Case Report

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Diagnostic challenges and management of kikuchi-fujimoto disease: a rare case report

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Introduction: Kikuchi-Fujimoto disease, otherwise referred to as histiocytic necrotizing lymphadenitis, is a rare and self-limiting disorder characterized by fever, lymphadenopathy, and upper respiratory symptoms. The main target of the illness is young Asian adults and is more prevalent in females. This disease probably has viral triggering or autoimmune responses, and diagnosis depends on histopathological examination.

Case Presentation: We present a case of an 18-month history of recurrent high-grade fever with marked weight loss and an enlarged occipital lymph node in a 42-year-old diabetic male from Karachi, Pakistan. The patient's symptoms did not subside despite being hospitalized several times and receiving multiple courses of antibiotics. Physical examination revealed a firm, non-tender occipital lymph node. Laboratory studies showed mild anemia and leukopenia, raised inflammatory markers, but unremarkable imaging studies and autoimmune tests. An excisional biopsy of the lymph node confirmed KFD with necrotizing lymphadenitis showing characteristic karyorrhectic debris.

Discussion: This case epitomizes the diagnostic challenges of KFD, which can mimic a host of conditions like tuberculosis and lymphoma. The recurrent fevers in the presence of significant weight loss and failure to respond to the usual treatments raised suspicion for further detailed investigation. Excisional biopsy established the diagnosis and differentiated it from other conditions. The patient's rapid improvement with corticosteroid therapy aligns with established treatment protocols for KFD, thus proving its efficacy.

Conclusion: KFD should be included in the differential diagnosis of fever of unknown origin. Diagnosis and management of KFD can avoid misdiagnosis and hence improve patient outcomes.

Keywords: corticosteroid therapy, fever of unknown origin, histiocytic necrotizing lymphadenitis, KIKUCHI-fujimoto disease, lymphadenopathy

Introduction

Kikuchi-Fujimoto disease (KFD), also referred to as histiocytic necrotizing lymphadenitis, is an uncommon, self-limiting disorder characterized by regional lymph node swelling, fever, night sweats, and upper respiratory symptoms[1]. It has a high occurrence rate among Asians, commonly affects young adults, and is more prevalent in females than in males[2]. In KFD, histiocytes and atypical lymphocytes are the primary cells involved, as its pathophysiology is hypothesized to involve viral infections or an autoimmune response. Reactive histiocytes and tubuloreticular inclusions support a viral origin, with Epstein-Barr virus and HTLV-1 being implicated. This disease shares histopathological features with systemic lupus erythematosus (SLE), suggesting a potential autoimmune component[1,2].

Most cases follow a benign course. The diagnosis relies on histopathological findings from an excisional biopsy, showing necrotizing lymphadenitis without granulocytic infiltration[2]. Recognizing KFD is crucial because it can often be mistaken for tuberculosis (TB), lymphoma, adenocarcinoma, or sometimes lymphadenitis associated with SLE[3]. This disease typically resolves within a few months and has a low recurrence rate of 3% to 4%, as its treatment focuses on supportive care, including rest, analgesics, and antipyretics[2]. In severe or relapsing cases, corticosteroids are the choice of treatment[1,2].

Here we report a case of a 42-year-old man with a high-grade fever, weight loss, and an enlarged cervical lymph node.

Case Presentation

A 42-year-old male with a history of diabetes mellitus, residing in Kemari, presented with a fever of unknown origin (FUO), was admitted to the Emergency Room (ER) with a high-grade fever occurring intermittently over the past 1.5 years and now persistent for the last 7 days. The fever had a sudden onset, reaching up to 102°F, associated with rigors, chills, and excessive sweating, occurring 2-3 times daily. It was unresponsive to oral antipyretics and resolved either spontaneously after 2-3 hours or

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immediately after IV antipyretics from nearby clinics. The patient reports each episode as a recurrent pattern of high-grade fevers lasting 7–10 days, followed by afebrile intervals of 2–3 months over the past 18 months. He has experienced significant, unintentional weight loss of 15-20 kg, anorexia, and reduced oral intake.

He has been hospitalized multiple times for similar issues. In July 2023, the patient was admitted to a peripheral hospital with a high-grade fever, generalized weakness, lethargy for 5 days, and a history of a fall, injuring his left hand without fractures or deformity; an EEG to exclude seizures was unremarkable. Despite receiving intravenous antibiotics, he was discharged from the hospital with a persistent fever. The patient denies experiencing symptoms across multiple body systems. Noteworthy symptoms include intermittent constipation, a mild cough with minimal sputum, left shoulder pain, and non-specific headaches.

He has had diabetes mellitus since 2011 and has managed with oral hypoglycemic drugs and insulin, but with poor compliance. There is no significant past surgical history. The patient's current medication regimen consists of Glucophage (metformin HCl) as needed for glycemic control, Lerace (Levetiracetam) [was initiated empirically during a prior hospitalization due to a suspicion of seizures following a fall attributed to dizziness. However, subsequent neurological evaluations, including an unremarkable EEG, ruled out epilepsy. The medication was later discontinued as no further episodes were reported, and the fall was attributed to a non-neurological cause], Rivotril (Clonazepam) at bedtime for sleep, Toujeo Solostar U-300 (Glargine Insulin) for diabetes management, and a recent course of Meropenem administered three times daily for 14 days. The patient has an allergy to Ceftriaxone, as evidenced by a pruritic skin rash experienced four months ago during a clinic visit, which was resolved with IV antihistamines. The patient is addicted to Naswar and has been an active smoker, consuming 2-3 cigarettes daily for 5 years, totaling 0.75 pack years.

Examination

On examination, the patient's temperature was 102°F. A single large palpable lymph node was noted in the occipital region, approximately 1 × 1 cm in size, firm, nontender, and fixed to the underlying muscle. The patient was stable, and the rest of the examinations were unremarkable.

Management

He was admitted to the male medical ward with a FUO. Initial ER blood work showed mild anemia, leukopenia, and normal platelet, renal, liver, and electrolyte functions. Elevated inflammatory markers (CRP, ESR) indicated inflammation without severe bacterial infection (Table 1), and an elevated HbA1c suggested poorly controlled diabetes. Imaging studies, including echocardiogram, abdominal ultrasound, and CT scans, were unremarkable. Autoimmune tests (ANA, anti-dsDNA, and ENA profile) were negative.

An ultrasound of the posterior neck revealed well-defined hypoechoic areas in the occipital region bilaterally: 1.5 × 0.4 cm on the right and 0.7 × 0.4 cm on the left, with no vascularity and well-defined borders, indicating benign lymph nodes. Figure 1 *and* 2 *demonstrate the ultrasound imaging of the posterior neck region.*

Table 1

Laboratory Findings

Test	Result	Reference Range
31/10/2023		
Complete Blood Count (CBC)		
Hemoglobin (HB)	11.6 g/dL	13.0–17.5 g/dL (males)
Mean Corpuscular Volume (MCV)	92 fL	80–100 fL
Total Leukocyte Count (TLC)	3.6 x 10^3/µL	4.0–11.0 x 10^3/µL
Neutrophils (N)	65%	40–70%
Lymphocytes (L)	30%	20–40%
Platelets (PLT)	219 x 10^3/µL	150–450 x 10^3/µL
Urinary creatinine excretion (UCE)		
Urea (Ur)	25 mg/dL	15–40 mg/dL
Creatinine (Cr)	0.76 mg/dL	0.6–1.2 mg/dL
Sodium (Na)	137 mmol/L	135–145 mmol/L
Potassium (K)	4.1 mmol/L	3.5–5.0 mmol/L
Chloride (Cl)	104 mmol/L	98–106 mmol/L
Bicarbonate (HCO3)	22 mmol/L	22–28 mmol/L
Liver Function Tests (LFT)		
Total Bilirubin (T.BILI)	0.46 mg/dL (Direct 0.2 mg/dL/Indirect 0.2 mg/dL)	0.1–1.2 mg/dL
Serum Glutamic Pyruvic Transaminase (SGPT)	27 U/L	7–56 U/L
Serum Glutamic Oxaloacetic Transaminase (SGOT)	29 U/L	5–40 U/L
Alkaline Phosphatase (ALP)	62 U/L	44–147 U/L
Gamma-Glutamyl Transferase (GGT)	67 U/L	9–48 U/L (males)
Prothrombin Time/ International Normalized Ratio (PT/INR)	10.4 sec/1.04	10–14 sec/0.8–1.2
Calcium (Ca)	8.9 mg/dL	8.5–10.5 mg/dL
Magnesium (Mg)	2.3 mg/dL	1.7–2.2 mg/dL
Phosphate (PO4)	4.6 mg/dL	2.5–4.5 mg/dL
Urine Detailed Report (URINE D/R)		
pH	6	4.5–8.0
Pus cells	1-2	0–5
Arterial Blood Gas Analysis (ABGS)		
pH	7.42	7.35–7.45
PaCO2	36 mmHg	35–45 mmHg
PaO2	104 mmHg	80–100 mmHg
HCO3	22 mEq/L	22–26 mEq/L
Troponin I (TROP I)	<0.10 ng/mL (NEG)	<0.10 ng/mL
Malaria Parasite-Immunochromatographic Test (MP-ICT)	NEGATIVE	Negative
Dengue Serology	IgM/IgG NEGATIVE	Negative
C-Reactive Protein (CRP)	4.79 mg/L	<5.0 mg/L
Procalcitonin (PCT)	0.39 ng/mL	<0.5 ng/mL
Erythrocyte Sedimentation Rate (ESR)	62 mm/hr	0–20 mm/hr (males)
Albumin	3.35 g/dL	3.5–5.5 g/dL
Hemoglobin A1c (HbA1c)	8.5 %	6.5% (diabetic)

Persistent fever prompted an excisional biopsy of an occipital lymph node and a bone marrow biopsy to rule out hemophagocytic lymphohistiocytosis (HLH). Histopathology of the posterior cervical lymph node biopsy (1.4 x 1.2 cm) revealed a partially distorted nodal architecture with focal paracortical pale areas containing eosinophilic granular material, karyorrhectic debris, and histiocytes, encircled by histiocytic cells, with no signs of neutrophils, granuloma, or malignancy.

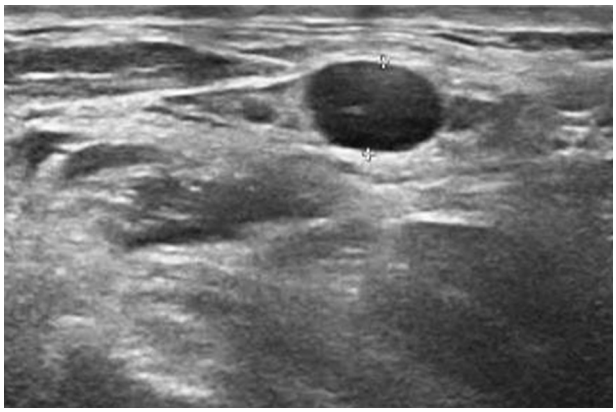

Figure 1. Transverse view of ultrasound of the back of the neck.

The bone marrow biopsy showed no hemophagocytosis, and cultures were negative. After consulting with infectious disease and hematology teams, the patient was started on oral steroids (prednisolone 5 mg; three times a day), resulting in rapid symptom improvement and decreased fever. The patient showed rapid improvement, becoming afebrile and symptom-free the next morning. He was discharged on oral steroids with a tapering protocol and follow-up scheduled in the outpatient department (OPD). During follow-up visits, the steroid dosage was tapered gradually to prednisolone 5 mg once daily over three weeks. The patient tolerated the reduced dosage without recurrence of fever or lymphadenopathy. Clinical monitoring included assessment of vital signs, resolution of symptoms, and repeat laboratory tests. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels, which were elevated at presentation, normalized during follow-up. The patient remained afebrile and asymptomatic, with no evidence of relapse during the subsequent follow-up period. *Laboratory findings are summarized in* Table 1.

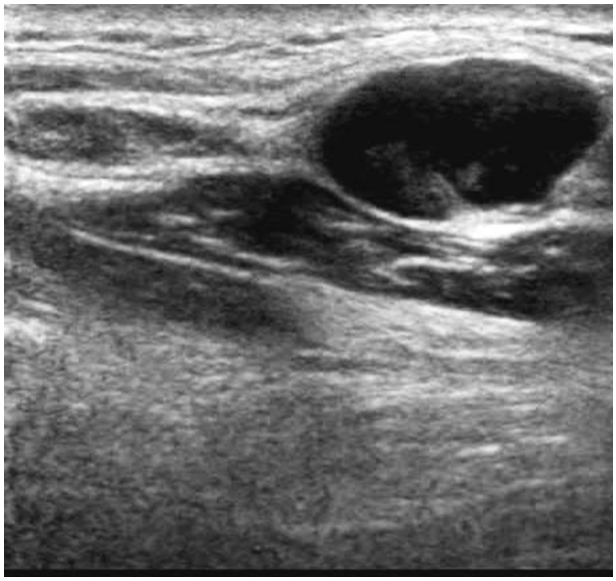

Figure 2. Longitudinal view of ultrasound of the back of the neck.

Discussion

KFD is a self-limiting condition primarily affecting lymph nodes, with a higher prevalence among Japanese and East Asian populations, though cases have been observed worldwide, including in South Asia[4]. It typically presents with mild fever and cervical lymphadenopathy[5]. The etiology of KFD remains unclear, with proposed triggers including various infectious agents and autoimmune responses, but no specific pathogen has been definitively identified. Diagnosis relies on invasive procedures, such as excisional biopsy, to observe characteristic cellular changes rather than solely on physical examination[3]. Although cervical lymph nodes are most frequently affected, other lymph node groups, such as the axillary and mediastinal nodes, can also be involved[4]. Patients often present with an unexplained fever, which our patient also experienced, although less common symptoms include headache, fatigue, arthralgia, myalgia, rash, weight loss, and abdominal pain[6], with our patient only reporting weight loss. Mortality from KFD is exceptionally rare and typically results from complications affecting the heart, kidneys, or lungs, such as pleural effusion, acute kidney injury, or cardiac tamponade. Rarely, the disease can also lead to neurological complications, including peripheral neuropathy[7].

In this case, a 42-year-old male presented with recurrent high-grade fevers, significant weight loss, and an occipital lymph node, reflecting the complexities of diagnosing KFD. The patient's episodic fevers, lasting 7–10 days with afebrile intervals, and unresponsiveness to antipyretics highlight the need for thorough evaluation. Initial tests were non-specific, which is common in KFD and complicates diagnosis.

The excisional lymph node biopsy was crucial. Histologic findings include paracortical areas of coagulative necrosis with abundant karyorrhectic debris. These karyorrhectic foci are surrounded by histiocytes, plasmacytoid monocytes, immunoblasts, and a mix of small and large lymphocytes, with a predominance of CD8 + T cells over CD4 + T cells[3]. This finding underscores the importance of biopsy in confirming KFD, as other diagnostic tests often fail to provide definitive results. Negative results from bone marrow biopsy and cultures helped exclude conditions such as HLH and other infections, which is vital due to symptom overlap.

The response to oral steroids observed in this case aligns with recommended treatment approaches for KFD, highlighting corticosteroids as effective for managing symptoms. This case emphasizes the importance of including KFD in the differential diagnosis of FUO, particularly when initial investigations are inconclusive. While diagnosing KFD can be challenging, its typical clinical presentation and favorable response to corticosteroid therapy are consistent with the literature, demonstrating that KFD generally responds well to appropriate treatment.

This case report has been conducted and reported in line with the SCARE 2023 guidelines to ensure the adherence to high-quality reporting standards[8].

Limitations

This case report highlights the diagnostic and therapeutic aspects of Kikuchi-Fujimoto Disease, but several limitations must be acknowledged. First, the study's findings are based on a single case, limiting generalizability to broader populations. Second, histopathological confirmation was obtained from

excisional biopsy, but advanced molecular diagnostic techniques were not employed, which may provide further insights into the disease etiology. Additionally, long-term follow-up was not performed, so the possibility of recurrence or chronicity could not be assessed. Finally, while corticosteroids proved effective in this case, comparative evaluation with other treatment modalities was not possible due to the scope of this report.

Conclusion

The case report reiterates that KFD needs to be considered in the differential diagnosis of FUO, especially when conventional diagnostic tests are not helpful. In this 42-year-old male patient with recurrent high-grade fevers and massive weight loss, accompanied by occipital lymphadenopathy, all the intricacies and difficulties associated with making a diagnosis of KFD were thoroughly explained. Histopathological diagnosis by excisional lymph node biopsy remains the key to definitive diagnosis, as it reveals characteristic features of necrotizing lymphadenitis. The rapid response of the patient to corticosteroid therapy underlines the effectiveness of this mode of treatment in managing KFD. This case illustrates that a high index of suspicion for KFD should be kept at all times for patients who present with persistent fever and lymphadenopathy, especially in areas where the incidence of the disease is higher than usual. Acknowledging and accurately identifying KFD avoids misdiagnosis and ensures proper effective management that would favorably affect the outcome of the patient.

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None.

Ethical approval

This case report does not contain any personal information that could lead to the identification of the patient. Therefore, it is exempted from ethical approval. Our institution does not require ethical approval for reporting individual case report or case series.

Patient consent

Written informed consent was obtained from the patient for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions:

J.M.: project administration, supervision, writing – original draft, writing – review & editing. A.K.: conceptualization, resources. L.A.: writing – original draft. A.A.Q.: writing – original draft, writing – review & editing. Z.F.: writing – original draft. S.K.: writing – original draft. V.K.: writing – original draft. S.M.N.: Writing – original draft.

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Data sharing is not applicable to this article.

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