6, pp. 1099–1102, 2004.
- [20]. W. T. Miller Jr. and L. A. Perez-Ja7e, "Cross-sectional imaging of Kikuchi disease," *Journal of Computer Assisted Tomography*, vol. 23, no. 4, pp. 548–551, 1999.
- [21]. T. R. Tong, O. W. Chan, and K. C. Lee, "Diagnosing Kikuchi disease on ?ne needle aspiration biopsy: a retrospective study of 44 cases diagnosed by cytology and 8 by histopathology," *Acta Cytologica*, vol. 45, no. 6, pp. 953–957, 2001.
- [22]. D. K. Das, B. I. Haji, R. A. Al-Boijan et al., "Kikuchi-Fujimoto disease in ?ne needle aspiration smears: a clinico-cytologic study of 18 pediatric cases and correlation with 68 adult patients," *Indian Journal of Pathology and Microbiology*, vol. 55, no. 3, pp. 333–338, 2012.
- [23]. B. Sopena, A. Rivera, C. Vázquez-Triñanes et al., "Autoimmune manifestations of Kikuchi disease," *Seminars in Arthritis and Rheumatism*, vol. 41, no. 6, pp. 900–906, 2012.
- [24]. E. J. Go, Y. J. Jung, S. B. Han, B. K. Suh, and J. H. Kang, "A case of Kikuchi-Fujimoto disease with autoimmune thyroiditis," *Korean Journal of Pediatrics*, vol. 55, no. 11, pp. 445–448, 2012. <http://wwi.com>



AAA A 4x viewAAAAAAAAA



B 40x view

A Low magnification showing circumscribed foci of necrosis .

. **B**, Area of histiocytic infiltrate and abundant karyorrhectic debris. Note the absence of neutrophils . Many phagocytic histiocytes, including a few “crescentic histiocytes.

Jasmine Khanna" Kikuchi–Fujimoto Disease in a Woman with axillary lymphadenopathy, a rare site of presentation: Case Report and Review of the Literature." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 9, 2019, pp 80-83.