Wild Mushroom Poisoning in North India: Case Series with Review of Literature

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Mushroom is an important constituent of diet in many ethnic tribes in India. Ethnic Indian tribes are known to consume nearly 283 species of wild mushrooms out of 2000 species recorded world over. Although they are experts in distinguishing the poisonous from edible mushrooms, yet occasional cases of toxicity are reported due to accidental consumption of poisonous mushrooms. We report amanita like toxicity in a family after consumption of wild mushrooms resulting in fatal outcome. (J Clin Exp Hepatol 2014;4:361–365)

Mushroom poisoning (aka mycetism) in humans has been described since time immemorial, which has been witnessed by ancient writings like "Rigveda" (at least 3500 B.C.) and "Atharvaveda" (at least 1500 B. C.) The first written record about a fungus is the death from fungal poisoning, of a mother, daughter and two full grown sons, an event, which Euripides (456–450 B.C.) commemorated by an epigram.[1]

In India, Mushroom has been a source of diet and article of commerce since long time and across many cultures. Poisoning results from unintentional consumption of poisonous wild mushrooms. The cases however remain undiagnosed, underreported and unpublished. A large number of suspected cases are reported in lay press. There have been small epidemics of mushroom poisoning culminating in mortality especially during monsoon. The published literature from India is sparse and mostly in the form of case reports.[2–4] The present case report depicts one such incident of accidental death of three members of a family, owing to consumption of wild mushrooms.

CASE REPORT

A family consisting of 35 yr old man, 33 yr old lady (mother), 14 yr old daughter and 13 yr old son residents of a village Trela, district Mandi, Himachal Pradesh, India consumed wild mushrooms harvested from mountains in September 2011. Subsequently all four of them developed pain abdomen, vomiting and bloody diarrhea 4–6 h after consumption. They were taken to community health center where intravenous (IV) fluids and anti-emetics were given and diarrhea and vomiting settled after 24–36 h and they remained relatively asymptomatic for 8–10 h. This was followed by progressive altered sensorium and behavior and irritability for which referred to district hospital Mandi, where found to have transaminitis >10 times elevated and jaundice. Provisional diagnosis of toxic hepatitis secondary to poisonous wild mushrooms was made. Patients were managed with IV fluids, antibiotics, anti-emetics and antacids. The man died on day 4 of the illness and in view of worsening sensorium the remaining three patients were referred to our center, a tertiary care hospital in North India. All the patients had similar complaints of jaundice and altered sensorium at admission. On Examination all three were afebrile, tachypneic (respiratory rate 26–32/min), had tachycardia (respiratory rate 120–160/min) with normal blood pressures at presentation.

Mother was pale with deep icterus, grade 3 hepatic encephalopathy, brisk deep tendon reflexes and down going planters. Investigations revealed anemia ((hemoglobin 7.6 g/dL), leukocytosis [total leukocyte counts (TLC) 16,000/mm^3], conjugated hyperbilirubinemia (total bilirubin/conjugated bilirubin 5.7/4.6 mg/dl), coagulopathy (prothrombin time >2 min), transaminitis [aspartate aminotransferase (AST)/alanine aminotransferase (ALT) 1580/2400 IU/ml)], deranged renal function test (creatinine 2.8 mg/dL) and hyperkalemia (K+ 5.6 mEq/L) with tall 'T' waves in electrocardiogram (ECG). Ultrasound abdomen showed fatty liver, liver span 13.4 cm, gall bladder wall thickening with pericholecystic fluid, bilateral renal parenchymal disease and mild ascites (Table 1).

Son had pallor, icterus, grade 3–4 hepatic encephalopathy, generalized hypertonia, absent deep tendon reflexes and mute planters. Investigations revealed anemia (hemoglobin 10.7 g/dL), normal leukocyte count, conjugated hyperbilirubinemia (total bilirubin/conjugated bilirubin

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Abbreviations: ALT: alanine aminotransferase; AST: aspartate aminotransferase; ECG: electrocardiogram; Hb: hemoglobin; ICU: intensive care unit; Inj: injection; IU/ml: international units/milliliter; IV: intravenous; NCCT: noncontrast computerized tomography; TLC: total leukocyte counts
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Table 1 Patient Characteristics.

Parameters	Patient 1: mother	Patient 2: son	Patient 3: daughter
Residence	Rural, hills	Rural, hills	Rural, hills
Type of mushroom consumed	Wild	Wild	Wild
Onset of symptoms after consumption	4 h	4–5 h	6 h
Initial symptoms	Pain abdomen, vomitings, bloody diarrhea	Pain abdomen, vomitings, bloody diarrhea	Pain abdomen, vomitings, bloody diarrhea
Resolution of initial symptoms	24–28 h	28–30 h	30–36 h
Period of convalescence	8–10 h	8–10 h	8–10 h
Progression of symptoms	Jaundice, altered sensorium	Jaundice, altered sensorium	Jaundice, altered sensorium
Day of admission to ICU	4th	4th	5th
General examination findings	Pallor, icterus	Pallor, icterus	Icterus
CNS examination	Grade 3 hepatic encephalopathy	Grade 3–4 hepatic encephalopathy	Grade 3 hepatic encephalopathy
	Hyperreflexia	Arreflexia	Hyperreflexia
	Planters down going	Planters mute	Planters down going
	Normal tone	Hypertonia	Normal tone
Investigations: Hemoglobin	7.6 g/dl	10.7 g/dl	12.1 g/dl
Leukocyte count	16000/mm^3	5000/mm^3	9200/mm^3
AST/ALT	1580/2400 U/L	2814/3759 U/L	573/1463 U/L
Bilirubin total/conjugated	5.7/4.6 mg/dl	5.2/3.1 mg/dl	5.2/3.6 mg/dl
Prothrombin time	>2 min	>2 min	>2 min
Serum sodium	125 meq/L	135 meq/L	137 meq/L
Serum creatinine	2.8 mg/dl	0.5 mg/dl	3.0 mg/dl
Arterial gases	Metabolic acidosis	Metabolic acidosis	Metabolic acidosis
Urine routine	Normal	Normal	Normal
USG abdomen	Raised liver echogenicity, 13.4 cm GB wall thickening, pericholecystic fluid, bilateral renal parenchymal disease, ascites	Raised liver echogenicity, 12.4 cm No ascites	Raised liver echogenicity, 11.5 cm GB wall thickening, pericholecystic fluid, bilateral renal parenchymal disease, ascites, bilateral mild pleural effusion
Management	ICU based including penicillin and silibinin	ICU based including penicillin and silibinin	ICU based including penicillin and silibinin
Course			
DIC	Present	Present	Present
Onset of hypotension	10 h	20 h	24 h
Demise	12 h	24 h	60 h
Terminal events	Refractory shock, MODS, sinus bradycardia	Refractory shock, MODS	Refractory shock, MODS, ventricular fibrillation, seizures

5.2/3.1 mg/dL), coagulopathy (prothrombin time > 2 min), transaminitis (AST/ALT 2814/3759 IU/ml), normal renal function test, electrolytes and ECG. Ultrasound abdomen showed fatty liver; span 12.4 cm and no free fluid. Noncontrast computed tomography (NCCT) head showed cerebral edema (Table 1).

Daughter had icterus, no pallor, grade 3 hepatic encephalopathy, brisk deep tendon reflexes and down going planters. Investigation revealed hemoglobin 12.1 g/dL, TLC 9200/mm^3, conjugated hyperbilirubinemia (total bilirubin/conjugated bilirubin 5.2/3.6 mg/dl), coagulopathy (prothrombin time >2 min), transaminitis (AST/ALT: 573/1463 IU/ml), normal Renal function test, electrolytes and ECG. Ultrasound abdomen showed fatty liver, liver span 11.5 cm, Gall bladder wall thickening with pericholecystic fluid, bilateral renal parenchymal disease, mild

ascites and mild bilateral pleural effusion. NCCT head showed cerebral edema (Table 1).

All three were managed in the liver ICU using standard protocol for treatment for acute liver failure including intensive monitoring, intubation for airway protection, IV fluids, IV broad spectrum antibiotics, IV mannitol, elevation of head end, hyperventilation, appropriate sedation, IV proton pump inhibitors, Inj vitamin K, Inj dextrose, vasopressor support and intensive monitoring and management of electrolytes imbalances and blood sugars. Inj penicillin G @1 million units/kg/d and silibinin @ 30 mg/kg/day were also given. Gastric aspirate from all three patients showed active upper gastrointestinal bleed, which was managed with fresh frozen plasma and packed red blood cell transfusions.

Mother developed hypotension requiring increasing doses of vasopressors with falling urine output and had progressive sinus bradycardia. She sustained cardiac arrest after about 12 h of ICU admission and could not be revived.

After about 20 h of ICU admission, the son developed worsening sensorium, falling urine output and hypotension requiring increasing vasopressor support. He was managed conservatively with fluids and blood products, however his condition kept on worsening. He sustained cardiac arrest after about 24 h of stay and could not be revived.

Daughter developed hypotension requiring vasopressors and seizures after 24 h of stay which responded to Inj levetiracetam. About 48 h of stay she had cardiac arrest following ventricular fibrillation and was revived in 10 min but her condition kept on deteriorating. She sustained another cardiac arrest after about 60 h of stay and could not be revived.

Post mortem liver biopsy from mother's liver showed features of cholestasis and autolytic changes. Liver biopsy from the son and daughter, revealed confluent areas of hepatic necrosis with few surviving hepatocytes showing intracytoplasmic cholestasis, features suggestive of fulminant hepatic damage.

DISCUSSION

Mushrooms are the fleshy, spore-bearing fruiting body of higher fungi, typically produced above ground on soil or on their food source. Traditional mycological knowledge of most Indian ethnic groups is known to be extensive and profound, Ethnic Indian tribes are known to consume nearly 283 species of wild mushrooms out of 2000 species recorded world over.[5] Around 100 species of mushrooms in India are known to be poisonous to humans,[6] hepatotoxicity is caused mainly by amatoxin and gyromitrin synthesized by a number of Amanita species and some members of the Galerina, Lepiota, and Conocybe genera.[7,8] Common poisonous mushroom species identified from Hills in South India are *Omphalotus olivascens*, *Mycena pura* and *Chlorophyllum molybdites* but human poisonings are uncommon as ethnic tribes are experienced in identifying poisonous from non poisonous mushrooms.[5,9,10] Previous case series from India include one which had fifteen cases of *Amanita phalloides* poisoning[11] with major clinical presentation with nausea, vomiting, diarrhea, jaundice and hepatic or renal failure after 48 h, or both. The early rise in serum AST/ALT levels was associated with high mortality. Study from the same institution has previously described prevalence of mushroom poisoning in children to be 3.2% out of all accidental poisonings.[12]

In our series acute liver failure and MODS resulted in fatality in all the three family members, after consumption of wild mushrooms harvested from hills of Himachal Pradesh. The species identification and toxin analysis could not be performed due to non-availability of mushroom specimen; however, the clinical presentation was similar to amanita poisoning. Amanita toxicity is characterized by an asymptomatic incubation period followed by the gastrointestinal and hepatotoxic phases, leading eventually to multi-organ failure and death (Table 2). This is probably the first reports of wild mushroom poisoning from Himachal Pradesh. In the absence of mushroom for species identification, syndromic approach to diagnosis and management is essential.[6] Similar case series from Assam has emphasized high mortality in patients aged less than 10 (83%) or more than 50 yr (100%) and major cause being acute liver failure and acute renal failure.[13]

C. molybdites poisoning also presents with gastrointestinal manifestations but colicky abdominal pain and explosive, bloody diarrhea are characteristic features.[3] Toxicity due to Clitocybe species of mushrooms results in muscarinic symptoms.[4] The toxicity of *A. phalloides* is related to two distinct groups of toxins: phallotoxins and amatoxins. The phallotoxins are toxic to cell membrane of enterocytes leading to initial diarrhea like illness whereas amatoxins

Table 2 Clinical Phases of Amatoxin Poisoning.

Phases	Onset from ingestion	Symptoms and signs
Stage 1.	Lag phase 0–24 h	Asymptomatic
Stage 2.	Gastrointestinal phase 6–24 h	Nausea, vomiting, crampy abdominal pain, and severe secretory diarrhea
Stage 3.	Apparent convalescence 24–72 h	Asymptomatic, worsening of hepatic and renal function indices
Stage 4.	Acute liver failure 4–9 days	Hepatic and renal failure → multi-organ failure → death

(α-amanitin and β-amanitin) are responsible for the toxic effect leading to acute liver failure, renal failure and potential toxicities to pancreas, adrenal glands, and testes.[14,15] Amanitins act via inhibiting eukaryotic RNA polymerase-II and thus interrupting transcription in humans resulting in decreased mRNA and protein synthesis and leading eventually to cell death. Since these toxins are not destroyed by cooking, the toxicity may occur after eating the cooked mushrooms. There is some evidence suggesting that parboiling can attenuate their toxicity but it has not being conclusively proven in studies.

Classically, Clinical manifestations occur in four stages as described in Table 2. Diagnosis is based on careful assessment of history, circumstantial evidence linking ingestion of mushroom to onset of symptoms. The identification by an experienced mycologist of the remaining mushrooms can be crucial for diagnosis. In the absence of these, the diagnosis is largely clinical and can best be probable.[6,7]

Since no specific antidote to amatoxins is currently available, management is largely supportive. Severe acute liver failure is a grade I indication for liver transplantation. Supportive measures including correcting dehydration, electrolyte abnormalities, and metabolic acidosis caused by the gastrointestinal phase of the intoxication remain the cornerstone.[6] The specific treatments consist of detoxification procedures including gastric lavage, multidose activated charcoal and extracorporeal purification using Molecular Adsorbent Recirculating System (MARS).[16,17] Other supportive drugs include Silibinin, Penicillin G and free radical scavenger like N-acetylcysteine. Silibinin is a silymarin derivative and acts via competing with amatoxins for trans-membrane transport and inhibits the penetration of amanitin into hepatocytes, thus having direct hepatoprotective effect. Recommended dose is 20–50 mg/kg/day intravenously for 48–96 h or oral dose from 1.4 to 4.2 g/d.[18,19] Penicillin G have a similar mechanism of action, displacing amanitin from the binding to plasma protein and thus promoting its excretion and preventing its hepatic uptake. It is recommended to administer it in continuous intravenous form as Na/K penicillin G (1,000,000 IU/kg for the first day, then 500,000 IU/kg for the next two days).[18,19] Early empiric administration may be beneficial. There is also some data suggesting hepatoprotection by N-acetylcysteine (NAC), in the management of amatoxin intoxication.[20]

All three specific measures were utilized in our patients but the outcome was not favorable. Despite these measures the mortality with *A. phalloides* poisoning ranges from 10 to 20%.[18,19] In present case report, the appropriate ICU care and specific measures like penicillin G, silibilin and N-acetylcysteine were instituted with a delay of 96–120 h after the onset of symptoms and all three had poor prognostic criteria i.e. grade III–IV encephalopathy, grossly deranged Coagulogram and mushroom being an etiology, hence mortality was high (100%).

Similar case report of three family members affected with mushroom toxicity and with similar clinical profile resulting in death of one in whom specific therapy was not instituted was reported from India in 2003. The remaining two who were fortunate to receive Inj. penicillin and silibinin survived.[21]

Liver transplantation has been described to improve mortality in amatoxin-induced acute liver failure in selected patients and before development of grade 4 hepatic encephalopathy.[22,23] Ganzert et al[24] retrospectively analyzed the outcome of a large series of amatoxin intoxication cases and found that predictors of death were the prothrombin index in combination with the serum creatinine level on 3–10 days after ingestion. Overall, the prognosis of amanitin-induced acute liver failure remains quite poor.[22,23]

In conclusion, amanita toxicity should be considered in the differential diagnosis of acute gastroenteritis and renal failure, especially during monsoon season in populations known for consuming wild mushroom. There is a need to educate the masses to recognize these poisonous mushrooms. In the absence of the culprit fungus and diagnostic tests, definitive diagnosis may be difficult. Management is focused on prompt recognition of the toxidrome, early hospitalization, gastric lavage, hydration, penicillin and silymarin therapy with hepatorenal support and the delay in treatment can result in nearly 100% mortality. Regional reference laboratories should be equipped for testing serum levels of amanitin levels to confirm the diagnosis.

CONFLICTS OF INTEREST

All authors have none to declare.

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