Electrocardiographic Changes Related to Hypersecretion of Catecholamine in a Patient with Fulminant Hepatitis

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A 48 year-old-man, with fulminant hepatitis complicated with myocarditis was treated. Despite intensive care, he died of fulminant hepatitis associated with hepatitis B virus infection. Electrocardiography (ECG) showed myocardial infarction-like changes when he went into a deep coma. Microscopically, scattered foci of myocardial cell damage and cell death associated with clusters of inflammatory cells were present in the heart at autopsy. However, there were no findings related to myocardial infarction and staining for hepatitis B surface antigen and core antigen were nil. The concentration of plasma catecholamine was elevated concomitantly with high level of ECG changes. We consider that abnormal ECGs may reflect a hypersecretion of catecholamine and suggest that our patient had a catecholamine cardiopathy.

Key Words: Cardiac manifestation from viral hepatitis, Hepatitis B virus, Myocarditis

Cardiac manifestations may be present in patients with viral hepatitis. Palpitation, dyspnea and anginoid chest discomfort were observed in a group of patients with icteric viral hepatitis. In this group of patients, the ECGs showed P wave, T wave and ST segment changes as well as abnormal QRS axis, tachycardia, bradycardia and other arrhythmias. These cardiac abnormalities seen in those individuals with viral hepatitis may be caused either directly by viral infection, or indirectly by immune-mediated mechanisms.

We report here a case of acute fulminant hepatitis with hepatitis B virus accompanied with myocardial infarction-like changes. Hypersecretion of catecholamines may have played a significant role in this case.

CASE REPORT

Y.S., a previously healthy 48 year-old male surgeon was admitted in January of 1985, with general fatigue, anorexia, sleeplessness and lumbago of four days duration. He denied any history of drug addiction, blood transfusion, alcoholism or homosexual relationships. However, he had operated on a hepatitis B surface antigen (HBsAg) positive patient three months earlier.

At the physical examination on admission, his pulse was 104/min., blood pressure was 76/32 mmHg and he was afebrile. He had a deeply icteric sclera and skin. The lungs were clear to auscultation and the first sounds of the heart were accentuated but pathological murmurs were not audible. There was a mild right upper quadrant tenderness but no hepatomegaly.

On admission, the leukocyte count was 21,900/mm³. Prothrombin time was 50.1 seconds (control value, 13 seconds) and hepaplastin test was under 10 per cent. Total serum bilirubin was 10 mg/dl with a direct fraction of 3.8 mg/dl. Serum glutamic oxaloacetic transaminase was 14,046 IU/L (normal 0-40), glutamic pyruvic transaminase was 7,896 IU/L (normal 0-40),...
lactate dehydrogenase was 9,016 IU/L (normal 120-250). Blood urea nitrogen was 26 mg/dl (normal 8-20). Plasma epinephrine was 624 pg/ml (normal < 120) and norepinephrine was 1,560 pg/ml (normal 40-350).

The serum sample taken was positive for HBsAg and IgM class of antibody to hepatitis B core antigen, but was negative for antibody to HBsAg and IgM class of antibody to hepatitis A virus. The serologic studies for Echo, Coxackie, and other cardiotropic viruses were negative.

The diagnosis on admission was fulminant hepatitis by hepatitis B virus infection. Despite treatment with plasmapheresis, charcoal hemoperfusion and β-interferon, the clinical condition deteriorated rapidly. On the third day after admission he went into a deep coma, which continued until the ninth day when he died.

The ECG (Figure 1) done on admission showed sinus rhythm and ST depression in leads V4 to V6. On the third day (Jan. 10) when the patient fell into a deep coma, the ECG changed; ST elevated in leads I, II, III, aVF, V5, V6 and ST remarkably depressed in leads aVR and V1 to V4. These findings continued for over 24 hours. Consequently, myocardial infarction was suspected. However, the echocardiogram showed movement of the intraventricular septum and the left ventricular inferior wall was not akinetic but hyperkinetic. There was a moderate effusion under the posterior left ventricular wall. From these data, myocardial infarction was ruled out. On the fourth day, pericardial effusion disappeared with the administration of prednisolone and a beta

![Fig. 1. The course of an electrocardiogram showing nonspecific ST segment changes. Calibration is 1/1](image)
ECG changes in fulminant hepatitis

On the sixth day a coronary T wave appeared and on the eighth day right bundle branch block appeared in the ECG.

Concentrations of plasma catecholamine, norepinephrine and epinephrine were 1,560 pg/ml and 624 pg/ml on admission, 2,000 pg/ml and 452 pg/ml on the third day, 663 pg/ml and 155 pg/ml on the fourth day, 3,320 pg/ml and 408 pg/ml on the eighth day and 5,700 pg/ml and 628 pg/ml on the ninth day when he died, respectively.

At autopsy, the liver weighed 680 g and was flabby and diffusely atrophic, with red mottling on the cut surface. The postmortem section of the liver showed that almost all hepatocytes in the hepatic area were necrotized with lymphocytes. Neither HBsAg nor hepatitis B core antigen were found by both orcein and peroxidase-antiperoxidase complex methods. The heart weighed 395 g and there were 20 ml of effusion in the pericardium. Scattered foci of myocardial cell damage and cell death associated with clusters of inflammatory cells were present (Figure 2). However, there were no findings related to myocardial infarction. Staining for HBsAg and hepatitis B core antigen was nil and the coronary arteries were free of stenosis and sclerotic changes.

**DISCUSSION**

Cardiac abnormalities may be a significant complication of hepatitis B virus infection. Evidence of myocardial involvement in those with a viral hepatitis was mainly based on ECG findings. In our patient, the first ECG showed ST-T changes suggestive of acute myocardial infarction or coronary spasm. However, evidence of myocardial infarction was not present at autopsy. Coronary spasm could be ruled out because the echocardiogram showed a hyperkinetic motion of the left ventricle during ischemic ST elevation, and this continued for long time over 24 hours. It is well known that ischemic ST changes accompany hypokinesis or akinesis.

At least, four theories have been formulated with regard to the pathogenesis of cardiac manifestations associated with hepatitis. First, inflammatory heart disease may be a direct effect of the infecting virus, second, it may be an indirect effect, resulting from an immune-mediated mechanism. In our patient, HBsAg and hepatitis B core antigen were absent in the cardiac tissues. Third, the heart of a patient with hepatitis may be affected by hyperbilirubinemia. The serum bilirubin in our patient was very high; however, other investigators have discounted the toxic effect of hyperbilirubinemia. Fourth, hemorrhage in the myocardium and pericardial cavity may lead to ECG changes. In our patient, hemorrhage and infarction were nil.

Byer et al. reported that the ECG showed abnormal changes much like those seen in case of myocardial infarction in those with an acute cerebrovascular accident (CVA). It was considered that the abnormal ECGs reflect hypersecretions of catecholamine in those with acute CVA. We
hypothesize that our patient had a catecholamine cardiopathy. This patient's state was likened to CVA, because he was in a hepatic coma and had brain edema. Consequently, noradrenaline in the plasma elevated and the ECG changes resembled findings in CVA. Histologically, myocardial degeneration and inflammatory cell infiltration in our patient resembled findings of catecholamine-induced cardiopathy. Fulminant hepatitis is generally accompanied by hepatic encephalopathy. Therefore, this disease causes catecholamine cardiopathy as does CVA in case of subarachnoid hemorrhage. Cardiac manifestations in patients with fulminant hepatitis must be given serious attention.

REFERENCES