CASE REPORT

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Combined Diagnosis of Systemic Lupus Erythematosus (SLE) and Tuberculosis (TB) in a Young Woman

Akanksha Singh, Jyotsana Prasad**, Subodh Kumar Mahto*, Nehal Aggarwal***, AK Malhotra*****

Abstract

Systemic lupus erythematosus (SLE) and tuberculosis present with a myriad of clinical manifestations and thus can mimic each other. The non-specific symptoms like unexplained fever, joint pains, lymphadenopathy, fatiguability, and serositis can be present in both diseases – thus can lead to misdiagnosis. We report a case of a 23-year-old woman who presented with fever, joint pains, recurrent oral ulcers and rash over face. The patient was evaluated and was diagnosed to have both SLE (lupus nephritis) and tubercular lymphadenitis.

Key words: Systemic lupus erythematosus, tuberculosis, extrapulmonary tuberculosis (EPTB).

Introduction

Systemic lupus erythematosus (SLE) is a chronic multisystem autoimmune disease. Tuberculosis (TB) remains one of the commonest infectious diseases globally with an estimated 10.0 million (range, 9.0 - 11.1 million) people diagnosed with TB in 2018[1]. Tuberculosis (TB) is a common infection among patients with SLE. Leading causes for high incidence of TB infection are immunosuppressive therapy and immune disturbances of lupus itself. We report a case of a young woman, who was diagnosed with SLE (lupus nephritis with secondary vasculitis) and TB (tuberculous lymphadenitis) simultaneously, with no prior history of any immunosuppressive therapy.

Case report

A 23-year-old woman presented with low-grade, continuous fever with joints pain and recurrent oral ulcers since 2 months and also rash over face since 1 month. Small and large joints of upper limbs and lower limbs were involved and the distribution of pain was symmetrical bilaterally. There was history of morning stiffness, and pain was inflammatory in nature. There was no history of smoking, alcohol consumption, or prolonged use of steroids or any other drug. The patient's pulse rate and blood pressure was 86/min and 126/82 mm Hg respectively. Pallor was present. Painless oral ulcers were present over the tongue and buccal mucosa. Maculopapular rash was present over the face involving the forehead, base of nose, and malar area (Fig. 1). Papular eruptions were present over the extensor surfaces of forearms (Fig. 2). Blackish discoloration of skin was present over the tip of the left ring finger (Fig. 3). Soft-to-firm, non-tender, non-matted, mobile cervical lymph nodes were present at level Ib, II, III, V on right side. Rest of the general physical and systemic examination was within normal limits.

Laboratory tests revealed haemoglobin of 7.3 gm% and total leukocyte count of 4,300/mm^3 with normal differential count and platelet count. The erythrocyte sedimentation rate was 42 mm/1st hour. Peripheral smear showed normocytic,

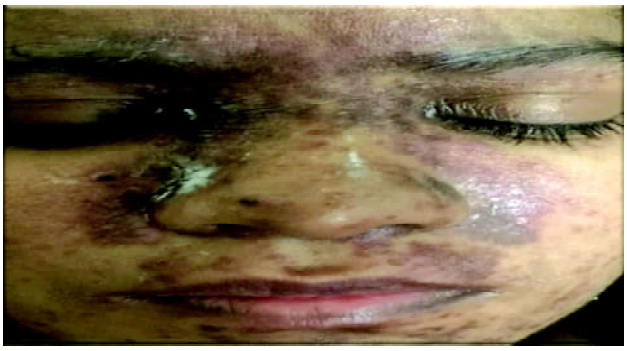

Fig. 1: *Maculo – papular rash present over face involving the forehead, base of nose, and malar area.*

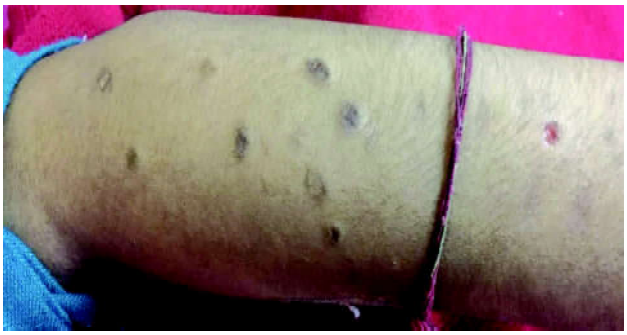

Fig. 2: *Papular eruptions present over the extensor sarface of forearm.*

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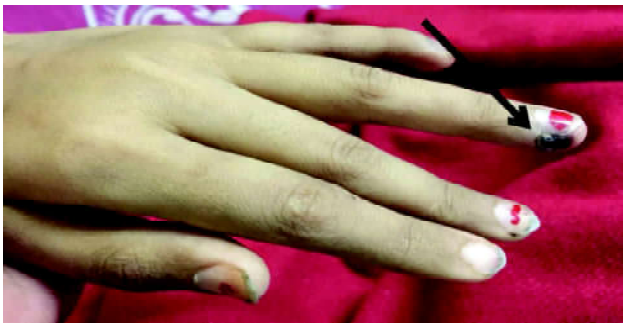

Fig. 3: *Blackish discolouration of skin present over tip of left ring finger.*

normochromic anaemia. Renal function tests were all within normal limits. Albumin/globulin ratio was reversed (2.8/4.5 gm/dl). Urine examination showed 6 - 8 RBCs, proteinuria (3+) with a 24-hr urinary protein of 1.6 gms/day. Urine for dysmorphic RBC was negative. HBsAg, anti-HCV and HIV were all negative. Coomb's test (Direct and indirect) was negative. Both Anti-Neutrophil Antibody level (ANA) and anti-ds DNA were positive. ANA (homogeneous pattern) in a titre of 1:360 by indirect immunofluorescence was positive. Complement levels, i.e., C3 (32 mg/dl) and C4 (5.20 mg/dl) were low. Fine needle aspiration cytology (FNAC) of cervical lymph nodes showed degenerated lymphoid cells, few fibrofatty fragments and necrosis in the background, with positive Ziehl Neelsen stain for acid-fast bacilli (AFB). Lymph node biopsy showed necrotising lymphadenitis (Fig. 4). Renal biopsy was done which showed lupus nephritis with moderate activity (class III A/C) (Fig. 5). Finally, the diagnosis of SLE with class III lupus nephritis with secondary vasculitis with tuberculous cervical lymphadenitis was made. Thus, patient was having TB with concomitant organ-threatening lupus. After consulting the Department of Rheumatology, it was decided to withhold immunosuppressive therapy. The patient was given pulse steroid (inj. methylprednisolone pulse therapy for 3 days) followed by oral steroids. She was started on a full course anti tubercular treatment (ATT), angiotensin converting enzyme (ACE) inhibitors, hydroxychloroquine and statins. The patient became afebrile and rashes over her face and forearm improved. She was thereafter discharged on oral steroids and ATT. It was planned to give her immunosuppressive therapy after completion of the full course of ATT.

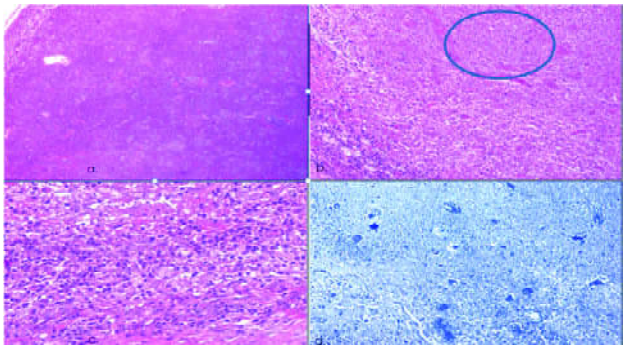

Fig. 4: *Lymph node biopsy showing necrotizing lymphadenitis (caseating necrosis has been encircled).*

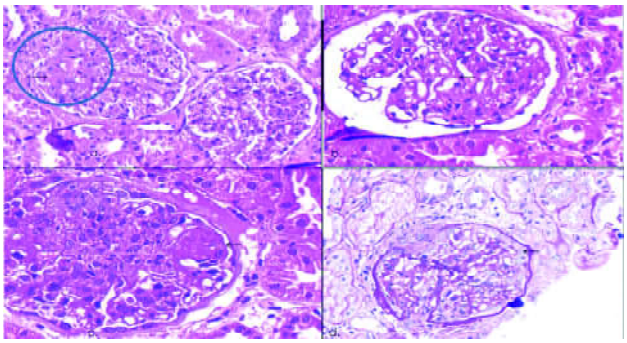

Fig. 5: *Renal biopsy showing Lupus Nephritis with moderate activity (class III A/C) (wire loop sesions are encircled).*

Discussion

SLE is characterised by genetically determined loss of self-tolerance and cellular activation dependent on non-genetic factors, such as environmental, hormonal, and infectious. Activation of T-lymphocytes by γ-interferon stimulates the sequence of progressive and persistent expansion of apoptosis-resistant polyclonal B-lymphocytes, which produce auto-antibodies characteristic of the disease[3]. Uncontrolled hyperactivity of the immune system actually makes SLE patients immunocompromised. Impaired cellular and humoral immune functions in SLE patients have been associated with predisposition to TB. Besides multiple immune abnormalities, immunosuppressive therapy given for treatment of lupus also leads to increased susceptibility to TB[4-6]. High doses of corticosteroids are a major risk factor.

Several global studies have documented a definite increase in the incidence of TB in patients with SLE[7]. A Spanish study reported a six-fold higher incidence of TB in the SLE group as compared to the general population[8]. Similarly, a study from Hong Kong reported a 5- to 15-fold higher risk of TB in the SLE group as compared to the general population[9].

In SLE patients, extra-pulmonary tuberculosis (EPTB) is more common than pulmonary TB[10]. TB in patients with SLE imparts a challenge to the clinical acumen especially in the setting of higher number of cases of EPTB. Presentation of EPTB is a constellation of non-specific symptoms like unexplained fever, joint pains, lymphadenopathy, fatiguability, and serositis, which are also seen in patients with SLE, making them mimickers of each other[11]. Moreover, some of the diagnostic laboratory investigations can be positive in both diseases. For instance, patients with TB are found to have positivity for rheumatoid factor and anti-nuclear antibodies, the latter of which are characteristically seen in lupus. Elevated ADA levels can be seen in conditions like para-infective effusions, empyema, malignancy, and autoimmune diseases

like RA and SLE. Pettersson *et al*[12], found that the mean ADA levels are significantly higher in patients with TB than in patients with SLE. Determination of isoforms of ADA activity is helpful in differentiating these conditions. Predominant ADA2 activity is seen in TB and predominant ADA1 activity is seen in empyema and para-infective effusions[13]. In another study, it was noted that the serum ADA levels are elevated in SLE and the isoform was ADA2, similar to that seen in TB[14]. Therefore, diagnosis of EPTB in lupus patients often requires tissue and body fluid analysis thus prolonging the time in reaching a definitive diagnosis. In our patient, we did a lymph node biopsy and renal biopsy which led to the simultaneous diagnosis of TB lymphadenitis with lupus nephritis.

It is also important to be aware of the impact of tuberculous infection in a SLE patient. There is growing evidence, which supports the crucial role of infections in the induction and exacerbation of SLE. Several mechanisms have been suggested by which microbes may trigger autoimmune reactions. Firstly, microbial antigens may get associated with self-antigens to form immunogenic strains and bypass the T-cell tolerance. Secondly, certain bacterial and viral products are non-specific polyclonal B-cell mitogens and may induce the formation of autoantibodies. Thirdly, infection may induce the suppression of T-cell functions[15]. Available literature links mycobacterial infections with humoral autoimmunity.

The treatment of TB in patients with SLE is same as for other patients with this disease. This regimen usually includes a combination therapy with isoniazid, rifampicin, ethambutol and pyrazinamide for 2 months followed by at least 4 months of isoniazid and rifampicin[16]. Also, before starting immunosuppressants and biologics, tuberculosis needs to be ruled-out. Patients should have risk assessment, physical examination, and chest radiograph. Tuberculin skin test only has sensitivity of 70%. Interferon-gamma Release Assays (IGRA) screening is recommended. IGRA are one of the recent innovations for the identification of latent tuberculous infection. These assays measure the release of interferon-gamma from sensitised T lymphocytes after stimulation with antigens from *Mycobacterium tuberculosis*. The IGRAs are performed in two ways, i.e., Quantiferon gold and T-SPOT TB. Screening tests decrease the reactivation of TB by 80%. Patients with latent MTB should delay biologic initiation until 1 month of latent TB therapy has been administered. They should receive a full course, i.e., 9 months ATT. Patients with active MTB should have a complete course of anti- tuberculosis therapy before starting a biologic (anti-TNF alpha agent)[17].

Lastly, most of the cases reported in literature demonstrated diagnosis of tuberculosis in already diagnosed Lupus patients[4]. These patients were usually on immunosuppressive therapies. Whereas, in our case, the diagnosis of TB and SLE was made simultaneously, with no prior history of any immunosuppressive therapy in the patient.

Conclusion

Our case highlights the fact that TB and SLE can mimic each other. This usually leads to delay in diagnosis and initiation of treatment. Also, extra-pulmonary TB is more common in SLE, thus a high suspicion is needed by the physician to diagnose these diseases.

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