Case Report

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Kikuchi–Fujimoto Disease with Multisystem Involvement: A Case Report with Review of Literature

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Abstract

Kikuchi-Fujimoto disease (KFD) is a self-limited, usually benign condition of unknown etiology characterised by fever and cervical lymphadenitis. Multisystem involvement is not very common.We report a case of a 14 year old boy who presented with prolonged fever, rashes, cervical lymphadenitis, oral ulcers, and weight losseventually diagnosedwith kikuchi's disease. This case is interesting as the child subsequently developed multisystem involvement secondary to Kikuchi disease. 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 SLE or other autoimmune disorders is required.

Keywords: Kikuchi's Disease; Fever; Lymphadenitis; SLE; Multisystem.

Introduction

Kikuchi disease (also known as histiocytic necrotizing lymphadenitis (HNL), Kikuchi-Fujimoto disease) 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 [1,2].

It most commonly affects adults younger than 40 years of age and of Asian descent [3]. Kikuchi disease occurs in a wide age range of patients (i.e., 2–75 years), but it typically affects young adults (mean age, 20–30 years). In general, a female preponderance has been reported with a female to male ratio of 4:1. But, recent reports suggest the ratio to be 1:1 [2]. Involved lymph nodes demonstrate paracortical areas of apoptotic necrosis with abundant karyorrhectic debris and a proliferation of histiocytes, plasmacytoid dendritic cells, and $CD8^+$ T cells in the absence of neutrophils. Kikuchi-Fujimoto disease is thought to have 3 evolving phases: proliferative, necrotizing, and xanthomatous. 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 sub-acute with fever and regional lymphadenopathy (mostly cervical). Extra-nodal 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 boy.

Case Report

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 one 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 withmultiple left cervical lymphadenopathy (1-2 cms

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in size, non-tender), hepatomegaly (2 cms) anderythematous maculopapular rash on trunk and limbs. Rest of the examination was unremarkable.

Child was extensively investigated for fever of unknown originand empirically treated with intravenous antibiotics (ceftriaxone and clindamycin). During his stay, we also requestedinput from our rheumatology, infectious disease & hematology colleagues.

Investigationsincluding blood, stool, urine cultures, Rickettsia, Toxoplasmosis, EBV, CMV, Salmonella serology, HSV PCR, TB (T -spot test), ANA and anti dsDNA were negative. He had raised ASOT (800 units), LDH 524 (170-283 U/L), ESR (170 mm/hr) and CRP (46 mg/l). Bone marrow showed no evidence of malignancy.

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 nodeexcision biopsy done (day 9 of inpatient stay) for suspicion of kikuchi's diseaseconfirmedKikuchi's lymphadenitis.

Child was started on oral prednisolone and discharged after 12 days of inpatient stay (day 3 of oral prednisolone at 1mg/kg/day, to be continued for another week) when symptoms improved and afebrile. He was given a follow up clinic appointment in a week.

Child got readmitted 4 days post hospital discharge with generalized seizures requiring anticonvulsants (intravenous lorazepam & phenytoin) and elective intubation & ventilation. Urgent CT brain scan performedwas normal. Child wasempirically treated for meningitis/encephalitis with intravenous ceftriaxone, acyclovir & ciprofloxacin (to cover for atypical organisms). LP was suggestive of aseptic meningitis (clear,colorless WCC; 9/mm^3, RBC: 12/ mm^3, Protein: 0.34g/L, Glucose: 3.3mmol/L). CSF studies including latex(bacterial antigen) agglutination, gram stain & culture,HSV/ Enterovirus (EV) PCR, Cryptococcus antigen, AFB smear & culture, CSF globulin were negative.

Liver function tests (LFT) were deranged (Totalbilirubin:50 umol/L, direct bilirubin: 36umol/ L, Albumin:24g/L, ALT:230U/L, AST:112U/L, GGT:1155 U/L. LDH:1596U/L, CRP:19mg/L, ESR:40mm/hr, serum ferritin 9174ug/l (significantly raised), serum triglycerides 0.8mmol/ L,lupus anticoagulant not demonstrated, complement levels were mildly raised (C3 1.45, C4 0.48 G/L), Anti NMDAR receptor antibodies (csf /blood) not detected, DCT positive anemia (Hb: 9.1g/dl). Skin biopsy of rash showed necrotic epidermis with features of interface dermatitis. MRI/MRA brain was normal.

Child was diagnosed with Kikuchi's disease with multisystem involvement (aseptic meningitis, raised liver transaminases, DCT positive anemia, and interface dermatitis) and treated with intravenousmethylprednisolone (3days) & antibiotics, followed by oral steroids and antibiotics on discharge.

Child has remained well and LFT's and anemia improved on subsequent clinic visits. He will continue to be monitored closely for the next few years for any evolving symptoms of SLE orany other autoimmune disorder.

Discussion

KFD patients can suffer classic symptoms, which include fe-ver, fatigue, and cervical lymph node enlargement and can also have unusual presentation, such as axillary and inguinal lymph node enlargement, skin rash, arthralgia, splenomegaly, and aseptic meningitis. KD can even be complicated with fatal outcomes like disseminated intravascular coagulopathy (DIC), and pulmonary hemorrhage [4].

The aetiology of Kikuchi's disease is unknown, although a viral, genetic and an autoimmune hypothesis have been proposed. Several infectious agents have been implicated, including Epstein-Barr virus, human herpes virus 6, human immunodeficiency virus, HTLV 1, herpes simplex virus, hepatitis B, dengue virus, parvovirus B 19, Yersinia enterocolitica, Bartonella, Brucella and Toxoplasma organisms [3].

Maria L et al [5] reported a case of a 14 year old boy presenting with severe systemic manifestations(fever up to 39.8°C for 1 week, malaise, odynophagia, arthralgia, myalgia, abdominal pain, and pruritic skin eruption , several multiple peripheral cervical, axillary, and inguinal adenopathies, hepato-splenomegaly and erythematous, flat-tipped papules on the face, back, and extremities) diagnosed with kikuchi disease (on lymph node biopsy) and treated empirically with corticoids (intravenous methylprednisolone) and antituberculosis drugs (INH, rifampicin, pyrazinamide) while awaiting definitive microbiologic test results, who developed transient fulminant hepatic failure in response antituberculous drugs.

Paradela S et al [6] reported a case of a 17-year-old woman with KFD (diagnosed on a lymph node biopsy), whoa month later developed an erythemato edematous rash on her upper body, with skin biopsy showinginterfacedermatitis. After 8 months, anti-

nuclear antibodies (ANA) at titre 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, haemolytic anaemia and lupus nephritis). This histopathological finding of interface dermatitis not previously considered significant, might be a marker of evolution into SLE.

Khishfe BF 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. 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 tuberculosis, CMV disease, toxoplasmosis, systemic lupus erythematosus (SLE), malignancy and kawasaki disease [1].

Diagnosis of Kikuchi's disease is confirmed by lymph node biopsy showing histiocytic necrotizing lymphadenitis. Systemic lupus erythematosus (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. Featuresthat favour Kikuchi's disease include predominanceof CD8 + cells, absence of neutrophils, and a relativepaucity 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 se-vere symptoms usually respond to steroids. Immunosuppressants have been recommended for complicated case to pre-vent fatal outcome [4].

Miri 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 a 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 fullblown SLE. Kikuchi's disease can also precede or coincide with the diagnosis of SLE, and SLE should always be excluded in patients presenting with necrotising 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

Symptoms of Kikuchi's disease can be very distressing to the patient, especially the lingering fever and fatigue. It is important for pathologists and clinicians to be aware of this possibility, especially when dealing with young female patient with fever and cervical lymphadenopathy.

Early recognition of Kikuchi's disease will minimize potentially harmful and unnecessary evaluations and thus prevent misdiagnosis and inappropriate treatment. We can thereby avoid laborious investigations for infectious and lymphoproliferative disorders.

References

1. Henry M. Feder, Jinli Liu, William N. Rezuke. Kikuchi disease in Connecticut. The Journal of Pediatrics 2014; 164:196-200.
2. Babu N Chaitanya, Sindura CS. Kikuchi's disease. Journal of Oral and MaxillofacialPathology. 2010; 14(1):6-9.
3. Kaur S, Mahajan R, Jain NP, Sood N, Chhabra S. Kikuchi's disease—A rare cause oflymphadenopathy and fever. J Assoc Physicians India. 2014; 62(1):54-7.
4. Miri Hyun, In Tae So, Hyun Ah Kim, Hyera Jung, and Seong-Yeol Ryu. Recurrent Kikuchi's disease treated by Hydroxychloroquine. Infect Chemother 2016; 48(2):127-131.
5. Maria L. Murga Sierra, Eva Vegas, Javier E. Blanco-González, Maria A. Calero. Kikuchi'sDisease with multisystemic involvement and adverse reaction to drugs. Pediatrics 1999; 104(2):e24.
6. Paradela S, Lorenzo J, Martínez-Gómez W, Yebra-Pimentel T, Valbuena L, Fonseca E.Interface dermatitis in skin lesions of Kikuchi-Fujimoto's disease: A histopathological marker of evolution into systemic lupus erythematosus? Lupus. 2008; 17(12): 1127-35.
7. Khishfe BF, Krass LM, Nordquist EK. Kikuchi disease presenting with aseptic meningitis.Am J Emerg Med. 2014; 32(10):1298.e1-2.

8. Cheng CY, Sheng WH, Lo YC, Chung CS, Chen YC, Chang SC. Clinical presentations, laboratory results and outcomes of patients with Kikuchi's disease. J Microbiol Immunol infect. 2010; 43(5):366-71.