Pleural Fluid Adenosine Deaminase in Rheumatoid Arthritis and Systemic Lupus Erythematosus

To the Editor:

The observation that the activity of adenosine deaminase (ADA) is higher in tuberculous pleural effusions than in malignant, para-pneumonic and transudative effusions was recently confirmed by Ocaña et al. These authors also reported high pleural fluid ADA activity in one patient with rheumatoid pleural effusion and asked for studies on more patients with connective tissue diseases.

We have measured the activity of ADA in pleural fluid and serum in a series of patients, comprising 14 with tuberculosis, six with rheumatoid arthritis (RA), and three with systemic lupus erythematosus (SLE). ADA activity was determined according to the method of Giusti with some minor modifications. The activity of ADA in pleural fluid from patients with tuberculosis, RA and SLE is shown in Figure 1. The mean pleural fluid ADA activity in patients with RA was comparable to that in patients with tuberculosis, but significantly higher than in patients with SLE (p<0.001), calculated using Student's t-test. Patients with tuberculosis or RA had significantly higher ADA activities in pleural fluid than in serum (p<0.001). In patients with pneumonia, nonspecific pleural effusion, cancer or congestive heart failure the pleural fluid ADA activity was significantly lower than in patients with tuberculosis or RA (p<0.001). The ADA activity in the serum of most patients (84 percent) with pleural effusion fell within the reference limits for ADA activity in normal human serum (16.2 ±10.2, mean ±2 SE).

Our study confirms earlier reports that the determination of ADA in pleural fluid is a valuable tool in the diagnosis of tuberculous pleurisy, but shows that it does not differentiate between tuberculous and rheumatoid pleurisy. This distinction can be made most reliably by measuring the glucose and complement (C3 and C4) concentrations in the effusion, rheumatoid effusions showing low values. The high ADA activities in rheumatoid pleural effusions, however, seem to distinguish these effusions from effusions caused by SLE, from other nontuberculous inflammatory effusions and from effusions caused by cancer. The markedly higher concentrations of ADA activity in pleural fluid than in serum suggests a local production of ADA in the pleural effusion. This may be related to local inflammatory processes within the pleural effusion and pleural membrane in which the secretion of T-lymphocytes and the maturation of monocytes to macrophages is accompanied by an increase in ADA activity. Differences in the local inflammatory reactions in pleural effusions probably reflect different pathogenic features in RA and SLE.

To the Editor:

Our findings concerning adenosine deaminase (ADA) activity in several types of pleural effusion confirm its diagnostic value in tuberculosis. The results of Pettersson et al in 14 further patients of tuberculous pleural effusion is in agreement with our experience. We have now tested 350 more cases, including 103 with pleural tuberculosis, and found results similar to our initial report; mean ADA activity in tuberculous fluid is 90.84 ± 29.27, with a sensitivity of 1 and a specificity of 0.85. As have Pettersson et al, we also studied ADA levels in 40 patients simultaneously in serum and pleural fluid, and no correlation could be found.

The three patients with SLE together with our three seem to demonstrate the value of ADA in the differential diagnosis of lupus pleuritis from tuberculous effusion, although the number of cases is still small.

In their six patients with rheumatoid arthritis, they found high levels of ADA as we did in the only case that we have studied at the time of our publication and in two new patients seen recently. The fact that both in tuberculous and rheumatoid pleural fluid ADA activity is high may be due to an activation of T-cell immunity; as it is well known in rheumatoid pleural effusion pleural biopsy may show granulomas.

The suggestion that ADA activity depends upon the lymphocyte maturative stage is in agreement with our previous work. As they stated, it is possible that in other granulomatous diseases with

References


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Figure 1. ADA activity in pleural fluid from 14 patients with tuberculosis (TB) six with rheumatoid arthritis (RA), and three with systemic lupus erythematosus (SLE). Horizontal bars indicate mean values in each group.
pleural effusion, such as rheumatoid arthritis, ADA activity may be high; nevertheless, further experience is needed.

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Acute Hepatotoxic Effect of Disopyramide

To the Editor:

Disopyramide is a quinidine-like antiarrhythmic drug. Because of its strong anticholinergic action, gastrointestinal disturbances are the most frequent side-effects. We report a case of hepatocellular toxicity following oral disopyramide treatment.

A 46-year-old woman with atrial fibrillation (AF) was admitted to our department for cardioversion. From the age of 16 years she suffered from mitral stenosis due to rheumatic heart disease. At the age of 43 years, because of paroxysmal AF, DC cardioversion was performed and quinidine was given to maintain the achieved sinus rhythm. After two months, however, AF reappeared and digoxin therapy was started. Because of two episodes of peripheral thromboembolism, coumadin was instituted and open mitral commissurotomy performed. Six months after the operation, while still on anticoagulant therapy, it was decided to attempt a repeat cardioversion, hoping that the better hemodynamic state could maintain sinus rhythm.

On admission, AF was noted on ECG. On physical examination, the first sound was strong and a diastolic murmur, grade 2-3/6, at mitral area was heard. The echocardiogram was compatible with mitral residual stenosis and the left atrium diameter was 4.5 cm. Routine laboratory findings were normal. The DC cardioversion was done, after oral quinidine 0.2 g x 6 was instituted the day before. Sinus rhythm was achieved, but AF reappeared after one hour. The following day a second trial of cardioversion was attempted by oral disopyramide, at a schedule dose of 300 mg every six hours on the first day. One hour after the second dose, sinus rhythm appeared on the monitor, but the patient began to complain of strong pains in the right hypocondrium, radiating to the back with nausea and vomiting; physical examination revealed a moderately enlarged and sensitive liver, but there was no sign of cardiac failure. Disopyramide was stopped and six hours after, the laboratory findings revealed: serum aspartate transaminase (SGOT) 127 IU (normal range 0-22 IU), serum alanine transaminase (SGPT) 127 IU (normal range 0-25 IU), lactic dehydrogenase (LDH) 67 IU (normal range 170-330 IU), prothrombin time (PT) activity 32 percent of normal. The peak of normal results of liver function tests was reached after three days: SGOT 443 IU, SGPT 770 IU, LDH 1992 IU; PT activity was still 30 percent of normal five days after the cessation of coumadin therapy.

Two days after disopyramide therapy was stopped, pain and hepatomegaly had disappeared, but the biochemical abnormalities returned to normal ranges after two weeks. Renal function tests, blood cell count, serum total lipids, cholesterol, bilirubin, alkaline phosphatase, creatinine kinase, glucose and electrolytes had always been in the normal range. Test for hepatitis antigen was negative. Disopyramide challenge test and liver needle biopsy were not performed, because they were not regarded by us as ethically and medically justifiable.

The strictly temporal relation between the onset of clinical symptoms and laboratory abnormalities after disopyramide administration and their return to normal after the drug was discontinued, strongly suggest that the hepatotoxicity was due to disopyramide. Quinidine, too, could be a cause of the liver dysfunction, but our patient had taken it in the past without any sign of intolerance.

Intrahepatic cholestasis has been previously described as a side-effect of disopyramide, but to the best of our knowledge, acute toxic reaction on hepatic cells has not been reported. The drug must therefore be considered a potential hepatotoxic agent.

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Erratum

To the Editor:

Regarding our paper entitled "Aristotle's triventricular heart and the relevant early history of the cardiovascular system," that was published in Chest in October, 1983, pages 462-468, several eagle-eyed friends pointed out two very unfortunate printing errors.

In the abstract at the beginning of the paper, two lines from the bottom, in the left hand column, the text presently reads: "... by Rufus and Ephesus ... ." This should be: by Rufus of Ephesus. . . .

The more important error, however, occurs on page 466, in the right hand column in the middle paragraph. The text presently reads: "The connecting passages from the left atrium to the lungs that also are obscure (small) must be the bronchial arteries or the patent ductus arteriosus (or both)."

This sentence obviously does not make sense. Going back to the original manuscript, I have discovered that it should be as follows:

"The connecting passages from the left atrium to the lungs that also are obscure (small) are obviously the pulmonary veins. The connecting passages from the left ventricle to the lungs, that also are obscure (small), must be the bronchial arteries, or the patent ductus arteriosus (or both)." Thus, 19 words were inadvertently omitted, which is why this part of the discussion makes no sense.

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