Case of severe alcoholic hepatitis with acute kidney injury, gastrointestinal tract bleeding, and rhabdomyolysis

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Abstract

We report a rare case of severe alcoholic hepatitis complicated by acute kidney injury, upper gastrointestinal tract bleeding, and rhabdomyolysis in a patient with heavy alcohol consumption. A 74-year-old man with heavy alcohol consumption was admitted to our hospital due to general fatigue and jaundice. The serological findings indicated liver and renal failure, anemia, and elevated muscle enzyme level (creatine kinase, 4,865 U/L). The upper gastrointestinal tract endoscopy revealed a hemorrhagic gastric ulcer that was treated with an endoscopic hemostatic technique. He was then diagnosed as having severe alcoholic hepatitis with acute kidney injury, upper gastrointestinal tract bleeding, and rhabdomyolysis. He died within 36 h after admission and corticosteroids were not administered. In conclusion, our patient had an early death mainly due to complications, such as AKI, and severity of the underlying liver disease.

Keywords
severe alcoholic hepatitis, acute kidney injury, upper gastrointestinal tract bleeding, rhabdomyolysis

Introduction

Alcohol abuse causes various liver diseases, including alcoholic steatosis, alcoholic hepatitis (AH), liver fibrosis, and cirrhosis (Yu et al, 2010). AH is characterized by serological and clinical features, such as jaundice, hepatomegaly, and leukocytosis, in patients with heavy alcohol consumption (Keating et al, 2022; Horie et al, 2014). The severity of the disease has been assessed by various scoring systems (Keating et al, 2022; Trebicka et al, 2022; Sehrawat et al, 2020; Veryan et al, 2019). Severe alcoholic hepatitis (SAH) is an acute liver disease associated with high mortality reaching up to 20%–50% within 30 days (Sehrawat et al, 2020; Hmoud et al, 2016). The estimated prognostic factors of SAH include the presence of infections, acute kidney injury (AKI), and gastrointestinal (GI) tract bleeding in addition to the severity of underlying liver dysfunction (Veryan et al, 2019; Hmoud et al, 2016; Maiwall et al, 2016; Horie et al, 2014).

Rhabdomyolysis is characterized by severe acute muscle injury that leads to the release of myofibers into the bloodstream and clinical features such as myalgia (Nance et al, 2015; Zutt et al, 2014; Zimmerman et al, 2013). Heavy alcoholic consumption is one of the risk factors causing myopathy, including rhabdomyolysis. However, to the best of our knowledge, there have been few case reports of rhabdomyolysis complicated by AH (Yoshida et al, 2002). We report a rare case of SAH complicated by AKI, upper GI tract bleeding, and rhabdomyolysis in a patient with heavy alcohol consumption.

Case presentation

A 74-year-old Japanese man presented to our hospital due to jaundice and shortness of breath. A few days prior, he had appetite loss and general fatigue. His social history was notable for frequent alcohol consumption; he had consumed ~40 g/day of ethanol for 35 years (from ages 30 to 64 years old). However, after his retirement (65 years old), he had consumed ~80 g/day of ethanol. When he was 71 years old, he was admitted to another hospital due to appetite loss and vomiting.

The serological findings recorded were as follows: white blood cell (WBC), 7,250/μL; hemoglobin (Hb), 12.1 g/dL; platelet, 12.5 × 10^4/μL; total protein, 6.8 g/dL; albumin, 3.6 g/dL; total bilirubin, 1.8 mg/dL; aspartate aminotransferase (AST), 418 U/L; alanine aminotransferase (ALT), 321 U/L; γ-glutamyl transpeptidase (γ-GTP), 356 (reference value: <70) U/L; creatinine, 0.78 mg/dL; and prothrombin time (PT), 71.8% (reference value: 80%–100%). He was diagnosed with alcoholic liver disease without cirrhosis. After discharge, his alcohol consumption was interrupted for four months. However, he continued to drink alcohol (approximately 100 g/day of ethanol) after the interruption.

At the time of the present consultation, his height was 171.4 cm, his body weight was 54.9 kg, and his body mass index was 18.7 kg/m^2. His blood pressure was 92/62 mmHg, his pulse rate was 98 beats/min, and his temperature was 37.2°C. He was alert and conscious. His palpebral and bulbar conjunctivas were pale and icteric, respectively. The results of the cardiopulmonary test were normal, and the liver was palpable. His whole skin was icteric. The lower extremities were edematous. The serological findings were as follows: WBC, 15,960/μL (neutrophils 90.5%); Hb, 8.7 g/dL; platelet, 10.2 × 10^4/μL; total protein, 4.6 g/dL; albumin, 2.3 g/dL; total bilirubin, 10.5 mg/dL; direct bilirubin, 9.2 mg/dL; AST, 2,408 U/L; ALT, 1,507 U/L; lactate dehydrogenase, 783 U/L; γ-GTP, 346 U/L; blood urine nitrogen (BUN), 52.1 mg/dL; creatinine, 1.53 mg/dL; creatine kinase (CK), 4,865 (reference value: 62–287) U/L; sodium, 133 mEq/L; potassium, 5.9 mEq/L; chloride, 94 mEq/L; phosphorus, 2.6 (reference value: 2.5–4.5) mg/dL; ammonia, 148 μg/dL; C-reactive protein (CRP), 2.4 mg/dL; Fischer ratio, 1.2 (reference value: 2.2–4.3); PT, 15.1%; PT-international normalized ratio 6.79 (reference value: 0.84–1.14); and activated partial thromboplastin time, 56.8 (control, 32.5) s. Hepatitis virus markers or autoantibodies, such as antinuclear or antimitochondrial antigen, were negative. A urinalysis indicated negativity for protein, but occult blood and bilirubin were noted. The abdominal echogram showed findings of a fatty liver. Plain computed tomography showed hepatomegaly without splenomegaly (Fig. 1).

The patient was admitted to our hospital on the same day. Upper GI tract endoscopy revealed the presence of a hemorrhagic gastric ulcer of the angulus (lesser curvature), which was treated by argon plasma coagulation (Fig. 2). Neither esophageal nor gastric varices were found. He was diagnosed with AH. Moreover, regarding the severity of AH, the patient's Model for End-Stage Liver Disease (MELD; a score of ≥21 indicates severe AH) and Maddrey's discriminant function (mDF; a score of ≥32 indicates severe AH) scores (Sehrawat et al, 2020; Maiwall et al, 2016) were 41 and 118, respectively. The patient's Glasgow Alcoholic Hepatitis Score (GAHS) (score is between 5 and 12, with ≥9 being associated with a poor prognosis) (Forrest et al, 2007) was 12, whereas his Japanese Alcoholic Hepatitis Score (≥10 indicates severe AH) (Horie et al, 2014) was 14. Consequently, he was diagnosed with SAH complicated by AKI, upper GI tract bleeding, and rhabdomyolysis. Transfusion and plasmapheresis with fresh frozen plasma were done. However, the renal dysfunction (BUN, 105.9 mg/dL; creatinine, 3.16 mg/dL) progressed on the next day from admission. He died within 36 h before corticosteroid was administered. Blood cultures performed before admission showed negative findings.

Discussion

We present a rare case of SAH complicated by AKI, upper GI tract bleeding, and rhabdomyolysis. Heavy alcoholic consumption is a common cause of liver diseases, such as AH, worldwide. The diagnosis of AH is usually made based on the social history of heavy alcohol consumption, clinical findings, elevated liver enzymes (AST and ALT), jaundice, and absence of other liver diseases (Sehrawat et al, 2020). Although histological findings are useful for the diagnosis of AH, liver biopsy is not always necessary for diagnosis (Veryan et al, 2019). Its pathogenesis has a multifactorial process; metabolism of alcohol to toxic products, Kupffer cell stimulation by endotoxin, oxidative stress, and nutritional impairment lead to liver injury and inflammation (Philips et al, 2019; Haber et al, 2003). Serological disorders of AH include an elevated transaminase level including AST (higher than the ALT level), hyperbilirubinemia, prolonged PT, low albumin level, elevated leukocyte level with a predominance of neutrophils, and elevated CRP level (Trebicka et al, 2022), which were all present in our case. AH severity is usually assessed by various scoring systems [MELD (≥21), mDF score (≥32), and Japanese Alcoholic Hepatitis Score

(≥10)] (Maiwall et al, 2016; Horie et al, 2014). SAH is often a life-threatening disease, and its prognostic factors include the complications of infections, AKI, and GI tract bleeding in addition to the severity of underlying liver dysfunction (Veryan et al, 2019; Hmoud et al, 2016; Maiwall et al, 2016; Horie et al, 2014; Yu et al, 2010).

AKI is a common complication observed in up to 30% of inpatients with SAH, and it considerably decreases survival, particularly in patients with SAH (Sujan et al, 2018). The presence of a systemic inflammatory response syndrome was reported to be a predictor of AKI development and progression and 90-day mortality of patients with SAH (Maiwall et al, 2016). Moreover, higher MELD scores seem to be associated with the development of AKI (Veryan et al, 2019). However, the precise pathophysiology of AKI associated with SAH remains unclear. The presence of GI tract bleeding was reported to be associated with early death in patients with SAH according to the review of data from placebo-controlled clinical trials (Yu et al, 2010). However, a retrospective study in a single facility among cirrhotic patients with SAH indicated that the survival rate was not significantly lower among patients with GI tract bleeding than among those without GI tract bleeding (Rudler et al, 2015). This result was due to the lower probability of developing an infection by antibiotic prophylaxis in cases with GI tract bleeding (Rudler et al, 2015). GI tract bleeding may deteriorate the hepatic blood flow and microcirculation that was associated with the pathophysiology of SAH (Horie et al, 2014). In present case, a hemorrhagic gastric ulcer was found and treated with argon plasma coagulation. Several abnormalities of coagulation complicated by severe liver dysfunction may be associated with GI tract bleeding (Bohania et al, 2021).

Rhabdomyolysis is characterized by severe acute muscle injury and the release of myofibers into the bloodstream (Nance et al, 2015; Zutt et al, 2014). It is usually diagnosed by the increase in serum CK levels, and many clinicians consider the cutoff level of 5–10 times the normal upper limit (Zimmerman et al, 2013). The complications of rhabdomyolysis include AKI that ranges from 15% to >50% (Melli et al, 2005). The causes of rhabdomyolysis vary, which include vigorous exercise, drugs, hypokalemia, seizures, trauma, infections, and endocrine disorders (Shizuma, 2022; Zutt et al, 2014). In the present case, there was no apparent cause, except for the heavy alcohol consumption. Muscle involvements are not uncommon in patients with a heavy alcohol consumption (Nance et al, 2015; Hewitt et al, 1995). A previous clinical study showed that 15.2% (23/151) of inpatients with chronic heavy alcohol consumption had an increased level of serum CK and 0.66% (1/151) presented with acute rhabdomyolysis (Martin et al, 1985). Another study showed that 18.2% (6/33) of patients with AH were positive for myoglobinuria (Sood et al, 2000). However, to the best of our knowledge, only one case of rhabdomyolysis complicated by AH has been reported (Yoshida et al, 2002). The patient was a 68-year-old man with rhabdomyolysis (serum CK level was approximately 40 times higher than the normal upper limit) without any complication of AKI, which was likely partially due to electrolyte imbalances (hyponatremia and hypophosphatemia) (Yoshida et al, 2002). To the best of our knowledge, case reports of rhabdomyolysis complicated by SAH are lacking. Muscle dysfunction as a consequence of alcoholic dysfunction is multifactorial and is attributable to a combination of immobilization, acid-base and electrolyte imbalances (i.e., hypokalemia and hypophosphatemia), vitamin deficiency, and/or direct myotoxicity (Abdulfattah et al, 2018; Yoshida et al, 2002; Hewitt et al, 1995). However, hypokalemia and hypophosphatemia, which sometimes develop due to chronic alcoholism (Abdulfattah et al, 2018), were not noted in our case. The direct toxic effect of ethanol on the skeletal muscles may be induced by the disruption of the adenosine triphosphatase pump function and breakdown of the muscle membrane (Maddison, 2002). Alcohol can reduce substrate availability by inhibiting gluconeogenesis, thereby further affecting the function of the already damaged muscle fibers (Maddison, 2002). Malnutrition, limited energy stores, and enzyme deficiencies may also predispose an individual with heavy alcohol consumption to rhabdomyolysis (Zimmerman et al, 2013).

Regarding the treatments for SAH, corticosteroid is the first-line therapy (Sehrawat et al, 2020; Hmoud et al, 2016), which has been also recommended by the American Association for Study of Liver Diseases and the European Association for Study of Liver Diseases (Philips et al, 2019; Hmoud et al, 2016). Although this study indicates that patients with a low GAHS (mild AH) do not appear to benefit from corticosteroid therapy (Forrest et al, 2007), it reduces the risk for short-term

mortality in patients with SAH (mDF score of ≥32) (Trebicka et al, 2022). Although corticosteroids are known to predispose patients to infections (Keating et al, 2022), a recent meta-analysis of randomized trials showed that corticosteroids do not increase the rate of occurrence of or mortality from bacterial infections in patients with SAH (Hmoud et al, 2016). In our case, corticosteroid was not administered immediately at admission due to the presence of upper GI tract bleeding and possibility of infections. Our case died within 36 h from admission. The possible causes of early death may include (1) presence of complications, such as progressive AKI, upper GI tract bleeding that may induce ischemia and reperfusion injury to the liver, and rhabdomyolysis and (2) severe liver failure as an underlying disease, as characterized by MELD and mDF scores of 41 and 117.5, respectively [the sensitivity for predicting 30-day mortality in patients with MELD score >30.5 was 100% (Philips et al, 2019)].

In conclusion, we reported a rare case of SAH with AKI, upper GI tract bleeding, and rhabdomyolysis. Our patient had an early death mainly due to complications, such as AKI, and severity of the underlying liver disease. Additional studies and strategies regarding the treatments for SAH are urgently needed.

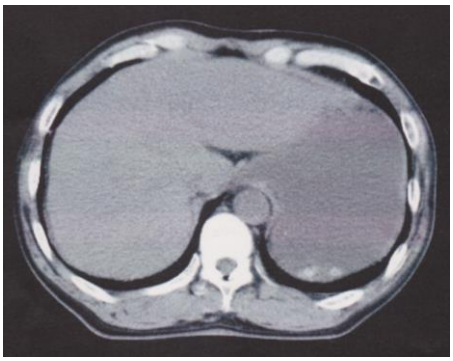

Fig. 1. Plain computed tomography of the abdomen showing hepatomegaly.

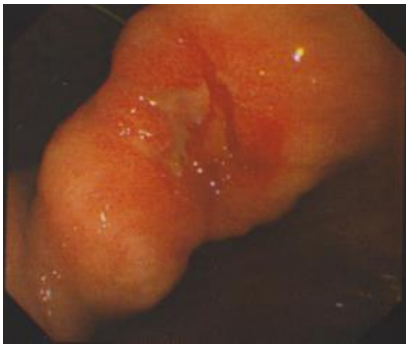

Fig. 2. Upper gastrointestinal tract endoscopy showing a hemorrhagic gastric ulcer of the angulus (lesser curvature).

Conflict of interests

There was no funding support and there is no conflict of interests to declare.

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