Kikuchi-Fujimoto disease with multisystem involvement: A case report

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ABSTRACT
Kikuchi-Fujimoto disease (KFD) is a self-limited, usually benign condition of unknown etiology characterized by fever and cervical lymphadenitis. Multisystem involvement is not very common. We report a case of a 14-year-old Chinese boy who presented with prolonged fever, rashes, cervical lymphadenitis, oral ulcers, and weight loss eventually diagnosed with Kikuchi’s disease. This case is interesting as the child subsequently developed multisystem involvement secondary to Kikuchi disease. The child recovered and remains well on follow-up clinic visits. KFD may have to be differentiated from many other infective, inflammatory, and malignant disorders. Diagnosis is confirmed by characteristic histopathological findings on excision lymph node biopsy. Long-term careful monitoring of these patients for signs and symptoms of evolving systemic lupus erythematosus or other autoimmune disorders is required.

Key words: Fever, Kikuchi’s disease, Lymphadenitis, Multisystem, Systemic lupus erythematosus

Kikuchi disease (also known as histiocytic necrotizing lymphadenitis [HNL], Kikuchi-Fujimoto disease [KFD]) was first reported in young Japanese females in 1972. It is a self-limited disorder of unknown etiology, characterized by focal painful lymphadenitis, fever, malaise, and weight loss [1]. Kikuchi disease affects a wide age range of patients (2-75 years) but typically affects young adults (mean age, 20-30 years) [2]. In general, a female preponderance has been reported with a female to male ratio of 4:1 [3]. The condition has been reported predominantly in the Asian population and occurs sporadically outside Asia [1]. Kikuchi’s disease typically is self-limited, usually resolving within 1-4 months. A low recurrence rate of 3% to 4% has been reported [3]. Diagnosis of KFD is based on characteristic histopathologic features on excision biopsy of affected lymph nodes. The onset of Kikuchi’s disease is usually acute or subacute with fever and regional lymphadenopathy (mostly cervical). Extranodal involvement in Kikuchi’s disease is rare and has been documented in skin, bone marrow, myocardium, and central nervous system [3]. We report a case of Kikuchi disease with multisystem involvement in a 14-year-old Chinese boy.

CASE REPORT
The child was admitted to our hospital with 3 weeks of fever (daily spikes >39°C), intermittent frontal headaches, rash, weight loss (2 kg), oral ulcers (for 1 week), and feeling tired. There was no history of any recent overseas travel or contact with any sick person. Clinical examination revealed a febrile child with multiple left cervical lymphadenopathy (1-2 cm in size, non-tender), hepatomegaly (2 cm), and erythematous maculopapular rash on trunk and limbs. Rest of the examination was unremarkable.

Child continued to spike fever for 9 days during inpatient stay in spite of being on above antibiotics (ceftriaxone for 9 days and clindamycin for 6 days). Finally, cervical lymph node excision biopsy was done (day 9 of inpatient stay) for suspicion of Kikuchi’s disease which confirmed the Kikuchi’s lymphadenitis (Figs. 1 and 2). The child was started on oral prednisolone and discharged after 12 days of inpatient stay (day 3 of oral prednisolone at 1 mg/kg/day, to be continued for another week) when symptoms improved and afebrile. He was given a follow-up clinic appointment in a week.
Urgent computed tomography brain scan was normal. The child was empirically treated for meningitis/encephalitis with intravenous ceftriaxone, acyclovir, and ciprofloxacin (to cover for atypical organisms). LP was suggestive of aseptic meningitis (clear, colorless, white blood cell; 9/mm$^3$, red blood cells: 12/mm$^3$, protein: 0.34g/L, glucose: 3.3 mmol/L). Cerebrospinal fluid (CSF) studies including latex (bacterial antigen) agglutination, Gram-stain and culture, HSV/enterovirus PCR, cryptococcus antigen, acid-fast bacilli smear and culture, and CSF globulin were negative.

Liver function tests (LFT) were deranged (total bilirubin: 50 umol/L, direct bilirubin: 36 umol/L, albumin: 24 g/L, ALT: 230 U/L, aspartate aminotransferase: 112 U/L, gamma-glutamyl transferase: 1155 U/L, LDH: 1596 U/L, CRP: 19 mg/L, ESR: 40 mm/h, serum ferritin 9174 ug/l (significantly raised), serum triglycerides 0.8 mmol/L, lupus anticoagulant not demonstrated, complement levels were mildly raised (C3 1.45, C4 0.48 G/L), anti-N-methyl-D-aspartate receptor antibodies (CSF/blood) not detected, DCT-positive anemia (hemoglobin: 9.1 g/dl). Skin biopsy of rash showed necrotic epidermis with features of interface dermatitis (Fig. 3). Magnetic resonance imaging/magnetic resonance angiogram brain was normal.

The child was diagnosed with Kikuchi’s disease with multisystem involvement (aseptic meningitis, raised liver transaminases, DCT-positive anemia, and interface dermatitis) and treated with intravenous methylprednisolone (3 days) and antibiotics, followed by oral steroids and antibiotics on discharge.

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microbiologic test results, who developed transient fulminant hepatic failure in response to antituberculous drugs.

Paradelas et al. [6] reported a case of a 17-year-old woman with KFD (diagnosed on a lymph node biopsy), who a month later developed an erythematous edematous rash on her upper body, with skin biopsy showing interface dermatitis. After 8 months, ANA at titer of 1/320, anti-DNA-ds antibodies, and marked decrease of complement levels were detected. During the following 2 years, she developed diagnostic criteria for SLE (arthralgias, pleuritis, aseptic meningitis, hemolytic anemia, and lupus nephritis). This histopathological finding of interface dermatitis not previously considered significant might be a marker of evolution into SLE.

Khishfe et al. [7] presented a case report of a patient who presented to the emergency department with signs and symptoms suggestive of aseptic meningitis and ultimately diagnosed with Kikuchi disease. The inclusion of Kikuchi disease in the differential diagnosis for meningitis may help establish a diagnosis in patients also presenting with regional lymphadenopathy.

Clinical differential diagnosis for Kikuchi disease includes infectious mononucleosis, bacterial lymphadenitis, cat scratch disease, mycobacterium TB, CMV disease, toxoplasmosis, SLE, malignancy, and Kawasaki disease [1].

Diagnosis of Kikuchi’s disease is confirmed by lymph node biopsy showing histiocytic necrotizing lymphadenitis. SLE presents the most challenging disorder from which it has to be differentiated. SLE lymphadenitis demonstrates aggregates of degenerated nuclear debris, degenerated nuclear material in walls of blood vessels, prominent reactive hyperplasia, abundant plasma cells, and capsular or pericapsular inflammation. Features that favour Kikuchi’s disease include predominance of CD8+ cells, absence of neutrophils, and a relative paucity of plasma cells [3].

Corticosteroid therapy may speed up recovery in patients with Kikuchi disease [1]. Patients with classic symptoms respond to NSAIDs or steroid, and those with severe symptoms usually respond to steroids. Immunosuppressants have been recommended for the complicated case to prevent fatal outcome [4]. Hyun et al. reported a case of a KD patient who was unresponsive to NSAIDs and steroids, and experienced symptom resolution after treatment with hydroxychloroquine (HC). This leads to the consideration about the use of HC for the treatment of KFD patients who have persistent symptoms, treated by NSAIDs and steroids [4].

Association between Kikuchi’s disease and SLE has been reported, with some patients of Kikuchi’s disease developing a full-blown SLE. Kikuchi’s disease can also precede or coincide with the diagnosis of SLE, and SLE should always be excluded in patients presenting with necrotizing lymphadenitis. It is recommended to perform ANA screening at the time of diagnosis, and the patients with Kikuchi’s disease should also have a follow-up evaluation for SLE [3]. The prognosis for Kikuchi is generally optimistic; however, a concurrent autoimmune disease or the risk of developing an autoimmune disease needs careful monitoring [8].

CONCLUSION

Our case report highlights the fact that although Kikuchi disease usually presents with fever and lymphadenopathy, it may also present with multisystem involvement. Awareness of this benign condition among clinicians and pathologists will help with early diagnosis and avoid expensive, extensive, and unnecessary investigations in a young child presenting with fever and lymphadenopathy.

REFERENCES


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