
Pulmonary Tuberculosis Associated with Autoimmune Hemolytic Anemia: An Unusual Presentation

Mehmet TURGUT*, Oğuz UZUN**, Engin KELKİTLİ*, Okay ÖZER*

* Department of Hematology, Medical School, Ondokuz Mayıs University,

** Department of Chest Medicine, Medical School, Ondokuz Mayıs University, Samsun, TURKEY

ABSTRACT

Coombs' positive hemolytic anemia is exceedingly rare in tuberculosis. We herein report a patient with tuberculosis associated with Coombs' positive hemolytic anemia that was responded to antituberculosis therapy. She was admitted to the hospital because of recent-onset fatigue, weakness, nonproductive cough, pallor and scleral jaundice. Coombs positive hemolytic anemia and pulmonary tuberculosis was diagnosed. Following antituberculosis therapy, laboratory and clinical finding related to autoimmune hemolytic anemia disappeared.

Key Words: Tuberculosis, Autoimmune hemolytic anemia, Coombs' positivity.

Turk J Haematol 2002;19(4): 477-480

Received: 29.04.2002

Accepted: 13.08.2002

INTRODUCTION

Tuberculosis is a multi-systemic specific infection, which can lead to protean manifestations in any organ-system. Therefore, the clinical presentation of the disease is quite diverse. Hematological findings in tuberculosis are not uncommon and usually due to non-immunological mechanisms. Normochromic normocytic anemia is the most frequent hematological finding at presentation and during the long clinical course of tuberculosis. Anemia is usually due to bone marrow granuloma, nutritional insufficiency, malabsorption and im-

paired iron utilization. Coombs' positive hemolytic anemia is exceedingly rare in tuberculosis. We herein report a patient with tuberculosis associated with Coombs' positive hemolytic anemia that was responded to antituberculosis therapy.

A CASE REPORT

A 30-year-old previously healthy woman was admitted to the hospital because of recent-onset fatigue, weakness, nonproductive cough, pallor and scleral jaundice. Physical examination revealed a blood pressure of 80/55 mmHg, pulse 92/min, respiration 35/min

and body temperature 39.5°C orally. In the examination of the respiratory system, there were fine rales heard in the left apical zone during inspiration and expiration together with a harsh bronchial noise. There was a systolic cardiac murmur of grade I-II heard all over the precordium. The laboratory findings on admission revealed a WBC 6600/mm³ (75% neutrophils, 13% lymphocytes, 11% monocytes and 0.5% eosinophiles), hemoglobin 4.6 g/dL, MCV 98.7 and MCH of 22.7 fL, platelet count 175.000/mm³ and reticulocyte 19.7%. Direct and indirect Coombs' test was positive without any transfusion. Erythrocyte morphology was polychromasytic together with macrocytosis, spherocytosis, anisopoikilocytosis and 6% normoblasts. Bone marrow examination disclosed significant erythroid hyperplasia and hypercellularity. Biochemical tests on admission were: Total bilirubin 4 g/dL, direct bilirubin 1.9 g/dL, AST 295 IU/L, ALT 81 IU/L, LDH 1902 U/L, ferritin 7685 ng/dL and haptoglobin 31 mg/dL. In the chest X-ray there was bilateral reticulonodular infiltration in the upper zones and in the high resolution computerized tomography bilateral apical reticulonodular infiltration and a cavitary lesion 2 cm in diameter seen in the right upper lobe posterior segment (Figures 1,2). Tests for ANA, anti-DNA, HIV and blood cultures were all negative. In the bronchoalveolar lavage obtained from the right upper pole there were acid-fast bacilli and *Mycobacterium tuberculosis* was cultivated in the Löwenstein-Jensen agar.

The drug regimen including INH 300 mg PO, rifampicine 450 mg PO, pyrazinamide 1500 mg PO and streptomycine 750 mg IM was initiated in April 2001. After one week time fever was subsided. Since the liver enzymes were elevated (ALT 540 IU/L and AST 560 IU/L), all of the drugs except streptomycin were holded and ethambutol 1500 mg PO was added to the treatment schema. When the enzymes (ALT and AST) were 39 IU/L and 100 IU/L respectively INH, pyrazinamide and rifampicine were added to the drug regimen with 5 days of intervals. There were no increments in the enzymes following the reinitiation of the treatment. The control laboratory tests of the patient are depicted in Table 1.

No blood or blood product was given to the patient and the clinical symptoms were gradually improved. Patient is discharged because of her will to continue the treatment at home in June 2001. The sputum examina-

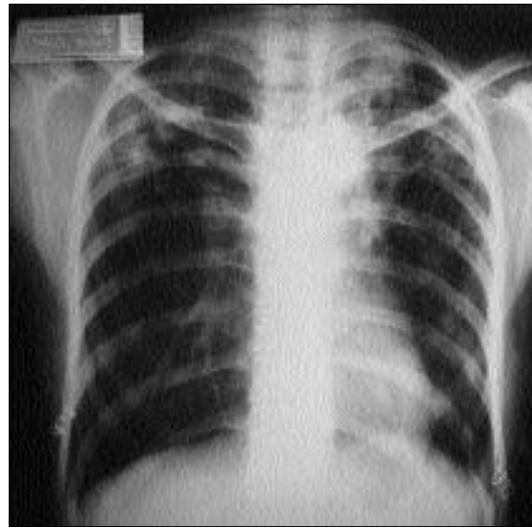


Figure 1. Anteroposterior X-ray of the chest on admission showing bilateral reticulonodular infiltration in upper zones.

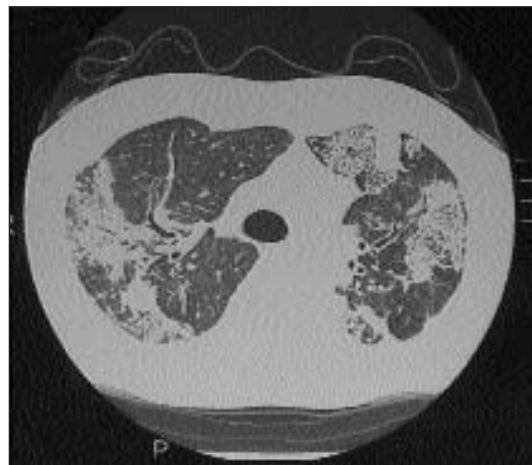


Figure 2. HRCT of the patient on admission showing bilateral apical reticulonodular infiltrations and cavitary lesions.

tion made at July 2001 revealed no acid-fast bacilli and there were no *M. tuberculosis* in the control cultures. The control Chest X-ray obtained in December 2001 showed no abnormalities except the bilateral apical fibrotic opacities.

DISCUSSION

A wide variety of hematological manifestations can be observed in patients with tuberculosis, which

Table 1. Essential laboratory findings and follow-up of the patient with tuberculosis and hemolytic anemia

Parameters	On admission	Eight months later
Hemoglobin (g/dL)	4.6	12.2
Reticulocyte (%)	19.7	0.98
LDH (IU/L)	1902	270
Bilirubin-total/direct (mg/dL)	4.6/1.9	0.32/0.05
AST (IU/L)	88	20
ALT (IU/L)	37	18
Haptoglobin (mg/dL)	31 (N above 50)	80

has a chronic inflammatory nature. The commonest of those are anemia and leukocytosis, which are reported as 60% and 40% respectively^[1]. Anemia is present in 63% of miliary tuberculosis patients^[2]. Anemia of tuberculosis is usually due to nutritional deficiency, failure of iron utilization, malabsorption syndrome and bone marrow suppression. However, autoimmune hemolytic anemia is exceedingly rare condition in tuberculosis.

Infection-associated hemolytic anemia is mostly related to virus and mycoplasmal infections. Four hemolytic anemia cases due to tuberculosis were previously reported in the English literature^[3-6]. Only two of those cases responded to antituberculous chemotherapy alone successfully^[3,4]. In the third patient, prednisolone 60 mg three weeks and splenectomy due to subcapsular hemotoma preceded antituberculosis therapy^[5]. The fourth patient required prolonged steroid therapy to prevent the recurrence of hemolysis^[6].

Another complicated issue while treating the patients is hemolytic effects of antituberculosis drugs, rifampisin, streptomycin and para-aminosalicylic acid induced hemolytic anemia reported in the literature^[7-9]. Our patient received both rifampisin and streptomycin, but we did not observe any hemolytic adverse effect of these drugs.

Disappearance of hematological abnormalities via antituberculosis therapy alone is an important proof that tuberculosis is the underlying cause of hemolytic anemia in our patient. Recovery of hemoglobin, reticulocyte, haptoglobin, bilirubin, levels and Coombs' negativity after antituberculous therapy were all strong

evidences of immune mediated hemolytic anemia due to tuberculosis.

In summary, pulmonary tuberculosis can cause autoimmune hemolytic anemia, although the exact mechanism of the association is not clear. Fiberoptic bronchoscopic procedure should be instituted in any suspected tuberculosis patient who do not produce sputum. Because any delay in the diagnosis of tuberculosis in anemic patients could be life-threatening.

REFERENCES

1. MacGregor RR. A year's experience with tuberculosis in a private urban teaching hospital in the postsanatorium era. *Am J Med* 1975;58:221-8.
2. Glasser RM, Walker RI, Hewrion JC. The significance of hematologic abnormalities in patients with tuberculosis. *Arch Intern Med* 1970;125:691-5.
3. Siribaddane SH, Wijesundera A. Autoimmune haemolytic anemia responding to antituberculous treatment. *Trop Doc* 1997;27:243-4.
4. Kuo PH, Yang PC, Kuo SS, et al. Severe immune hemolytic anemia in disseminated tuberculosis with response to antituberculosis therapy. *Chest* 2001;119:1961-3.
5. Blance P, Rigolet A, Massault PP, et al. Autoimmune hemolytic anemia revealing miliary tuberculosis. *J Infect* 2000;40:292.
6. Cameron SJ. Tuberculosis and the blood: A special relationship? *Tubercle* 1974;55:55-72.

7. Oğuz A, Kanra T, Gökalp A, et al. Acute hemolytic anemia caused by irregular rifampicin therapy. Turk J Pediatr 1989;31:83-8.
8. Letona JM, Barbolla L, Frieyro E, et al. Immune hemolytic anemia and renal failure induced by streptomycin. Br J Haematol 1977;35:561-71.
9. Mueller-Eckhardt C, Kretschmer V, Coburg KH. Allergic, immunohemolytic anemia due to para-aminosalicylic acid (PAS). Immunohematologic studies of three cases. Dtsch Med Wochenschr 1972;97:234-8.

Address for Correspondence:

Mehmet TURGUT, MD

Denizevler Mahallesi

Erzurum Apartman No: 349/8

TR-55200, Atakum, Samsun, TURKEY

e-mail: mturgut@omu.edu.tr