

## Kikuchi-Fujimoto Disease: a Case Report

Mozaffar Aznab<sup>1</sup>, Naser Kamalian<sup>2</sup>, Jaffar Navabi<sup>3</sup>, and Kaveh Kavianimoghadam<sup>4</sup>

<sup>1</sup> Department of Internal Medicine, Taleghani Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran

<sup>2</sup> Department of Pathology, Tehran University of Medical Sciences, Tehran, Iran

<sup>3</sup> Department of Internal Medicine, Taleghani Hospital, Kermanshah, Iran

<sup>4</sup> Department of Paramedical, School of Medicine, Kermanshah of University Medical Sciences, Kermanshah, Iran

Received: 17 Dec. 2013; Accepted: 6 Jun. 2014

**Abstract-** Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis is an idiopathic, self-limiting disorder and predominantly affects young women. We report a 35-year-old female who presented with soft to firm cervical lymphadenopathy and neck pain. She had multiple enlarged cervical nodes. Examination of other systems was normal. Lymph node biopsy was performed, and the histological features, and immunohistochemistry confirmed the diagnosis. The Patient was treated with non-steroidal anti-inflammatory drugs and low-dose prednisolone. A significant decrease in the size of lymph node and relief of neck pain occurred. During four years of follow-up, the patient developed no malignant disease or systemic and autoimmune diseases such as systemic lupus erythematosus. Kikuchi-Fujimoto disease is rare, clinicians should be aware of this condition as early diagnosis of the disease will lessen concerns of the patient's family. © 2015 Tehran University of Medical Sciences. All rights reserved.

*Acta Med Iran* 2015;53(11):725-727.

**Keywords:** Kikuchi-Fujimoto disease; Histiocytic necrotizing lymphadenitis

### Introduction

Kikuchi-Fujimoto Disease (KFD) or histiocytic necrotizing lymphadenitis is an idiopathic, self-limiting disorder that typically causes lymphadenitis of cervical lymph nodes, usually is accompanied by mild fever and night sweats. This disease was first described in 1972 in Japan (1).

Kikuchi-Fujimoto disease is more common in female gender (2,3). People under 30 years of age are more affected by this disease than any other age group (4). The cause of KFD is unknown. Infections such as Epstein-Barr virus (EBV) (5), Human T-lymphotropic virus 1 (HTLV-1) (6) or autoimmune cause has been reported in the pathogenesis of KFD, but none of these factors have been found to be consistently associated with this condition (7,8). Blood tests classically show a mild leukopenia (neutropenia) with the rise in erythrocyte sedimentation rate; many patients show atypical lymphocytes in their peripheral blood (4,9).

Although serologic tests such as antinuclear and anti-DNA antibodies should be performed to exclude systemic lupus erythematosus; but the KFD is generally diagnosed on the basis of an excisional biopsy of affected lymph nodes. Histopathologic

feature and immunohistochemistry help differentiation of KFD from the other causes of lymphadenopathy including lymphoma, malignancy or collagen vascular diseases such as systemic lupus erythematosus.

Features that distinguish KFD from malignant lymphoma include incomplete architectural effacement with patent sinuses, the presence of numerous reactive histiocytes, relatively low mitotic rates, fragmentation, necrosis, karyorrhexis, and absence of Reed-Sternberg cells. No specific staining for the KFD is available. KFD is diagnosed by the combination of histopathological and immunohistochemical findings.

Patients with KFD should be followed-up for several years to survey the possibility of the development of systemic lupus erythematosus. The disease process continues for approximately two to three months before resolving spontaneously. Spontaneous recovery occurs in one to four months. Treatment is generally supportive. Non-steroidal anti-inflammatory drugs may be used to alleviate lymph node tenderness and fever. The use of corticosteroids has been recommended in the severe form of the disease. The disease usually runs a benign course and the condition is self-limiting; usually resolves in several weeks to months. There are patients that the

**Corresponding Author:** M. Aznab

Department of Internal Medicine, Taleghani Hospital, Kermanshah University of Medical Science, Kermanshah, Iran  
Tel: +98 918 1313925, Fax: +98 83 18370139, E-mail address: draznab@yahoo.com

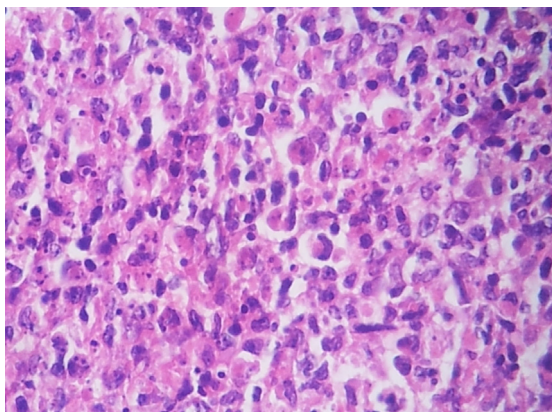
## Kikuchi-fujimoto disease

response to chloroquine is observed (10). A high initial oral dose of prednisolone with a subsequent reducing dose is the advocated regime (11).

### Case Report

In December 2008, a 35-year-old Iranian female presented with pain and swelling in the neck for three weeks, she denied any fever, weight loss or night sweats. The lymph nodes were multiple, 1-2.5 cm in diameter, soft to firm in consistency, mobile, discrete in both jugulodigastric, and posterior cervical chains. On examination, there were no abnormalities in the ears, oral cavity, oropharynx or larynx. The rest of examination was normal.

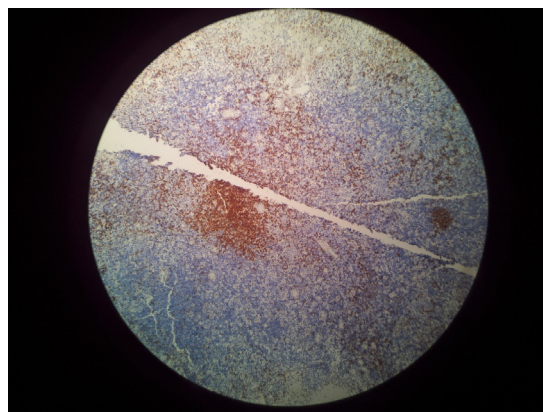
Complete blood count showed mild neutropenia, ESR was 35 mm/h, and the patient had normal chest-X-ray. Neck ultrasonography showed multiple nodal enlargements in both jugulodigastric, posterior cervical chains and also in the submandibular region. Antinuclear antibody and anti-double-stranded DNA was negative. Excision biopsy of a lymph node from the same area was performed. Figure 1 shows parenchyma that represents focal areas of karyorrhectic necrosis surrounded by histiocytes of which some has eccentric nuclei, and plasmacytoid, intervening ones are small lymphoid cells.



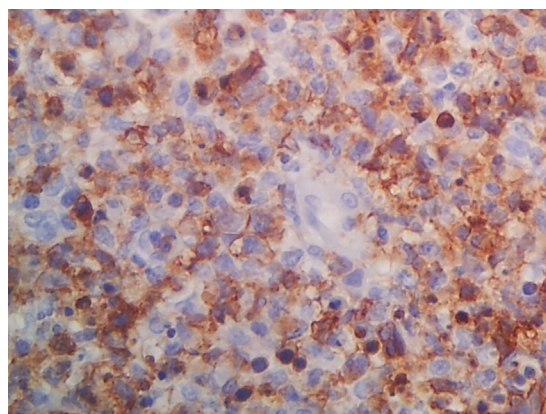
**Figure 1.** Expansion of paracortical areas with necrosis (H&E) X800

IHC stains for CD20 show highlight germinal centers (Figure 2) and IHC stains for CD45RO, express in interfollicular lymphoid cells and cellular element around foci (Figure 3) and no expression of CD15 and CD30, myeloperoxidase (MPO) in lymphoid cells.

At 4-year follow-up of patients no malignant disease or systemic and autoimmune diseases such as systemic lupus erythematosus, as it did in the case.



**Figure 2.** IHC stains for CD20 show highlight germinal centers



**Figure 3.** CD45RO express in interfollicular lymphoid cells and cellular element around foci X 400

### Discussion

The exact etiology and pathogenesis of KFD is still not fully understood. An autoimmune mechanism, viral agents such as EBV, HIV (5), HTLV1 (6), have been suggested as possible etiological agents, but none of these factors has confirmed a role in the pathogenesis of KFD. There are two important points in dealing with the disease: 1- differential diagnosis of KFD, 2 - being a self-limiting disease (12) and calm and reassure the patient and his family that the disease is not dangerous. Pathology reports and performing appropriate tests can provide great help. Specific staining helps us to rule out lymphoma, particularly Hodgkin's lymphoma. Appropriate follow-up also is recommended to rule out lupus erythematosus. Anti-inflammatory medications are often prescribed for pain. Low-dose prednisolone should be prescribed in severe cases, especially the patients that the examination has revealed severe tenderness, (10) severe extranodal or generalized KFD.

This disorder must be considered in the differential

diagnosis when a young female patient presents with fever and cervical lymphadenopathy. Clinically KFD may mimic lymphoma or systemic lupus erythematosus. Early diagnosis of the disease is of crucial importance in reducing concerns the patient's family.

## References

1. Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytes. *Acta Hematol Jpn* 1972;35:379-80.
2. Fujimoto Y, Kozima Y, Yamaguchi K. Cervical subacute necrotizing lymphadenitis: a new clinicopathologic entity. *Naika* 1972;20:920-7.
3. Bosch X, Guilabert A, Miquel R, et al. Enigmatic Kikuchi-Fujimoto disease: a comprehensive review. *Am J Clin Pathol* 2004;122(1):141-52.
4. Lin HC, Su CY, Huang CC, et al. Kikuchi's disease. A review and analysis of 61 cases. *Otolaryngol Head Neck Surg* 2003;128(5):650-3.
5. 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.
6. Lee HY, Huang YC, Lin TY, et al. Primary Epstein-Barr virus infection associated with Kikuchi's disease and hemophagocytic lymphohistiocytosis: a case report and review of the literature. *J Microb Immunol Infect* 2010;43(3):253-7.
7. Atarashi K, Yoshimura N, Nodera H, et al. Recurrent histiocytic necrotizing lymphadenitis (Kikuchi's disease) in an human T lymphotropic virus type I carrier. *Intern Med* 1996;35(10):821-5.
8. Pileri SA, Sabattini E, Costigliola P, et al. Kikuchi's lymphadenitis and HIV infection. *AIDS* 1991;5(4):459-61.
9. Hollingsworth HC, Peiper SC, Weiss LM, et al. An investigation of the viral pathogenesis of Kikuchi-Fujimoto disease: lack of evidence for Epstein-Barr virus or human herpesvirus type 6 as the causative agents. *Arch Pathol Lab Med* 1994;118(2):134-40.
10. Chen PH, Huang YF, Tang CW, et al. Kikuchi-Fujimoto disease: an amazing response to hydroxychloroquine. *Eur J Pediatr* 2010;169(12):1557-9.
11. Jang YJ, Park KH, Seok HJ. Management of Kikuchi's disease using glucocorticoid. *J Laryngol Otol* 2000;114(9):709-11.
12. Dorfman RF. Histiocytic necrotizing lymphadenitis of Kikuchi and Fujimoto. *Arch Pathol Lab Med* 1987;111(11):1026-9.
13. George TI, Jones CD, Zehnder JL, et al. Lack of human herpesvirus 8 and Epstein-Barr virus in Kikuchi's histiocytic necrotizing lymphadenitis. *Hum Pathol* 2003;34(2):130-5.