MILIARY TUBERCULOSIS IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS WITH ABSCESS FORMATION IN THE UPPER EXTREMITIES

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SUMMARY
A 53-year-old man with arthritis and fever was admitted to hospital. He had been followed with systemic lupus erythematosus for the last seven years. He was on corticosteroid therapy. Laboratory work-up revealed tuberculous abscesses on both hands and the patient died of respiratory failure due to miliary tuberculosis on the fourth day of anti-tuberculous therapy. It should be kept in mind that tuberculosis is frequently encountered in the systemic lupus erythematosus patient population due to nature of the disease and the therapy given. It may be fatal unless treated aggressively.

Key Words: Abscess, Systemic Lupus Erythematosus, Miliary Tuberculosis

Tuberculosis had been a long dreaded disease until development of antituberculosis drugs. The relief was not long lasting, since the number of immunocompromised patients infected with tuberculosis are increasing with the widespread use of immunosuppressants and increasing infection rate with acquired immunodeficiency syndrome AIDS (1). About one third of the world population is infected with tuberculosis at present, and about 90 million new cases are being reported every year. In Mexico, the incidence of tuberculosis in patients with systemic rheumatic diseases was %2.5 in 1994 (1). In Korea, in a recent study it was shown that tuberculosis incidence rate was 20/1000 patients - years of tuberculosis in the same patient group (2).

In Turkey, we know that tuberculosis is still an epidemic with an annual incidence of 39.4 cases per 100000 (as reported in 1993).

Patients with rheumatic diseases are more susceptible to infection with mycobacterium species because of the nature of the disease and

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because of the immunosuppressive treatment regimens (1). Infection is a frequent problem in patients with systemic lupus erythematosus (SLE), especially in those hospitalized with complications of disease. Infections increase morbidity of disease and often are the cause of death. Most are due to gram positive or negative bacteria. However, there is increasing evidence that opportunistic infections contribute greatly to infectious mortality in SLE. However diagnosis of these infections is difficult and most are superimposed with SLE activation (3).

Here we present a male patient with SLE who developed miliary tuberculosis associated with severe abscess formation bilaterally in the forearms and hands and who died on the fourth day of anti-tuberculous treatment because of respiratory failure.

Case Report

A 53 - year - old farmer was admitted to our department with arthralgia and fever. He was diagnosed with SLE based on the ARA classification criteria of presence of arthritis, proteinuria, malar rash and anti-ds-DNA and ANA positivity, seven years ago. He was started on steroids and nonsteroidal anti-inflammatory drugs. He was being followed by the outpatient department on an irregular basis. He was incompliant to the follow-up plans for the last few years and was taking 10 mg of glucocorticoid daily.

His recent complaints had started about seven months previously, with cellulitis and abscess formation on the right forearm. The abscess was drained and a course of antibiotics was given. Six months later he was rehospitalized because of abscess formation on the left forearm. Abscess was drained and cultures of the material revealed Staph. aureus. He was treated with amoxicillin 1gr and clavulonic acid (Augmentin) tid for three weeks. He was admitted to the department of clinical immunology and rheumatology because of SLE activation. He had spiking fevers and arthritis of the hands despite antibiotic therapy and drainage of the abscess.

He had smoked 1 pack/day for 20 years. He quit smoking two months ago. His family history was insignificant.

He was an obese man showing his age. On physical examination, blood pressure was 130/90mmHg, pulse rate was 70/minute and body temperature was 36.2°C. There were no lymphadenopathies. Breath sounds were roughened and bilaterally there were basilar rales. Cardiovascular examination revealed a systolic murmur of the second degree. There was no hepatosplenomegaly, ascites, intraabdominal masses. Extremity examination revealed pretibial (+++) pitting edema bilaterally and instability of the right knee.

Laboratory examination revealed mild anemia, due to chronic illness. Serum Vit B12, folate and iron levels were within normal limits. Biochemistry of the blood showed altered renal functions. Urinalysis showed proteinuria (4.2 g/day) and microscopically erythrocytes, leukocytes and granular casts. Immunological parameters were as follows: ANA: ++++, homogenous pattern; anti-ds-DNA: 496 IU/ml (0 - 7 IU/ml); CRP: 21.9 IU/L (0 - 5 IU/L); ESR: 74 mm/hour; C3c: 0.642 g/L (0.9 - 2 g/L); C4: 0.0851 g/L (0.1 - 0.4 g/L); protein electrophoresis revealed hypergammaglobulinemia (26.1%).

His chest X-ray findings were insignificant. There were no signs of a past tuberculosis infection such as calcified lymph nodes, apical fibrosis or cavity formation.

Direct radiographs of the hands, wrists and elbows did not show any significant changes other than soft tissue swelling of the hands. Magnetic resonance imaging (MRI) of the right knee revealed rupture of posterior horn of medial meniscus and anterior horn of lateral meniscus; patella alta; erosion of cartilage and cortex of medial plato of tibia; a Baker’s cyst and changes secondary to operation done for the knee trauma three years ago.

High resolution thoracic computed tomography showed pretracheal, precarinal, aorticopulmonary and axillary lymphadenopaties not reaching pathological
sizes; minimal pericardial effusion. Signs for diffuse interstitial pathology were not observed. There were fibrotic bands in the basal regions and a 1 cm subpleural nodule in the right middle lobe.

On the third day of his admission glucocorticoid was increased to a dose of 40mg/day. 18 days later azathioprine (Imuran) 50 mg bid was added to the therapy. Steroid doses were slowly decreased. His clinical condition seemed to be improving with immunosuppressive treatment.

On the sixth week of admission, arthritis on second, third and fourth metacarpophalangeal (MCP) joints of the left hand and first MCP of the right hand was observed. Steroids had been decreased to a dose of 25mg/day. There was no demonstrable site of infection and because the involvement was bilateral and it occurred during steroid dose reduction, this was accepted as SLE flare–up. Steroid dose was increased to a dose of 30 mg/day and azathioprine to 50 mg tid. Amoxicillin – clavulonic acid was added to the treatment at a dose of 1 gr. bid PO in case there was an undetected infection. However the condition of the arthritis worsened, extending to uninvolved joints of both hands, to include the wrists.

On day 59, auscultation revealed rales all over the right lung. Chest X-ray revealed right paracardiac pneumonic infiltration. Leukocyte count was 2100 /mm3. Imuran was stopped. Meropenem (Meronem) 500 mg qid I.V. was started after samples for culture were obtained. Sputum culture revealed Staph. aureus. Blood culture results were negative. Teicoplanin (Targocid) was added to therapy on a dose of 400 mg every 36 hours (dosage adjusted for renal failure) I.V. after a loading dose of 800mg. On the third day of the new antibiotic, there was no response, fever continued, steroid dosage had been decreased to 15 mg/day. On the day 75, abscess formation was observed in both hands. Spontaneous drainage of the right hand occurred.

On day 80, he was operated on as an emergency case for abscess drainage. Abscess material was sent again for culture and microscopic examination. This time microscopic examination revealed many acid fast bacteria.

Figures 1 - 2: On the day 75, abscess formation was observed in both hands. Spontaneous drainage of the right hand occurred.

Figure 3: A new thorax CT revealed axillary lymphadenopathies, largest being 1.5 cm in diameter. Parenchymal micronodules were present mainly on the right side. Multiple parenchymal and subpleural nodules were observed, largest being 1 cm in diameter. Findings were interpreted as compatible with miliary tuberculosis.

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Anti-tuberculosis treatment was started with isoniazid (INH) 300 mg/day, rifampicin (Rifcap) 600 mg/day, ethambutol (Embutol) 1250 mg/day and morphazinamide (Morfozid) 1000 mg tid PO. However, by this time his pulmonary functions were deteriorating. He was hypoxemic. Upon auscultation, there were rhonchi and rales over the lungs. However there were no new findings on the chest X-rays. A new thorax CT revealed axillary lymphadenopathies, largest being 1.5 cm in diameter. Parenchymal micronodules was present especially on the right side (picture 3). It was accepted as a sign for an inflammatory pathology, not SLE involvement. Multiple parenchymal and subpleural nodules were observed, largest being 1 cm in diameter. Findings were interpreted as compatible with miliary tuberculosis.

On day 81 melena was detected. Steroid and aspirin were discontinued. Anti-ulcer treatment with antacids and parenteral H1 blockers was started, two units of erythrocyte suspensions were transfused. Vit K replacement was given. Patient vital signs were stable, hemoglobin and hematocrit levels were stable. However melena continued. Fibrinogen levels were high, d-dimer levels and bilirubin levels were normal, excluding a diagnosis of disseminated intravascular coagulation.

On the fourth day of the anti-tuberculosis treatment, and on the 85th day of admission, massive gastrointestinal bleeding started and a short while after patient respiratory distress increased. Respiratory arrest occurred a few hours later and was not responsive to cardiopulmonary resuscitation.

**Discussion**

A similar case was reported from Malaysia: a 28-year-old lady with SLE was on oral cyclophosphamide and prednisolone when presented with cellulitis of the left lower limb. It failed to respond to usual antibiotics and prompted reevaluation of the condition. The diagnosis was made on the presence of granulomas, multinucleated giant cells and acid fast bacilli on the skin biopsy (4).

As in the case presented, the clinical manifestations of the systemic rheumatic disease activation and tuberculosis infection can be quite confusing as fever, weight loss, asthenia are present under both conditions (1,3).

SLE patients are accepted as immunocompromised hosts although they are nonleukopenic (3). Host resistance to *Mycobacterium tuberculosis* is mediated by cellular immunity, a defense system that is deficient in these patients both due to the nature of their disease and due to the treatment (chronic high dose steroid and cyclophosphamide therapy) they are receiving. These factors cause the rheumatic disease patient to be prone to tuberculosis infection, and a delay in diagnosis.

In the evaluation of 33 patients with systemic rheumatic disease and tuberculosis by Hernandez – Cruz et al, it was shown that 10 patients had pulmonary tuberculosis and 20 had extra pulmonary disease (the three patients were excluded because they had tuberculosis before the diagnosis of rheumatic disease). Six of the seven patients with miliary tuberculosis had concomitant SLE (13 patients out of 30 had SLE). The commonest clinical manifestations were fever and weight loss. Only 16 patients had abnormal chest X-rays. Only 18 had positive cultures, of these six were with pulmonary tuberculosis and six had miliary tuberculosis. Two women with SLE and miliary tuberculosis died because of acute respiratory failure after 5 and 15 days of anti-tuberculosis therapy, like our patient. The period between the initial symptoms of tuberculosis and hospitalization was 46 and 78 days respectively, and the interval to initiation of therapy was 48 and 93 days respectively (1).

Higher proportion of extra pulmonary tuberculosis and miliary tuberculosis cases were found in patients with systemic rheumatic disease, 42% and 24% respectively. There was an association with miliary tuberculosis and SLE (1).

In a study reported from Slovakia in a group of 388 patients with SLE tuberculosis was diagnosed in 3.6%. The occurrence of septic fevers in SLE patients that did not respond to
glucocorticoid treatment indicated the possibility of complication with tuberculosis. SLE associated tuberculosis included miliary and far advanced pulmonary and extra pulmonary forms (5).

Düzgün et al. reported a case of lupus vulgaris in a patient with systemic lupus erythematosus and corticosteroid induced hypogammaglobulinemia. This was the first case of lupus vulgaris in a patient with systemic lupus erythematosus reported (6).

Much tuberculosis cases in adult age classes groups be caused by reactivation of a latent infection, as opposed to reinfection (7). This is important in a country like Turkey where the incidence of latent infections is high. During rheumatic disease activation or due to treatment given, these latent infections may reactivation.

Mortality rates in SLE patients with tuberculosis were especially high. This could be related to delay in diagnosis, need for higher doses of immunosuppressive therapy, and concomitant disease exacerbation with infection (1). Besides, the screening test results were different in this patient group. PPD response >10 mm was found to correlate highly with tuberculosis activity, whereas milder responses did not rule out the disease. Furthermore, patients with extra pulmonary tuberculosis and miliary tuberculosis tended to have milder responses (1).

In the immunocompromised host without neutropenia any pathogen may produce a variety of clinical conditions and tuberculosis may be the cause of any clinical or radiological situation. It must be kept in mind that new extra pulmonary symptoms or signs with a rapid progression of fever, diffuse opacities or nodules on chest X-ray may sign tuberculosis. Sputum, blood samples should be obtained for microscopic evaluation and cultures. A CT scan of the thorax may be useful to characterize the lesions especially if there is concomitant pleural effusion. Where plausible, bronchoalveolar lavage (BAL) may be performed. Yet, BAL results may be negative occasionally (8).

Advisory council for the elimination of tuberculosis suggests, PPD reaction > 5 mm should be considered significant in patients with organ transplants and other immunosuppressed patients (receiving the equivalent of > 15 mg/d of prednisone for a month or more) (9).

In the case of miliary tuberculosis, early empiric therapy can be started if there is sufficient clinical suspicion based on the presenting signs and symptoms as well as the pattern of organ involvement. As with all infections, particularly of the immunosuppressed early implementation of treatment is essential and life saving (3,5).

In conclusion, in dealing with systemic rheumatic disease patients, one should always be aware of the possibility of concomitant tuberculosis infection. Keeping in mind that most patients will have extra pulmonary disease, any clinical finding that cannot be explained by rheumatic disease activity should raise the suspicion of tuberculosis infection. Also, any infection unresponsive to standard antibiotic regimens, when cultures are nondiagnostic, should prompt search for a specific infection. They should be evaluated promptly and treatment should be started immediately. Tuberculosis can be fatal in these patients.
REFERENCES


