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A CASE OF ACUTE LIVER FAILURE CAUSED BY THE INGESTION OF GALERINA FASCICULATA

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Abstract

A 76-year-old man presented to another hospital with a two-day history of severe diarrhea and vomiting. A laboratory analysis revealed liver dysfunction. He was admitted to that hospital, but the laboratory data showed the exacerbation of patient's liver dysfunction and renal dysfunction. He was therefore transferred to our hospital for multidisciplinary treatment. According to patient's laboratory data and medical history, he was diagnosed with acute liver failure due to mushroom poisoning. This mushroom was identified as *Galerina fasciculata*. An investigation at the prefecture's agricultural center revealed that the mushroom contained amatoxin.

Key words : acute liver failure, mushroom, *Galerina fasciculata*, amatoxin

Introduction

Among the more than 5,000 species of mushrooms, approximately 52 species are poisonous to humans[1]. *Galerina fasciculata* belongs to *Galerina* genus of amatoxin-containing mushrooms. The ingestion of amatoxin-containing mushrooms causes various gastroenterological symptoms such as epigastric abdominal pain, nausea, vomiting, and severe watery diarrhea[2]. Acute liver failure due to ingestion of amatoxin-containing mushrooms is relatively rare[3]. The diagnostic criteria for acute liver failure were established in Japan in 2011. From 2011, the criteria were expanded to include cases other than hepatitis and non-coma cases[4]. Viral infection, in particular hepatitis B virus infection, is a major cause of acute liver failure in Japan. The other major causes include : drug-induced, and autoimmune ; however, there are some reports of acute liver failure due to mushroom poisoning.

We herein report a successfully treated case of acute liver failure caused by *Galerina fasciculata*.

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Case Report

A 76-year-old man presented to another hospital with a two-day history of severe diarrhea and vomiting. Five days prior to the visit, he ate a wild mushrooms which he picked behind his house. A laboratory analysis revealed liver dysfunction : aspartate aminotransferase (AST), 375 IU/l ; and alanine aminotransferase (ALT), 511 IU/l. He was admitted to that hospital but his liver dysfunction, renal dysfunction, prothrombin time percentage activity (PT%), and serum ammonia level showed exacerbation. Seven days after eating the mushroom, he was transferred to our hospital. The patient was 164.0 cm tall and weighed 53.8 kg. His body temperature was 36.4℃, his heart rate was 86 bpm, and his sitting blood

Table 1. The patient's laboratory data on admission to our hospital

WBC	7,400/μl	BUN	31 mg/dl	HBsAg	(−)
RBC	540×10^4/μl	Cre	0.62 mg/dl	IgM-HBc Ab	(−)
Hb	17.2 g/dl	Na	131 mEq/l	HCV Ab	(−)
Ht	49.8%	K	3.7 mEq/l	IgM-HA Ab	(−)
Plt	5.5×10^4/μl	Cl	98 mEq/l	IgA-HEV Ab	(−)
AST	2,773 IU/l	CRP	0.81 mg/dl	Anti-VCA IgM	(−)
ALT	6,128 IU/l	BS	136 mg/dl	IgM-CMV Ab	(−)
ALP	268 IU/l	NH3	118 μg/dl	IgM-HSV Ab	(−)
LDH	1,777 IU/l	PT%	31%	ANA	40
γ-GTP	64 IU/l	APTT	31.5 s	AMA-M2	(−)
T-Bil	4.2 mg/dl	FDP	3.4 μg/ml		
D-Bil	1.8 mg/dl	Fib	222.0 mg/dl		
TP	6.5 g/dl	AT-3	61.6%		
Alb	4.1 g/dl	D-dimer	1.03 μg/ml		
ChE	360 IU/l				
T-Chol	183 mg/dl				

pressure was 114/76 mmHg. He had no significant past medical history and had not consumed alcohol, or any medication. On admission he showed jaundice, but no other remarkable physical abnormalities such as hepatomegaly, splenomegaly, or flapping tremor. The laboratory data was as following follows : AST, 2,773 IU/l ; ALT, 6,128 IU/l ; alkaline phosphatase (ALP), 268 IU/l ; lactate dehydrogenase (LDH), 1,777 IU/l ; γ- glutamyltransferase (γ-GTP), 64 IU/l ; total bilirubin (T-Bil), 4.2 mg/dl ; blood urea nitrogen (BUN), 31.0 mg/dl ; creatinine (Cre), 0.62 mg/dl ; C-reactive protein (CRP), 0.81 mg/dl ; ammonia (NH_3), 118 μg/dl ; and prothrombin time% (PT%), 31.0% ; activated partial thromboplastin time (APTT), 31.5 s (Table 1). The patient was negative for hepatic viral markers (Table 1). Abdominal ultrasonography (US) and contrast-enhanced multidetector-row computed tomography (CE-MDCT) showed no remarkable abnormalities such as hepatomegaly, splenomegaly, or ascites. According to the above results and patient's medical history, he was diagnosed with acute liver failure without hepatic coma due to mushroom poisoning. This mushroom was identified as *Galerina fasciculata* after an investigation by the staff in the prefectural agricultural center (Figure 1). Treatment was initiated with glucose infusion, gabexate mesilate, antithrombin-3, and platelet transfusion. The patient's AST, ALT, and PT% continued to improve smoothly (Figure 2). US-guided biopsy of the liver showed hepatic necrosis around central vein, mild inflammatory cell infiltration, hemorrhage, hemosiderin deposition, but no findings of specific hepatitis (Figure 3). On seventeen days in the hospital, he discharged to home on foot without any symotoms.

Figure 1. *Galerina fasciculata,* the species of mushroom that was ingested by this patient.

Discussion

Sugawara et al. reported that the etiologies of acute

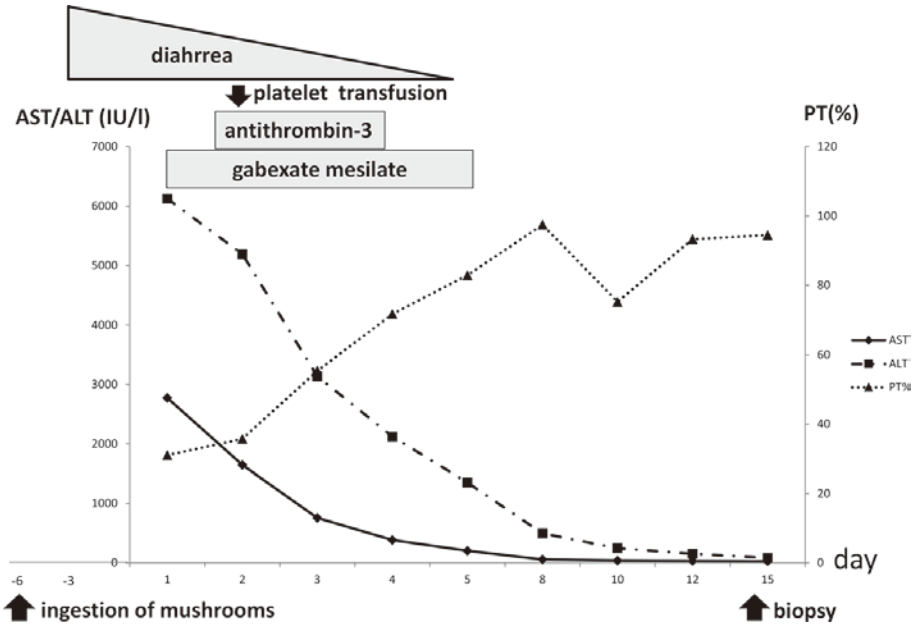

Figure 2. The clinical course of the patient.

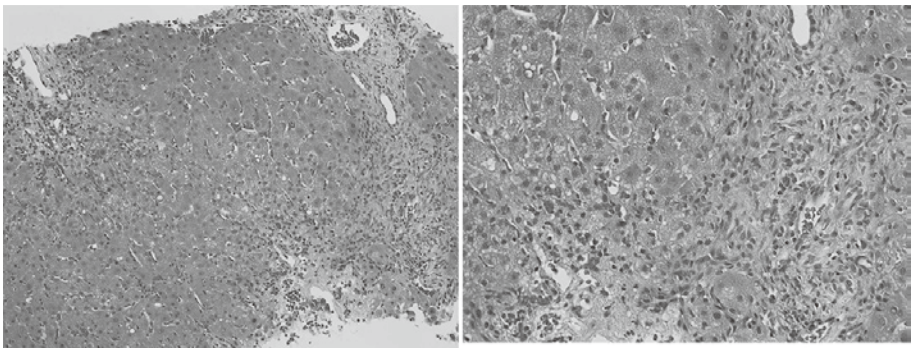

Figure 3. The histopathological findings of the liver showed hepatic necrosis around the central vein, mild inflammatory cell infiltration, hemorrhage, hemosiderin deposition, but no findings of specific hepatitis.

liver failure without hepatic coma were as follows : viral infection (44.8%), indeterminate (28.1%), liver damage without hepatitis (11.5%), autoimmune hepatitis (9%), drug allergy (4%) ; with the etiologies in the remaining cases unknown due to insufficient examination[4]. Although viral infection is the major cause of acute liver failure without hepatic coma, the proportion of mushroom poisoning cases is largely unknown. In a survey of patients with acute liver failure in Spain, only 10 out of 267 cases (4%) were caused by amatoxins[3]. Amatoxins account for 90% of fatal mushroom poisonings, with their most significant impact being on liver dysfunction[5].

Galerina fasciculata, which contains amatoxin, belong to the *Galerina* genus. Amatoxin is absorbed by the gastrointestinal tract and transported to the liver, where it is absorbed into the liver cells by two hepatocyte membrane proteins organic anion transporting peptide (OATP) 1B3 and sodium taurocholate co-transporter (NTCP)[6,7,8].

In hepatocytes, amatoxin inhibits mRNA synthesis, leading to cell death[8]. The ingestion of the amatoxin - containing mushrooms causes various gastroenterological symptoms. Amatoxin can be detected in urine only within 36 hours after ingestion[9]. In contrast, liver dysfunction typically peaks at approximately 48–72 hours after ingestion, where levels of AST and ALT may elevate to greater than 2,000IU/l. In some cases, liver dysfunction develops into fulminant hepatitis or acute liver failure[10]. Since the present case was transferred to our hospital 7day after ingestion, we did not determine urine amatoxin levels. There are several reports of cases of acute liver failure caused by amatoxin poisoning, however, the exact incidence of amatoxin poisoning cannot be estimated[11]. The treatment of acute liver failure caused by amatoxin poisoning is the same as acute liver failure of other causes. Several substances (steroids, cimetidine, thioctic acid, etc) have been documented to be ineffective in amatoxin poisoning[11]. A number of previous reports demonstrated the effects of benzylpenicillin ; however, a retrospective analysis revealed that benzylpenicillin had poor clinical efficacy in cases of amatoxin poisoning[12]. Eventually, the major parameter in the treatment of amatoxin poisoning was found to be the time of admission to hospital after the ingestion of mushroom[11]. Other reports have investigated the efficacy of the liver transplantation, fractionated plasma separation and an adsorption system in the treatment of acute liver failure caused by amatoxin poisoning[13,14]. Kaneko et al. reported a case of amatoxin poisoning from the ingestion of Japanese Galerina mushrooms[15]. A search of PubMed with keywords “amatoxin” and “acute liver failure” revealed only nine reports describing cases of acute liver failure due to amatoxin poisoning. In these reports, 10 of 13 patients died due to acute liver failure[1,5,11,16-18]. Sevki Hakan et.al conducted a retrospective analysis of 294 cases of mushroom poisoning, and reported that AST and ALT levels were elevated in 8.1 % of the cases[5]. Furthermore, they noted that there was a significant relationship between mortality and liver enzyme levels, and that liver enzyme levels could possibly be a good prognostic marker of amatoxin poisoning or an indication for liver transplantation. It can be said that cases of acute liver failure caused by mushroom poisoning are relatively rare ; however, the development of acute liver failure is associated with a high mortality rate.

We herein demonstrated the successful treatment of acute liver failure caused by *Galerina fasciculata*. Acute liver failure caused by amatoxin- containing mushroom is associated with a high mortality rates ; however, rapid treatment may be helpful in improving the prognosis. In this prefecture, some people pick wild mushrooms as in the mountains. Thus, accidental consumption of poisonous mushrooms sometimes occurs. In cases where mushroom poisoning is suspected from patient’s medical history, it is recommended that they be promptly transferred to a large institution. Moreover, an effective antidote is needed to further improve the prognosis associated with mushroom poisoning.

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