A CASE OF MYOCARDIAL DAMAGE FOLLOWING
ACUTE PARACETAMOL POISONING

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A 24-year-old woman was admitted to our hospital with acute paracetamol poisoning, and severe hepatic injury. The peak blood level of GOT, GPT and LDH were 32,600 U, 119,200 U and 36,500 U respectively. Glucagon-insulin and glutathione were administered to save the liver function. On the third hospital day, hemodialysis was administered to treat acute renal failure. On the 16th hospital day, when the liver and renal functions recovered, severe pulmonary congestion occurred and right heart catheterization revealed high pulmonary pressure. Echocardiography showed left ventricular enlargement accompanied by a severe diffuse impairment of left ventricular wall motion. Multi-focal ventricular arrhythmia was frequent during this period. Hemodialysis and artificial respiration were carried out for the treatment of heart failure. Three months after admission, myocardial perfusion scintigram showed patchy reduction in the uptake of TI-201 throughout the myocardium, and left ventriculography showed mild diffuse impairment of the LV wall motion (ejection fraction: 49%). In this case, acute heart failure appeared approximately 2 weeks after the severe hepatic injury. Apparently myocardial damage following paracetamol overdosage is caused not only by direct toxicity but by severe metabolic derangement.

Paracetamol (acetaminophen) has been widely used as a mild analgesic and antipyretic agent, and it is normally a very safe drug, but in case of overdosage it can cause acute centrilobular hepatic necrosis and renal tubular damage. Pimstone et al. first reported a case of acute centrilobular liver necrosis accompanied by acute myocardial damage following administration of a massive overdose of paracetamol. Subsequently, a few cases have been reported concerning acute myocardial damage in paracetamol poisoning.

We describe a patient with acute severe left ventricular failure following an overdose of paracetamol. In this case, we could evaluate cardiac performance during the acute stage and follow the patient for 7 months after the drug overdose.

A 24-year-old woman was admitted to Yamaguchi University Hospital with severe hepatic injury after taking an overdose of paracetamol (4.8 g) in a suicide attempt. She was found in an unconscious state, and was brought to the hospital. Saline solution was administered and gastric lavage was performed. The consciousness level improved within a few hours. The blood level of paracetamol (estimated by gas chromatography) was 47.1 µg/ml at 8 hours, and 10.7 µg/ml at 24 hours after ingestion.

The next day, the patient was transferred to an intensive care unit for the treatment of severe
Fig. 1. Time course of the treatment and the blood levels of serum enzymes. CHF; congestive heart failure, GOT; glutamate oxaloacetate transaminase, GPT; creatinine phosphokinase, LDH; lactate dehydrogenase, CAVH; continuous arteriovenous hemodialysis, HD; hemodialysis, ECUM; extracorporeal ultrafiltration method.

N.1 24 Female

Oct 25 '85  Nov 9 '85  Jan 21 '86

Pulmonary Congestion

Fig. 2. Chest X-ray films. Oct. 25 '85; on admission, Nov. 9 '85; at the day showing pulmonary congestion, Jan. 21 '86; at steady state condition.
Fig. 3. Electrocardiograms
Oct. 24 '85; on admission, Nov. 14 '85; during severe heart failure, Jan. 27 '86; at chronic steady state.

Fig. 4. The time course of M-mode left ventricular echograms obtained by 2-D echocardiography. The wall motion of the left ventricle was normal on Oct. 28 '85 (3 days after admission). However, on Nov. 15 '85 (22 days after admission with severe heart failure) the left ventricle size increased and diffuse hypokinesis of the ventricular wall were evident. The wall motion recovered at Jan. 27 '86.

hepatic damage. The time courses of the blood levels of serum enzymes, pulmonary artery pressure (by Swan-Ganz catheter), and treatment of hemodialysis are shown in Fig. 1. The peak blood level of serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) and lactate dehydrogenase (LDH) were 32,600 U (normal: 1-20), 119,200 U (1-17), and 36,500 U (130-240) respectively. Glucagon-insulin and glutathione were administered to save the liver function.

On the 3rd day, the urinary output decreased. Furosemide was administered intravenously, but oliguria persisted. Continuous arteriovenous hemofiltration (CAH) and hemodialysis (HD) were performed to treat the acute renal insufficiency.

On the 16th hospital day, orthopnea appeared. A chest X-ray film (center panel, Fig. 2) revealed marked pulmonary congestion. At this time, the pulmonary artery pressure was 47/38 (mean 43) mmHg, and cardiac output was 3.28 L/min/m². Electrocardiogram showed (Fig. 3) markedly low voltage in the limb leads throughout the clinical course, and when congestive heart failure was far advanced, multi-focal ventricular arrhythmia appeared (center panel, Fig. 3). Two dimensional echocardiography taken on the sixth hospital day revealed normal cardiac size with normal systolic performance (ejection fraction 68%, evaluated by M-mode echocardiogram, Fig. 4). However, on the 24th hospital day, when severe congestive heart failure was present, cardiac enlargement and diffuse impairment of the left ventricular wall motion (ejection fraction 41%) appeared (center panel, Fig. 4). Hemodialysis and a positive end-expiratory pressure with a respirator were administered to treat pulmonary edema. On the 37th day, cardiac failure was improved and the patient could do well in general hospital life.

Myocardial perfusion imaging with thallium-201, performed 3 months after admission, showed a patchy reduction in the uptake of radionuclide throughout the myocardium, especially in the anteroseptal region.

Cardiac catheterization performed 3 months after admission showed normal right and left heart pressures, and the cardiac index was reduced (2.16 L/min/m²). The peak value of the first derivative of left ventricular pressure was markedly reduced (723 mmHg/sec) and the time constant of LVP decay during the isometric relaxation period was prolonged (54 msec). Left ventriculography showed a generalized hypokinesis of the left ventricle and the calculated ejection fraction was 48%. The mean circumferential shortening velocity of LV was 0.63 cm/sec. The left and right coronary arteries appeared normal in a coronary angiography.

A few papers have addressed paracetamol toxicity on organs other than the liver, including the heart. In these reports, acute cardiac arrest and/or severe ventricular arrhythmia accompanied by severe hepatic injury occurred within a few days after the ingestion of an overdose of paracetamol. In all cases, myocardial degeneration and necrosis were found at autopsy. However, it is still undetermined whether the cardiac abnormalities are caused by the severe metabolic derangement of liver failure or by the pharmacology of the agent directly. Lesna et al reported that there have been no cardiac arrest cases in the absence of liver failure. In the present report, we have a patient with severe congestive heart failure following acute paracetamol poisoning. The heart failure appeared about 2 weeks following severe hepatic injury. In that time, the hepatic function had returned to normal, and there was no paracetamol in the blood. This suggests that, in this case, the myocardial damage may be attributable to the severe metabolic derangement of liver failure.

Three months after ingestion, when she had no clinical symptoms, the cardiac output, ejection fraction of the left ventricle, and the first derivative of left ventricular pressure were still under the normal range. The time constant of the left ventricular pressure decline was markedly prolonged, indicating impairment in the relaxation of the ventricle. A patchy reduction in the uptake of radionuclide throughout the myocardium may have indicated the existence of the patchy myocardial necrosis in the left ventricular wall. We found no case report of cardiac function being examined in detail with echocardiography, myocardial scintigraphy and cardiac catheterization during the chronic steady stage following acute severe heart failure caused by paracetamol poisoning. This brief report may be useful in understanding the clinical course and etiology of the myocardial damage after a paracetamol overdose.

REFERENCES

