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Case Report

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Kikuchi–Fujimoto disease associated with systemic lupus erythematosus

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Abstract
A cervical lymph node biopsy from a 38-year-old woman initially revealed necrotising lymphadenitis. Her case is presented herein. An exhaustive examination that included renal biopsy did not suggest systemic lupus erythematosus (SLE). She was diagnosed with Kikuchi–Fujimoto Disease (KFD) and was treated with prednisone. One year later, a renal biopsy performed for renal failure revealed Class IV SLE. It was proposed that lymphadenitis in this KFD patient should be considered as SLE so that the SLE would be properly treated. In our patient, this hypothesis was partially correct, because even though SLE could not be verified at initial presentation, it evolved into full SLE after a year interval.

Keywords: Kikuchi–Fujimoto disease; lymph node biopsy; renal biopsy; SLE

Background

Kikuchi–Fujimoto disease (KFD), or histiocytic necrotising lymphadenitis, is a benign and self-limiting condition, which usually affects females under the age of 30 years. KFD was first described in Japan in 1972 [1, 2]. The aetiology is unknown, although a viral or autoimmune pathogenesis has been suggested. A possible relationship between KFD and systemic lupus erythematosus (SLE) has been investigated but it appears complex and is not completely understood. Previous reports indicate that SLE may be dormant in KFD patients, that it may develop along with KFD or that it may develop after the clinical appearance of KFD [3]. Pathological similarities between lymphadenopathy of KFD and SLE have led to speculation that KFD is an SLE-like autoimmune disease [4].

Case-report

A woman aged 38 years presented with a history of fever, major and minor joint pains, oral ulcers, ulcers over the upper back and hair loss over a period of 2 months. During the previous 5 days, she experienced swelling of the feet and face, oliguria and breathlessness. She was not diabetic. On examination, she was found to be anaemic and oedematous and had a blood pressure of 180/100 mmHg, a pulse rate of 110 bpm, and left ventricular S3 present with bilateral diffuse crackles. Other clinical findings are given in Table 1. After two haemodialysis sessions, a renal biopsy was performed.

A year previous to admission, she had complaints of joint pains, fever and maculopapular rash on the face. She had been examined by a physician elsewhere. A fine needle aspiration cytology of the cervical lymph nodes was performed, but the findings were not made available. She was started on antituberculous therapy. She discontinued the medication after 3 months because there was no reduction in the size of the lymph nodes or rash. At our institute, a cervical lymph node biopsy was performed in addition to other investigations. These results are also shown in Table 1.

Because none of these features were suggestive of lymph node tuberculosis or fulfilled American Rheumatism Association criteria for the diagnosis of SLE, she was diagnosed with KFD. Within 2 weeks of oral prednisolone administration (1 mg/kg/day), the rash disappeared and both joint pains and fever subsided. She received the prednisolone for 8 weeks and was reduced to a maintenance dose of 10 mg/day.

More recently, she was initiated on three doses of injected methyl prednisolone (15 mg/kg/day) on successive days followed by injection of cyclophosphamide (500 mg/m^2). She has completed six monthly doses of cyclophosphamide. Her present serum creatinine is 1.2 mg/dL and 24 h urine protein is 124 mg.

Discussion

KFD is histopathologically characterized by a patchy necrotising process in paracortical areas of the lymph node. The necrotising process comprises circumscribed areas of

Table 1 Investigations[a]

Measurement	At admission	1 year before admission
Blood urea (mg/dL)	92 → 107 → 125	49
Serum creatinine (mg/dL)	3.4 → 4.8 → 6.3	1.2
Serum proteins (g/dL)	4.8	5.8
Serum albumin (g/dL)	2.5	3.5
C3 (reference range: 55–120 mg/dL)	38	74
C4 (reference range: 10–40 mg/dL)	13	23
Haemoglobin (g/dL)	7.3	6.2
Ultrasound abdomen	RK: 9.4 × 4.3 cm; LK: 9.5 × 4.2 cm	RK: 9.6 × 4.2 cm; LK: 9.4 × 4.8 cm
Urine examination		
Albumin	1+	Trace
Sugar	Nil	Nil
RBC (/hpf)	15–20 (/hpf), RBC cast 10–12 (/hpf)	1–2
WBC (/hpf)		20–25
24 h urine protein (mg)	475	128
ANA and anti-dsDNA	Positive	Negative
Montoux with 5 TU	Not done	Negative
Skin biopsy	Not done	Normal study
Lymph node biopsy	Not done	Necrotising lymphadenitis, no acid fast bacilli (Figure 1)
Renal biopsy	14 glomeruli. Mesangial cellularity increased. Neutrophilia present. Wire loop lesions were noted. Capillary lumina showed hyaline thrombi. Interstitium showed neutrophilic infiltrate. There was 'full house' pattern on immunofluorescence. Impression: SLE Class IV. (Figure 2)	11 glomeruli, normal study

[a]RBC, Red blood cells; WBC, white blood cells; RK, right kidney; LK, left kidney.

eosinophilic fibrinoid material associated with karyorrhexis. Fragments of nuclear debris ('nuclear dust') are distributed irregularly throughout these areas of necrosis and are associated with the presence of apparently atypical mononuclear cells. Foamy histiocytes are present in a majority of patients and are prominent around the foci of necrosis. A consistent histologic feature of these lymphnodes is the absence of granulocytes and paucity of plasma cells [5]. The lymphadenitis of SLE is differentiated by the prominent presence of plasma cells; haematoxyphillic bodies are aggregated towards the edges of the necrotising areas often in sinuses, and the necrosis tends to be seen as extensive areas of acellular necrosis, devoid of viable cells or nuclear dust. There is a similar lack of granulocytes in SLE lymphadenitis.

Hu *et al.* [4] suggested that the lymphadenitis that coexists with SLE should be regarded as lupus lymphadenitis, especially when it is of the necrotising type, so that diagnosis of the underlying SLE will not be overlooked. In their study, Hu *et al.* [4] analysed 18 patients having KFD-like lymphadenitis and found that KFD did not always occur simultaneously with SLE. There were 10 patients that had KFD coexisting with SLE, and they most likely had lymphadenitis due to SLE rather than to KFD.

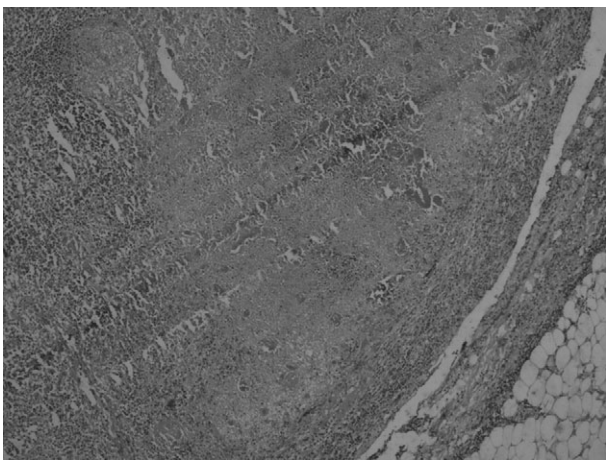

Fig. 1. Lymph node biopsy (×40): necrotic area with karyorrhexis.

In another analysis of 244 patients, 32 (13%) KFD patients had SLE [6]. Of these, 56% had both KFD and SLE together, 19% developed SLE later, 12% had a previous diagnosis of SLE and 12% did not fulfil criteria for the

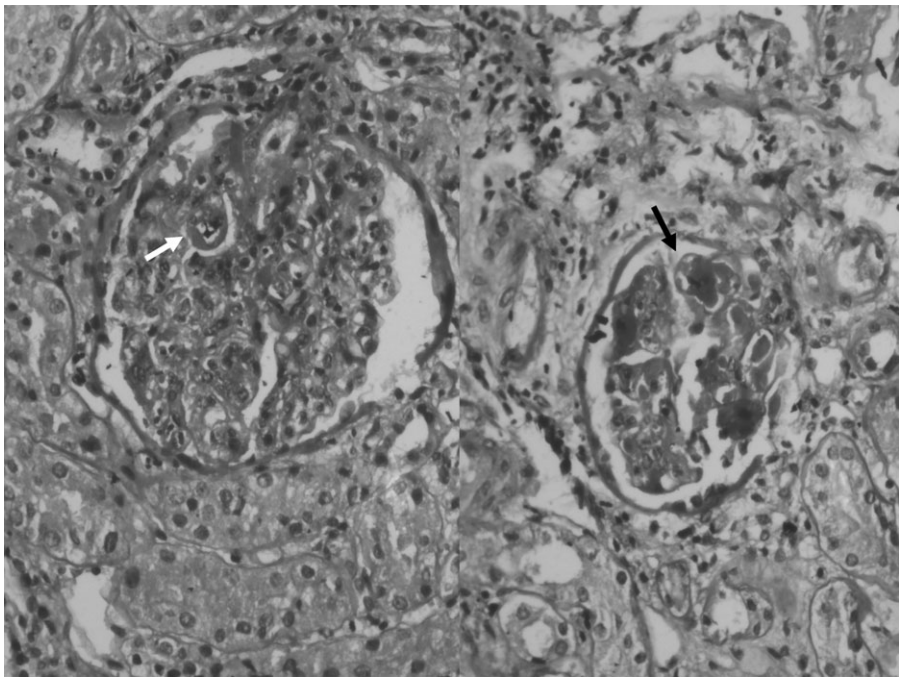

Fig. 2. Renal biopsy: diffuse proliferative glomerulonephritis wire loop lesion (white arrow) and hyaline thrombi (black arrow).

definition of SLE and were designated as incomplete SLE. In a large study examining KFD patients, the frequency of suspected SLE cases was 5 of 108 [5].

We have diagnosed eight KFD patients at our institute during the last 3 years. The mean age of this cohort was 20.3 years (range: 13–42 years), and there were six females. Diagnosis in all patients was achieved through lymph node biopsy. In all patients, antinuclear antibody (ANA) and anti dsDNA was negative. Renal biopsies were not performed in these patients. All were successfully treated with steroids (K. P. Adiraju, S. Vangipurapu Rangacharlu, unpublished results). Other reports also from India have shown similar findings [7, 8].

In the patient described in this report, the initial lymph node biopsy suggested KFD; however, subsequent investigations of anti-dsDNA and complement levels were not suggestive of SLE. The renal biopsy was also normal. After a year, the second renal biopsy had confirmed SLE. The anti-dsDNA and ANA were positive. C3 and C4 levels were low. It has been suggested [9] that lymphadenitis in KFD patients should be considered as part of SLE so that the SLE would be properly treated. In our patient, this hypothesis was partially correct because even though SLE could not be verified at initial presentation, it evolved into full SLE after a year interval.

Supplementary data

Supplementary Table is available online at http://ndt.oxfordjournals.org/.

Conflict of interest statement. None declared.

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