Case report

Recurrent Kikuchi Fujimoto Disease with Aseptic Meningitis and Familial Occurrence: A Rare Presentation

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Abstract

Recurrent Kikuchi Fujimoto Disease (KFD) with neurological manifestations is a rare entity. It usually presents with fever and cervical lymphadenopathy. Diagnosis is based on clinical grounds and typical histological findings of lymph node biopsy. Mostly KFD is self-limiting. Treatment with non-steroidal anti-inflammatory drugs or steroids may be needed in severe recurrent disease.

We report a case of recurrent KFD in a 28-year-old male presenting with aseptic meningitis who has a family history of KFD.

Keywords: Kikuchi Fujimoto Disease, Aseptic meningitis, Recurrence, Familial

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Introduction

Kikuchi Fujimoto disease (KFD) is a rare benign condition which is characterized by necrotizing lymphadenitis. This condition was first described by two Japanese pathologists, Kikuchi and Fujimoto simultaneously in 1972. Although many studies have been done afterwards, the etiopathology remains unknown [1]. It is common among Asian females between the ages of 20-30 years [2]. The usual presentation is mild fever with cervical lymphadenopathy. Involvement of skin, eyes, bone marrow and hepatic dysfunctions are documented [3]. Various neurological manifestations are also reported, and the incidence of neurological manifestations is 11% [4-6]. Recurrent KFD is a rare entity with a rate of 3-4% [7]. Familial cases of KFD are rarely reported in the literature [8].

We report a case of recurrent KFD with aseptic meningitis occurring among siblings.

Case history

28-year-old male from Galle, Sri Lanka, presented with high spiking fever for two weeks associated with generalized headache with vomiting.

There were no respiratory or urinary symptoms. On examination, he was conscious and rational and had bilateral papilledema without neck stiffness or other neurological deficits. There was bilateral tender cervical lymphadenopathy. The other system examination was normal.

He had two previous hospital admissions during the last 6 weeks as well as several admissions during the last 20 years due to similar symptoms.

Three years ago, he has undergone a lymph node biopsy. Histology revealed necrotizing lymphadenitis which is suggestive of KFD. His sister had been investigated for similar symptoms and KFD was confirmed by lymph node biopsy.

In his investigations, Complete blood count, renal functions, and liver functions were normal (Table 1). Chest radiograph, non-contrast computer tomography brain, and 2D ECHO also were normal.

Table 1: Summery of investigations

Investigation	Value	Reference value
Full blood count		
White blood cells	8500 /microliter	4500-11000 /microliter
Haemoglobin	14.8 g/dl	13.8 – 17.2 g/dl
Platelets	226 /microliter	15o – 450 / microliter
Liver function tests		
AST	25 U/L	8 – 33 U/L
ALT	38 U/L	7 55 U/L
ALP	60 U/L	44 – 150 U/L
GGT	35 U/L	5 – 40 U/L
T. bilirubin	0.6 mg/dl	0.1 -1.2 mg/dl
Direct bilirubin	0.2 mg/dl	< 0.3 mg/dl
Albumin	44 mg/dl	34 – 54 mg/dl
INR	1.1	<1
C reactive protein	125 mg/dl	<5 mg/dl
Renal functions		
Creatinine	1.1 mg/dl	0.7 – 1.3 mg/dl
Blood urea	8 mg/dl	6 – 24 mg/dl
Sodium	136 mEq/L	135 -145 mEq/L
Potassium	4.1 mEq/L	3.5 – 5 mEq/L
Erythrocyte sedimentation rate	82 mm/1st hour	< 14mm/1st hour
Serum ferritin	3946 ng/ml	12 – 300 ng/ml
Cerebrospinal fluid analysis (CSF)		
Appearance	Crystal clear	
Polymorphs	20 / mm^3	Nil
Lymphocytes	152 / mm^3	< 5 /mm^3
Protein	75 mg/dl	20 – 40 mg/ dl
Glucose	52 mg/dl	50-75 mg/dl

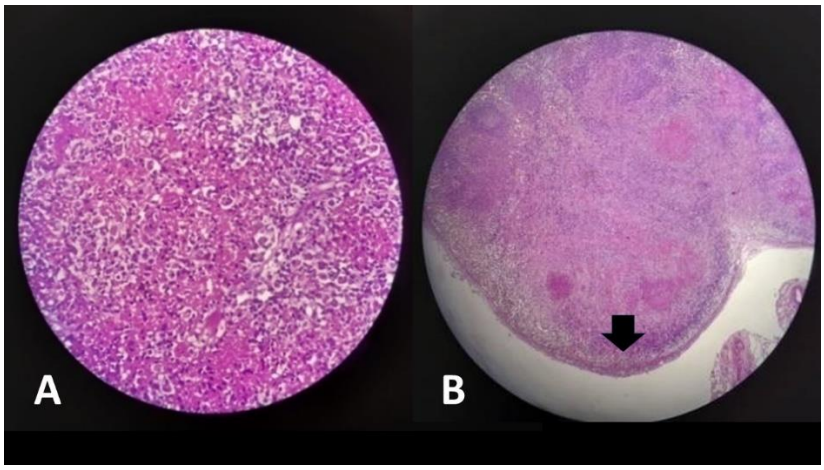

Figure 1: Histological findings of left cervical lymph node biopsy. Hematoxylin-eosin staining showing **A**, histiocytes; **B**. sub-cortical necrosis

Indian ink staining of CSF for *Cryptococcus neoformans*, polymerase chain reaction for tuberculosis, herpes simplex virus and bacterial and fungal cultures were negative. With the above findings CSF analysis is suggestive of aseptic meningitis.

Serology for Epstein-Barr virus, cytomegalovirus, and toxoplasma were negative. Cervical lymph node biopsy histology revealed necrotizing lymphadenitis with histiocytic cellular infiltrate suggestive of KFD (Figure 1). His Antinuclear antibody (ANA) was found to be positive at a titer of 1:80.But he did not have other features of systemic lupus erythematosus (SLE) and his anti-Ds DNA was negative.

With these investigations, the diagnosis of recurrence of KFD with aseptic meningitis was made. Treatment started with prednisolone 40mg daily. Within 24 hours of starting steroids vomiting settled and by the second-day headache and fever completely resolved. The patient was observed for another 24 hours and discharged to be received at the clinic.

On clinic visit in two weeks, he had completely recovered, and lymph nodes had disappeared. Steroids were tailed off over the next two weeks and stopped. The patient was followed up for several months and he was completely asymptomatic.

Discussion

Here we report a case of recurrent KFD associated with aseptic meningitis and it is a very rare entity. The patient had fever, headache, vomiting and tender bilateral cervical lymphadenopathy. He has several previous hospital admissions with similar symptoms and three years back been treated for histologically confirmed KFD. This time his CSF findings were suggestive of aseptic meningitis and lymph node biopsy revealed necrotizing lymphadenitis. The diagnosis was recurrence of KFD with aseptic meningitis and treated with steroids. The patient was completely recovered.

KFD is a rare, benign, self-limiting disease that primarily affects young adults, especially females and is characterized by lymphadenopathy and fever. Lymphadenopathy presents in 60% of cases and usually, it is cervical. Lymphadenopathy from other sites can vary from 2% to 40%. Generalized lymphadenopathy is rarely reported [9]. Our patient had bilateral cervical lymphadenopathy without involvement of other sites.

Uncommon extra nodal manifestations include skin manifestations such as erythematous papules, plaques, indurated lesions and ulcers, and gastrointestinal manifestations such as nausea, vomiting, enlarged liver, spleen and upper respiratory symptoms with fever. Nonspecific symptoms such as fatigue, joint pains, weight loss and night sweats have also been reported [9].

The main complaint of our patient was headache and vomiting with non-specific symptoms such as joint pains and fatigue. There was papilledema which suggests central nervous system involvement.

Other neurological manifestations of KFD are aseptic meningitis, mononeuritis multiplex and acute cerebellar ataxia [10]. The total incidence of neurological manifestation is 11% [5]. Aseptic meningitis is the most common complication observed in 2.8%-9.8% of cases [6].

There can be fatal outcomes such as pulmonary haemorrhages and disseminated intravascular coagulopathy [11].

The recurrence rate of KFD is reported as 3%-4% [7]. The site of lymphadenopathy is usually the same in recurrent cases. The clinical features or severity of symptoms do not affect the recurrence rate. However, a higher recurrence rate has been reported in patients with non-classic symptoms [2].

Our patient had recurrent episodes of fever with lymphadenopathy for around 20 years. However, a clear diagnosis of KFD was made only once with the help of a lymph node biopsy.

Recurrent KFD should be distinguished from conditions such as tuberculosis, SLE and lymphomas [12]. We have successfully excluded these conditions in our patients.

In some cases of KFD, ANA positivity showed a higher recurrence rate [13]. Higher ANA positivity is reported in Asian patients than in European patients [2]. Our patient also had positive ANA which is supportive for his high recurrence rate.

KFD is a self-limited disease, and most patients do not require specific treatment. Non-steroidal anti-inflammatory drugs (NSAIDS) can be used as conservative management [2].

Patients with classic symptoms of KFD respond well to NSAIDS. In cases where symptoms are severe or complications arise, treatment with glucocorticoids may be considered. Immunosuppressants are recommended in complicated cases for the prevention of fatal outcomes [14].

Our patient was initially treated with NSAIDS, but due to poor response steroids was started which showed a dramatic response.

KFD occurrence among family members is reported very rarely in literature [8]. Our patient's sister has a history of Kikuchi lymphadenitis without a history of recurrence.

Conclusion

Recurrent KFD and KFD with aseptic meningitis both are extremely rare. KFD should be considered as a differential diagnosis in a patient with fever and lymphadenopathy. With patients who have concomitant headache aseptic meningitis should be suspected. An early lymph node biopsy can be done to confirm KFD. When aseptic meningitis is suspected lumbar puncture is beneficial to avoid unnecessary antibiotic use and to prevent complications. Familial occurrence of KFD is rare but has been reported.

Consent

Informed written consent was obtained from the patient for this case report.

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