Increased Lactate Dehydrogenase Isoenzyme-5 (LD₅) Activity Evidently Caused by Persistent Diaphragmatic Pressure on a Congested Liver

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A patient with congestive cardiac failure owing to severe bradycardia had a transvenous cardiac pacemaker inserted, resulting in complete alleviation of the cardiac failure. Later, however, the pacer became displaced high into the superior vena cava, where it ceased to pace the heart but instead stimulated the right phrenic nerve. Consequently, the rapid movement of the right hemidiaphragm pressing on the dome of an increasingly congested liver, for about one week before hospital admission, was associated with an unusually elevated LD₅ (lactate dehydrogenase, EC 1.1.1.27) activity in the serum.

An increased activity of serum LD₅, the slow-moving isoenzyme, is a sensitive and nearly specific indication of hepatocyte damage (1). Increase in LD₅ activity may be observed when the total serum LD activity is within normal limits, but usually the total serum LD is also elevated. This is the case in liver hypoxia, which is a common sequela of severe congestive cardiac failure, when elevations of up to twice the upper limit of normal may be seen (2). This case report documents enzyme activity changes in a patient with congestive cardiac failure caused by displacement of a cardiac pacemaker. These enzyme changes were complicated by hepatic compression from a fluttering diaphragm induced by impulses from the displaced cardiac pacemaker.

Case History

X.L., an 82-year-old man was admitted on 12 March with a history of progressive congestive cardiac failure associated with bradycardia.

Physical Examination and Relevant Initial Laboratory Findings

On admission this patient was found to have ventricular enlargement with murmurs of aortic stenosis and regurgitation. The ECG pattern indicated sinus bradycardia (50/min) and confirmed the left ventricular hypertrophy. The roentgenogram of the chest showed cardiomegaly and bilateral pulmonary edema.

Hemoglobin and serum electrolyte concentrations were normal but the blood urea nitrogen was 39 mg/dl, serum creatinine 1.5 mg/dl, and uric acid 9.4 mg/dl. Activities of serum enzymes [aspartate aminotransferase (L-aspartate:2-oxoglutarate aminotransferase, EC 2.6.1.1), creatine kinase (ATP:creatinine phosphotransferase, EC 2.7.3.2), and lactate dehydrogenase (L-lactate:NAD oxidoreductase, EC 1.1.1.27)] were within normal ranges.

Treatment and Subsequent Course

As cardiac failure could not be controlled in the face of severe bradycardia, a cardiac transvenous pacemaker was inserted on 13 March. The tip of the pacemaker was positioned in the lower portion of the right ventricle close to the tricuspid valve. The patient was discharged on 20 March without evidence of cardiac failure and with a stable cardiac rhythm of 70/min. He was re-admitted at 2355 hours on 5 April because of an attack of nocturnal dyspnea without chest pain and a history of increasing exertional dyspnea of seven days duration (associated with, but preceded by, right-sided diaphragmatic contractions synchronous with his pacemaker). On admission he was in left ventricular failure, had Cheyne-Stokes respirations, and was cyanotic. Rapid right-sided diaphragmatic contractions were also noted. His heart rate was 60/min and ECG
showed no cardiac response to the pacer stimulus. On monitoring, the heartbeat showed variable rates of between 40 and 75/min. Chest roentgenogram showed marked bilateral pulmonary congestion and the tip of the transvenous pacemaker high in the superior vena cava. In this position the pacemaker had been stimulating the right phrenic nerve, which lies directly lateral to the superior vena cava (3). The patient denied that he had been twisting the battery pack of the pacemaker but the pacemaker wire was wrapped around the generator.

He was given intravenous digoxin and furosemide and a temporary transvenous pacemaker was inserted, pacing the heart at 80/min. On the evening of 6 April he developed ventricular fibrillation. In spite of immediate defibrillation and resuscitation measures he went into irreversible ventricular asystole and died at 2230 hours on 6 April.

Relevant Laboratory Findings
(1000 Hours, 6 April)

Clinical laboratory values for serum: Na+ 137, K+ 6.2, Cl− 102, CO2 22 (all mmol/liter); urea nitrogen 35, creatinine 1.9, uric acid 11.4, total bilirubin 1.3 (all mg/dl), and albumin 3.5 g/liter. Serum lactate dehydrogenase activity was three times the upper limit of normal, creatinine kinase normal, and aspartate aminotransferase eight times the upper limit of normal. The LD electrophoreogram, performed on agarose (see Figure 1), showed a very high LD5 value. The values listed were corrected for substrate depletion in the isoenzyme assay, giving values of LD2 6%, LD3 6%, LD4 10%, and LD5 72%.

Autopsy Report (Relevant Features)

Immediate cause of death: Extensive bilateral pulmonary edema.

Liver: Gross appearance: Hyperemic, nutmeg liver with thickened capsule. Microscopic appearance: Central necrosis and atrophy of the hepatocyte. No histologic evidence of hepatitis.

Discussion

This case report records an elevated serum LD in a patient with gross congestive cardiac failure. It is unusual because over 70% of serum LD activity originates from the liver. Since serum creatine kinase was normal, muscle origin of the LD5 can be ruled out. Liver autopsy demonstrated only centriflobular necrosis and atrophy, and the possibility that liver damage was due to an early viral hepatitis can therefore be excluded. The serum was negative for hepatitis-associated antigen. We have only been able to find a single case report (4) of a patient with severe congestive cardiac failure after myocardial infarction with such a marked (75.3%) rise in LD5, and this was associated with a serum LD activity of 60 times the upper limit of normal, aspartate aminotransferase activity of 290 times the upper limit of normal, and numerous hepatic necrotic loci. Our own experience and those of others (2) indicate that only a modest rise in serum LD5 usually results from congestive cardiac failure. We postulate therefore that the rapid movement of the right hemidiaphragm induced by the displaced cardiac pacemaker is responsible for the marked LD5 elevation, by pressing on the dome of the congested liver. A similar elevation is noted after handling the liver during abdominal surgery (5).

References
2. idem, p 54.