Case Report:

Disseminated tuberculosis in a patient with systemic lupus erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder. Intercurrent infections and nephritis are important causes of mortality in SLE. Among infections, tuberculosis (TB) is of particular importance as SLE patients are more susceptible to develop active TB, prior TB can precipitate SLE in genetically susceptible individuals and similar clinical presentations of SLE flare and TB may lead to delayed diagnosis. We report a patient with SLE, who developed disseminated TB. The present case highlights the importance of a high index of suspicion and focussed evaluation in the diagnosis of intercurrent infections, particularly TB in patients with SLE

Key words: *Systemic lupus erythematosus, Disseminated tuberculosis*

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INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune systemic disorder of unknown cause with various manifestations involving multiple organ systems. Infections and nephritis are major causes of mortality in SLE.[1] They are more prone to infections because of immunosupression due to several factors intrinsic to SLE and immunosuppressive treatment.[2] Among infections, tuberculosis (TB) has special importance in patients with SLE. Not only SLE patients are more prone to develop active TB,[3] in genetically predisposed individuals TB can precipitate SLE.[4] Furthermore, as the clinical presentation of TB and SLE flare overlap with each other, the diagnosis of TB in SLE patients is challenging and delayed.[2,5]

CASE REPORT

A 19-year-old unmarried female student presented to Medicine out-patient service at our tertiary care teaching hospital in south India with chief complaints of fever for the past 6 months and breathlessness on exertion for the past 3 months. She was apparently well 6 months back when she noticed the occurrence of low grade fever with evening rise of temperature associated with generalized weakness and myalgias. She complained of exertional breathlessness for the past 3 months, which was insidious in onset and was gradually progressive. There was no history of paroxysmal nocturnal dyspnoea, orthopnoea,wheeze, chest pain, or syncope. She complained of progressive swelling of both lower limbs for the past 1 month that was more obvious by the evening. She also complained of weight loss of 5 kg and loss of appetite over the last one month. There was no history of rash, joint pain/swelling, alopecia, nasal/oral ulcers, parotid swelling, dysphagia, xerostomia, digital ulcers, claudication pain, or Raynaud's phenomenon. She did not travel recently and there was no contact with ill persons and pets.

At the time of initial evaluation, she was conscious and coherent. Her body mass index (BMI, kg/m^2) was 18. She was febrile, sinus tachycardia was evident (heart rate 120 beats/ min). Physical examination revealed pallor, bilateral pitting pedal oedema, firm, painless, mobile, enlarged right cervical and left axillary lymphadenopathy measuring 2×2 cm. Abdominal examination revealed tender hepatomegaly, palpable 3 cm below the right costal margin in mid-clavicular line; spleen was

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not palpable. Examination of cardiovascular, respiratory, nervous systems and rest of the physical examination was unremarkable.

Laboratory investigations revealed: haemoglobin 7.4 g/dL, mean corpuscular volume 72 fL, peripheral blood smear revealed a microcytic hypochromic blood picture and neutrophilic leukocytosis. Erythrocyte sedimentation rate (ESR) was elevated (120 mm at the end of first hour; Westergren method). Serum biochemistry including liver, renal functional tests; urinalysis were within normal limits. Quantitative buffy coat (QBC) test for malarial parasite was negative. Serologic tests for human immunodeficiency virus (HIV), hepatitis B and C viruses, leptospirosis, scrub typhus and dengue fever were negative. Serum iron levels (38 µg/dL) were low; serum ferritin was elevated (410 ng/mL). Blood and urine cultures were sterile. Chest radiograph showed cardiomegaly (Figure 1), 2D-echocardiography showed mild pericardial effusion; ultrasonography of abdomen showed hepatomegaly (liver span 17 cm).Computed tomography (CT) of the chest showed pericardial effusion (Figure 2) and calcified sub-centimetre right paratracheal and pre-vascular mediastinal lymphadenopathy (Figure 3). Fine needle aspiration cytology (FNAC) from the right cervical lymph node and excision biopsy of the left axillary lymphnode biopsy revealed reactive lymphoid hyperplasia. Serological tests for rheumatoid factor, anti cyclic citrullinated protein were negative, anti-nuclear antibody (ANA), anti-double stranded deoxyribonucleic acid (dsDNA); anti-cardiolipin antibody were positive by enzyme linked immunosorbent assay (ELISA). The ANA profile was positive for anti-Smith (Sm) antibody.

The patient was diagnosed to have systemic lupus erythematosus (SLE) and was started on oral prednisolone (0.75 mg/kg body weight). At 2-months follow-up, she was afebrile, generalized weakness subsided, and the haemoglobin had increased to 9.6 g/dL; tapering of prednisolone was initiated. Two months later, she again presented to medicine out-patient service with low grade fever, dry cough and generalized weakness of 10 days duration. Investigations revealed normocytic normochromic anaemia (haemoglobin10.4 g/dL), neutrophilic leukocytosis, raised ESR (56mm at the end of first hour). Biochemical tests including liver, renal functional tests;

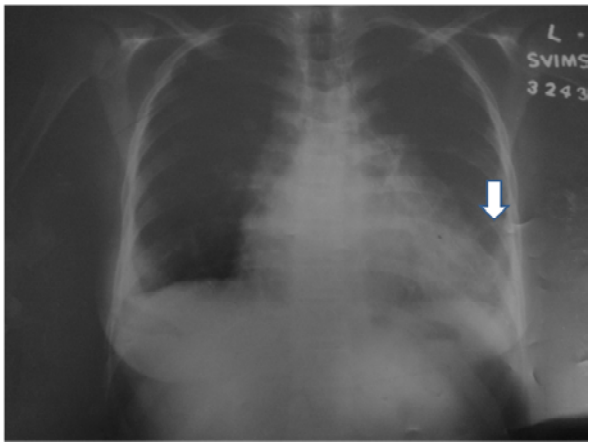

Figure 1: Chest radiograph (postero-anterior view) showing fibrotic bands in left middle and lower zones (arrows) and cardiomegaly

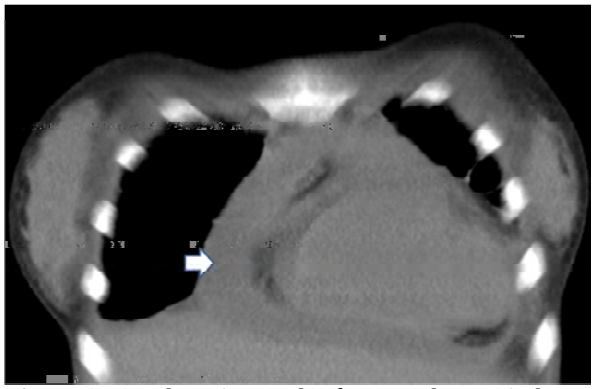

Figure 2: CT chest (coronal reformatted image) showing pericardial effusion (arrows)

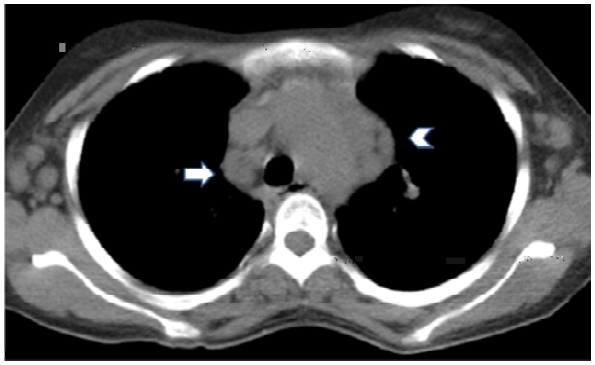

Figure 3: NCCT chest (axial image) showing bilateral axillary, sub-centimeter right paratracheal (arrows) and pre-vascular (arrow-head) lymphadenopathy

urinalysis were within normal limits. QBC test for malarial parasite was negative. Sputum did not reveal acid-fast bacilli; sputum and blood culture were sterile. Chest radiograph showed right and left paratracheal and right hilar lymphadenopathy, and left mid-zone consolidation (Figure 4). CT chest (Figure 5) showed right paratracheal lymphadenopathy and increase in the left pre-vascular lymphadenopathy compared to the previous CT done 4 months earlier (Figure 3). Other salient CT chest findings included bilateral hilar lymphadenopathy (Figure 6), bilateral diffuse randomly distributed pulmonary nodular opacities (Figure 7) and hypodense enhancing lesions in right lobe of liver suggestive of abscesses (Figure 8).

In view of increase in the mediastinal lymphnode size, a CT guided FNAC from right paratracheal lymph node was done (Figure 9).

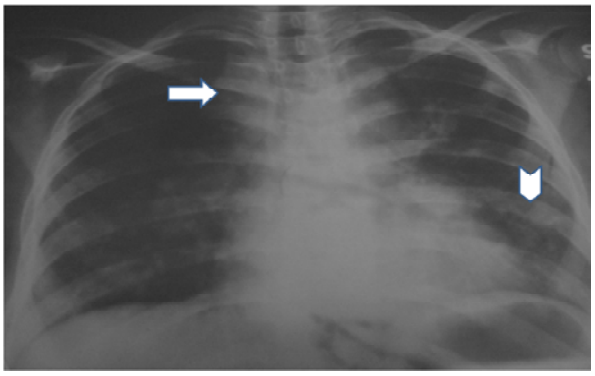

Figure 4: Chest radiograph (postero-anterior view) showing lobulated opacity in right and left paratracheal regions, and right hilar region, suggestive of lymphadenopathy (arrows), non-homogeneous opacity in left mid-zone suggestive of consolidation (arrows head)

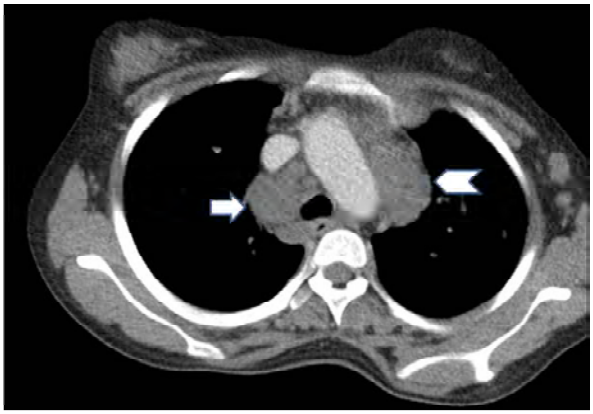

Figure 5: CECT chest (axial image) showing right paratracheal lymphadenopathy (arrow) and increase in the left prevascular lymphadenopathy (arrow-head)

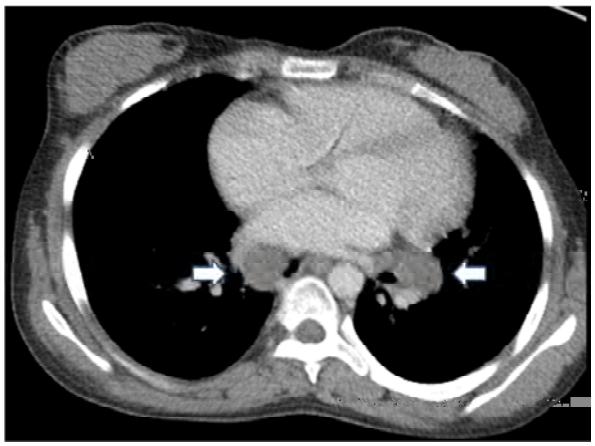

Figure 6: CECT chest (axial image) showing bilateral hilar lymphadenopathy (arrows)

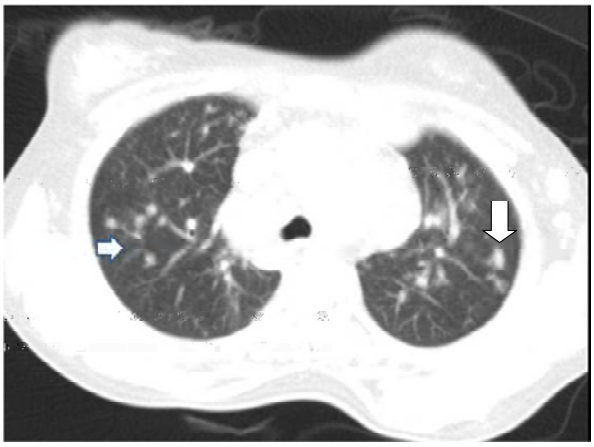

Figure 7: CECT chest (axial image, lung window) showing nodules in bilateral upper lobes (arrows)

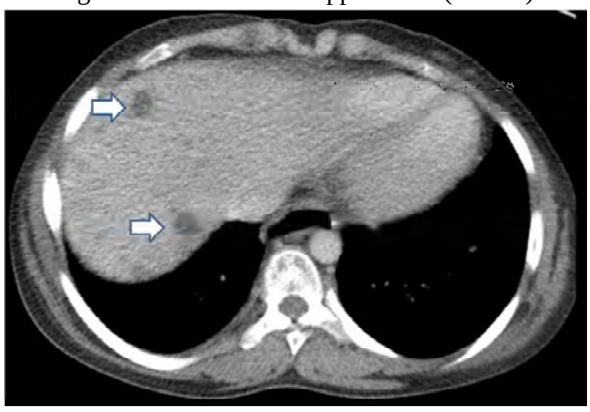

Figure 8: CECT upper abdomen(axial image) showing hypodense enhancing lesions in right lobe of liver suggestive of abscesses (arrows)

Cytological examination showed caseation necrosis with lymphocytes (Figure 10) and a few AFB suggestive of TB lymphadenitis. She was started on thrice-weekly intermittent Category I DOTS antituberculosis treatment as per the Revised National TB Control Programme (RNTCP). The patient became

afebrile after 3 weeks and her generalized weakness improved. On follow up after further 2 months, considerable regression of the mediastinal lymphadenopathy was evident on the chest radiograph and the patient continues to do well on follow-up.

The patient was thus, diagnosed to have SLE with disseminated TB involving lung; hilar, intrathoracic and cervical lymphnodes and possible hepatic TB.

DISCUSSION

SLE is an autoimmune systemic disorder of unknown cause with myriad manifestations involving multiple organ systems. Patients with SLE are prone to develop intercurrent infections because of: (i) compliment deficiency; (ii) mannose binding lectin (MBL) deficiency; (iii) chronic inflammation and tissue damage; and (iv) use of immunosuppressive therapy.[2] TB is a common infection in SLE patients and the prevalence of TB in patients with SLE ranges from 5% - 11.6% in studies reported from India.[6,7] The relation between SLE and TB is complex, intriguing and not yet fully understood. The incidence of TB in SLE patients is considered to be 15-fold higher; extra-pulmonary involvement and disseminated TB are more common; and an increased occurrence of TB in SLE patients who are renal transplant recipients has also been observed.[3,8] TB and SLE share several similar clinical manifestations like fever, constitutional symptoms, cough, breathlessness, chest pain and arthralgias. So, differentiating disease flare from active TB disease in patients with SLE based on clinical manifestations alone remains a challenge.[9]

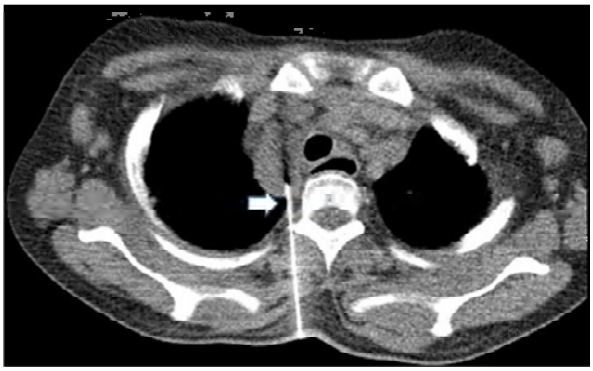

Figure 9: CT guided FNAC of right paratracheal lymph node with needle in-situ (arrows)

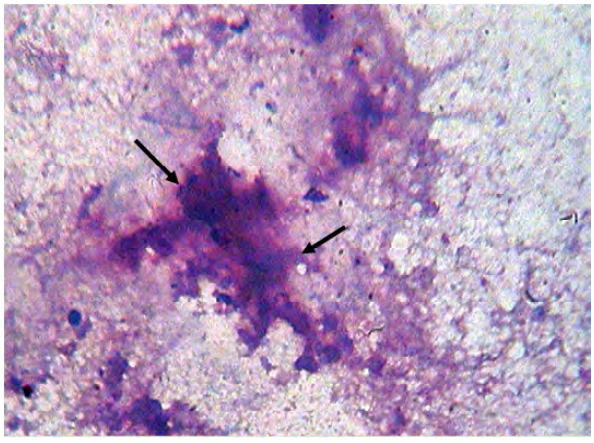

Figure 10: Photomicrograph showing caseation necrosis (arrows) and occasional lymphocytes (Haematoxylin and eosin, × 400))

Several genetic and environmental factors play a role in the causation of SLE. Infections play important role in the expression of SLE in genetically predisposed individuals.[10] Evidence is available suggesting that monoclonal antibodies raised against TB can cross react with DNA,[11] features of autoimmunity are evident in mycobacterium induced arthritis in experimental models,[12] and detection of antibodies in patients with TB similar to that found in SLE.[13] Evidence is also available suggesting that prior TB infection may precipitate SLE in genetically susceptible patients. Ghosh et al[14] reported that prevalence of antecedent TB in patients with SLE to be 21%, i.e., 40 times higher than the prevalence of TB in general population. In a study from Taiwan[4] among 2721 patients with SLE antecedent TB was present in 44 (1.8%) of patients; TB patients were found to have an odds ratio of 2.09 for subsequent development of SLE after controlling for other potential risk factors. Some workers have even advocated isoniazid prophylaxis in patients with SLE receiving long term corticosteroid treatment.[15]

The present case highlights the importance of a high index of suspicion and focussed evaluation in the diagnosis of intercurrent infections, particularly, TB in patients with SLE.

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