Kikuchi-Fujimoto disease

Ashraf ALAkkad[1] and Mohamed Alakkad[1]

[1]Affiliation not available

October 6, 2022

International Journal of Advances in Medicine
Alakkad A et al. Int J Adv Med. 2021 Sep;8(9):1419-1422
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20213248

Case Report

Kikuchi-Fujimoto disease

Ashraf Alakkad[1]*, Mohamed Alakkad[2]

[1]Department of Internal Medicine, Madinat Zayed Hospital, UAE
[2]Department of General Surgery, Hatta Hospital, UAE

Received: 29 June 2021
Accepted: 31 July 2021

***Correspondence:**
Dr. Ashraf Alakkad,
E-mail: ashraf.alaqqad@gmail.com

ABSTRACT

A lady from Sudan was referred to our medical clinic as a case of cervical lymphadenopathy with gradual enlargement. She had no complaint. The cervical lymphadenopathy was not associated with pain, fever, weight loss, cough, neither bleeding nor other associated swellings. There was no history of chronic medical problems including TB and underwent thorough investigations including LN biopsy. Lymphoma was initially suspected. Fine-needle aspiration and excision biopsy were undertaken. Histological analysis later suggested Kikuchi-Fujimoto disease, also known as histiocytic necrotizing lymphadenitis. Kikuchi-Fujimoto disease (KFD) was described in 1972 as lymphadenitis with focal proliferation of reticular cells accompanied by numerous histiocytes and extensive nuclear debris. KFD, frequently found in East Asian countries, is rare in the UK. No definite etiology of KFD is known despite autoimmune and infection factors being suggested. The diagnostic hallmark is histological findings from lymph nodes. Steroid therapy could be used in severe cases. KFD is relatively unknown and this case report aims to highlight its occurrence in our population.

Keywords: KFD, Histiocytic necrotizing lymphadenitis, Cervical lymphadenopathy

INTRODUCTION

Cervical lymphadenopathy can be caused by a wide range of conditions, from benign infectious diseases to malignant lymphomas. According to NICE guidelines, cervical lymphadenopathy persisting>3 weeks should be considered as cancer and referred to the ENT clinic. Kikuchi-Fujimoto disease (KFD) is also known as histiocytic necrotizing lymphadenitis. These were first described in 1972 by Kikuchi and Fujimoto independently. It is a rare syndrome with no known etiology, self-limited and benign, characterized by localized tender lymph nodes, fever, and night sweats.[1] KFD is prevalent in adult patients with the mean age of diagnosis around 21 pre-ponderances of 4:1 with females.[2]

This article reports a case of persistent tender cervical lymphadenopathy which had confounded diagnosis until a histological specimen was obtained from the lymph tissue which encased the internal carotid artery close to the base of skull. It emerged that our patient had KFD, otherwise known as histiocytic necrotizing lymphadenitis. We also performed a literature review of KFD to provide an evidence-based understanding of this disease.

CASE REPORT

A female patient from Sudan who came to follow the result of biopsy of her lymph node was seen in the clinic as a case of cervical LNs with gradual enlargement. She had no complaint. The cervical lymphadenopathy was not associated with pain, fever, weight loss, cough, neither bleeding nor other associated swellings. There was no history of chronic medical problems including TB and underwent thorough investigations including LN biopsy. Her histopathology report showed: preserved nodal architecture and expansion of the paracortical zone by focal collections of pale staining mononuclear cells. Scattered melanin-laden macrophages were detected. Hyperplastic lymphoid follicles were found. There were scattered few eosinophils and plasma cells infiltrating the lymph node parenchyma. There was a proliferation of the

small endothelial venules and no apparent malignancy. The histological report was suggestive of active dermatopathic lymphadenitis. No significant cytologic atypia was seen. Special stains for fungus and acid-fast bacilli were negative.

Viral infection was excluded, normal blood picture, inflammatory markers remark of mild elevation of ESR 25, no organomegaly in abdominal ultrasound, breast ultrasound clear except left axillary LNs persistent cervical lymphadenopathy involving anterior/posterior groups matted together no significant change in sizes compared with the last visit. Histopathology suggests the diagnosis of Kikuchi disease (necrotizing histiocytic lymphadenitis). All autoimmune work up negative.

The overall findings of the above lymph node tissue are most consistent with Kikuchi disease (necrotizing histiocytic lymphadenitis). Correlation with clinical/serological/culture findings, and follow-up were recommended.

Diagnosis

Cervical lymph node, excisional biopsy: Consistent with necrotizing histiocytic lymphadenitis (Kikuchi disease), based on the histological findings.

A diagnosis of Kikuchi disease was made and she was treated symptomatically with Nonsteroidal anti-inflammatory drug. At follow up visit the patient is asymptomatic and lymph nodes have almost subsided.

Management and treatment

She was given course of antibiotics because of the inflamed lymph node along with non-steroidal anti-inflammatory drugs. The infection subsided. She underwent excision biopsy of cervical lymph node.

DISCUSSION

History

Dr. Masahiro Kikuchi published a case of lymphadenitis in the Japanese journal of the hematological society in 1972. It was characterized by localized proliferation of reticular cells, dense histiocytes, and substantial nuclear debris.[1] Dr. Fujimoto submitted a related case in another Japanese article the same month.[2]

Epidemiology

KFD is most commonly prevalent in East Asia and Japan and rare in the UK and continental Europe. Larger case series reports suggest that Kikuchi disease is roughly equal prevalent among males and females with slight preponderance in female and mainly affects individuals with mean age <30 years old.[3]

Etiology

No evidence of any etiological factor. This subject is mainly concentrated either on an infection or autoimmune disorder.

Infection

Many viruses and bacteria have been isolated in case reports of KFD. Among bacteria brucellosis, +, *Entamoeba histolytica*, *Mycobacterium szulgai*, *Toxoplasma gondii* and *Yersinia enterocolitica*, have been isolated. Among viruses' herpes viruses, hepatitis B virus, human T-lymphotropic virus type 1, human immunodeficiency virus (HIV), Epstein-Barr virus, cytomegalovirus, paramyxovirus, parvovirus, parainfluenza virus, dengue and rubella virus are all implicated to causation of KFD.

However, further research has been unable to corroborate these findings. The fact that most KFD patients are resistant to medications shows that these microorganisms were discovered by chance. None of them have been consistently linked to this condition.[3]

Autoimmune immunological testing in KFD

Antinuclear antibodies (ANA), rheumatoid factor, and lupus erythematosus preparations are generally negative. Some patients initially diagnosed with Kikuchi disease have subsequently developed systemic lupus erythematosus (SLE), and an ANA test should be performed in patients with suspected Kikuchi syndrome who have features suggestive of SLE in order to exclude this diagnosis. Serology for Epstein Barr virus (EBV), cytomegalovirus, human immunodeficiency virus (HIV), toxoplasmosis, Yersinia enterocolitica, cat scratch disease, and other infectious agents is often per formed since these infections are considered in the differential diagnosis of fever and lymphadenopathy.[10]

Clinical features

The typical pattern of presentation is widespread flu-like symptoms with painful lymph adenopathy in the posterior cervical region. Arthralgia, weariness, headache, and nausea are some of the less prevalent non-specific symptoms. The condition progresses for around two to three months before spontaneously resolving.[6] Our patient's MRI scans revealed several enlarged lymph nodes on the right side. Following that, they were biopsied.

Diagnosis

Due to its relative obscurity, ambiguous symptoms, and imprecise histological diagnosis, KFD is difficult to diagnose. Histological evaluation of a lymph node excision sample is currently the only reliable method of diagnosis. Unfortunately, fine-needle aspiration samples are often not sensitive enough to provide a valid diagnosis,

with an accuracy of 56.3% overall. Mild neutropenia is typically detected in blood testing, with modesty elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). CT, diagnostic results. In many cases, an inaccurate provisional diagnosis of lymphoma or tuberculosis is established. Kwon et al discovered that instances of confirmed KFD exhibited the following common appearances on CT scanning in a study of 96 retrospective scans of confirmed KFD: (i) numerous homogenous lymph adenopathy involving levels II to V; (ii) 94% were smaller than 2.5 cm, allowing some differentiation from lymphoma, which normally develops fewer but larger nodes; and (iii) peri-nodal infiltration and necrosis are common findings. Lymph nodes with a hypoechoic centre and a hyperechoic ring are frequently seen on ultrasonography scans. These characteristics have a low specificity for KFD once again. These findings strongly suggest that imaging techniques cannot be used diagnosis KFD. However, based on the clinical history, KFD rather a neoplastic lesion should be suspected.[7,8]

Histological findings

Kim et al found the following among epidermal (coetaneous) Kikuchi illness in such a 2010 study: (i) minor dominance of CD8 + lymphocytes, (ii) lymphohistiocytic infiltration and non-neutrophilic karyorrhexis (typically). Kikuchi illness has a dominant immunophenotype of mature CD8-positive and CD4-positive T cells. Apoptosis is also prevalent in lymphocytes histiocytes. B cells are scarce whereas natural killers (NK) are plentiful. Kikuchi illness has positive immune-staining results with the monoclonal antibody Ki-M1P, while malignant lymphoma does not.

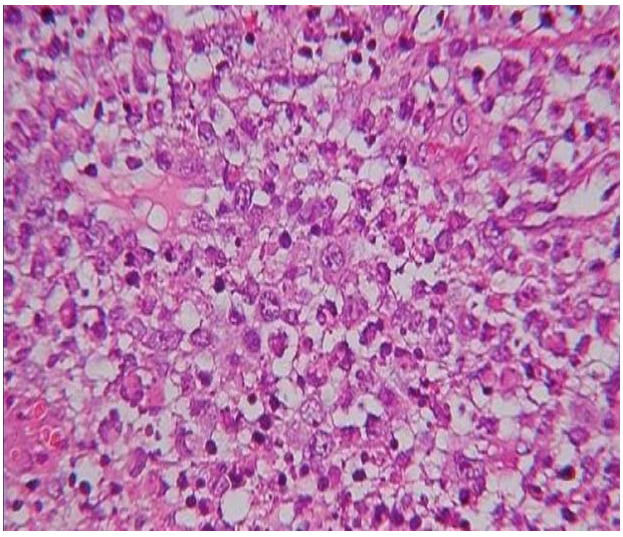

Figure 1: Biopsy specimen of lymph node in KFD.

Differential diagnosis

Such as sarcoidosis, infectious mononucleosis, tuberculosis, Kawasaki disease, lymphoma, syphilis and systemic lupus erythematosus (SLE).

Management

In most cases, KFD is a self-limiting illness that does not require specific therapy. As a result, management is primarily on supportive therapies such as analgesics and anti-inflammatory drugs. Immunosuppression with corticosteroids appears to improve the condition quickly in individuals with neurological symptoms or in cases where KFD is diagnosed in conjunction with another medical disease. The recommended regimen is a high initial oral dosage of prednisolone followed by a tapering dose. Significant responses have been reported to immunoglobulins and minocycline, hydroxychloroquine.[9] KFD recurrence is estimated to be 3%.[3]

CONCLUSION

KFD is a rather uncommon disorder, especially in Western countries. KFD is the subject of extensive research. Unfortunately, the etiology, pathology, diagnosis, and therapy of this disease are all still largely unknown and debated. Ongoing research on this disease might possibly provide an understanding of a variety of other autoimmune diseases.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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 subacute necrotizing lymphadenitis. A new clinicopathological entity. Naika. 1972;20:920-7.
3. Lin HC, Su CY, Huang CC, CF Hwang, Chien CY. Kikuchi's disease: a review and analysis of 61 cases. Otolaryngology. 2003;128(5):650-3.
4. Hollingsworth HC, Peiper SC, Weiss LM, Raffeld M, Jaffe ES. 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.
5. Goldblatt F, Andrews J, Russell A, Isenberg D. Association of Kikuchi–Fujimoto's disease with SLE. Rheumatology (Oxford). 2008;47:553-4.
6. Hutchinson CB, Wang E. Kikuchi-Fujimoto disease. Arch Pathol Lab Med. 2010;134:289-93.
7. Kwon SY, Kim TY, Kim, Lee KY, Lee NJ, Seol HY. CT findings in Kikuchi disease: analysis of 96 cases. Am J Neuroradiol. 2004;25(6):1099-102.
8. Douglas M, Bradbury R, Kannangara S, Mitchell D. Arthritis as an unusual manifestation of Kikuchi-Fujimoto disease. Rheumatology. 2003;42(8):1010-2.
9. Rezai K, Kuchipudi S, Chundi V, Ariga R, Loew J, Sha BE. Kikuchi-Fujimoto disease:

hydroxychloroquine as a treatment. Clin Infectious Diseases. 2004;39(12):e124-6.
10. 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.

Cite this article as: Alakkad A, Alakkad M. Kikuchi-Fujimoto disease. Int J Adv Med 2021;8:1419-22.