

# Kikuchi-Fujimoto's Disease: Clinicopathological Correlation

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## Abstract

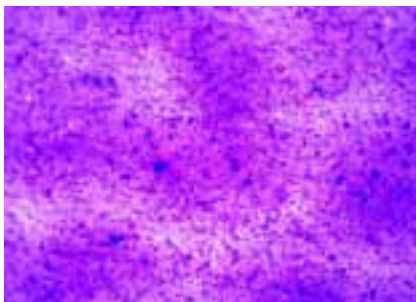
Kikuchi-Fujimoto's disease is a benign, self-limiting disorder characterized by regional tender lymphadenopathy fever and night sweats. It most commonly affects Asian adult females younger than 40 years of age. We report a case of 26 year female who presented with cervical lymphadenopathy, which on FNAC revealed Necrotizing Granulomatous inflammation which was unresponsive for three months of antitubercular therapy. A diagnosis of Kikuchi Fujimoto's disease was suggested on review of the slides at our institute and a biopsy confirmed the diagnosis.

## Introduction

Kikuchi Fujimoto disease was first described in Japan by Dr Masahiro Kikuchi and independently by Y. Fujimoto in 1972.<sup>1,2</sup> Also known as histiocytic necrotizing lymphadenitis, it is a rare, self-limiting disorder, typically affecting the cervical group of lymph nodes. It is mainly seen in Japan, has a slight female preponderance and affects mainly young adults of 20 to 30 years age group. Isolated cases are reported from Europe and Asia.<sup>1-5</sup>

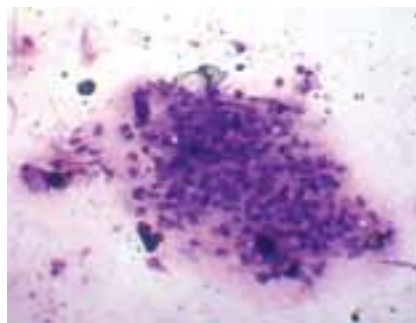
## Case Summary

A 26 year old female doctor presented with solitary right cervical lymphadenopathy which was gradually increasing in size. The swelling was painless and non-tender. Her vital parameters were within normal limits and general physical examination did not yield any positive findings. FNAC of the swelling was done elsewhere and reported as necrotizing granulomatous inflammation favouring a diagnosis



**Fig. 1: FNAC smear showing abundant necrosis along with karyorrhectic debris, devoid of neutrophils (Giemsa, 100x)**

of tuberculous lymphadenitis. Ziehl-Neelson stain for acid fast Bacilli was negative. The aspirate was sent for AFB culture which was also negative. The patient was started on anti-tubercular therapy. After 3 months of treatment, the swelling showed no signs of regression, hence the slides were brought in for review. Smears studied showed abundant necrosis (Figure 1) along with numerous macrophages containing karyorrhectic debris and small lymphocytes along with few plasma cells (Figure 2). However, neutrophils were not seen. A cytological diagnosis of Kikuchi Fujimoto disease was offered and a histological confirmation was sought. A biopsy from the swelling was done and it showed polymorphous population of cells consisting of numerous histiocytes, small and large



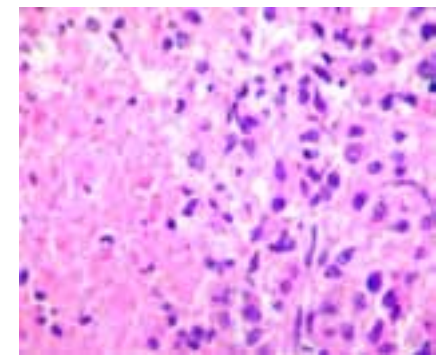
**Fig. 2: Final smear showing aggregates of histiocytes were observed in the smears studied, some containing cellular debris (Giemsa, 400x)**

lymphocytes, atypical mononuclear cells surrounding large areas of necrosis and nuclear debris (Figure 3). Few cells showed plasmacytoid appearance and apoptosis. A diagnosis of Kikuchi-Fujimoto's disease was offered. The biopsy material was sent for PCR which was again negative for Mycobacterium Tuberculosis. AFB culture was negative. The postoperative period was uneventful and the patient was followed up for next two months. She was symptom free and recovered completely.

## Discussion

Kikuchi-Fujimoto disease (KFD) is an enigmatic, benign and self-limited condition characterized by regional tender lymphadenopathy, predominantly involving the cervical region, with or without fever and night sweat.<sup>4</sup>

Described independently in 1972 by Kikuchi and Fujimoto et al., this subacute necrotizing lymphadenitis has been recognized in Asia and sporadically in Western countries.<sup>1-5</sup> Affected patients are most often young adults under the age of 30 years; with a female predominance.<sup>1-5</sup> The disease is seldom reported in children.



**Fig. 3: General lymph node histopathological sections showed vast areas of necrosis along with histiocytes, cellular debris and small lymphocytes. (H&E, 400x)**

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There is much speculation about the etiology of KFD. A viral or autoimmune cause has been suggested. Several infective agents including EBV, parvovirus B19 and HHV-65 have been postulated as causative although no relationship has yet been established.<sup>5</sup> A viral infection is nonetheless possible by virtue of clinical manifestations that include upper respiratory infection prodrome, atypical lymphocytosis and lack of response to antibiotic therapy and certain histopathologic features (i.e., T-cells as revealed by immunological marker studies).<sup>6</sup>

The differential diagnosis of enlarged cervical lymph nodes is huge but the principal conditions to be distinguished are lymphoma, metastatic tumour from local or distant site, drainage from infective lesions in the dependent skin, and systemic conditions such as infectious mononucleosis, human immunodeficiency virus (HIV) infection and most commonly, in our part of the world, tuberculous lymphadenitis. There are several reports suggesting an association between Kikuchi's disease and Systemic Lupus Erythematosus (SLE).<sup>5</sup> However no convincing evidence is available to confirm such association.

The pathogenesis of Kikuchi's disease is still not fully understood. It has been proposed that the primary event may be the activation of T-lymphocytes and histiocytes. Here, the proliferating T cells enter the cycle of apoptosis, which may form the areas of necrosis in lymph nodes and then the histiocytes clear the apoptosed cellular debris and fragments.<sup>5</sup>

In FNAC smears, the characteristic findings are of large numbers of pale, phagocytosing histiocytes with eccentric, crescent nuclei, debris with nuclear fragments, absence of neutrophils and a reactive background of lymphoid cells. The histiocytic cells are CD68, CD163 and myeloperoxidase positive. Necrosis in lymph nodes may also occur in systemic lupus erythematosus.<sup>5</sup> In SLE there may be significant numbers of plasma cells and/or hematoxylin bodies, which may help to distinguish it from Kikuchi-Fujimoto disease. The presence of necrosis may also lead one towards a possibility of tubercular lesion. A negative Ziehl-Neelson stain can help, to some extent.

A definitive diagnosis can be made on lymph node biopsy. Characteristic histopathologic findings of KFD include irregular central or paracortical areas of necrosis with abundant karyorrhectic debris.<sup>3</sup> The nodal architecture can be distorted. Abundant histiocytes at the margin of the necrotic areas are seen. The karyorrhectic foci are formed by predominantly histiocytes and plasmacytoid monocytes but also immunoblasts and small and large lymphocytes.<sup>3</sup> An important characteristic feature is absent or scarce neutrophils. Plasma cells are either absent or scarce.<sup>3</sup> Importantly, atypia in the reactive immunoblastic component is not uncommon and can be mistaken for lymphoma. The typical immunophenotype consists predominantly of T-cells, with few B-cells. Histiocyte-associated antigens like CD68, lysozyme, myeloperoxidase (MPO) are expressed by the histiocytes.<sup>3,4</sup>

Kikuchi-Fujimoto disease is typically self-limiting with a course ranging from one to four months.<sup>4,5</sup> Symptomatic treatment like analgesics-antipyretics and NSAIDs help relieve the distressing local and systemic complaints. The use of corticosteroids has been recommended but its efficacy is uncertain.<sup>4</sup>

## Conclusion

Kikuchi Fujimoto's disease is an uncommon, perhaps under diagnosed. Condition of unknown cause with excellent prognosis. Recognition of this condition is crucial as it may mimic tuberculous lymphadenitis, lymphoma, metastatic disease, or a local inflammatory / infective process. Awareness, not only by the clinicians but also the pathologists, may help prevent misdiagnosis and over-treatment.

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