CASE REPORT

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Necrotising Lymphadenitis in a Rare Overlap of SLE with Ankylosing Spondylitis

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Key words: Systemic lupus erythematosus, Kikuchi's disease, Necrotising lymphadenitis.

Introduction

Lymphadenopathy results from reticulo-endothelial cell proliferation secondary to infection, autoimmunity, or malignancies. Getting a necrotising lymph node in a back ground of Disease Modifying Antirheumatic Drugs (DMARDs) therapy, tuberculosis is most likely. We are presenting a case report of a patient with a rare overlap of Ankylosing spondylitis (AS) and Systemic Lupus Erythematosus (SLE) presenting with a necrotising lymph node.

Case presentation

A 16-year-old female presented with fever for 3 months and persistent headache. Fever was moderate to high grade and was associated with anorexia and weight loss. She also gave a history of recurrent oral ulcers. On examination, she had bilateral cervical lymphadenopathy involving the posterior triangles, which were non tender, firm in consistency, and surface temperature was normal. Apart from lymphadenopathy, there was mild hepatosplenomegaly. There was no sternal tenderness or any bleeding manifestation. Her sensorium was normal and there was no neurological deficit. Fundus examination revealed grade 1 papilloedema.

In the past (nine years ago) she had been diagnosed as Ankylosing Spondylitis (AS) for her backache, bilateral sacroiliac joint involvement, positive HLA B 27 and family history. She was on Sulfasalazine for the same.

Her haemogram revealed leukopenia and thrombocytopenia. Her renal and liver function tests (including Prothrombin time) were normal. Her albumin was low and globulin was high suggesting a chronic inflammatory state. Inflammatory markers were found to be elevated (Erythrocyte sedimentation rate was 106 mm in first hour and ferritin was 3,455 ng/ml). But Procalcitonin and C-reactive protein was low. Mantoux test was negative and serology for HIV was non-reactive. Blood and urine cultures were sterile and Brucella serology was negative. Her chest X-ray was normal. A contrast-enhanced CT was done which revealed mediastinal, cervical, axillary, retroperitoneal and iliac lymphadenopathy with hepatosplenomegaly, but no focal lesion in the lung parenchyma, no fluid collection in serosa or bowel thickening (Fig. 1). Radiological diagnosis was lymphoma. MRI brain showed hyperintensity in bilateral thalamoganglionic regions, mesial temporal lobe and subtle cortical gyral hyperintensity with minimal post-contrast enhancement. CSF revealed mildly elevated protein (95 mg/dl), normal sugar and mild lymphocytosis pleocytosis (35 cells, 95% lymphocyte) and Viral panel and TB PCR were negative in CSF, thereby suggesting sterile meningitis.

A lymph node biopsy was done and she was put on intravenous antibiotics but there was no improvement in the fever pattern even after two weeks. The work-up for multisystem involvement revealed ANA to be elevated (1:1000, speckled pattern) with high titre of anti ds DNA, anti Smith antibody and low C3 and C4 level. Her urine examination was unremarkable and proteinuria was 120 mg/day. Based on clinical and immunological evidence, the patient fulfilled the 2012 SLICC criteria for the diagnosis of SLE. A diagnosis of SLE with high disease activity with

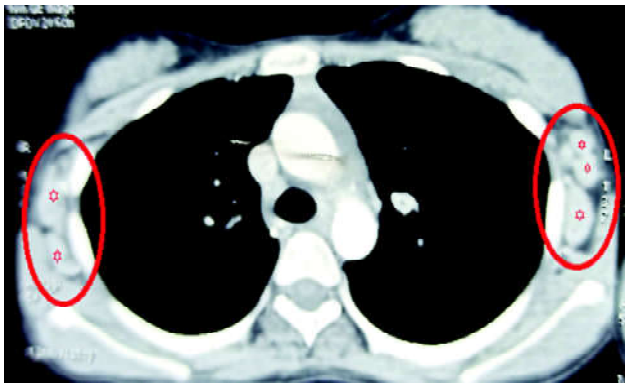

Fig. 1: *Contrast-enhanced CT showing heterogeneously enhancing bilateral axillary lympadenopathy. Largest LN 3.8 cm in the left axilla.*

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haematological, mucocutaneous, musculoskeletal and neurological involvement was made.

Biopsy report revealed necrotizing lymphadenitis with epithelioid histiocytosis with no architectural distortion (ruling-out lymphoma). And also the associated likelihood of Kikuchi's disease in a background of SLE needed to be looked in. Detailed review suggested foci of necrosis within the LN with numerous karyorrhexic bodies, fibrin deposits surrounded by Histiocytes which were CD 68 positive (Fig. 2) and lymphocytes predominantly CD 8 and few CD 4 cells, with absence of neutrophils and eosinophils. There was no caseation, no granuloma, nor any giant cell aggregation (thereby ruling-out TB). There was presence of Haematoxylin bodies (Fig. 3) and cells were negative for CD 30 marker ruling out KFD in a background of SLE (Fig. 4). Hence a final diagnosis of SLE lymphadenitis was made.

Accordingly, we gave her Methylprednisolone pulse therapy

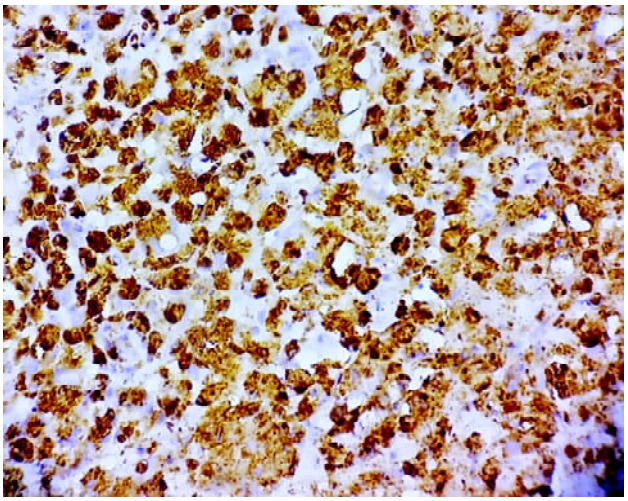

Fig. 2: *Cells stains with CD 68 marker suggesting presence of Histiocytes.*

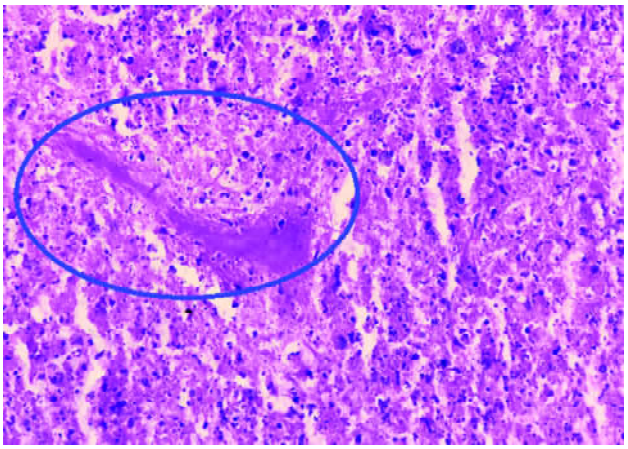

Fig. 3: *Showing high power view of LN biopsy. The encircled area marked above shows Haematoxylin bodies.*

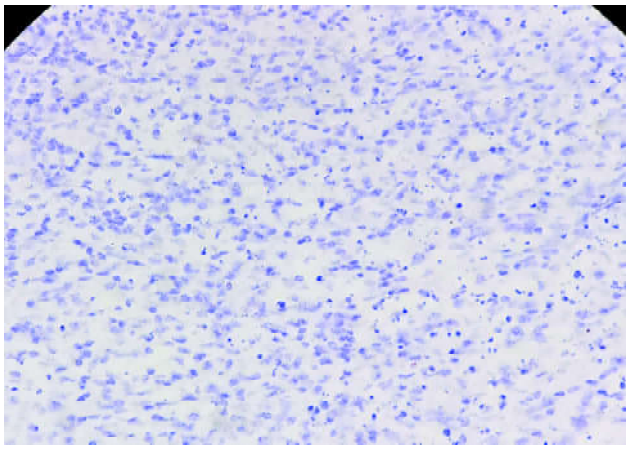

Fig. 4: *CD 30 marker is negative thus ruling-out KFD.*

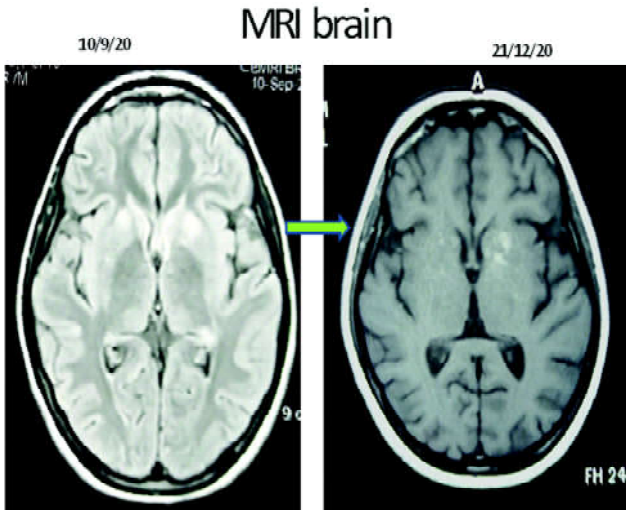

Fig. 5: *Showing comparison between the images of two MRI of brain at the level of Basal ganglia. The left side image (10.09.2020) is showing hyper-intensity in the ganglio-thalamic region bilaterally. The right side image (21.12.2020) is showing normal intensity with some residual changes in the left caudate nucleus.*

(1 g intravenous for 3 days) followed by oral prednisolone 1 mg/kg/d for one month and then tapered off. She dramatically responded to it with regression of the lymphadenopathy and fever. Her biochemical reports and MRI brain (Fig. 5) also showed marked improvement. Hydroxychloroquine was added. She showed no signs of relapse till reporting this case.

Discussion

Lupus lymphadenopathy has an estimated prevalence of 12 to 59%[1]. But, it rarely is an initial manifestation of SLE (5 - 7% at the onset). Usually it involves the cervical and axillary region. Rarely, mediastinal and retroperitoneal involvement may occur in a fulminant form of the disease. Lymph nodes (LNs) are soft, mobile, painful, and non-adherent to the

deep planes. Biopsy commonly shows reactive follicular hyperplasia which is a non-specific finding. Coagulative necrosis with haematoxylin bodies (condensed complexes of DNA and anti dsDNA antibodies) are typical findings in SLE, but it is rarely seen[2]. There is always an increased risk of lymphomas, especially non- Hodgkin's lymphoma in lupus patients that should be kept in mind while approaching such patients[3].

KFD is a rare entity, also termed as histiocytic necrotizing lymphadenitis. It is a disease of young people, predominantly females, of Asian descent. KFD generally presents with lymphadenopathy (localised – especially cervical, or generalised), organomegaly and constitutional symptoms. Diagnosis is made by LN biopsy. The disease is self-limiting. It usually takes 4 - 6 months. Treatment is of supportive care. However, corticosteroids are of benefit in severe or relapsing disease.

Review of the literature from 1991 onwards indicates that SLE predominantly predates or concurs with KFD[4]. An autoimmune origin with an infectious trigger of viruses has been suspected as aetiology of KFD. A strong autoimmune link with SLE has been implicated. A positive ANA has been found to be associated with a high chance of relapse. There is a significant overlap between pathomorphological features of KFD and lupus lymphadenitis. Pathognomonic feature of SLE being the presence of haematoxylin bodies that are condensed complexes of DNA and anti-dsDNA-antibodies, but it is very difficult to identify. Some of the studies documented that CD 30 cells are increased more in KFD than SLE that might also help them to separate[5]. Cramer *et al* in their report suggested that KFD may be a histopathologic alternative form of lupus lymphadenitis representing a '*forme fruste*' rather than being an independent disease entity[6]. Lupus lymphadenitis and KFD could in fact belong to the same entity. It is possible that the factors that induce lymph node proliferation are also responsible for the development of auto-antibodies. KFD should be a differential in SLE patients with necrotizing lymphadenopathy, due to its benignity and self limitedness.

In the present case, patient was on follow-up for AS and was on DMARDs – Sulfasalazine. In the light of necrotizing lymphadenopathy and background of DMARDs intake, secondary infection like tuberculosis was more a possibility. But during work-up, patients was found to have SLE (due to haematologlical, mucocutaneous, musculoskeletal, and neurologic involvement along with ANA positivity) as overlapping disease. The overlap of SLE with AS is very rare and only ten cases have been reported in the literature till date[7].

References

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