CASE REPORT

Case report of a lupus patient with a severe flare and miliary tuberculosis: need for proper guidelines for management

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Abstract
Systemic lupus erythematosus (SLE) is an autoimmune disease that is frequently treated with high doses of corticosteroids and other immunosuppressive drugs. Thus patients with SLE are at increased risk for infections with several pathogens including Mycobacterium tuberculosis. There are no established guidelines available for treatment of tuberculosis in SLE patients with high disease activity due to lack of relevant studies and management based more on physician expertise. We report a case of a young SLE patient with high disease activity index (SLEDAI19) as evidenced by the presence of a vasculitic rash, non-healing ulcer on forearm and proteinuria of >1 g/d along with miliary tuberculosis. She was treated with intravenous methylprednisolone pulse up to 3 g and antituberculous therapy, but the result was a fatal outcome. This case report emphasizes the need for formal guidelines for co-management of active tuberculosis and SLE with high disease activity.

INTRODUCTION
Systemic lupus erythematosus (SLE) is an autoimmune disease that is frequently treated with high doses of corticosteroids and other immunosuppressive drugs. Thus patients with SLE are at increased risk for infections with several pathogens including Mycobacterium tuberculosis. There are no established guidelines available for treatment of tuberculosis in SLE patients with high disease activity due to lack of relevant studies and management based more on physician expertise. We report a case of a young SLE patient with high disease activity index (SLEDAI19) as evidenced by the presence of a vasculitic rash, non-healing ulcer on forearm and proteinuria of >1 g/d along with miliary tuberculosis. She was treated with intravenous methylprednisolone pulse up to 3 g and antituberculous therapy, but the result was a fatal outcome. This case report emphasizes the need for formal guidelines for co-management of active tuberculosis and SLE with high disease activity.
CASE PRESENTATION

A 22-year-old woman with SLE for 2 years, was diagnosed on the basis of malar rash, photosensitivity, oral ulcers, arthralgias, vasculitic rash, ANA positivity and anti double stranded DNA (anti dsDNA) titre of 740 IU/ml (normal value <25 IU/ml). She was previously treated with oral prednisolone 10 mg/d and azathioprine 100 mg/d with improvement in her symptoms. She continued these medications but was lost to follow-up soon after diagnosis and presented after 2 years with generalized petechial rash along with non-healing ulcer on right forearm with new onset proteinuria of >1g/d for 2 months, high grade fever and dry cough for 2 weeks. On examination she had Cushingoid features with malar rash, painless oral ulcers with thrush and thin hair on scalp. She also had generalized petechial, blanch able, non-tender, non-palpable rash all over her body with tender nodules over palms, a well demarcated ulcer of size 6 x 5 cm² with granulation tissue on right forearm near elbow. Her chest examination revealed bilateral normal vesicular breathing with no added sounds. Her disease activity score SLEDAI was high 19.

Intravenous methylprednisolone pulse therapy was started for her high disease activity. On same day a chest radiograph showed bilateral nodular opacities. HRCT Chest report showed enlarged pretracheal, paratracheal, pre and subcarinal lymph nodes. Lung windows show extensive nodular infiltrates findings pointing toward miliary tuberculosis. As Pakistan is an endemic area empirical antituberculous treatment was started on the next day after starting intravenous pulse methylprednisolone that given 500 mg/d up to 3 g.

Later her broncho alveolar lavage was positive for AFB on smear. GeneXpert test also showed no resistance to Rifampicin. Prior to discharge she was switched to oral prednisolone 0.5 mg/kg/d and azathioprine 100 mg/d in addition to antituberculous therapy. She presented in the emergency department (ED) 4 days after discharge from hospital with weakness of both legs for which she was under evaluation by a neurologist. He ordered an MRI of the thoracolumbar spine but no further details were written in her emergency chart. Within 2 h after her ED admission she suddenly developed respiratory distress and her blood oxygen saturation fall to 50% and she collapsed. Cardiopulmonary resuscitation was attempted but she died, without any further investigation and her family refused autopsy.

DISCUSSION

Pulmonary tuberculosis in SLE patients may manifest differently from immunocompetent patients [6] and tends to have a higher incidence of miliary disease due to delay in diagnosis and non-specific clinical symptoms that mimic lupus [7]. Therefore early diagnosis of pulmonary tuberculosis is essential for proper treatment.
High dose steroid therapy is a major risk factor. Several studies have demonstrated a higher cumulative dose as well as higher mean daily dose of prednisolone in SLE patients before diagnosis of tuberculosis. One study suggested that for each gram dose of prednisolone, there is a 23% increment in the chance of acquiring tuberculosis [2]. To more convincingly prove the role of steroids in increasing the risk of tuberculosis, the effect of cortisol on the immune response to Mycobacterium tuberculosis antigens was studied in vitro [8]. It demonstrated that cortisol, within physiological range can inhibit the mycobacterial antigen-driven proliferation of cells as well as production of interferon-gamma, signifying that endogenous levels of cortisol may contribute to the decreased lymphoid cell response to mycobacterium antigens [2, 8].

On the other hand, a growing body of literature supports the pivotal role of infections in the induction or exacerbation of SLE [9]. A high index of suspicion is required to diagnose tuberculosis especially in endemic areas. Studies revealed that the period between tuberculosis onset and diagnosis may vary from 1 month to 1 year as it often mimics SLE flares [10].

In a retrospective study done by Victorio et al. of 390 patients with SLE from Philippines, 13.8% had active tuberculosis and 75% had pulmonary involvement. This study also reported that patients with disseminated infection had a higher lupus disease activity index regardless of the corticosteroid doses they received at the time of diagnosis [11].

Priscilla et al. [12] reported fatal outcomes in four patients with juvenile SLE and miliary tuberculosis. In conclusion SLE patients with miliary tuberculosis have high mortality. Our case report reinforces the need of formal detection of tuberculosis among patients with systemic lupus erythematosus. Ann Rheum Dis 1982; 41: 11-4

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