A young pregnant woman was hospitalized due to hepatitis B virus (HBV)-related acute liver failure (ALF). The cardiac function was normal on admission. However, she developed ALF concurrently with a coma and severe cardiac failure. The patient was diagnosed with severe acute cardiomyopathy due to diffuse hypokinesis of the left ventricle wall on ultrasound cardiography. Following intensive treatment, both the liver and cardiac function dramatically recovered. Although some factors, such as HBV, pregnancy and systemic inflammatory response syndrome, are possible causes of acute cardiomyopathy in the present case, ALF itself may be a risk factor for heart failure.

Key words: acute heart failure, acute liver failure, fulminant hepatitis, hepatitis B virus, pregnancy

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give priority to her treatment. However, she developed grade II hepatic encephalopathy (6) on day 5 and was diagnosed with ALF with a hepatic coma, the acute type. Plasma exchange (PE) and hemodiafiltration (HDF) was started via a catheter inserted into the right femoral vein to the inferior vena cava. Cardiomegaly appeared, the heart rate increased and the blood pressure decreased gradually. Ultimately, it became difficult to withdraw large flows of blood for HDF. Therefore, HDF was changed to continuous HDF (CHDF) for the proper adjustment of the circulating fluid volume (blood flow rate: 75 mL/min, dialysate flow rate: 700 mL/h, replacement flow rate 300 mL/h, and filtration flow rate: 300 mL/h). Moreover, she was intubated under sedation by an intravenous anesthetic and connected to a mechanical ventilator because she was in an excited state and restless. On day 7, the patient suddenly developed cardiac arrest. Although she recovered to sinus rhythm immediately by a chest compression, a chest X-ray showed cardiomegaly, pulmonary congestion and bilateral alveolar infiltration (Fig. 3). ECG showed advanced left axis deviation and rSR pattern in precordial lead V1, but there were no findings of ST segment elevation or pathologic Q wave (Fig. 2). Ultrasound cardiography (UCG) of the wall motion of the left ventricle revealed diffuse-severe hypokinesis or akinesis in areas other than the base to central part of the posterior wall. The ejec-

![Image](https://via.placeholder.com/150)

**Figure 1.** A chest X-ray on day 2. A central vein catheter was inserted into the right internal carotid vein. There were no findings of cardiomegaly or pulmonary congestion.
Figure 2. 12-lead electrocardiograms. Normal findings were observed on day 2 (a). Following the cardiac arrest on day 6 (b), an advanced left axis deviation and rsR' pattern in lead V1 was observed.

tion fraction (EF) was estimated to be approximately 17.5% (Fig. 4). The patient was diagnosed with acute cardiac myopathy, rather than myocardial ischemia and myocarditis, because the blood flow of the coronary arteries on UCG was normal and the serum levels of myocardial enzymes, such as creatine kinase (CK), were not elevated. Ultrasound showed intrauterine fetal death; however, it was difficult to induce abortion due to DIC.

The patient was complicated with severe cardiomyopathy, ARF, DIC and intrauterine fetal death, as well as ALF with a hepatic coma. Her hemodynamics were stabilized by the continuous administration of noradrenaline, and CHDF was effective for the removal of the excess water from the body. The serum ALT levels and prothrombin activity subsequently improved. She spontaneously delivered a dead fetus with minimum hemorrhaging on day 8. UCG on day 11 indicated an improvement of the left ventricular lateral and septal wall motion (EF=33.6%, Fig. 4). CHDF was terminated on day 11 and she was extubated on day 13. The EF had dramatically improved to 57.2% on day 20 (Fig. 4). Although the patient required long-term rehabilitation to improve her respiratory condition, she was discharged from our hospital on day 33.

Discussion

The diagnostic criteria for ALF in Japan were defined in 2011 by Mochida et al. as follows: acute liver injury associated with prothrombin time values of 40% or less of the standardized value, or international normalized ratios (INRs) of 1.5 or more due to severe liver damage within 8 weeks of the onset of disease symptoms. ALF is classified as “ALF without a hepatic coma” and “ALF with a hepatic coma,” where no or grade I hepatic encephalopathy is present in the former type, and grade II or more severe hepatic encephalopathy is found in the latter type. ALF with a hepatic coma is further subclassified into the “acute type” and “subacute type.” ALF with a hepatic coma corresponds to the former classification of “fulminant hepatitis” (6). Furthermore, according to the classification of ALF taking into consideration the etiologies (7), the present case was diagnosed with HBV-related ALF with a hepatic coma, the acute type. The annual incidence of fulminant hepatitis in Japan is estimated to be approximately 400 cases (1). According to the annual reports by the Intractable Hepato-Biliary Diseases Study Group of Japan, a nationwide survey of the patients with ALF between 2010 and 2012 reported that fulminant hepatitis accounted for 42.3% of ALF cases. Therefore, there are approximately 950 cases of ALF. Most of the cases of ALF are caused by viral infections with HBV infection being the most frequent (2).

The patient in the present study developed severe acute heart failure, and we speculated that HBV, pregnancy and/or ALF may have been related to the heart failure. Approximately 20% of HBV infected patients are complicated with extrahepatic disorders that include dermatologic disease, polyarthralgia and arthritis, glomerulonephritis, polymyositis, aplastic anemia, neuropathy and vasculitis (8, 9). Although cardiac manifestations due to hepatitis have been recognized for a long time, there are few reports of myocarditis associated with HBV (10, 11). There are two hypotheses regarding HBV related myocarditis; one proposes an indirect mechanism with immune complexes (12), whereas the other proposes a direct myocardial cell injury by HBV. Some authors have reported that HBV proteins and nucleic acids were found in a number of non-hepatic tissues, including the myocardium (11, 13). However, the acute heart failure in the present case was not myocarditis but myopathy because the serum levels of CK, which is a sensi-

Figure 3. A chest X-ray on day 7. An X-ray showed cardiomegaly, pulmonary congestion and alveolar infiltration.
Figure 4. Clinical course. The patient was treated with ETV and mPSL from day 2, but the CTR increase on X-rays and the body weight increased gradually. She developed acute liver failure with a coma on day 5 and cardiac arrest on day 6. Following treatment with PE, CHDF and the continuous administration of NAD, the liver and cardiac functions immediately improved. ETV: entecavir, mPSL: methylprednisolone, PE: plasma exchange, CHDF: continuous hemodiafiltration, NAD: noradrenaline, CTR: cardio thoracic ratio, EF: ejection fraction.

tive marker of myocardial injury, were within the normal range. It was therefore difficult to diagnose the present case as HBV-related myocarditis, although a subclinical myocardial injury by HBV may have existed.

Peripartum cardiomyopathy (PPCM) is a representative disease of pregnancy-associated heart failure (14). PPCM is an idiopathic cardiomyopathy presenting with the left ventricular systolic dysfunction, and the EF typically decreases to less than 45% without dilatation of the left ventricle. PPCM is defined as cardiomyopathy that develops in the last month of pregnancy or within 5 months post-partum. Therefore, the cardiac dysfunction of the present case was most likely not due to PPCM, because the patient was in the middle stage of pregnancy and had no symptoms of delivery when she developed cardiopulmonary arrest. However, a significant physiological hemodynamic change occurs even during a normal pregnancy, with increases in both the cardiac output and blood volume (15). Therefore, pregnancy itself may be a risk factor for the stress-related cardiac dysfunction.

Congestive heart failure is a complication in approximately 10% of the patients with fulminant hepatitis and late onset hepatic failure (4). It has been previously reported that most ALF patients had significantly high levels of serum troponin I regardless of the etiology (16, 17). Troponin is a specific marker of myocardial cell injury (18). These studies found that ALF patients had subclinical myocardial injury and elevated troponin I levels were associated with a significant increase in the morbidity and mortality. In addition, this phenomenon was observed in certain circumstances, such as acute stroke or sepsis (19, 20) and was closely related to the prognosis (21). Therefore, it is speculated that the elevated troponin I is due to subclinical myocardial cell injury, such as necrosis or increased membrane permeability; however, troponin I was not measured in the present patient because the measurement of troponin I was not possible in our hospital.

Recently, a new cardiac syndrome, “takotsubo cardiomyopathy,” was proposed. The clinical feature is transient cardiac failure with chest pain despite the absence of coronary artery abnormalities (22). The wall motion of the left ventricle shows akinesis or dyskinesis from the middle to apical area in contrast with hyperkinesis in the basal area, and the electrocardiogram demonstrates either ST elevation or T wave inversion (23). Because the onset is typically preceded by emotional or physical stress, catecholamine-
mediated myocardial dysfunction has been proposed as a potential mechanism. Moreover, the involvement of estrogen has also been reported recently, as most of the patients are postmenopausal elderly women (24). In the present study, the diagnosis of takotsubo cardiomyopathy could not be made due to results different from the established criteria in the ECG findings (Fig. 2b) and the insufficiency of the exclusion diagnosis. However, the clinical course and UCG findings in the present case were similar to takotsubo cardiomyopathy. Hayashi et al. reported a case of fulminant hepatitis with the transient hypersecretion of catecholamine (25). Therefore, ALF with a hepatic coma is a very stressful condition and may be a predisposing condition for takotsubo cardiomyopathy.

We performed the proper administration of the extracorporeal circulation and additional drugs; however, we cannot completely rule out the possibility that the treatment may have had an effect on the patient’s condition. The exact mechanism of the heart failure in the present case remains unclear. However, we speculate that ALF may itself be a risk factor for heart failure, directly or indirectly. Physicians must therefore be aware of the possibility of heart failure during the treatment of ALF even in younger patients who present with a normal cardiac function.

The authors state that they have no Conflict of Interest (COI).

References