Histiocytic necrotizing lymphadenitis, Kikuchi-Fujimoto’s disease, associated with systemic lupus erythematosus


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Summary

Histiocytic necrotizing lymphadenitis, Kikuchi-Fujimoto’s Disease (KFD), is a condition rarely associated with systemic lupus erythematosus (SLE). The diagnosis of KFD can precede, postdate or coincide with the diagnosis of SLE. Lymphadenopathy is a common clinical presentation of KFD and SLE, and is histologically indistinguishable in both conditions. We describe two cases of KFD associated with SLE. The diagnosis of KFD in one case was made several years before the diagnosis of SLE, and the other was simultaneous. Both showed large lymphadenopathy, but neither fever nor neutropenia. Lymph-node biopsy showed necrosis, with proliferation of histiocytes and immunoblasts, paucity of neutrophils and absence of hemathoxilin bodies. Both patients responded favourably to steroid treatment. Patients with KFD should be assessed for SLE and have long-term follow-up checking for development of SLE. KFD should be ruled out in SLE flare-up accompanied by lymphadenopathy.

Introduction

Histiocytic necrotizing lymphadenitis, Kikuchi-Fujimoto Disease (KFD), is a rare self-limiting condition characterized by lymphadenopathy, fever and neutropenia.1 The aetiology of KFD is controversial,2–4 and its diagnosis is confirmed histologically.1,5 Although KFD has rarely been reported associated to SLE, KFD should be ruled out given its different prognosis and management. KFD has been reported over the last decade in Western countries, with varying characteristics.1–5 We describe clinical and biopsy findings in two cases of KFD associated to SLE; and review previous KFD-SLE cases in the literature.

Case reports

Patient 1

A 27-year-old White woman was admitted with a history of malaise and large cervical lymphadenopathy. She had been diagnosed as having SLE 7 years earlier, based on the presence of photosensitivity, discoid lupus, large symmetric joint arthritis, leucopaenia, positive ANA and positive anti-DNA. A non-specific lymphadenitis was reported on a lymph-node biopsy. She responded favourably to steroid treatment, and ANA and anti-DNA became negative.

On admission, the patient complained of malaise, nausea and vomiting. On physical examination, vital signs were normal. Photosensitivity, and large and tender cervical lymphadenopathy were noted. Laboratory tests revealed normal blood cell count, ESR 60 mm/h, and serum LDH 547 U/l (normal 230–460). Serum ANA was negative and serum C3 and C4 were normal. Serum serology for Epstein-Barr virus, cytomegalovirus (CMV) and toxoplasma were positive for chronic infection. Lymph-node biopsy showed effacement of nodal architecture, abundant foci of necrosis with marked karyorrhexis; aggregates of plasmocytoid monocytes and...
histiocytes with phagocytic activity. Scattered neutrophils and absence of haemathoxilin bodies were reported. A comprehensive investigation for mycobacteria was negative. The patient had clinical improvement on oral methylprednisolone 1 mg/kg, and the cervical lymphadenopathy disappeared. On follow-up, the patient showed relapse of cervical lymphadenopathy, photosensitivity and arthralgia, with good response to prednisone and hydrochloroquine.

Patient 2

A 27-year-old male patient was transferred to our Lupus and Arthritis Unit with night sweats, weight loss and lymphadenopathy. Thrombocytopenia, positive ANA and anti-DNA were reported. A lymph-node biopsy was reported as a questionable lymphoma.

On admission, he complained of night sweats and weight loss for 2 months. Vital signs were normal. Large cervical, axillary and inguinal lymphadenopathy were present. Laboratory studies revealed normal CBC and chemical tests except a mild thrombocytopenia. Serum ANA was 1/243 (normal 70–160) and serum C3 and C4 were normal. Serology for hepatitis B and C viruses was negative. Toxoplasma, CAN and Epstein-Barr virus were positive for a chronic infection. A lymph-node biopsy showed massive coagulative necrosis and frequent karyorrhexis. Marked aggregation of immunoblasts and histiocytes with eccentrically crescentic nuclei and phagocytic activity was noted. Neutrophils were few, and haemathoxilin bodies were absent. A stain for acid-fast bacilli was negative. In the next few days, the patient developed progressive anaemia and thrombocytopenia. A direct Coombs test was negative and a bone-marrow biopsy was normal. Clinical improvement was noted on prednisolone 1 mg/kg/day, and the anaemia and thrombocytopenia disappeared. Six months later, the patient was asymptomatic on prednisolone 15 mg/day

Discussion

Clinical and pathological results of these two patients support the association of KFD and SLE. Only 17 cases of KFD have been reported as associated with SLE worldwide.1–16 KFD diagnosis can be prior, simultaneous or after the diagnosis of SLE.1 KFD has been considered as SLE-like, caused by an strong immunological response to a viral antigen.17 Unfortunately, repeated efforts have failed to show any relationship with Epstein-Barr virus and Herpes virus 6.4,5

Histologically, the two conditions have been considered indistinguishable.5 Lymphadenitis in patients with SLE is characterized by prominent necrosis similar to that described in patients with KFD.1 Haemathoxilin bodies are a typical finding in SLE.5,13 Similar to our previous report,18 haemathoxilin bodies were absent in these two patients with KFD and SLE. The presence of coagulative necrosis, paracortical necrotizing nodules, proliferation of histiocytes and immunoblasts, and absence or paucity of neutrophils confirm the diagnosis of KFD.1,19 Finally, the diagnosis cannot always be ruled out histologically, thus patients should have a long-term follow-up.

KFD and SLE are conditions with different management and prognosis. Our cases showed atypical clinical presentation compared with patients with KFD alone.16 Fever was absent, and lymphadenopathy disappeared only after steroid treatment. Neutropenia occurs in almost half of the patients with KFD, and few go on to have SLE, so neutropenia does not seem to be a marker of this progression, as has been suggested.8 Similarly to previous reports of KFD,1,5 neutropenia was absent in our two cases. We considered lymph-node biopsy with examination by expert pathologists as the procedure of choice to confirm the diagnosis of KFD associated to SLE.1,3,8–13 The favourable response to steroids in our cases and in previous reports, support steroids as the appropriate treatment. Patients with KFD should be assessed for SLE and have a long-term follow-up considering possible onset of SLE. KFD should be ruled out in SLE flare-up accompanied by lymphadenopathy.

References

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