RESEARCH ARTICLE

Kikuchi-Fujimoto disease in a tertiary care teaching hospital in Coastal South India: A 8-year retrospective study. [version 1; peer review: 3 approved]

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Abstract

Background: Kikuchi-Fujimoto disease (KFD) is a rare, benign condition of unknown etiology, presenting as cervical lymphadenitis. Lymphadenopathy is usually tender and maybe associated with systemic symptoms. Despite the extensive literature on this disease, it continues to be misdiagnosed owing to its misleading clinical presentation.

Methods:
A retrospective hospital-based descriptive cross-sectional study was conducted in tertiary care hospitals from 2011 to 2019. All patients with confirmed KFD diagnosis were included and after ethics committee approval the clinical details and histopathological data was retrieved from the medical records department and analyzed.

Results:
A total of 67 cases were included. The mean age was 26.9±11.3 years with a female: male ratio of 1.9:1. There were 50 patients with tender cervical lymphadenopathy which was the most common clinical presentation. The mean length and width of palpable lymph nodes were 2.3±1.0 cm and 2.2±0.7 cm respectively. Histology revealed proliferative stage in majority of patients (n=40, 59.7%). Lymphadenopathy resolved in 83.6% within 2 months. There were 42 patients who had complete recovery with symptomatic treatment within a period of 9 months.

Conclusions:
KFD is prevalent in young, female patients of Asian descent and often presents as tender cervical lymphadenopathy. Early diagnosis with excisional lymph node biopsy is crucial to avoid unnecessary investigations and treatment. Treatment is symptomatic unless
Kikuchi-Fujimoto disease, Histioytic necrotizing lymphadenitis, Lymphadenopathy, Fever, Kikuchi disease, Rare diseases.

Keywords

Kikuchi-Fujimoto disease, Histioytic necrotizing lymphadenitis, Lymphadenopathy, Fever, Kikuchi disease, Rare diseases.

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Introduction

Kikuchi-Fujimoto disease (KFD), also known as “histiocytic necrotizing lymphadenitis” is a rare condition of unknown etiology. This benign condition presents as cervical lymphadenopathy, usually tender and is often associated with systemic symptoms like fever. Identified first by two Japanese pathologists, independent of each other in the year of 1972, KFD was noted to have a higher incidence in Asian patients and continues to be misdiagnosed till date. Therefore, the awareness of this condition amongst clinicians and pathologists alike would be fruitful as it would aid in the early detection and prevention of life-threatening sequelae such as malignancies.

KFD is seen more frequently in young adults, with a mean age between 20–30 years, but it can occur in any age group. Even though a female predominance is reported in many previous cases, some studies done in Asia show a male to female ratio of 1:1. The rare involvement of the heart, liver and lungs increases the fatality of an otherwise self-limiting disease.

The most common clinical feature is cervical lymphadenopathy, with or without systemic features such as fever, fatigue, headache and night sweats. The lymphadenopathy is usually under 4 cms, and in most cases can be tender or painful. Hepatosplenomegaly has been reported in a few cases.

Both the etiology and pathogenesis of this disease is still unknown. Clinically and histologically, the disease has overlapping features with tuberculosis, lymphoma or systemic lupus erythematosus (SLE) resulting in dilemmas in diagnosis and management. KFD can be seen in patients with previous history of SLE, it can coexist with SLE or complicate into SLE. This association with SLE was more common in Asian than European patients. Meanwhile, a significant number of patients were found to have underlying viral infections.

The gold standard investigation for diagnosis is by histopathological examination of an excisional biopsy obtained from the affected lymph node. Histologically, altered lymph node architecture by nodules of necrosis in the cortex, paracortical expansion, apoptotic cells with accumulation of crescentic histiocytes, and the absence of granulocytes especially neutrophils are typical fine-needle aspiration cytology features seen in KFD. Due to challenges faced in diagnosing KFD, three evolving histological patterns have been proposed by pathologists based on key morphologic features. They are proliferative, necrotizing and xanthomatous based on the dominant histological pattern. Most patients have normal laboratory findings. However, a few cases with mild anemia, elevated Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) along with leucopenia and elevated Lactate Dehydrogenase (LDH) have been reported rarely.

Even though, this disease almost always runs a benign course and resolves in several weeks to months in most patients, it is seen to increase the risk of SLE and lymphoma. Treatment if necessary is symptomatic with analgesics and antipyretics. KFD has a very low recurrence rate and only a few fatalities have been reported. The use of corticosteroid therapy is still under debate for the management of recurrent cases.

Despite the extensive studies done on KFD, it continues to be misdiagnosed till date. The objective of this study was to promote awareness among clinicians and pathologists alike. Therefore, this study discusses the clinico-epidemiological presentations of the disease, the histomorphology commonly found in these cases and the importance of follow-up of these patients to ensure complete recovery and avoid possible sequelae and complications.

Methods

The study was a retrospective hospital based descriptive cross-sectional study carried out among all patients diagnosed with KFD in Mangalore. The diagnosis was confirmed following histopathological examination of the excision biopsy of the lymph nodes of suspected patients in the Pathology Department in Kasturba Medical College (KMC), Mangalore. The inclusion criteria consisted of all the patients diagnosed with KFD in KMC teaching hospitals from 2011–2019, while exclusion criteria were patients not diagnosed with KFD and cases diagnosed before 2011 and after 2019.

The Institutional Ethics Committee (IEC) of Kasturba Medical College, Mangalore (Manipal Academy of Higher Education) approval (Reference No. IEC KMC MLR 03-17/41) was obtained. The permission to access the medical records of KFD patients and a waiver of consent was obtained from the Institutional ethics committee.

The records of KFD patients during the period of April 2011 to April 2019 were reviewed and information on demographics, clinical profile and histopathological data of KFD patients seeking medical care was recorded in a data extraction sheet. The proforma included the relevant clinico-epidemiological information about the patient inclusive of clinical presentation, associated co-morbidities, examination findings, investigations done, pathological morphology as well as any complications or sequelae on follow-up over a period of 9 months.
Histopathological examination of the excision biopsy of all suspected cases of KFD was carried on formalin-fixed paraffin embedded sections stained with Hematoxylin and Eosin, Ziehl–Neelsen stain, Periodic acid-Schiff and Gomori Methenamine silver stains in the Pathology Department. The results obtained were categorized into 3 phases as proliferative phase, xanthomatous phase and necrotizing phase. The classic presentation of the proliferative stage was histiocytes, dendritic cells, lymphocytes and nuclear fragments. In the xanthomatous phase the predominant feature was foamy histiocytes within the lesions. Necrotizing phase typically showed extensive necrosis with karyorrhectic nuclear debris and coagulative necrosis and complete loss of lymph node architecture. The diagnosis of KFD was confirmed based on these morphological findings.

Data collected was analyzed using IBM Corp. Released 2017. IBM SPSS Statistics (RRID:SCR_016479) for Windows, Version 25.0. Armonk, NY: IBM Corp to analyze the clinico-epidemiological data, clinical presentation, local examination findings, histopathological presentation as well as outcomes on follow-up. This data was expressed as proportions, mean, standard deviation, median and Inter Quartile Range (IQR).

Results
The baseline characteristics of the patients are shown below in Table 1. The age of our study population ranged from 4 to 77 years. The mean age was 26.9±11.3 years and a median age of 27 years (IQR: 18–32 years). As shown below KFD commonly affects younger adults between the ages of 21 to 40 years (n=44, 65.7%) and was seen more in female patients (n=44, 65.7%). When the occupation of the study population was analyzed, most of the patients were found to be homemakers (n=27, 40.3%).

Table 2 demonstrates the distribution of chief complaints at presentation in KFD patients. A vast majority of the patients presented with tender swelling over the side of the neck (n=50, 74.6%). Following local examination, excision biopsies were performed on patients with positive findings. These biopsies revealed, the length and width of the cervical lymph nodes ranged from 0.5 to 5 cm and 1 to 5 cm respectively. The excised cervical lymph nodes had a mean length of 2.3±1.0 cm and mean width of 2.2±0.7 cm.

Patients also presented with complaints of fever (n=35, 52.2%) and hepatosplenomegaly (n=10, 14.9%) due to the systemic involvement of the disease. Hepatosplenomegaly was assessed by abdominal examination in all the patients. Computerized tomography (CT) scan of the abdomen was used for the patients with positive findings on clinical examination. Axillary lymph nodes were assessed by clinical examination and were found to be enlarged in 6 patients.

The histopathological profile of all patients was analyzed after classifying the findings of excision biopsies into the three morphological stages (Table 3). Most of the patients presented during the proliferative stage (n=40, 59.7%). The duration
of lymphadenopathy in KFD patients ranged from a few days to 6 months (Table 4). In most patients, lymphadenopathy resolved in less than 2 months ($n=56$, $83.6\%$).

The patients were followed-up over a period of 9 months to observe the outcomes of KFD. A vast majority of the patients recovered with symptomatic treatment ($n=42$, $62.7\%$). Here, the lymphadenopathy was assessed using ultrasound examination of neck once the symptoms improved following treatment. Meanwhile steroid use was successful in treatment of KFD patients with systemic symptoms ($n=17$, $25.4\%$), and one such patient presented with signs of neurological involvement which also resolved following treatment with steroids. A few patients were found to have a self-limiting course of KFD ($n=6$, $12.2\%$). Recurrence of KFD was observed after treatment in 2 patients in this study. Both these patients developed tuberculosis over the next 2 to 3 months. Antinuclear antibody (ANA) levels were elevated in 3 patients, one of these patients was later diagnosed with SLE (positive for dsDNA). One elderly male patient who was diagnosed with necrotizing lymphadenitis of axillary nodes developed generalized lymphadenopathy, a repeat fine needle aspiration cytology (FNAC) and excision biopsy 6 months later confirmed a diagnosis of Non-Hodgkin Lymphoma.

### Discussion

KFD is a rare, self-limiting condition that is usually prevalent in Asian countries, clinically presenting as tender cervical lymphadenopathy with or without systemic symptoms. The etiology of the disease is yet to be uncovered, although certain studies have suggested an underlying viral infection or autoimmune disease to trigger the onset of KFD. A retrospective hospital-based descriptive cross-sectional study was conducted on 67 patients diagnosed with KFD, to determine the sociodemographic profile, clinical presentation, and the outcome of the disease.

The mean age of KFD prevalence was found to be 27.1 years in this study while in a study done in Sub-Saharan Africa, an average of 21 years was recorded. The youngest patient in our study was a 4-year-old girl and the eldest, a 77-year-old man. Of the study population, 16 were children (ranging from 4–18 years old) with confirmed cases of KFD. A study done on pediatric cases of KFD by Guleria S et al. reported a mean age of 10.8 years. A study based on the characteristics of
KFD based on age showed the mean age of children and adults to be 13.2 ± 4.8 and 32.7 ± 8.8 years respectively, which was similar to the range observed in our study.12

On analysis of the gender prevalence, a female predominance of 1.91:1 was observed which was similar to a study done in South India which had a significant female majority of 2.4:1.9 A ratio of 1:1 was observed in the results obtained from a study conducted by Pepe F et al. in Italy. A reversal of the gender ratio was observed in two studies carried out in Korea and North India with a significant male majority of 2.8:113 and 2:111 respectively.

Younger females were noted to be more predisposed to KFD in our study with ages ranging from 4 to 38 years with all considerably younger than their male counterparts. A case series of 9 patients was conducted by Abeysekara RA et al., where all the cases were female patients in the age group of 12–30 years.14 Adhikari RC et al. carried out a similar study where 5 out of the 6 cases were females and the age range were 13–32 years.15

The most common clinical presentation of these patients was tender swelling on the side of the neck (74.6%). Similar results were obtained from a study done in Michigan with 60–90% of the cases having posterior cervical lymphadenopathy.1 Systemic symptoms such as fever (52.2% of the cases) and hepatosplenomegaly (14.9% of the cases) was found abundantly in this study. Fever was noted to be associated frequently with tender cervical lymphadenopathy (n=30, 44.8%). This coexistence of symptoms was replicated in the Michigan study in 35–77% of the patients.1 Tender cervical lymphadenopathy was the most common symptom in studies done in Italy9 (60–98%), Saudi Arabia15 (56–98%) and Michigan1 (60–90%). The involvement of axillary lymph nodes was encountered in 9% of the cases in this study, whereas 13% were reported in a study conducted by Supari D et al.9

One 22-year-old male patient in our study presented with symptoms of cervical lymphadenopathy for 15 days duration associated with systemic symptoms of fever, neck stiffness and meningitis. He was treated with steroids and tapered over a period of one month. Follow-up over 2 years revealed that lymphadenopathy subsided in 3 months and the patient recovered fully with no recurrence reported. In correlation to the above case, a study done in Japan reported 5 cases of recurrent KFD associated aseptic meningitis which resolved within several months with 3 of the cases requiring steroids.16 Thus, the use of steroids in patients with recurrence of KFD with neurological involvement is considered beneficial following extensive investigation to ensure its safety.16,17

The histopathology findings of the excisional lymph node biopsy remains a gold standard for confirming KFD. In this study, the findings were grouped into 3 morphological phases as done in previous studies5–7,8 and a vast majority of the confirmed cases presented in proliferative phase of KFD (n=40, 59.7%). Two of the patients whose lymph nodes showed proliferative phase with histiocytic aggregates later developed tuberculosis. Thus, histology of early tuberculosis can mimic KFD resulting in misdiagnosis. Similarly, two patients with predominance of necrosis went on to be diagnosed with SLE and Non-Hodgkin’s Lymphoma. Follow-up is thus crucial in KFD patients. Immunohistochemistry studies are ancillary techniques to support or exclude a diagnosis of lymphoma in suspicious cases.

A study conducted in Bangalore revealed that the duration of lymphadenopathy lasted from 1 week to 3 months,9 however our study results suggested a longer duration of symptoms and it varied from 2 weeks to 6 months. The follow-up outcomes our patients over a period of 9 months revealed that all the cases completely recovered with no complications.

Regarding the treatment aspect, majority of our patients recovered after symptomatic management (62.7%), which was the choice of initial treatment in previous studies as well.1,11,16 One fourth of the patients in this study were treated successfully with steroids (25.4%) and a similar result was obtained in two more studies where 2 out of the 6 patients required steroid therapy13 and the utilization of methylprednisolone exhibited a drastic response within 24 hours.6

Studies conducted in Florida had self-limiting KFD which typically lasted 1 to 4 months6 and in England their symptoms resolved spontaneously within 6 months. On the contrary, even though KFD is known to be a self-limiting condition, our study showed that only a small fraction of patients recovered completely without any treatment (9%).

Recurrence is always a matter of concern for the treating physician. Studies done have reported a recurrence rate of 3 – 4%1,2,18 in adults which was similar to our study recurrence rate of 3%. In comparison to children, we observed no recurrence which was a paradoxical finding when compared to a study by Han HJ et al.16 which had a recurrence of 27% after a one year follow-up. Recurrence can present as late as 8 years after initial presentation according to Deaver D et al.5 Therefore, long-term follow-up is essential to determine the rate of recurrence of KFD.
Conclusion
KFD is a rare, idiopathic condition which presents as a diagnostic challenge to both pathologists and clinicians due to its misleading presentation. Demographically, the disease is prevalent in young, Asian, female patients and often presents as cervical lymphadenopathy. Early diagnosis with excisional lymph node biopsy is crucial to avoid unnecessary investigations and treatment for this self-limiting condition. Treatment is only symptomatic unless complicated, where steroid therapy is considered. KFD has an excellent prognosis with almost no risk of fatality. Long term follow-up of patients is vital to look for recurrence, complications of this condition and a few of them can evolve into SLE, lymphoma and TB.

Data availability
Underlying data
Figshare: Underlying data for ‘Kikuchi-Fujimoto disease in a tertiary care teaching hospital in Coastal South India: A 8-year retrospective study. https://figshare.com/s/b11d971a3f430af2f3d4. CC BY 4.0 license.

This project contains the following underlying data:

- Data sheet in excel format

Author contributions
Basavaprabhu Achappa - Conceptualization; Data curation; Formal analysis; Methodology; Project administration; Resources; Supervision; Writing - original draft, review & editing.

Nipuni Chamathka Herath - Data curation; Formal analysis; Resources; Writing - original draft, review & editing.

Bodhi Sebastian - Data curation; Formal analysis; Writing - original draft.

Nikhil Victor Dsouza - Data curation; Formal analysis; Resources; Supervision; Writing - original draft, review & editing.

Pavan Manibettu Raghuram - Conceptualization; Formal analysis; Methodology; Project administration; Supervision; Writing - original draft, review & editing.

Ramesh Holla - Formal analysis; Methodology; Project administration; Resources; Supervision; Writing - original draft, review & editing.

Nithyananda Chowta - Formal analysis; Project administration; Resources; Supervision; Writing - original draft, review & editing.

Jyoti Ramanath Kini - Data curation; Formal analysis; Resources; Supervision; Writing - original draft, review & editing.

References
1. Perry AM, Choi SM: Kikuchi Fujimoto disease: A Review. Arch. Pathol. Lab. Med. 2018; 142(11): 1342-1346.
2. Jamal AB: Kikuchi Fujimoto disease. Clin. Med. Insights Arthritis Musculoskelet. Disord. 2012; 5: 63-66. PubMed Abstract | Publisher Full Text
3. Dalugama C, Gawarammana IB: Fever with lymphadenopathy - Kikuchi Fujimoto disease, a great masquerader: a case report. J. Med. Case Rep. 2017; 11(1): 349. PubMed Abstract | Publisher Full Text
4. Tarig H, Gaduputi V, Raffiq A, et al.: The enigmatic kikuchi-fujimoto disease: a case report and review. Case Rep. Hematol. 2014; 2014: 1-4. PubMed Abstract | Publisher Full Text
5. Pepe F, Disma S, Teodoro C, et al.: Kikuchi-Fujimoto disease: a clinicopathologic update. Pathologica. 2016; 108(3): 120-125. PubMed Abstract
6. Deaver D, Horna P, Cualing H, et al.: Pathogenesis, diagnosis, and management of Kikuchi-Fujimoto disease. Cancer Control. 2014; 21(4): 313-321. PubMed Abstract | Publisher Full Text
7. Salamat S, Chan J, Jolly K, et al.: Kikuchi-Fujimoto Disease and Prognostic Implications. Head Neck Pathol. 2020; 14(1): 272-275. PubMed Abstract | Publisher Full Text
8. Das DK, Mallik MK, Hawara A, et al.: Kikuchi-Fujimoto disease in fine-needle aspiration smears: a clinicocytologic study of 76 cases of KFD and 684 cases of reactive hyperplasia of the lymph node. Diagn. Cytopathol. 2013; 41(4): 288-295. PubMed Abstract | Publisher Full Text
9. Supari D, Ananthamurthy A: Kikuchi-fujimoto disease: a study of 24 cases. Indian J. Otolaryngol. Head Neck Surg. 2014; 66(1): 69-73. PubMed Abstract | Publisher Full Text
10. Lame CA, Loun B, Fall AK, et al.: Kikuchi-Fujimoto disease, a rare cause of lymphadenopathy in Africa. Description of the first case in Senegal and review of the literature. *Eur. Ann. Otorhinolaryngol. Head Neck Dis.* 2017; 134(5): 347-349. PubMed Abstract | Publisher Full Text

11. Guleria S, Gupta A, Pilania RK, et al.: Kikuchi-Fujimoto Disease: An Under Recognized Cause of Fever with Lymphadenopathy. *Indian J. Pediatr.* 2020; 87(1): 85. PubMed Abstract | Publisher Full Text

12. Kim HY, Jo HY, Kim SH: Clinical and Laboratory Characteristics of Kikuchi-Fujimoto Disease According to Age. *Front. Pediatr.* 2021; 9: 745506. PubMed Abstract | Publisher Full Text

13. Han HJ, Lim GY, Yeo DM, et al.: Kikuchi's disease in children: clinical manifestations and imaging features. *J. Korean Med. Sci.* 2009; 24(6): 1105-1109. PubMed Abstract | Publisher Full Text

14. Abeyesekara RA, Kularatne SA, Waduge R, et al.: Kikuchi-Fujimoto's disease: a case series from Sri Lanka. *Ceylon Med. J.* 2013; 58(1): 31-33. PubMed Abstract | Publisher Full Text

15. Adhikari RC, Sayami G, Lee MC, et al.: Kikuchi-Fujimoto disease in Nepal: a study of 6 cases. *Arch. Pathol. Lab. Med.* 2003; 127(10): 1345-1348. PubMed Abstract | Publisher Full Text

16. Komagamine T, Nagashima T, Kojima M, et al.: Recurrent aseptic meningitis in association with Kikuchi-Fujimoto disease: case report and literature review. *BMC Neurol.* 2012; 12: 112. PubMed Abstract | Publisher Full Text

17. Sekiguchi S, Yamamoto Y, Hatakeyama S, et al.: Recurrent Aseptic Meningitis Associated with Kikuchi’s Disease (Histiocytic Necrotizing Lymphadenitis): A Case Report and Literature Review. *Intern. Med.* 2021; 60(11): 1779-1784. PubMed Abstract | Publisher Full Text

18. Bosch X, Guilabert A, Miquel R, et al.: Enigmatic Kikuchi-Fujimoto disease: a comprehensive review. *Am. J. Clin. Pathol.* 2004; 122(1): 141-152. PubMed Abstract | Publisher Full Text
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Version 1

Reviewer Report 28 June 2022

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Farhan Fazal
Al Rahba Hospital, Abu Dhabi, United Arab Emirates

This is a retrospective study of a very important misdiagnosed entity. The authors have elaborated on the clinical as well as histological features of the disease. Since the study was retrospective it is not clear how the follow-up was done?. The authors have commented on the duration of lymph nodes that the patients had, but did not mention if the patients came for regular follow-up or was it done whenever the patient came for follow-up. Also what type of steroids and their dosage are used have not been mentioned. Overall the paper is well written.

Is the work clearly and accurately presented and does it cite the current literature? Yes

Is the study design appropriate and is the work technically sound? Yes

Are sufficient details of methods and analysis provided to allow replication by others? Yes

If applicable, is the statistical analysis and its interpretation appropriate? I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility? Partly

Are the conclusions drawn adequately supported by the results? Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Infectious disease
I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 23 June 2022

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Chaitanya Tellapragada Achyutha Krishna
Division of Clinical Microbiology, Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden

The article by Achappa B et al. is well written and provides important information regarding the baseline demographic and clinical features of patients with Kikuchi-Fujimoto disease (KFD) in South India.

I have few minor suggestions for the authors to add in their discussion:
- How many of these 67 patients were subjected to microbiological investigations for infectious aetiology (mainly viral infections) at the time of their initial presentation.
- Histopathological profiles of the study subjects are described in table 3 and duration of lymphadenopathy in table 4. It would be interesting if the authors could further discuss (based on their experience or previous studies) whether patients with any one or more of the three morphological phases (by histopathology or based on duration of lymphadenopathy) would benefit more from the steroid therapy.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Not applicable

Are all the source data underlying the results available to ensure full reproducibility?
No source data required

Are the conclusions drawn adequately supported by the results?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Microbiology; Epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 13 June 2022

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Thejaswi K. Poonacha

Department of Internal Medicine, University of Minnesota Medical Center, Minneapolis, USA

The authors have done an excellent retrospective observational study on Kikuchi-Fujimoto disease (KFD). While the sample size is relatively small, and no conclusions of real statistical significance can be concluded, it is still a landmark article considering the 8 year study, and the similarities noted in other studies. The authors' conclusion cannot be overstated with regard to the need for follow up in these patients. Nevertheless, this study deserves full merit.

Please consider the following points:

1. The authors particularly focus on the clinical signs and symptoms, histopathology and the demographics. For the sake of completeness, they should include pathophysiology of the disease.

2. The authors could elaborate on the viral etiology of disease for academic significance.

3. As a follow-up project, I urge the authors to consider doing a meta-analysis study for this disease. There has been a meta analysis done on the causative agents.

**References**

1. Iguchi H, Sunami K, Yamane H, Konishi K, et al.: Apoptotic cell death in Kikuchi's disease: a TEM study. *Acta Otolaryngol Suppl.* 1998; 538: 250-3 PubMed Abstract
2. Chong Y, Kang CS: Causative agents of Kikuchi-Fujimoto disease (histiocytic necrotizing lymphadenitis): a meta-analysis. *Int J Pediatr Otorhinolaryngol.* 2014; 78 (11): 1890-7 PubMed Abstract | Publisher Full Text

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes
Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Hematology/ Oncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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