Lactic Dehydrogenase Anomaly in a Patient with Chronic Renal Failure

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A 67-year-old man with chronic renal failure (CRF) was defined to have lactic dehydrogenase (LDH)-immunoglobulin A (IgA) complex, the so-called “LDH anomaly”, in his serum and pleural effusion. He was found to have a pleural effusion on the right side during maintenance dialysis at a satellite hospital. A LDH-IgA complex was detected in the serum and pleural effusion by the method of current electrophoresis. The immunoglobulin class was found to be IgA (K) by counter immunoelectrophoresis. LDH anomaly is extremely rare in patients with CRF; the clinical significance of this substance in serum and pleural effusion remains unclarified. (Internal Medicine 32: 316–318, 1993)

Key words: enzyme-linked immunoglobulin, maintenance hemodialysis, pleural effusion, serum IgA (K)

Introduction

Enzyme-linked immunoglobulin (ELI) was initially reported in 1964 as macroamylase (1) and then LDH anomaly (2). ELIs for glucose 6-phosphodehydrogenase, alkalinephosphatase, glutamic oxalopyruvic transaminase (GPT), creatinine phosphokinase (CPK), glutamic oxaloacetic transaminase (GOT) and lipase were subsequently discovered (3–5). ELI has a large molecular weight, however, the biological significance of ELI remains unknown. ELI may not be associated with specific disorders and the mechanism of production remains unknown.

LDH anomaly is known to often occur in certain diseases such as neoplasms, liver damage and cardiovascular accidents (6, 7). Moreover, LDH-immunoglobulin complex is rarely detected in healthy human serum; the biological role of this complex remains unknown. It is clear that the LDH component of this complex is an antigen, as there have been no reports of immune complex disease. In chronic renal failure (CRF), certain immunological disorders which affect cellular and humoral immunity are present and often induce systemic infections and neoplasms (8). LDH-IgA complex, however, has not yet been reported in CRF. This is the first case of CRF in which this complex has subsequently been found in serum and pleural effusion.

Case Report

The patient, a 67-year-old man on hemodialysis for CRF due to diabetes mellitus since 1984, had a past history of colon diverticulum, arrhythmia, gallbladder polyp and calculi, syphilis and mild dementia of unknown origin. Recently he has been undergoing hemodialysis 3 times a week at a satellite hospital but he was found to have pleural and abdominal effusions of unknown etiology, for at least 4 months. On admission on June 10, 1991, this patient had no fever, upper respiratory symptoms, appetite loss, skin eruptions or malaise.

Physical examination revealed an arteriovenous shunt for hemodialysis on his right forearm. Overhydration was diagnosed based on his increased body weight in comparison with his dry weight. Laboratory studies showed moderate anemia: erythrocyte count 247 x 10⁴, hematocrit 23.8%, hemoglobin 8.3 g/dl. Liver damage reflected in GOT of 35 u/l, GPT of 53 u/l, γ-glutamic transpeptidase of 332 u/l, LDH of 485 mg/dl and leucine aminopeptidase of 893 u/l, was induced by fatty liver defined by abdominal ultrasound. LDH isozyme analysis showed a slight elevation of the LDH5 component. HBs and HCV antibodies were positive. No glucose intolerance was observed based on FBS of 78 mg/dl and hemoglobin A1c of 5.7%. Tumor markers were almost normal, except for DUPAN 2 of 16,000 unit. Serum immunoglobulin levels were: IgG 1200 mg/dl, IgA 260
mg/dl, and IgM 103 mg/dl. No findings were positive for infection except for a positive Wassermann reaction, however, anti-syphilis treatment had already been performed. Consequently, the patient was not infected.

A chest x-ray showed the presence of a pleural effusion on right side (Fig. 1) and a thoracocentesis was performed. Pleural fluid was characterized by LDH of 151 mg/dl, total protein of 4.1 g/dl, and albumin of 2.3 g/dl; rivalta reaction was negative, and pathological examination was negative for malignancy. Figure 2 shows the results of counterimmunoelectrophoresis of pleural effusion. The anomalous band was identified as LDH isoenzyme and included IgA (K) type immunoglobulin. This LDH-IgA complex was also detected in the patient’s serum. Thereafter, serum LDH level was normalized to 246 mg/dl, and LDH isozyme was almost within normal limit at the stage of discharge.

This patient was aggressively dialyzed to reduce the effusions in pleura and abdomen, and both of these effusions disappeared. Pleural effusion and ascites appeared to have been induced by overhydration.

Discussion

ELI complex was first reported for macroamylase in 1964 by Wilding et al (1). Ganrot (2) found this complex in 1967 in LDH anomaly; this represents the highest prevalence report for ELI. Several numbers more than 300 cases has been reported to date in Japan (9). Diseases associated with LDH anomaly consist of liver diseases such as hepatoma, stomach carcinoma, and cardiovascular diseases including hypertension and ischemic heart disease. However, there have been no reports of renal disease with LDH anomaly, except a few cases of nephrotic syndrome and renal transplantation. The present CRF case is the first report of the presence of LDH-IgA complex in the serum and pleural effusion. No other enzyme anomalies have been detected in patients with CRF. Collagen diseases often exhibit LDH anomaly (6), but there are no data showing whether the LDH anomaly disappears when these patients develop CRF or not.

LDH anomaly accounts for the highest proportion of ELI. The present patient had IgA-class binding globulin and the light chain was of K type. IgA-type LDH anomaly is the most common especially in cardiovascular disease and chronic hepatitis (10). On the other hand, the IgG type of LDH anomaly is associated with liver cirrhosis, hepatitis, multiple myeloma and hepatoma; collagen disease can give several types of immunoglobulin, such as IgG, IgA and IgM (6, 7).

ELI is usually detected by high serum levels of enzyme or by serum isoenzyme imbalance (11, 12). The present patient did not show these marked changes, and ELI was discovered as a result of a moderate elevation in a LDH in pleural effusion. There have been no reports of the presence of ELI in pleural effusion. The pleural effusion in our patient was a transudate, and the LDH-IgA complex appears to have originated in the blood stream. The same LDH-IgA complex might have been detected in the abdominal effusion, if a careful analysis had been performed.

It is known that the frequency of ELI for LDH anomaly in healthy controls is less than 0.3%, and then the highest binding immunoglobulin is IgA (9). Thus, the relationship between LDH-IgA and CRF is not confirmed at present. The decrease in the LDH-IgA level after aggressive hemodialysis in the present patient may be due to the reduction of the serum level of LDH. Although the origin and clinical significance of ELI
remain unknown, it may form immune complexes, and this may play a role in the pathogenesis of certain diseases such as glomerulonephritis or vasculitis. In the present case, CRF might be accompanied by an unknown immunologic abnormality which induced the LDH-IgA complex. Anti-syphilis antibody was also present. In fact, several autoantibodies such as anti-nuclear, anti-DNA and anti-smooth muscle antibodies are sometimes found in hemodialysis patients (13).

LDH-IgA may exist as a circulating immune complex, and this can induce serositis resulting in the retention of pleural or abdominal fluid. Further studies are required to determine the precise significance of LDH-IgA in the serum and pleural effusion.

References