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Case Series

Wild mushroom poisoning in Kumaon region of Uttarakhand: a case series

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ABSTRACT

Mushrooms have been dietary source in hilly and ethnic tribes of India. More than 5000 mushroom species are known worldwide and nearly 100 species are known to be poisonous for humans. Mushroom poisoning occurs due to unintentional and accidental ingestion of poisonous mushroom due to misidentification of poisonous variety as edible one. There has been increasingly incidence of reporting of mushroom poisoning cases nowadays. Here we are reporting case series of 4 patients admitted hailing from same village with accidental ingestion of poisonous mushrooms with clinical-laboratory profile and outcome at our institution. Mushroom Poisoning is an emerging healthcare concern nowadays. Education and mass awareness for identification of poisonous mushrooms is an important preventive measure. Early hospitalization, proper hydration, gastric decontamination, silibinin and N- acetyl cysteine therapy with hepato-renal support constitutes mainstay of treatment. Delay in treatment and complications results in poor prognosis and mortality.

Keywords: Wild mushroom, *Amanita* poisoning, Poisoning

INTRODUCTION

Mushroom are the fungal reproductive structures with cap and gills which produces spores and help in propagation of fungus also. Out of more than 5000 mushroom species worldwide 200 to 300 species are found to be edible ones and nearly 100 species are known to be poisonous for humans. Mushroom poisoning had been known since ancient times all over world ("Rigveda" at least 3500 BC and "Atharvaveda" at least 1500 BC, Roman emperor Claudius.[1,2]

Mushrooms have been dietary source in various ethnic tribes in north eastern states, Uttarakhand, Jammu and Kashmir and Himanchal Pradesh of India. With increasing influence of other cuisines commercial farming as well as local foraging consumption of mushroom is increasing nowadays.

Mushroom poisoning occurs due to unintentional and accidental ingestion of poisonous mushroom due to misidentification of poisonous variety as edible one.

There has been increasingly incidence of reporting of mushroom poisoning cases nowadays. Here we are reporting case series of 4 patients admitted of same village with accidental ingestion of poisonous mushrooms with clinical-laboratory profile and outcome at our institution.

CASE SERIES

Four patient's resident of village Dulagiri, Dwarahaat (Almora) were admitted to Base hospital Haldwani with history of consumption of wild mushroom during social gathering on 23rd July 2020. Subsequently all 4 patients developed pain abdomen, vomiting, 2 of the patients developed loose stools and decreased urine output. Patients were referred to nearby district hospital where

gastric lavage, intravenous fluid and antiemetic were prescribed. After 8 to 10 hours patients developed severe abdominal pain and progressive altered sensorium and referred to Base hospital Haldwani. A provisional diagnosis of acute hepatitis secondary to wild mushroom ingestion was made.

Patient 1: A 44-year-old male presented with pain abdomen, vomiting. On examination patient had icterus, mild hepatomegaly with no signs of encephalopathy. Investigations revealed conjugated hyperbilirubinemia (Total bilirubin/conjugated bilirubin 5.7/3.0 mg/dl). Rest biochemical parameters including ECG were within normal limit.

Patient 2: A 45-year-old male presented with abdominal pain, vomiting, loose stools, decreased urine output and altered sensorium. On examination patient was afebrile, tachycardia (heart rate 120-130/min), tachypnea (rate 30-32/min), pallor, icterus, grade 2-3 hepatic encephalopathy, deep tendon reflex were brisk and planters were flexor. Investigation revealed hemoglobin 10.4 gm/dl, TLC 9800/mm^3, platelets 1.3 lac/mm^3, conjugated hyperbilirubinemia (total bilirubin/conjugated bilirubin 5.8/3.2 mg/dl), elevated liver enzymes (aspartate aminotransferase (AST)/alanine aminotransferase (ALT) 1180/820 IU/ml)], coagulopathy (prothrombin time >2 min), deranged renal function test (creatinine 2.2 mg/dl) and hyperkalemia (K+ 5.8 mEq/L) with metabolic acidosis and abnormal electrocardiogram (ECG) in form of tall T waves, ST segment depression. Ultrasound abdomen was suggestive of raised liver echogenicity with thickened gall bladder wall, mild ascites and bilateral renal parenchymal disease.

Patient 3: A 37-year-old male presented with abdominal pain, nausea, vomiting, loose stools and irritability. On examination patient had icterus, no pallor, mild hepatomegaly, grade 1 hepatic encephalopathy, brisk deep tendon reflex, flexor planter. Investigation revealed hemoglobin 12.4 g/dl, TLC 5400/mm^3, conjugated hyperbilirubinemia (total bilirubin/ conjugated bilirubin 4.5/2.4 mg/dl), transaminitis (AST/ALT: 488/240 IU/ml), normal coagulation profile, renal function test, electrolytes and ECG.

Patient 4: A 45-year-old male presented with severe abdominal pain, vomiting with altered sensorium. On examination icterus was present with tachycardia (heart rate 130-140/min) and tachypnea (rate 38-40/min) with grade 3-4 hepatic encephalopathy, absent deep tendon reflex and no planter response. Investigation suggested anemia (hemoglobin 9.8gm/dl) TLC 8070/mm3, conjugated hyperbilirubinemia (total bilirubin/conjugated bilirubin 11.7/6.2 mg/dl), coagulopathy (prothrombin time >3 min), transaminitis (AST/ALT: 1340/1227 IU/ml), deranged renal function test (urea 88mg%, creatinine 1.4 mg%), normal electrolytes and ECG. Metabolic acidosis was present. ECG was suggestive of Sinus tachycardia with ST/T inversion. Ultrasound abdomen was suggestive of raised liver echogenicity with gall bladder wall thickening with ascites with mild bilateral pleural effusion.

All four patient were managed using standard treatment protocol of acute liver failure including:

IV fluids (hepatic drip), IV broad spectrum antibiotics, IV mannitol, head end elevation, appropriate sedation, IV proton pump inhibitors, injection vitamin K, inotropic support and intensive monitoring and management of electrolytes imbalances and blood glucose. Inj NAC and silibinin were also given. Penicillin G was not available.

Patient 2 developed hypotension and bradycardia on 3rd day of admission and started on vasopressor support. With progressive derangement of renal function and worsening sensorium patient was intubated and kept on ventilatory support. Patient sustained cardiac arrest on 4th day of admission and couldn't be revived.

Patient 4 developed upper gastrointestinal bleed on 4th day of admission, which was managed with fresh frozen plasma and packed red blood cell transfusion. Patient developed hypotension and bradycardia for which vasopressor were started. On day 6th in view of worsening sensorium and higher requirement of vasopressor patient was put on ventilatory support. Patient sustained cardiac arrest on 7th day of admission and could not be revived.

Patient 1 and 3 responded well with treatment with improvement in liver function and sensorium. Both were discharged on 7th and 10th day respectively.

Patient characteristics

Following Table 1 showed patients characteristics:

Table 1: Patient's characteristics.

Parameters	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	44	45	37	45
Gender	Male	Male	Male	Male
Residence	Rural/ hill	Rural/ hill	Rural/ hill	Rural/ hill
Type of mushroom	Wild	Wild	Wild	Wild
Initial symptoms	Pain abdomen vomiting	Pain abdomen, vomiting, loose stools, decreased urine output, altered sensorium	Pain abdomen, nausea, vomiting, loose stools and irritability	Pain abdomen, vomiting, altered sensorium

Continued.

Parameters	Patient 1	Patient 2	Patient 3	Patient 4
Examination findings	Icterus, mild hepatomegaly	Tachycardia (120-130/min), tachypnea (30-32/min), pallor, icterus, grade 2-3 hepatic encephalopathy, brisk deep tendon reflex, planters were flexor	Icterus, mild hepatomegaly, grade 1 hepatic encephalopathy, brisk deep tendon reflex, flexor planter	Icterus, tachycardia (130-140/min), Tachypnea (38-40/min) hepatic encephalopathy grade 3/4, absent deep tendon reflex and planter response
Investigations: Hb	12.2	10.4	11.6	9.8
TLC	12100	9800	11050	8070
Total /conjugated bilirubin	5.7/3.0	5.8/3.2	4.5/2.4	11.7/6.2
AST/ALT	356/212	1180/820	488/240	1340/1227
Coagulopathy	Absent	Present	Absent	Present
Renal function	Normal	Serum urea 76 mg%, creatinine 2.2 mg/dl with hyperkalemia (5.8 mEq/L)	Normal	Serum urea 88 mg%, creatinine 1.4 mg/dl
Arterial blood gas analysis	Normal	Metabolic acidosis	Normal	Severe metabolic acidosis
ECG	NSR	Sinus tachycardia, Tall T waves, ST segment depression	Sinus tachycardia	Sinus Tachycardia with ST/T inversion
Ultrasonography abdomen	-	Raised liver echogenicity with thickened gall bladder wall, mild ascitis and bilateral renal parenchymal disease.	-	Raised liver echogenicity with gall bladder wall thickening with ascitis with mild bilateral pleural effusion.
Management	Standard ICU based protocol, inj. Silibinin, inj. NAC	Standard ICU based protocol, inj. Silibinin, inj NAC, vasopressors, Ventilatory support	Standard ICU based protocol, inj. Silibinin, inj. NAC	Standard ICU based protocol, inj Silibinin, inj NAC, vasopressors, ventilatory support, packed RBCs, fresh frozen plasma
Outcome	Discharged on day 7	Expired on day 4	Discharged on day 10	Expired on day 7

DISCUSSION

Mushroom poisoning profile varies from benign symptoms to fatal multi-organ failure to death. The clinical manifestation ranges from type of species, toxins, amount ingested and time of presentation. 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.[3,4] *Amanita* phalloides is the most poisonous mushroom, which causes severe hepatotoxicity.[5]

Due to non-availability of mushroom specimen, species identification and toxin analysis was not possible however the clinical presentation was similar to *Amanita* poisoning.

Amanita toxicity is characterized as an asymptomatic incubation period followed by the gastrointestinal and hepatotoxic phases, leading eventually to multi-organ failure and death.

Clinical phases of amatoxin poisoning consist of stages 1 to 4 (Table 2).

Stage 1 is asymptomatic and has a lag phase of 0 to 24 hours. This is followed by stage 2 of gastrointestinal symptoms (6-24 h) of nausea, vomiting, crampy abdominal pain, and severe secretory diarrhea. Stage 3 of apparent convalescence (24-72 h) consists of asymptomatic, worsening hepatic and renal function indices. Finally, stage 4 of acute liver failure (4-9 days) of hepatic and renal failure/multi-organ failure/death.[6]

Table 2: Clinical stages of *Amanita* poisoning.

Stages	Onset from ingestion	Sign and symptoms
Stage 1	Lag Phase 0-24 hour	Asymptomatic
Stage 2	Gastrointestinal phase 6-24 hour	Nausea, vomiting, crampy abdominal pain, and severe secretory diarrhea
Stage 3	Apparent convalescence 24-72 hour	Asymptomatic, worsening of hepatic and renal function indices
Stage 4	Acute liver failure 4-9 days	Hepatic and renal failure/multi-organ failure/death

Amatoxins are a group of ten heat-stable bicyclic oligopeptides. The toxicity of *A. phalloides* is attributed to two distinct groups of toxins: phallotoxins and amatoxins. They inhibit RNA polymerase II and so prevent transcription of DNA to mRNA, thus blocking the biosynthesis of many proteins (enzymes, structural proteins, peptide hormones, membrane receptors). The phallotoxins are toxic to cell membrane of enterocytes leading to initial diarrhea like illness whereas amatoxins (a-amanitin and b-amanitin) are responsible for the toxic effect leading to acute liver failure, renal failure and potential toxicities to pancreas, adrenal glands, and testes.[7,8] *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.

The minimum lethal dose for amatoxin is 0.1 mg/kg of body weight (5-15 mg of amatoxin is contained in about 15-20 dried *Amanita* caps which is sufficient to kill a healthy adult) overall mortality is between 5-40%.[9]

The baseline investigations include complete hemogram, liver and renal function tests, PT/INR, PTT, creatinine kinase, urinalysis, serum lactate, ammonia, LDH followed by serial measurement every 6 to 8 hourly. Although blood tests for functional liver impairment give positive results after organ damage has already occurred.

The treatment for mushroom poisoning is mainly symptomatic as no specific antidotes are available includes fluid and electrolytes replacement and correction of metabolic acidosis as patient may be dehydrated due to GI phase or even in shock. Urine output monitoring is crucial as toxins are eliminated primarily through kidneys.

Gastrointestinal decontamination using activated charcoal is most effective when patient presents within one hour of ingestion. It interrupts the enterohepatic circulation at oral dosage of 0.5 to 1 g/kg body weight or up to a maximum of 50 gm as a bolus in adults.[10]

Other supportive therapy includes penicillin G, silibinin and N-acetylcysteine. Silibinin is derived from the milk thistle and is the pharmacologically active substance in the silymarin complex.

Penicillin G and silibinin exhibit hepato-protective effect via OATP-1B3 transporter (OATP, organic anion transporting polypeptide) it competes with amatoxins for trans-membrane transport and inhibits the entry of amanitin into hepatocytes and results in the diversion of amatoxin back into the general circulation for renal clearance, therefore maintaining renal function and a brisk urine output is crucial to the success of the drug.

Recommended dose of silibinin is 5 mg/kg IV followed by a continuous infusion at a dose 20 mg/kg/day for 6 days or until clinical recovery.

Penicillin G is administered in continuous intravenous form 1,000,000 IU/kg for the first day, then 500,000 IU/kg for the next two days. Early empiric administration may be beneficial.[11,12]

NAC has antioxidant and glutathione-regenerating effects. It can be given either as an alternative (if silibinin is not available) or as an adjunct to silibinin. Recommended protocol is initial loading dose of 150 mg/kg (max 10 gm), followed by 4 hourly infusions at 12.5 mg/kg/hr, then a 16-hour infusion at 6.25 mg/kg/hr. The 16-hour dose can be repeated if significant hepatic dysfunction persists.

There is a rationale for combining silibinin and NAC therapy, since these two substances have different mechanisms of action.[13]

Severe acute liver failure is indication of liver transplantation. The Clichy criteria and Munich criteria provides a basis for decision making on whether a liver transplant is indicated.[14,15] The Clichy criteria include the latency period, coagulopathy, and encephalopathy, while the Munich criteria are based on coagulopathy and renal function.

Extracorporeal purification and dialysis using molecular adsorbent recirculating system (MARS) have no significant effect in terms of toxin elimination, but can be utilized as surrogate measure until liver transplantation can be planned out.[16]

Biliary drainage by percutaneous cholecystostomy has been emerging modality nowadays. Removing amatoxin laden bile from the gallbladder provides definitive protection to uninvolved hepatocytes by eliminating further enterohepatic exposure to the poison. Simple ultrasound guided gallbladder aspiration appears to be the fastest, safest, easiest, and most efficient means of

permanently removing accumulated amatoxin from the biliary tract.[17]

In present study along with ICU care NAC and silibinin was administered to patients however penicillin G was not available in our institute. Out of four, two patients couldn't survive owing to progressive hepato-renal dysfunction, deranged coagulogram and multi-organ failure. Despite appropriate measures mortality with *A. phalloides* poisoning ranges from 10 to 20%.[12]

A similar case series from Himanchal Pradesh shown *Amanita* like poisoning in family of four members with high mortality owing to acute liver failure with multi-organ.

Failure (MODS) by Verma et al.[6] Another case report from India in 2003 described three family members with similar clinical profile affected with mushroom toxicity and resulting in mortality in one member whom specific therapy couldn't be administered.[9]

CONCLUSION

Mushroom poisoning is an emerging healthcare concern nowadays due to increased consumption and early reporting of cases. Any patient presenting with delayed onset of vomiting and diarrhea six hours or more following consumption of foraged mushrooms must be presumed an amatoxin poisoning until proven otherwise. Education and mass awareness for identification of poisonous mushrooms is an important preventive measure. Management includes early hospitalization, gastrointestinal decontamination, proper hydration, correction of electrolyte imbalance and metabolic acidosis, hepato-renal support. Other supportive measures like silibinin, N-acetyl cysteine and penicillin G also have favorable role in early administration. Liver transplantation is reserved for patient with fulminant hepatic failure with poor prognosis.

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