Relation of serum adenosine deaminase (ADA) levels with sputum smear conversion in patients with pulmonary tuberculosis

To the Editor: Adenosine deaminase (ADA) plays a role in the proliferation and differentiation of lymphocytes. It is present more in T lymphocytes than B lymphocytes and increases during T cell differentiation. In pulmonary tuberculosis the increase of serum ADA levels and its value for diagnosis has been shown in many studies.[1-3] The studies also showed a decrease of serum ADA activity after treatment.[4]

In fact, a decrease in such acute phase reactant levels as erythrocyte sedimentation rate (ESR) was found after initiation of therapy. However, these reactants were not enough for follow up in this disease. Conversion of a sputum smear is accepted as an important indicator for the beginning of recovery in tuberculous therapy. Do serum ADA levels decrease during sputum conversion? Does sputum conversion, which is an indicator of the efficacy of treatment, correlate with serum ADA levels? Lymphocytic activity may be continued during the course of the disease. If serum ADA levels reflect lymphocytic activity, they can be a reliable marker of the effectiveness of tuberculous therapy. To answer these questions we measured serum ADA levels of smear positive pulmonary tuberculous patients at the beginning of therapy and during conversion.

We included 48 smear-positive pulmonary tuberculosis patients and 15 healthy men of similar age as a control group. All the patients were men, and their mean age was 22.8±5.3 years (range, 20-42 years). Lesions determined on their pulmonary radiographies were classified as minimal, moderately advanced or far advanced.[5] All patients were analyzed by a complete blood count, blood biochemistry, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and tuberculin skin test. All patients were treated with standard antituberculous treatment. The two-week sputum smear negativity determined consecutively was accepted as conversion week. ESR, serum ADA, CRP analysis and radiologic evaluations were made in this period. All samples for serum ADA measurements were evaluated with Gusti's colorimetric method.[6] The Statistical Package for the Social Sciences (SPSS) software was used in all analyses and a *P* value of <0.05 was considered statistically significant.

Mean serum ADA levels were 35.6±15.3 U/L (range, 17-91 U/L) in smear positive pulmonary tuberculosis patients and 19.0±7.1 U/L (range, 9-32 U/L) in the control group (*P*<0.0001). Sputum smear conversion occurred at 4.2±2.1 weeks (range, 2-9 weeks). When smear conversion occurred, serum ADA levels were 38.2 ± 13.9 U/L (range, 13-76 U/L). The differences in serum ADA levels between the measurement at the beginning of the treatment and sputum conversion time were not significant (*P*=0.3), but ESR and CRP levels decreased significantly (Table 1). There was not a significant correlation between radiologic extent and serum ADA levels at the beginning of the treatment (*P*=0.2). The radiologic changes during smear conversion were not significant either. A significant change in the serum ADA levels of both new cases and old cases either at the beginning of the treatment or at the time of conversion was not found (*P*=0.1). In one study of the efficacy of serum ADA activity in evaluating the response to tuberculous therapy, the investigators reported a decrease in serum ADA levels in the first two months and a return to normal at the end of treatment.[4] In our study, sputum smear conversion time was 4 weeks on average, but serum ADA levels did not decrease in this period. Our studies do not correlate with results from other studies that show a decrease in serum ADA levels in the early period. No significant difference was found in serum ADA levels between the early or late sputum conversion time. Although ESR and CRP, known as acute phase reactants decrease during conversion, disease activity is thought to be continuous. This may be the reason why our patient's ADA levels did not de-

Table 1. ESR, CRP, sADA, hemogram results at the beginning of the treatment and at conversion time

Measurements (mean±SD)	Before treatment	During conversion	*P* value
sADA (U/L)	35.6 ± 15.3	38.2 ± 13.9	0.3
ESR (mm/hour)	74.3 ± 22.5	48.9 ± 27.8	<0.001
CRP mg/L	69.6 ± 42.1	39.8 ± 39.2	0.001
Leukocyte (/mm3)	9793 ± 2447	10189 ± 2974	0.4
Lymphocyte (/mm3)	1487 ± 504	1676 ± 428	0.051

crease during the conversion period. We also observed that there were no changes in leukocyte and lymphocyte counts. We found no studies that evaluated serum ADA activity during sputum conversion in the literature so there is no data to compare with our results. Also, serum ADA activity in drug-resistant cases is not known. In these cases, serum ADA levels are expected to be high as the sputum positivity continues. The relationship between ADA and lymphocytes may be clarified by new studies in drug-resistant cases. Finally, the serum ADA level is a highly specific parameter in pulmonary tuberculosis patients. Despite acute phase reactants during sputum smear conversion, serum ADA levels do not decrease. For this reason serum ADA may be a good parameter in the follow-up of a chronic disease like tuberculosis.

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References

1. Kuyucu N, Karakurt C, Bilaloglu E, et al. Adenosine deaminase in childhood pulmonary tuberculosis: diagnostic value in serum. J Trop Pediatr 1999;45:245-7.
2. Mishra OP, Yusaf S, Ali Z, et al. Adenosine deaminase activity and lysozyme levels in children with tuberculosis. J Trop Pediatr 2000;46:175-8.
3. Canbulat O, Ulusdoyuran S, Ozgen G, et al. The comparison of adenosine deaminase activity values with polymerase chain reaction results in patients with tuberculosis. J Clin Lab Anal 1999;13:209-12.
4. Collazos J, Espana P, Mayo J, et al. Sequential evaluation of serum adenosine deaminase in patients treated for tuberculosis. Chest 1998;114:432-5.
5. Seaton A, Seaton D, Leitch AG. Crofton & Douglas's Respiratory Diseases 4th Ed. Oxford: Blacwell Scientific Publications, 1989:409-10.
6. Guisti G. Adenosine deaminase. In: Bergmeyer UH (ed). Method of enzymatic analysis. New York: Academic Press, 1974:1092-9.

Lung involvement in inflammatory bowel diseases

To the Editor: The rate of extraintestinal involvement in inflammatory bowel diseases (IBD) was reported as 21% to 41%.[1] Pulmonary involvement patterns include tracheobronchitis, tracheal stenosis, bronchitis, bronchiectasis, interstitial lung disease, necrobiotic nodule, serositis, and pulmonary vasculitis.[2,3,4,5,6,7] Our aim was to evaluate lung involvement in IBD. Seventeen IBD patients were included in the study with the approval of a local ethics committee. IBD activity was evaluated by clinical, endoscopic, and histopathological findings. Patients with a previous history of lung disease were excluded. Pulmonary function tests (PFT) were carried out using a Jaeger Master Screen Pneumo device. Patients with normal PFT values were examined for bronchial hyperreactivity with methacholine. High-resolution computed tomography (HRCT) was obtained using a Siemens Emotion 2003 Spiral CT (Munich, Germancy) device. Fiberoptic bronchoscopy was applied to 15 of 17 patients who accepted the procedure. Bronchoalveolar lavage (BAL) was performed by standard technique. Mucosal biopsies were also taken from the middle lobe through the lower lobe carina on the right, and the upper lobe through the lingua carina on the left. SPSS software was used for the analysis of the data. Fisher's exact test was used for comparison of disease activity to other parameters.

Of the 17 patients, 15 had ulcerative colitis and 2 had Crohn's disease. The mean age of 10 female (58.8%) and 7 male (41.2%) cases was 41.0±12.5 years and the mean duration of disease was 5.6±5.9 years. Six of the cases were regarded as active IBD. Respiratory symptoms were observed in 4 (23%) cases. PFT parameters were normal in all patients except one, who had restriction. Bronchial hyperreactivity was positive in 5 cases irrespective of respiratory symptoms. HRCT revealed pathology (air-trapping, emphysema, peribronchial thickening, bronchectasis, fibrosis, frosted glass, bullae) in 15 cases (88.2%). In BAL, the cell count of 7 cases (46,6%) indicated alveolitis (lymphocytic 40% and neutrophilic 6.6%) was present whereas in the mucosal biopsy of 2 cases (11.8%), submucosal inflammatory cell infiltration was observed. No relationship was found between disease activity and thorax HRCT findings, PFT, and BAL values (P=0.5).

Despite the amount of research carried out on extraintestinal findings in IBD, the pathogenesis still needs clarification. In such diseases, since there is an impairment in the mucosal immune regulation of gastrointestinal system antigens, digestive enzymes, and bacteria in the luminal content; activation of immune regulatory cells by the systemic circulation occurs.[8] Respiratory system pathologies can be classified as airway disease (upper airway obstruction, acute bronchitis, chronic bronchitis, chronic bronchial suppuration, bronchiectasis, bronchiolitis), parenchymal disease (cryptogenic organising pneumonia, pulmonary infiltrates and peripheral