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Kikuchi-Fujimoto: A Clinicopathological Perspective to Cervical Lymphadenitis

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Abstract:- Kikuchi-Fujimoto disease is a form of benign necrotizing lymphadenitis also known as histiocytic necrotizing lymphadenitis. While Kikuchi disease is a globally prevalent disease, it is predominantly seen in the Asian population. Etiology can be traced back to dysregulated immune responses triggered by viral or autoimmune factors. Here we present a case report to emphasize the importance of considering Kikuchi disease and possible etiologies, highlighting the need for increased awareness and recognition of this rare condition. A 28-year-old female with a history of hypothyroidism, IBS, and GERD complained of sore throat, intermittent epigastric pain, mild heartburn, and fever and was taking PPIs without any improvement. Abdominal USG was negative for any pathology. She presented with bilateral enlarged cervical lymph nodes and worsening of symptoms 1.5

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months later. Ciprofloxacin was prescribed which failed to improve the symptoms. CT scan of the neck showed an enlarged thyroid gland with diffuse lymphadenopathy. Labs showed elevated TSH, for which the levothyroxine dose was increased, despite that she still continued to have symptoms. LDH and CRP were normal. Rheumatology, oncology, and infectious disease specialists were called upon for further evaluation. Excisional Lymph node biopsy showed areas of extensive necrosis with karyorrhectic debris, surrounded by histiocytes and small lymphocytes, suggestive of necrotizing lymphadenitis, specifically consistent with Kikuchi disease. Immunophenotyping by flow cytometry demonstrated normal CD4+ and CD8+ T cell populations without any evidence of clonal lymphoid expansion. AFB and GMS stains were negative for infection. Hydroxychloroquine 200 mg twice daily was given, which resulted in the resolution of her symptoms. Kikuchi disease's origins can be traced back to Japan, where it was initially documented. More prevalent in the young female Asian population under the age of 30. It presents as tender, enlarged nodes, primarily in the cervical region along with lymphadenopathy, fever, erythematous rash, joint pain, fatigue, arthritis, and hepatosplenomegaly. It becomes important to consider Kikuchi disease in patients presenting with symptoms that can be attributed to sore throat related to GERD, followed by the development of fever with cervical lymph node enlargement.

Keywords:- *Kikuchi-Fujimoto disease, benign necrotizing lymphadenitis, Asian population, dysregulated immune response, cervical lymphadenopathy.*

I. INTRODUCTION

"Kikuchi disease: a mysterious, self-limiting condition that challenges clinicians with its elusive nature, resembling infections, autoimmune disorders, and even the specter of lymphoma."

Kikuchi-Fujimoto disease is a form of benign necrotizing lymphadenitis also known as histiocytic necrotizing lymphadenitis. [1,2] In 1972, Kikuchi and Fujimoto independently published a case series describing Kikuchi disease, marking its initial description in Asia. [3,4] Its origins can be traced back to Japan, where it was initially documented. [5] While Kikuchi disease is a globally present condition, it demonstrates a notable inclination towards Asian populations, particularly affecting individuals under the age of 30 and showing a higher incidence among females with a male-to-female ratio of 1:1.9. [5–7]. Nevertheless, cases have also been reported in patients ranging from 6 to 80 years old. [8] Initially regarded as a disorder specific to Asian ancestry, the first case series in a European cohort was described by Pileri et al, leading to subsequent reports of Kikuchi disease in various ethnic backgrounds across the world. [6] It is characterized by tender, enlarged nodes, primarily in the cervical region, and most prevalent manifestations include lymphadenopathy (100%), fever (35%), erythematous rash (10%), joint pain (7%), fatigue (7%), arthritis (5%), and hepatosplenomegaly (3%). [2,5] While the exact etiology remains unknown, it is believed to involve a dysregulated immune response triggered by viral or autoimmune factors. Here, we present a case report to emphasize the importance of considering Kikuchi disease in the differential diagnosis of patients presenting with initially attributed symptoms, such as sore throat related to gastroesophageal reflux disease (GERD), followed by the development of fever. The complexity of this case underscores the diagnostic challenges faced in differentiating Kikuchi disease from other possible etiologies, highlighting the need for increased awareness and recognition of this rare condition.

II. CASE PRESENTATION

A 28-year-old female with a medical history significant for hypothyroidism, irritable bowel syndrome, and gastroesophageal reflux disease presented to the primary care clinic with complaints of sore throat, intermittent epigastric pain, mild heartburn, and fever. She reported no black stools, blood in the stool, nausea, or vomiting. The patient had been taking omeprazole and famotidine without experiencing any improvement in her symptoms. An abdominal ultrasound performed previously showed no significant findings, and she was advised to continue the antacid medications.

The patient returned to the clinic after 1.5 months with bilateral enlarged cervical lymph nodes which were diagnosed by ENT and worsening symptoms, including sore throat, heartburn, high-grade fever (104°F), fatigue, and weakness. On physical examination, bilaterally palpable and tender cervical lymph nodes were noted. She finished a ciprofloxacin course without any relief in his symptoms. To further investigate the cause of enlarged lymph nodes, a CT scan of the neck was performed, revealing an enlarged thyroid gland and diffuse lymphadenopathy.

Laboratory investigations revealed an elevated thyroid-stimulating hormone (TSH) level, indicating poor control of her hypothyroidism. Consequently, her levothyroxine dose was increased from 50 mcg to 100 mcg once daily. Despite the adjustment in medication, the patient continued to experience persistent fever with chills, myalgia, and difficulty swallowing. Blood tests indicated increased lactate dehydrogenase (LDH) levels, while C-reactive protein (CRP) was within the normal range.

Given the complexity of the presentation, the patient was referred to rheumatology, oncology, and infectious disease specialists for further evaluation. An initial lymph node biopsy was inconclusive, showing only reactive lymphocytes. However, a repeat excisional biopsy from a level 2, right-sided neck lymph node revealed areas of extensive necrosis with karyorrhectic debris, surrounded by histiocytes and small lymphocytes, suggestive of necrotizing lymphadenitis, specifically consistent with Kikuchi disease.

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Immunophenotyping by flow cytometry demonstrated normal CD4+ and CD8+ T cell populations without any evidence of clonal lymphoid expansion. Special stains for acid-fast bacilli (AFB) and Grocott's methenamine silver (GMS) stain for fungi were negative. Notably, the patient also developed external hemorrhoids during the course of her illness.

The patient was initiated on Hydroxychloroquine 200 mg twice daily for Kikuchi disease. Concurrently, the antacid medications and levothyroxine were continued as part of her ongoing management. Regular follow-up visits were scheduled to monitor the patient's clinical course, with a focus on the resolution of fever, myalgia, and improvement in other symptoms.

III. DISCUSSION

The kikuchi disease commonly presents as an acute onset lymphadenopathy associated with a fever or flu-like syndrome. [1] The most common clinical presentation is acute cervical lymphadenopathy with or without the presence of systemic features. [2–5] In addition to cervical lymphadenopathy, axillary and supraclavicular lymphadenopathy has also been reported. [6,7] Usually, the lymph nodes associated with KFD are firm and mobile and of size <3 cm, but there have been reports of lymph nodes reaching 5 to 6 cm in dimensions. [8] Lymphadenopathy is isolated to a single location in 83% of the cases, but multiple chains may be involved. The nodes are usually described as painless or mildly tender. [1] Additional signs and symptoms include fever, hepatosplenomegaly, headache, anorexia, nausea, vomiting, skin lesions, and constitutional symptoms like night sweats, weight loss, and malaise. [9] Certain studies have shown that fever associated with KFD usually lasts for about 1-7 weeks with temperatures ranging from 38.6 C to 40.5 C. [6] It has been reported that about 30% of KFD had developed cutaneous symptoms. [7] Skin lesions usually manifest as rashes, nodules, erythematous papules, indurated erythematous lesions, erythema multiforme, and erythematous maculopapular lesions. [7,10] A study reported that in seven patients with cutaneous involvement, most had facial lesions. [7,10,11] These dermatologic findings are not pathognomonic, and no particularly characteristic skin lesion specific to KFD has been yet identified. In our case, the patient initially presented with heartburn, sore throat, and epigastric pain which was initially believed to be due to gastroesophageal reflux, and the high-grade fever and lymphadenopathy developed later. In our case, The lymph nodes were surprisingly tender, leading to ciprofloxacin treatment without any relief.

Although the precise cause of Kikuchi disease is not known, the histologic alterations and clinical manifestations point to a T cell and histiocyte immune response to an infectious agent. Numerous viral infections, such as Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), herpesvirus 8 (HHV-8), and B19 parvovirus. (2,12,13) Interferon-alpha and other proteins are produced at higher levels thanks to 2',5'-oligoadenylate synthetase and tubuloreticular structures are examples of interferon-alpha targets. The cytoplasm of histiocytes, vascular endothelium, and stimulated lymphocytes are consistent with a viral cause. (10)

The primary mechanism of cell death is apoptosis, which is mediated by cytotoxic CD8-positive T cells. Histiocytes could function as enhancers. The Fas-Fas ligand system appears to be responsible for inducing apoptosis. Transmission electron microscopy reveals the morphological features of apoptotic cells, such as nuclear chromatin condensation and disintegration along the nuclear membrane with intact organelles and histiocytes phagocytosing karyorrhectic debris (apoptotic bodies). [12]

Generally, the lab work may show slightly elevated inflammatory markers like erythrocyte sedimentation rate, ferritin, elevated aminotransferases, C-reactive protein, and elevated lactate dehydrogenase. In 25% of patients, unusual peripheral lymphocytes may be found. [13,14] However, there are no pathognomonic or particular laboratory results for Kikuchi illness. [15] Serology should be obtained for numerous viral causes of lymphadenitis, including acute EBV, CMV, Hepatitis B, Herpes simplex, HIV, parvovirus B19, and viral respiratory causes such as parainfluenza. The tuberculin skin test (TST) or interferon-gamma release assay (IGRA) can be used to begin testing for tuberculous causes of lymphadenitis.

Our patient, who has a history of hypothyroidism, underwent laboratory tests which revealed an elevated thyroid-stimulating hormone (TSH) level, indicating poor control of her hypothyroidism. Consequently, her levothyroxine dose was increased from 50 mcg to 100 mcg once daily. Despite the adjustment in medication, the patient continued to experience persistent fever with chills, myalgia, and difficulty swallowing. Blood tests indicated increased lactate dehydrogenase (LDH) levels, while C-reactive protein (CRP) was within the normal range.

Given the complexity of the presentation, the patient was referred to rheumatology, oncology, and infectious disease specialists for further evaluation. An initial lymph node biopsy was inconclusive, showing only reactive lymphocytes. However, a repeat excisional biopsy from a level 2, right-sided neck lymph node revealed areas of extensive necrosis with karyorrhectic debris, surrounded by histiocytes and small lymphocytes, suggestive of necrotizing lymphadenitis, specifically consistent with Kikuchi disease.

Histologically, the lymph nodes of a KFD patient exhibit follicular hyperplasia with largely intact lymph node architecture. At the border of necrosis, karyorrhexis cells and a considerable buildup of histiocytes are detected. To further assess for further lymphadenopathy and organomegaly, a chest radiograph and abdominal ultrasound can be employed. [16] In our patient, to further investigate the cause of enlarged lymph nodes, a CT scan of the neck was performed, revealing an enlarged thyroid gland and diffuse lymphadenopathy.

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Immunophenotyping by flow cytometry was performed in our patient, which demonstrated normal CD4+ and CD8+ T cell populations without any evidence of clonal lymphoid expansion. Special stains for acid-fast bacilli (AFB) and Grocott's methenamine silver (GMS) stain for fungi were negative. Notably, the patient also developed external hemorrhoids during the course of her illness. A skin biopsy can also be obtained concomitantly if any vasculitis or other skin condition is suspected. [15,17]

In most cases of Kikuchi- Fujimoto disease (61.5%), no therapy is necessary since the clinical symptoms spontaneously subside and the biological parameters return to normal within 1-4 months. [17] Pharmacological modalities include anti-inflammatory drugs such as NSAIDs for symptomatic treatment and immunosuppressants such as glucocorticoids and hydroxychloroquine for moderate to severe cases. [18] For the treatment of patients with SLE and Kikuchi-Fujimoto illness, glucocorticoids have been used alone or in conjunction with hydroxychloroquine. [18] Interestingly, hydroxychloroquine has been shown to be effective in patients with Kikuchi-Fujimoto illness without associated SLE. The anti-inflammatory effects of hydroxychloroquine seem to be contributing to the resolution of symptoms. The profile of hydroxychloroquine is safer and has fewer side effects than glucocorticoids. [19] Additionally, a study found that removing the affected lymph node has both a diagnostic and therapeutic effect. [20] In our patient, Hydroxychloroquine 200 mg was prescribed twice daily and regular follow-up visits were scheduled to monitor disease progression.

KFD is usually a self-limiting disease with a relapse rate of 3-4 % in adults. The pediatric population was found to have a better prognosis than adults. [21,22] One interesting finding is the possible association between KFD and Systemic lupus erythematosus (SLE). It has been found that SLE patients may be diagnosed with Kikuchi's disease early in the course of the disease, and SLE may develop 10 months to 3 years following Kikuchi's disease diagnosis. [23,24] Hemophagocytic lymphohistiocytosis (HLH), with or without disseminated intravascular coagulation (DIC) in very rare cases was found to be associated with KFD. [25] Neurologic complications such as meningoencephalitis, cerebellar ataxia, and encephalitis with CNS lesions were also found to occur in rare cases. [26] In our case, the patient developed external hemorrhoids during the course of this disease.

IV. CONCLUSION

KFD is one of the rare diseases presented with necrotizing lymphadenitis, having its connections with autoimmune conditions like SLE. It is one of the differential diagnoses with a self-remitting course, so it should be ruled out if a patient exhibits clinical conditions like sore throat, fever, lymphadenopathy, and/or hypothyroidism. Lymph node biopsy can provide a distinct histological pattern that is characteristically seen in KFD. Patient education about Kikuchi sickness is crucial given the condition's rarity. Patients should be informed of the management, which includes symptomatic treatment with analgesics and antipyretics. Our patient is currently on Hydroxychloroquine and regular follow-up is scheduled for disease progression and monitoring. Patients should be informed of the significance of following up with their primary care physician and rheumatologist for long-term monitoring because it is crucial for symptom monitoring and remission.

The table containing previously published articles including characteristics, investigations, and treatment:

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B. Abbreviations :

- IBS - Irritable bowel syndrome
- GERD - Gastroesophageal reflux disease
- PPI - Proton pump inhibitor
- USG - Ultrasonography
- CT - Commuted tomography
- TSH - Thyroid stimulated hormone
- LDH - Lactate dehydrogenase
- CRP - C-reactive protein
- AFB - Acid-fast bacilli
- GMS - Gomori methamine stain
- ENT - Eye nose throat
- KFD - Kikuchi Fujimoto disease
- EBV - Epstein barr virus
- HIV - Human Immunodeficiency virus
- CMV - Cytomegalovirus
- TST - Tuberculin skin test
- IGRA - Interferon-gamma release assay
- NSAIDs - Non-steroidal anti-inflammatory drugs
- SLE - Systemic lupus erythematosus
- HLH - Hemophagocytic lymphohistiocytosis
- DIC - Disseminated intravascular coagulation
- CNS - Central nervous system.

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REFERENCES

[1.] Lo KB, Papazoglou A, Chua L, Candelario N: Case Report: Kikuchi: The great mimicker. F1000Res. 2018, 7:520. 10.12688/f1000research.14758.1

[2.] Kucukardali Y, Solmazgul E, Kunter E, Oncul O, Yildirim S, Kaplan M: Kikuchi-Fujimoto Disease: analysis of 244 cases. Clin Rheumatol. 2007, 26:50–4. 10.1007/s10067-006-0230-5

[3.] Shirakusa T, Eimoto T, Kikuchi M: Histiocytic necrotizing lymphadenitis. Postgrad Med J. 1988, 64:107–9. 10.1136/pgmj.64.748.107

[4.] Fujimoto Y: Cervical subacute necrotizing lymphadenitis. Naika. 1972, 30:920–7.

[5.] Longaretti P, Savasta S, Caimmi D, Possenti I, Marseglia GL: Kikuchi-Fujimoto disease complicated by peripheral neuropathy. Pediatr Neurol. 2012, 46:319–21. 10.1016/j.pediatrneurol.2012.02.024

[6.] Bosch X, Guilabert A, Miquel R, Campo E: Enigmatic Kikuchi-Fujimoto Disease: A Comprehensive Review. Am J Clin Pathol. 2004, 122:141–52. 10.1309/YF081L4TKYWVYVPQ

[7.] Lin H-C, Su C-Y, Huang C-C, Hwang C-F, Chien C-Y: Kikuchi's disease: a review and analysis of 61 cases. Otolaryngol Head Neck Surg. 2003, 128:650–3. 10.1016/S0194-59980223291-X

[8.] Pepe F, Disma S, Teodoro C, Pepe P, Magro G: Kikuchi-Fujimoto disease: a clinicopathologic update. Pathologica. 2016, 108:120–9.

[9.] Chaitanya BN, Sindura C: Kikuchi's disease. J Oral Maxillofac Pathol. 2010, 14:6–9. 10.4103/0973-029X.64300

[10.] Baumgartner BJ, Helling ER: Kikuchi's disease: a case report and review of the literature. Ear Nose Throat J. 2002, 81:331–5. 10.1177/014556130208100511

[11.] Kuo TT: 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, 19:798–809. 10.1097/00000478-199507000-00008

[12.] Lee BC, Patel R: Kikuchi-Fujimoto disease: a 15-year analysis at a children's hospital in the United States. Clin Pediatr . 2013, 52:92–5. 10.1177/0009922811436338

[13.] Spies J, Foucar K, Thompson CT, LeBoit PE: The histopathology of cutaneous lesions of Kikuchi's disease (necrotizing lymphadenitis): a report of five cases. Am J Surg Pathol. 1999, 23:1040–7. 10.1097/00000478-199909000-00006

[14.] Yen H-R, Lin P-Y, Chuang W-Y, Chang M-L, Chiu C-H: Skin manifestations of Kikuchi-Fujimoto disease: case report and review. Eur J Pediatr. 2004, 163:210–3. 10.1007/s00431-003-1364-y

[15.] Sumiyoshi Y, Kikuchi M, Takeshita M, Yoneda S, Kobari S, Ohshima K: Immunohistological study of skin involvement in Kikuchi's disease. Virchows Arch B Cell Pathol. 1992, 62:263–9. 10.1007/BF02899691.

[16.] Yen A, Fearneyhough P, Raimer SS, Hudnall SD: EBV-associated Kikuchi's histiocytic necrotizing lymphadenitis with cutaneous manifestations. J Am Acad Dermatol. 1997, 36:342–6. 10.1016/s0190-9622(97)80413-6

[17.] Huh J, Kang GH, Gong G, Kim SS, Ro JY, Kim CW: Kaposi's sarcoma-associated herpesvirus in Kikuchi's disease. Hum Pathol. 1998, 29:1091–6. 10.1016/s0046-8177(98)90419-1

[18.] Yufu Y, Matsumoto M, Miyamura T, Nishimura J, Nawata H, Ohshima K: Parvovirus B19-associated haemophagocytic syndrome with lymphadenopathy resembling histiocytic necrotizing lymphadenitis (Kikuchi's disease). Br J Haematol. 1997, 96:868–71. 10.1046/j.1365-2141.1997.d01-2099.x

[19.] Rich SA: De novo synthesis and secretion of a 36-kD protein by cells that form lupus inclusions in response to alpha-interferon. J Clin Invest. 1995, 95:219–26. 10.1172/JCI117643

[20.] Ohshima K, Shimazaki K, Kume T, Suzumiya J, Kanda M, Kikuchi M: Perforin and Fas pathways of cytotoxic T-cells in histiocytic necrotizing lymphadenitis. Histopathology. 1998, 33:471–8. 10.1046/j.1365-2559.1998.00532.x

[21.] Perry AM, Choi SM: Kikuchi-Fujimoto Disease: A Review. Arch Pathol Lab Med. 2018, 142:1341–6. 10.5858/arpa.2018-0219-RA

[22.] Zuckerman R, Damiani L, Ayyad HA, Alpert DR: Persistent cervical lymphadenitis in a patient with prior thyroid cancer attributed to Kikuchi-Fujimoto disease. BMJ Case Rep. 2018, 2018.: 10.1136/bcr-2018-226457

[23.] Joean O, Thiele T, Raap M, Schmidt RE, Stoll M: Take a second look: it's Kikuchi's disease! A case report and review of literature. Clin Pract . 2018, 8:1095. 10.4081/cp.2018.1095

[24.] Lelii M, Senatore L, Amodeo I, et al.: Kikuchi-Fujimoto disease in children: two case reports and a review of the literature. Ital J Pediatr. 2018, 44:83. 10.1186/s13052-018-0522-9

[25.] Cuglievan B, Miranda RN: Kikuchi-Fujimoto disease. Blood. 2017, 129:917. 10.1182/blood-2016-08-736413

[26.] Rezai K, Kuchipudi S, Chundi V, Ariga R, Loew J, Sha BE: Kikuchi-Fujimoto disease: hydroxychloroquine as a treatment. Clin Infect Dis. 2004, 39:e124–6. 10.1086/426144

[27.] Frankel AM, Frenkel S, Aminlari A, Chan T: Kikuchi Disease: A Case Report. J Emerg Med. 2020, 59:927–30. 10.1016/j.jemermed.2020.07.031

[28.] Rauniyar R, Acharya K, Mishra A, Pathak N, Chaudhary G, Bhandari P, Gaire P: Kikuchi-Fujimoto disease: A rare case report from Nepal. Clin Case Rep. 2021, 9:e05031. 10.1002/ccr3.5031

[29.] Song Y, Liu S, Song L, et al.: Case Report: Histiocytic Necrotizing Lymphadenitis (Kikuchi-Fujimoto Disease) Concurrent With Aseptic Meningitis. Front Neurol. 2021, 12:565387. 10.3389/fneur.2021.565387

[30.] Kellner D, Temelkovska T, Greeley A, Saito A: Kikuchi-Fujimoto Disease: A Case Report of Fever and Lymphadenopathy in a Young White Man. Fed Pract. 2023, 40:22–7. 10.12788/fp.0347
[31.] Khan AM, Ahmad M, Muhammad O, Taj S, Shiza ST: Kikuchi-Fujimoto Disease in a Young Female: A Case Report and Literature Review. Cureus. 2021, 13:e19321. 10.7759/cureus.19321
[32.] Kataria R, Rao P, Kachhawa D, Jain VK, Tuteja RK, Vijayvargiya M: Kikuchi-Fujimoto Disease, the Masquerading Menace: A Rare Case Report. Indian J Dermatol. 2016, 61:348. 10.4103/0019-5154.182465
[33.] Dalugama C, Gawarammana IB: Fever with lymphadenopathy - Kikuchi Fujimoto disease, a great masquerader: a case report. J Med Case Rep. 2017, 11:349. 10.1186/s13256-017-1521-y
[34.] D'Introno A, Perrone A, Schilardi A, Gentile A, Sabbà C, Napoli N: Kikuchi-Fujimoto Disease in an Old Italian Woman: Case Report and Review of the Literature. Case Rep Med. 2017, 2017:7257902. 10.1155/2017/7257902.

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Author's Name	Age/ Sex	Ethnicity	Initial presenting Symptoms	Laboratory Findings	Imaging findings	Biopsy Findings	Treatment
Frankel et al. [27]	42-year-old male	Japanese	1-month history of fever, painful cervical lymphadenopathy, malaise, bilateral ear crusting, necrosis, a maculopapular rash on his thighs, and a malar rash.	WBC count: 3.7X10^3 cells/mL with 75% neutrophils and 14% monocytes, Hb: 11.7 g/dL, Platelet count: 129,000 cells/mL. ALT: 299 U/ L, AST:to 238 U/L. ESR:112 mm/h, C-reactive protein: 8.2 mg/dL, and ferritin: 2051 ng/mL. Urinalysis and creatinine: Normal.	A computed tomography scan of the neck revealed numerous prominent and enlarged lymph nodes in the right cervical jugular chain, right basicervical, and supraclavicular regions. Two of these lymph nodes exhibited central hypoattenuation.	Necrotizing lymphadenitis in the background of histiocytes and mixed B-cells as well as T-cells.	Hydroxychloroquine and prednisone.
Rauniyar et al. [28]	34-year-old female	Tibeto-Burman Nepalese	3 weeks of low-grade fever, painful swelling in the right side of the neck, and fatigue.	Hb: 13.0 g/dl, and WBC count: 2800/cubic mm, with neutrophils 52%, lymphocytes 40%, eosinophils 1%, and monocytes 7%. ESR: 25 mm in the first hour (normal range: <20 mm/h in females) with a positive CRP.	Ultrasound showed multiple, prominent, round structures with a hypoechoic center and a hyperechoic rim, suggestive of enlarged lymph nodes.	Encapsulated lymphoid tissue with effaced architecture, paracortical expansion with areas of fibrinoid necrosis, numerous apoptotic bodies, and crescentic macrophages with ingested debris could be seen	Symptomatic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs).
Song et al. [29]	20-year-old male	Chinese	5 days of headache and fever.	Normal complete blood count, coagulation tests, ESR, procalcitonin, CRP, antistreptolysin O, rheumatoid factor, tumor markers, antinuclear antibody (Ab), anti-dsDNA Ab, and anti-cardiolipin Ab. The initial intracranial pressure (ICP) measured was 220 mmH2O (normal range, 80–180 mmH2O).	Ultrasonography of the neck revealed multiple swollen bilateral cervical lymph nodes, some as large as 21 × 8.5 mm.	A cervical lymph node biopsy demonstrated numerous lympho-histiocytic cells and karyorrhectic debris without neutrophils.	Oral Methylprednisolone.
Lo KB et al. [1]	20-year-old female	African American	3 weeks of late afternoon fevers associated with night sweats, frontal headache, tender cervical lymphadenopathy, anorexia, and malaise.	WBC: 2.9 × 10^3 /mcL (65% neutrophils, 13% lymphocytes, 13% bands), Hb: 8.5 gr/dL (mean corpuscular volume 65 fL) and 181 × 10 3 /mcL platelets. C-reactive protein (CRP) and erythrocyte	Computed Tomography of the neck revealed bilateral cervical lymphadenopathy, enhancement and mild enlargement of the parotid and lacrimal glands, and diffuse swelling of the pharyngeal mucosa, and	Excisional biopsy of the left cervical lymph node revealed geographic necrosis with fibrinoid deposits and apoptotic cells surrounded by a	Oral Prednisone.

				sedimentation rate (ESR) levels were markedly elevated at 51 and 84 respectively. Lactate dehydrogenase (LDH), ferritin, and haptoglobin were also elevated.	marked enhancement of bilateral cervical soft tissue planes.	mononuclear infiltratee characteristically without neutrophils and eosinophils	
Kellner et al. [30]	27-year-old male	Caucasian	1 week of subacute, progressive right-sided neck pain and swelling, intermittent fevers, night sweats, and abdominal pain.	WBC count: 3.7 × 10^9/L with 57.5% neutrophils and 27.0% lymphocytes, Hb: 12.3 g/dL with a mean corpuscular volume of 85.1 fL.	Computed Tomography (CT) scan of the neck revealed multiple heterogeneously enlarged lymph nodes along the right anterior cervical chain with necrotic changes.	Lymphohistiocytic inflammation with plasmacytoid dendritic cells, areas of necrosis, and scattered karyorrhectic nuclear debris.	Oral Prednisone.
Khan et al. [31]	22-year-old female	-	2 months of fever, fatigue, anorexia, and cervical lymphadenopathy.	Hb: 11.7gm/dL, WBC count: 12000 cells/mm^3, ESR: 51, and CRP: 3.2md/dL.	Neck ultrasonography confirmed cervical lymphadenopathy with preserved lymph node architecture.	Partially affected architecture and areas of necrosis, nuclear dust, and mononuclear cells within surrounding tissues.	Oral Prednisone.
Kataria et al. [32]	30-year-old female	Indian	2 months of intermittent high-grade fever, weakness, pain in knee, wrist, and ankle joints, oral ulcers, erythematous rashes on face and upper chest, hemorrhagic crusting on lips and multiple, firm, tender enlarged bilateral cervical lymph nodes in the posterior cervical region.	Blood tests showed anemia, thrombocytopenia, and mild leukocytosis. All other lab findings were normal.	Chest X-ray was normal	Paracortical, well-circumscribed necrotic lesions, with karyorrhectic debris, fibrin deposits, with the proliferation of phagocytic foamy histiocytes, and infiltration of plasmacytoid monocytes, histiocytes, and lymphocytes surrounding karyorrhectic debris. Staining for acid-fast bacilli was also negative.	Antibiotics, nonsteroidal anti-inflammatory drugs, and oral steroids.
Joean et al. [23]	18-year-old male	-	2 weeks of recurrent episodes of high-grade fever, night sweats, generalized lymphadenopathy, and painful swelling in his	Mild anemia and lymphopenia. CRP, procalcitonin, and ferritin were moderately elevated. Large rise in NT-pro BNP levels and slightly increased liver enzymes with mild coagulopathy.	Ultrasonography showed multiple enlarged lymph nodes, the largest of them was (37×25×36 mm) in the left axilla.	Extensive necrosis and presence of histiocytes.	Symptomatic treatment with analgesics and

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			left axilla.				antipyretics.
Dalugama et al. [33]	18-year-old female	Sri Lankan	1 month of high grade fevers with sweating, weight loss, anorexia, swollen neck glands, and symmetric joint pain in the morning.	Hb: 7.4 g/dL with a mean corpuscular volume of 74 fL, WBC count:3 × 10^6/ml with a normal platelet count, ESR:144 mm, CRP: 60 mg/L. Serum albumin: 35 g/L(low), LDH: 1254 u/L, serum ferritin: > 1200 mg/mL.	Chest X-ray was normal.	Mononuclear cells could be seen in the surrounding tissue of the partially effaced architecture and necrotic areas that were also infiltrated with nuclear dust.	Oral prednisolone.
D'Introno et al. [34]	66-year-old female	Italian	2 months of low-grade fever, malaise, fatigue, night sweats, decrease in appetite, 4kg weight loss. 1 month of painful right laterocervical lymph nodes.	CRP: 20 mg/L (normal < 2.9), LDH: 705 UI/L (normal< 450), and ESR: 54 mm/h.	With a low peripheral flow, eccentric cortical thickening, and deviation of the hila, ultrasonography showed enlarged right-sided hypoechoic laterocervical (maximum size of 1.7 cm) and submental lymph nodes (size 1 cm).	Paracortical necrotic foci with the presence of small to large T lymphocytes, in addition to numerous histiocytes and abundant apoptotic nuclear debris.	Symptomatic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs).