CASE REPORT

Acute Renal Failure Caused by Mushroom Poisoning

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Despite the abundance of wild mushrooms growing in a variety of habitats in Taiwan, mushroom poisoning is rarely reported. Here, we report two cases of mushroom poisoning, possibly due to *Amanita smithiana* or a related species. A 54-year-old man and his 52-year-old wife presented with acute anuric renal failure 1 day after ingesting some white mushrooms they had collected when mountain climbing; they made a full recovery following hemodialysis and supportive treatment. Although rare, mushroom poisoning should be considered in the differential diagnoses of acute renal failure. [*J Formos Med Assoc* 2006;105(3):263–267]

Key Words: acute renal failure, *Amanita smithiana*, hemodialysis, mushroom poisoning

Despite an abundance of wild mushrooms in Taiwan, mushroom poisoning is rarely reported. A previous study indicated a much lower reported incidence of mushroom poisoning in Taiwan than in America and Europe, with an incidence of 0.023 exposures per 100,000 people per year.[1] Among these previously reported cases, the incidence of major organ failure is even rarer. Most cases present with self-limited gastrointestinal symptoms such as nausea, vomiting and abdominal pain.[1] Notable in the literature is a report of an outbreak of nine cases of rhabdomyolysis caused by *Russula subnigricans* in 1998.[2] Here, we report mushroom poisoning in a 54-year-old man and his 52-year-old wife, both of whom presented with acute renal failure after eating wild mushrooms presumed to be *Amanita smithiana*. They both recovered completely following hemodialysis and supportive treatment. *A. smithiana* is a white mushroom with white spores. Before the year 2000, only 13 cases of poisoning due to ingestion of this species and causing acute renal failure had been reported in North America.[3–5] The prevalence rate of mushroom poisoning in Taiwan is much lower than that reported in the West;[1] however, underdiagnosis might contribute to this difference. Therefore, the gravity of mushroom poisoning should not be overlooked.

Case Reports

Case 1

A 54-year-old previously healthy man presented with a 2-day history of nausea and vomiting, and a 1-day history of reduced urine output after eating some wild mushrooms. The ingested mushrooms measured approximately 15 cm tall, and the cap was about 5 cm in diameter. They were white and also produced a whitish spore print. The mushrooms were collected while the patient was mountain climbing at about 2000 m above sea level in central Taiwan. As the mushrooms were pulled directly out from the soil, no detailed observations on the root structure could be made. However, some wart-like structure was noted over the caps of the younger mushrooms. The patient and his wife had both tried a small amount

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of the mushrooms for 2 consecutive days, and no immediate adverse effect had been noted. Therefore, they cooked a larger quantity, which they consumed at supper on the 3rd day. Four hours later, the patient experienced increased production of urine. Six hours after the meal, abdominal pain, nausea and vomiting developed. These symptoms persisted to the next day.

On initial presentation at a local hospital, he was treated for presumed acute gastroenteritis with intravenous fluid and antiemetic agent. However, he subsequently became anuric on the same day and visited our emergency department on the 3rd day. He denied any medication or Chinese herb use, and there was no animal contact or insect bite during the mountain climbing trip when the mushrooms were collected.

At this stage, the patient was conscious, alert and oriented. His height was 165 cm, and he weighed 61 kg. His body temperature was 36.4° C, pulse rate was 79 bpm, respiratory rate was 16 breaths per minute, and blood pressure was 143/81 mmHg. Physical examination revealed only mild abdominal tenderness without peritoneal sign or hyperactive bowel sounds. Skin turgor was normal and there was no sign of dehydration. Sclera were anicteric, the liver and spleen were not palpable, and there was no costovertebral angle tenderness. The rest of the physical examination was unremarkable.

Figure 1. A photograph of *Amanita smithiana*. It has a long, bulbous stipe (stem) and a cup (volva) at the root. (Reprinted with permission from Reference 5.)

Laboratory data showed elevated blood urea nitrogen (BUN) of 61.5 mg/dL (normal range, 4.5–24 mg/dL), elevated serum creatinine (Cr) of 7.2 mg/dL (normal, 0.6–1.3 mg/dL), and a BUN/Cr ratio of 8.54. Serum sodium was 137 mmol/L and potassium was 5.0 mmol/L. Liver enzymes were mildly elevated, with aspartate aminotransferase (AST) of 30 U/L and alanine aminotransferase (ALT) of 110 U/L; bilirubin was in the normal range. Initial white blood cell count was 10,150/μL, with 81.8% neutrophils, which declined soon after admission. There were no signs of infection and there was no recent use of antibiotics. Arterial blood gas showed mild metabolic acidosis with respiratory compensation, pH 7.38, $PaCO_2$ 32.8 mmHg, and bicarbonate 19.6 mmol/L. Urinalysis showed a specific gravity of 1.010, a spot urine protein of 30 mg/dL, and hyaline and granular casts 0–2/high power field (hpf). Although muscle enzymes were not checked, urinalysis revealed only 1+ occult blood, which was attributed to Foley catheter insertion causing microscopic hematuria of 10–20 red blood cells/hpf. Fractional excretion of sodium (FE_{Na}) was 5.6%, and the renal failure index (urine sodium multiplied by plasma Cr, then divided by urine Cr) was 7.65. The influence of pre-renal factors, such as dehydration due to nausea and vomiting, was considered to be limited based on the values of serum BUN/Cr ratio, arterial blood gas, urine specific gravity, FE_{Na} and renal failure index. Renal ultrasonogram showed normal-sized bilateral kidneys (both 10 cm in longitudinal axis), non-distended urinary bladder and no evidence of hydronephrosis. Acute renal failure, presumably mushroom poisoning-related, was highly suspected.

He and his wife recognized *A. smithiana* (Figure 1) from a mushroom field guide as the species that they had eaten, and the physical appearance they described matched the species as well, except for

a cup-like structure on the root, the volva, which cannot be seen if the mushrooms are pulled out instead of dug up. With a presumptive diagnosis of acute anuric renal failure caused by *A. smithiana*, emergency hemodialysis was started and treatment with N-acetylcysteine and silymarin was also given. Urine output started to increase 9 days after the poisoning (Figure 2A). Liver enzymes returned to normal soon after admission. Renal biopsy was suggested but the patient refused. His systolic blood pressure remained elevated at 150 mmHg and required treatment. Mild hyperkalemia and hyperphosphatemia were treated with calcium polystyrene sulfonate, aluminum hydroxide and calcium carbonate. He was discharged 17 days after mushroom ingestion; 4 weeks after discharge, his blood pressure normalized, and antihypertensive treatment was discontinued. His serum Cr level at that time was 1.3 mg/dL.

Case 2

This 52-year-old previously healthy woman was married to Case 1 and had eaten the same mushrooms. She shared the same symptoms and signs as her husband, except that she did not have initial polyuria. On presentation to the emergency department, BUN was 40.4 mg/dL, Cr was 5.2 mg/dL, and AST/ALT was 224/398 U/L, slightly higher than her husband but which also normalized within days after admission. Urinalysis was unremarkable. She described a similar clinical course to her husband's (Figure 2B), but had neither hypertension nor electrolyte disturbances. Two weeks after discharge, all her physical findings and laboratory data were normal.

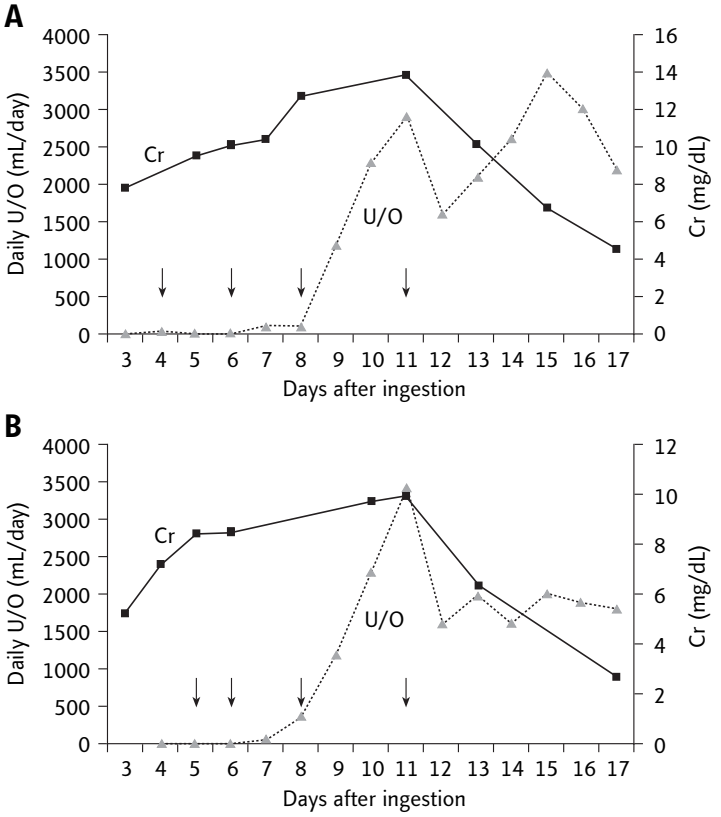

Figure 2. Daily urine output (U/O) and serum creatinine (Cr) in: (A) Case 1; and (B) Case 2. Arrows indicate hemodialysis sessions.

Discussion

Mushroom poisoning is usually classified into the following eight toxin categories:[1,6] cyclopeptide (amanitin, phalloidin) with hepatocyte damage accounting for most fatalities; orellanine (in *Cortinarius*) with late-onset renal failure; monomethylhydrazine (gyromitrin) with red blood cells, hepatocyte and neuronal damage; coprine with disulfiram-like reactions taken with alcohol; muscarine with parasympathomimetic reactions; psychoactive ibotenic acid (muscimol) with gamma-aminobutyric acid (GABA) agonist activity; psilocybin with LSD-like hallucinations; and finally, miscellaneous gastrointestinal irritants accounting for most poisoning.[1,6] *A. smithiana* poisoning, however, cannot be classified into any of these eight categories and has its own unique presentation.

In Taiwan, cyclopeptide-containing species, the most deadly ones, have only been found at high altitudes (> 1000 m above sea level), where few people live.[1] For this reason, severe poisoning is fairly rare in Taiwan. In most cases of mushroom poisoning, the exact species involved cannot be identified due to a lack of an available specimen for examination, or poor preservation of the specimen due to rapid decomposition of the fresh mushroom at room temperature or in moist environments. A previous study reported that in

Taiwan, the offending species was identified in only 28.6% of cases (4 of 14 incidents).[1]

The unique toxic effects of *A. smithiana* were first reported in a mycology journal in 1992.[3] Prior to that, acute renal failure was only recognized as a complication secondary to the fulminate liver failure caused by the amatoxins found in *Amanita* spp.; the most well-known of these species being *Amanita phalloides* (the "Death Cap");[7] victims may require a liver transplantation to survive.[7] However, despite being in the same family, *A. smithiana* does not share the same toxins, and its nephrotoxic agents have been identified as allenic norleucine and chlorocrotylglycine.[4] Another well-known group of toxins in mushrooms known to cause renal failure are the orellanines found in *Cortinarius* spp. With this group, the latent period from the onset of trivial gastrointestinal symptoms to permanent chronic renal failure is longer; from 2 days up to 14 days. Mortality has declined with modern dialysis, but about 17–41% of patients require long-term renal replacement therapy or kidney transplantation.[8] Renal biopsies reveal tubular lesions, interstitial nephritis and progressive fibrosis.[8] Acute renal failure caused by *A. smithiana* ingestion differs from that due to orellanine intoxication in that it takes place more rapidly, but may allow full recovery without permanent renal impairment.

Our review of the literature found that since 1992, three case series including 13 patients with *A. smithiana* intoxication have been reported in North America.[3–5] Most patients mistook *A. smithiana* for the edible pine mushroom *Tricholoma magnivelare*. In addition, the white "innocent" appearance of *A. smithiana* misled its victims to believe that it was harmless. Gastrointestinal irritation usually occurred within 4–11 hours and renal failure within 3–5 days.[4,5] In some cases, a short polyuric phase was also noticed before the development of anuric renal failure.[4] Most patients required temporary hemodialysis for up to several weeks, but all eventually returned to their baseline renal function.[4,5] Elderly patients or patients with diabetes or hypertension appear to have more rapid onset, and more severe and longer periods of renal failure;[4] they are also prone to have the initial polyuric phase as well.[4] However, even those with mild baseline renal function impairment can make a full recovery as well.[4] Despite severe gastrointestinal symptoms, most patients did not appear to be dehydrated and oliguria did not respond to fluid replacement.[4] As in our patient, the physical findings, BUN/Cr ratio and arterial blood gas in previously reported cases showed no evidence of dehydration.

No specific treatment for *A. smithiana* poisoning is available. Hemodialysis for acute renal failure and symptomatic treatment are the most important therapies.[4,5] N-acetylcysteine and silymarin are the only two reported treatments specific to amatoxin intoxication, but their benefit remains debatable.[7] Furthermore, use of these treatments has not been reported in *A. smithiana* poisoning. As in most cases of mushroom poisoning in which no samples of the mushroom were available, our patients recognized the species they ate from a mushroom atlas. Due to the similarity in appearance among certain members of the *Amanita* family, N-acetylcysteine and silymarin were added as treatment in case of misidentification, although their use in these two cases might actually have been redundant. Activated charcoal may break the hepatoenteral circulation of amatoxins,[7] but no such circulation has been documented with allenic norleucine and chlorocrotylglycine, so activated charcoal may not be applicable in *A. smithiana* poisoning.

In conclusion, with appropriate supportive care, total recovery can be achieved, and neither end-stage renal disease nor hepatic failure have been reported.

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