KBB ve BBC Dergisi 24 (1):17-20, 2016

Kikuchi-Fujimoto Disease: Case Report

Kikuchi-Fujimoto Hastalığı

Hacer BARAN, MD,[1] Özgür Çakır KAYA, MD[2]

[1] Private Zeytin Medical Center Surgery, Clinic of Ear, Nose and Throat,
[2] Bursa Medical Park Hospital, Ear, Nose And Throat, Bursa

ABSTRACT

Kikuchi-Fujimoto Diseaase is a rare, self-limiting, benign disease that is presents with cervical lymphadenopathy, fever and transient leucopenia. There is a higher incidence of Kikuchi- Fujimoto Disease in young women and Asian populations. It mimics malignant lymphoma on presentation, and therefore an accurate clinicopathological differential diagnosis is crucial. Herein, we report a 33-year-old female who presented with relapsing fever, cervical lymphadenopathy and fatigue. We discussed clinical and pathological findings of the disease with a review of the literature.

Keywords
Kikuchi Fujimoto Disease; histiocytic necrotizing lymhadenitis; immunity

ÖZET

Kikuchi-Fujimoto hastalığı; servikal lenfadenopati, ateş ve geçici lökopeni ile seyreden nadir, kendini sınırlayan, benign bir hastalıktır. Genç kadınlarda ve Asya popülasyonunda Kikuchi-Fujimoto Hastalığı yüksek insidansta izlenir. Malign lenfomayı taklit eder ve bu yüzden kesin klinikopatolojik ayırım çok önemlidir. Biz çalışmamızda tekrarlayan ateş, servikal lenfadenopati ve halsizlik şikayeti ile gelen 33 yaşında kadın hastayı bildirdik.

Anahtar Sözcükler
Kikuchi-Fujimoto Hastalığı; histiositik nekrotizan lenfadenit; immünite

Çalışmanın Dergiye Ulaştığı Tarih: **20.09.2015** Çalışmanın Basıma Kabul Edildiği Tarih: **01.03.2016**

≈

Correspondence
Hacer BARAN, MD
Private Zeytin Medical Center Surgery,
Clinic of Ear, Nose and Throat, Bursa
E-mail: baranhacer@hotmail.com

INTRODUCTION

Kikuchi-Fujimoto Disease (KFD), also known as histiocytic necrotizing lymphadenitis, was first described in 1972 by Kikuchi and Fujimoto independently.[1,2] KFD occurs frequently in young adults below 40 years of age. Female predominance was considered initally, but recent literature indicates a male/female ratio as 1/1.[3] The exact etiology of KFD is unknown. Recent literature has emphasized viral or autoimmune causes.[4] The initial presentation of KFD is cervical lymphadenopathy, fever, headache, sore throat, and fatigue. Nausea, vomiting, night sweats, and cutaneous manifestations are other less common symptoms. Leukopenia, anemia, elevated sedimentation and C-reactive protein are the common laboratory findings.[5,6] In addition, atypical lymphocytes have been reported in the peripheral blood.[4] Excisional biopsy of the involved lymph nodes is performed for diagnosis.

Apoptosis which results in the formation of nuclear debris is one of the characteristic features of histiocytic necrotizing lymphadenopathy. Histological findings include paracortical necrosis, karyorrhexis, increased number of phagocytic histiocytes and atypical lymphocytes. It is generally a self limiting disease that regresses spontaneously in 1-4 months.[7] Reccurence of the disease is observed in 3-4% of the patients.[8] Symptomatic relief with analgesics and antipyretics is offered for local or systemic complaints of the patients. Rarely steroids can be used especially in severe extranodal involvement or generalized clinical course.[9] In this report, we reported KFD in a 33-year- old woman, and reviewed current literature.

CASE REPORT

A 33-year-old women presented with a painful neck mass, fever, sore throat, headache, night sweats, and myalgia for 2 months. She had no significant medical history before presentation. On physical examination, body temperature of the patient was 39°C. She had multiple lymphadenopathies on anterior and posterior triangles of her neck. Lymph nodes were tender, erythematous, and mobile.

There was no ulceration or drainage. Her skin was warm to palpation, but there was no rash, petechia, or purpura. There was no hepatosplenomegaly or lymphadenopathies in the other regions of the body.

White blood cell count was 2100/mm^3, hemoglobin level was 10.7 g/dL, platelet count was 148,000/µL, polymorphonuclears were 50%, and lymphocytes were 33.3%. Well defined lymphadenopathy on the left side extending along the carotid sheath and adjacent to anterior and posterior borders of the sternocleidomastoids were observed on ultrasonography. A fine-needle aspiration biopsy was performed, and the final diagnosis was atypical lymphoid hyperplasia. The pathology department recommended an additional biopsy to rule out lymphoproliferative disorder. A lymph node was removed from the posterior triangle of the neck.

Zones of coagulative necrosis with surrounding proliferation of histiocytes and foci of karyorrectic debris were shown on histopathological examination. KFD was diagnosed. The patient was treated with anti-inflammatory drugs. Symptoms resolved in four weeks and the patient did not have any recurrent lymphadenopathies.

DISCUSSION

Kikuchi-Fujimoto lymphadenopathy/histiocytic necrotizing lymphadenitis (HNL) is an uncommon, idiopathic, benign and generally self limiting disease. Kikuchi first described the disease in 1972 in Japan. Fujimoto and colleagues independently described Kikuchi's disease in the same year. They described the disease as "lymphadenitis with focal proliferation of reticular cells accompanied by numerous histiocytes and extensive nuclear debris."[1,2] The disease is seen primarily in the Asian population, but it has been reported in all races. It is rare in Europe and North America.[10] The incidence of KFD is unknown. It typically occurs in patients during third and fourth decades of life.[11] At first, a female predominance was considered, but in recent literature male to female ratio was reported as 1:1.[3,4] The exact etiology is unknown. It is thought that viral or autoimmune causes were effective in etiology.[4] Current data suggests that it may be due to the excessive immune response of histiocytes to an infectious agent. Many viruses like Epstein Barr virus, human herpes virus, human immunodeficiency virus, parvovirus B19, and paramyxoviruses have been implicated in its pathogenesis.[12,13]

KFD begins as an acute or subacute condition. Patients with KFD usually present with tender cervical lymphadenopathies (56-98%).Generally, lymph nodes are located in the jugular-carotid chain, and the posterior

triangle. Sometimes generalized diffuse lymphadenopathy may occur.[14,15] Diameters of lymph nodes are usually 3 cm or less; however they may reached to 5-6 cm.[16] Fever, headache, nausea, fatigue, weight loss, arthralgia, sore throat, night sweats, splenomegaly and skin rash are other nonspesific symptoms.17 The laboratory findings may include leukopenia (25-58%), increased

lactate dehydrogenase, and elevated erythrocyte sedimentation rate.[15,18,19] Atypical lymphocytes have been reported in the peripheral blood. Extranodal involvement is rare; however skin, eye and bone marrow may be involved.4 Skin lesions have been identified in approximately 30% of the patients with KFD. They are non-specific acneiform eruptions, facial erythema, indurated, erythemic papules and plaques, purpura, and nodules.[20-22]

Lymph node excisional biopsy and histopathological examination are done for definitive diagnosis of KFD.[23] Characteristic histological findings are coagulative necrosis with ample karyorrhetic debris in paracortical areas of the involved nodes.[17] The histopathological features are classified into three stages: proliferative stage expressing various histiocytes, plasmacytoid monocytes, lymphoid cells containing karyorrhectic nuclear fragments, and eosinophilic apoptotic debris; necrotizing stage showing a degree of coagulative necrosis; and xanthomatous stage predominantly containing foamy histiocytes. The absence of granulocytes is also an important feature. The lack of monoclonal lymphocyte receptors rules out the possibility of a lymphoma.[24,25]

The differential diagnosis of a slow-growing neck mass is extensive including malignant lymphoma, tuberculosis, Kawasaki's disease, systemic lupus erythematosus (SLE), Hodgkin's disease, toxoplasmosis, metastatic carcinoma, infectious mononucleosis, acquired immunodeficiency syndrome, cat scratch disease, and angioimmunoblastic lymphadenopathy.[4,11,24,26] Differentiation of KFD from SLE is difficult because of similar clinical and histological findings. It has also been reported that KFD is associated with SLE.[17]

KFD is typically a self-limiting disease that rarely requires specific treatment, and it resolves within one to four months.[23,26] Usually symptomatic relief is adequate for the local and systemic complaints of the disease. Lymph node tenderness and fever are treated with analgesics, antipyretics, and non- steroid anti-inflammatory drugs. Rarely, steroids can be used especially in severe extranodal involvement or generalized clinical course.9 Patients with KFD should be examined systemically, and must be under regular follow-up in order to monitor the manifestations of SLE.[17]

Histiocytic necrotizing lymhadenitis is an idiopathic, extremely rare disease and predominantly involves the posterior cervical lymph nodes. Kikuchi's disease seems to be more prevalent in Asian individuals. KFD has an excellent prognosis. Early recognition of KFD has prime importance to avoid extensive and expensive investigations related to malignant lymphoma or other related disorders. Unfortunately, the etiology, pathogenesis, diagnosis, and management of KFD still remain enigmatic and further research is required to answer these questions.

REFERENCES

1. Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytosis. Nippon Ketsueki Gakkai Zasshi 1972;35:379-80.
2. Fujimoto Y, Kojima Y, Yamaguchi K. Cervical subacutenecrotizing lymphadenitis. A New Clinicopathological Entity 1972;20:920-7.
3. Tsang WY, Chan JK, Ng CS. Kichuchi's Lymphadenitis: a morphologic analysis of 75 cases with special reference to unusual features. Am J Surg Pathol 1994;18(3):219-31.
4. Bosch X, Guilabert A, Miquel R, Campo E. Enigmatic Kikuchi-Fujimoto disease: a comprehensive review. Am J Clin Pathol 2004;122(1):141-52.
5. Kulak J, Smith LP, Acar BC, Weed DT. Kikuchi-Fujimoto disease. Ear Nose Throat J 2009;88(9):1108-9.
6. Bosch X, Guilabert A. Kikuchi-Fujimoto disease. Orphanet J Rare Dis 2006;23(1):18.
7. Tariq H, Gaduputi V, Rafiq A, Shenoy R. The enigmatic kikuchi-fujimoto disease: a case report and review. Case Rep Hematol 2014;2014:648136.
8. Dorfman RF. Histiocytic necrotizing lymphadenitis of Kikuchi and Fujimoto. Arch Pathol Lab Med 1987;111(11): 1026-9.
9. Jang YJ, Park KH, Seok HJ. Management of Kikuchi's disease using glucocortcoid. J Laryngol Otol 2000;114(9):709-11.
10. Satavahana Chowdary V1, Vinay Kumar EC, Swarna Latha G, Sudha Rani R. Kikuchi and Fujimoto Disease. Indian J Otolaryngol Head Neck Surg 2006;58(3):287-90.

11. Bennie MJ, Bowles KM, Rankin SC. Necrotizing cervical lymphadenopathy caused by Kikuchi-Fujimoto disease. The British Journal of Radiology 2003;76(909):656-8.
12. Rosado FG, Tang YW, Hasserjian RP, McClain CM, Wang B, Mosse CA. Kikuchi- Fujimoto lymphadenitis: role of parvovirus B-19, Epstein-Barr virus, human herpesvirus 6, and human herpesvirus 8. Human Pathology 2013;44(2):255-9.
13. Imamura M, Ueno H, Matsuura A, Kamiya H, Suzuki T, Kikuchi K, Onoe T. An ultrastructural study of subacute necrotizing lymphadenitis. Am J Pathol 1982;107(3):@292-9.
14. Melikoglu MA, Melikoglu M. The clinical importance of lymphadenopathy in systemic lupus erythematous. Acta Reumatol Port 2008;33(4):402-6.
15. Yilmaz M, Camei C, Sari I, Okan Sevine A, Onat AM, Buyukhatipoglu H. Histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto's Disease) mimicking systemic lupus erythematous: a review of two cases. Lupus 2006;15(6):384-7.
16. Kucukardali Y, Solmazgul E, Kunter E, Oncul O, Yildirim S, Kaplan M. Kikuchi-Fujimoto Disease: analysis of 244 cases. Clin Rheumatol 2007;26(1):50-4.
17. Jamal AB. Kikuchi fujimoto disease. Clin Med Insights Arthritis Musculoskelet Disord 2012;5:63-6.
18. Hudnall SD. Kikuchi-Fujimoto Disease: Is Epstein - Barr virus the culprit? Am J Clin Pathol 2000;113(6):761-4.
19. Qadri F, Atkin G.K, Thomas D, Das SK. Kikuchi's disease: an important cause of cervical lymphadenopathy. Clin Med 2007;7(1):82-4.
20. Paradela S, Lorenzo J, Martínez-Gómez W, Yebra-Pimentel T, Valbuena L, Fonseca E. Interface dermatitis in skin lesions of Kikuchi Fujimoto's disease: a histopathological marker of evolution into systemic lupus erythematosus? Lupus 2008;17(12):1127-35.
21. Jang JM, Woo CH, Choi JW, Song DJ, Yoo Y, Lee KC, et al. A case of Kikuchi's disease with skin involvement. Korean Journal of Pediatrics 2006;49(1):103-6.
22. Murthy SC, Dandin SM, Dandin AS, Patwardan MY. Kikuchi's disease associated with systemic lupus erythematosus. Indian J Dermatol Venereol Leprol 2005;71(5): 338-41.
23. Bennie MJ, Bowles KM, Rankin SC. Necrotizing cervical lymphadenopathy caused by Kikuchi-Fujimoto disease. Br J Radiol 2003;76(909):656-8.
24. Ade AS, Soares JM, Sá Santos MH, Martins MP, Salles JM. Kikuchi-Fujimoto disease: three case reports. Sao Paulo Med J 2010;128(4):232-5.
25. Kuo T. Kikuchi's disease (histiocytic necrotizing lymphadenitis). A clinicopathologic study of 79 cases with an analysis of histologic subtypes, immunohistology and DNA ploidy. Am J Surg Pathol 1995;19(7):798-809.
26. Archibald DJ, Carlson ML, Gustafson RO. Kikuchi-Fujimoto disease in a 30-year-old caucasian female. Int J Otolaryngol 2009;2009:901537.
27. Parappil A, Rifaath AA, Doi SA, Pathan E, Surrun SK. Pyrexia of unknown origin: Kikuchi- Fujimoto disease. Clin Infect Dis 2004;39(1):138-43.