

# Pulmonary Tuberculosis in a Patient with Systemic Lupus Erythematosus – A Case Study

HUSSAIN N.,<sup>1</sup> JAFFERY G.,<sup>2</sup> SABRI A.N.,<sup>3</sup> HASNAIN S.,<sup>4</sup> MIR N.<sup>5</sup>

<sup>1,3,4</sup>Department of Microbiology and Molecular Genetics

Quaid-e-Azam Campus, University of the Punjab, Lahore – Pakistan

<sup>2</sup>Department of Pathology, Services Institute of Medical Sciences, Lahore – Pakistan

<sup>5</sup>Department of Rheumatology, Fatima Memorial Hospital, Lahore - Pakistan

**For correspondence:** Dr. Nageen Hussain, Qualification: M.Sc. in Microbiology and Molecular Genetics, PhD Scholar.

Designation: Lecturer in the Department of Microbiology and Molecular Genetics

Quaid-e-Azam Campus, University of the Punjab, Lahore - Pakistan

Systemic Lupus Erythematosus (SLE) patients have an increased susceptibility to tuberculosis; such a case was reported in a 28-year old man. It is believed that Methotrexate used to reduce the activity of systemic lupus erythematosus and of rheumatoid arthritis had decreased the activity of his immune system and tends to develop tuberculosis.

**Key words:** Systemic Lupus Erythematosis, tuberculosis, Methotrexate.

## Introduction

Systemic lupus erythematosus is an autoimmune disease characterized by the production of autoantibodies that react with the self antigens and form immune complexes.<sup>1,2</sup> These complexes get deposit on the tissue, results in tissue injury and ultimately bring about the symptoms of lupus. The cellular and molecular mechanisms of lupus are unknown but it is believed that genetic, non-genetic and immunological factors are involved.<sup>4,5</sup>

Long lasting inflammation results in lupus so the only treatment is to reduce inflammation.<sup>6</sup> Commonly, prescribed medications are Non steroidal anti-inflammatory drugs, Acetaminophen, Corticosteroids, Antimalarial, Immunomodulating Drugs and anticoagulants.<sup>7,8</sup> Recently, Methotrexate has come into use as a treatment for autoimmune diseases.<sup>9,10</sup> It is formerly known as amethopterin, which competitively and reversibly inhibits dihydrofolate reductase, an enzyme that participates in the tetrahydrofolate synthesis.<sup>11,12</sup> Folic acid is needed for DNA synthesis and also for purine base synthesis, so all purine base synthesis will be inhibited.<sup>13,14</sup> Therefore, Methotrexate inhibits the synthesis of DNA, RNA, thymidylates, and proteins. This drug is still in the investigational phase for lupus.<sup>15</sup>

## Case Report

A boy with the age of 16 years was diagnosed with SLE; he had noticed fever, fatigue, joint pains, and vasospasm of fingers and toes. There was no family history of SLE. The patient was diagnosed as having SLE based on the 1982 revised criteria proposed by the American College of Rheumatology. Results of laboratory investigation include Hemoglobin-12.7 g/dl, ESR-85 mm/hr, Total leukocyte count- $4.2 \times 10^9/L$ , Platelet count- $216 \times 10^9/L$ , C3-124 g/dl (50-120 mg/dl), C4-24.5 mg/dl (20-50 mg/dl), BUN-13.8 mmol/L (7-18 mmol/l), Albumin-3.7 g/dl (3.8-5 g/dl), CRP-6 mg/dl

(<6 mg/l), RA factor-32 U/ml (<8 U/ml). Furthermore, ANA, anti-dsDNA and anti-Sm were positive while anti-Ro, anti-La, anti-Histone, anti-Rib-P were negative.

In September 2006, the patient was treated with the double dose of Methotrexate for the management of Rheumatoid arthritis and to control the symptoms of lupus. On January 2007, the patient was hospitalized as fever, cough, fatigue, weight loss, and breathing difficulty appeared. Examination of the lungs by stethoscope revealed crackles, fluid was detectable around the lungs. The patient was diagnosed with tuberculosis as chest X-ray was abnormal, there were multiple opacities located in the upper area of the lungs toward the back. Sputum and blood samples obtained for microscopic evaluation and cultures were also abnormal. The administration of anti-tuberculosis drugs such as isoniazid, ethambutol hydrochloride, and Rifampicin was started. The symptoms were improved after 1 week and the administration of anti-tuberculosis drugs was terminated in 10 months. Moreover, lower dose of Methotrexate was started for the effective management of rheumatoid arthritis in such SLE patient.

## Discussion

Microbes may trigger autoimmune reactions in several ways. First microbial antigens and autoantigens may become associated to form immunogenic subunits and bypass T-cell tolerance. Secondly, some viral and bacterial products are nonspecific polyclonal B-cell mitogens and thus may induce the formation of autoantibodies. Third, infection may result in loss of suppressor T-cell function.<sup>16</sup>

SLE patient are accepted as immunocompromised hosts although they are non-leukopenic. Mortality rate in SLE patients with tuberculosis is especially high.<sup>17</sup> Host resistance to *Mycobacterium tuberculosis* is mediated by cellular immunity, a defense system that is deficient in this patient

both due to the nature of the disease and due to the treatment they are receiving.

Measurement of CRP is important in monitoring the disease activity and response to therapy. CRP is synthesized as a non-glycosylated protein, comprises of five identical non-covalently bound subunits with 206 amino acids arranged in a cyclic symmetry around a central pore. Here, elevated CRP indicates an infection and ESR arise with the disease activity mainly due to arthritis.<sup>18</sup>

Methotrexate acts by damping the immune system and reducing inflammatory in joints.<sup>19</sup> But some of the side effects that we have seen in our patient are breathlessness, fever, sweating, and hair loss. Methotrexate is responsible for pulmonary tuberculosis in our patient as double dose has reduced the activity of immune system. Cough, breathlessness are the common manifestations of Pulmonary Tuberculosis.

Thus, patients with systemic lupus erythematosus have a higher predisposition to infection as a result of immunosuppressive therapy and underlying abnormalities of the immune system such as impaired phagocytosis or deficient cell-mediated immunity. Tuberculosis is one of the key opportunistic infections that should be considered in such patients.

## Reference

1. Boumpas D.T. Systemic Lupus Erythematosus: emerging concepts. *Ann. Intern. Med.* 1995; 122: 940.
2. Mills JA. Systemic Lupus Erythematosus. *New Eng. J. Med.*, 1994; 330: 1871-1872.
3. McShane D.J., and Rothfield N.J. The 1972 revised criteria for the classification of SLE. *Rheum. Dis.*, 1986; 45: 435-437.
4. Kotzin BL. Systemic Lupus Erythematosus. *Cell Biology* 1986; 85: 303-306.
5. David P.D. Systemic Lupus Erythematosus. *B.M.J.*, 2006; 15: 890-894.
6. Theofilopoulos A.N. The basis of autoimmunity. *Immunol. Today* 1995; 16: 90.
7. Abbas A.K., Lohr J., Knoechel B., and Nagabhushanam V. T-cell tolerance and autoimmunity. *J. Autrev.*, 2004; 3: 471-475.
8. Davies K.A., Peters A.M., Beyon H.L., and Walport M.J. Immune complex processing in patients with SLE. *In vivo* imaging and clearance studies. *J. Clin. Invest.*, 1992; 90: 2075-2083.
9. Fairweather D., and Rose N.R. Women and autoimmune diseases. *Emer. Infect. Dis.*, 2004; 10: 2005-2011.
10. Paton N.I. Infections in SLE patients. *Ann. Acad. Med.*, 1997; 26: 694-700.
11. Anderson R.M. Tuberculosis: Old problems and new approaches. *Proc. Natl. Acad. Sci.*, 1998; 95: 13352-13354.
12. Kalerskod L., Vander Heijde D., de Jager J.P., Gough A., Kalden J., Malaise M., Martin Mola E., Pavelka K., Sany J., Settas L., Wajdula J., Pedersen R., Fatenejad S. and Sanda M. Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomized controlled trial. *Lancet.*, 2005; 363: 675-81.
13. Kowl C., Weinstein A. and Diamond B. Molecular mimicry between bacterial and self antigen in a patient with Systemic Lupus Erythematosus. *Eur. J. Immunol.*, 1999; 29: 1901-11.
14. Manson J.J. and Isenberg D.A. The pathogenesis of systemic lupus erythematosus. *Neth. J. Med.*, 2003; 61: 343-5.
15. ohen M. Systemic Lupus Erythematosus: diagnosis and classification. *Intern. Med. J.*, 2004; 34 (12): 701-2.
16. Johnston A., Gudjonsson J.E., Sigmundsdottir H., Ludviksson B.R., Valdimarsson H. The anti-inflammatory action of methotrexate is not mediated by lymphocyte apoptosis, but by the suppression of activation and adhesion molecules. *Clin. Immunol.*, 2005; 114: 154-163.
17. Sjowall C., Bengtsson T. and Skogh T. CRP and anti-CRP autoantibodies in SLE. *Curr. Rheum. Rev.*, 2005; 1: 81-89.
18. Manson J.J. and Rehman A. Systemic Lupus Erythematosus. *Orphanet Encyclopedia*, 2005.
19. Hashimoto M., Nonaka S., Furuta E., Wada T., Suenaga Y., Yasuda M., Shinqu M. and Nobunaga M. Methotrexate for steroid resistant systemic lupus erythematosus. *Clin. Rheumatol.*, 2005; 13: 280-283.