GYROMITRA MUSHROOMS

Gyromitra are unique among the toxic mushrooms because they are avidly sought by some mushroom enthusiasts for their gastronomic value. The toxicity of these mushrooms is largely related to their method of preparation—if they are eaten raw or prepared incorrectly, their consumption can elicit a clinical picture ranging from gastrointestinal symptoms and headaches, to hemolysis, renal failure, hepatic failure, seizures, methemoglobinemia, coma and death.

There are a number of poisonous gyromitra containing species, the most well known being Gyromitra esculenta, the false morel or “wood ear.” This mushroom has a distinctive wrinkled, brain-like appearance that could potentially be mistaken for the tasty morel by inexperienced gatherers. They commonly grow on rotting logs and are frequently associated with coniferous trees. They are found throughout North America and Europe and tend to fruit in early spring — hence, poisonings with these mushrooms are more common at that time. The Amanita species, in contrast, classically causes poisonings in the fall.

The North American Mycological Association has reported 59 cases of non-fatal Gyromitra poisonings in the United States since 1969, however this figure is acknowledged to underestimate the prevalence due to inconsistent reporting. The majority of Gyromitra poisonings have historically occurred in Europe, where the mushroom is more enthusiastically consumed. Recently, shipments of canned and dried, supposedly edible morel mushrooms have been detained in France due to the presence of Gyromitra esculenta.

Toxin

The main toxin, known as “gyromitrin” (N-methyl-N-formyl-acetyl-hydrazone) is an unstable compound that undergoes 2-step hydrolysis to monomethylhydrazine (MMH), a potent substance that has been used as a rocket propellant. It was well known that aerospace industry workers exposed to MMH exhibited a syndrome identical to gyromitrin poisoning, and much of the research on this compound has been done because of its utility as a rocket fuel. Moreover, MMH has a structural kinship to isoniazid, a hydrazide; it is no coincidence that gyromitrin toxicity closely resembles isoniazid poisoning and is treated similarly.

MMH has a relatively low boiling point (87.5°C) and can be inhaled as a vapor. As a consequence, a cook standing over a boiling pot of these mushrooms may inhale a toxic and clinically relevant dose. Provided there is adequate ventilation, boiling will release the toxin and render the mushrooms harmless as long as the water is changed and discarded a number of times.

The lethal dose of MMH in humans has been estimated to be between 10 and 50 milligrams/kilogram, which translates to between 12-60 kg of mushrooms for a 70 kg male, an unrealistic quantity given the fact that lethal poisonings do occur. Recent studies have indicated a potentially significant variation in the amount of toxin contained in mushrooms collected at different times and in different geographical areas, and it has been postulated that this disparity may account for the sporadic nature of these poisonings.

Clinical Pharmacology

Gyromitrin is converted to acetaldehyde and the intermediate N-methyl-formyl-hydrazone (MFH) in the stomach. MFH subsequently hydrolyzes to MMH, the primary toxic component that serves as an alkylating agent and potent cytotoxin. While the exact mechanisms of toxicity are not clear, studies have demonstrated numerous effects in multiple organ systems.

MMH appears to exert its central nervous system effects by blocking pyridoxine kinase, an enzyme responsible for the conversion of pyridoxine to pyridoxal phosphate. The deficiency of pyridoxal phosphate impedes the body from making y-aminobutyric acid (GABA), an inhibitory neurotransmitter. This, in turn, leads to altered mental status, increased neuromuscular excitability and ultimately seizure activity or coma.

MMH affects the liver as well, possibly by inducing lipid peroxidation and inhibiting the transaminases that use pyridoxal phosphate as a cofactor. Additionally, MFH may interact with the cytochrome P-450 enzyme systems of the liver.

MMH has also been shown to be a hemolytic agent, and an oxidizer capable of inducing methemoglobinemia. Its action on the diamine oxidase enzyme of gut mucosa has been posited to explain the gastrointestinal component of poisoning.

Finally, it has been extensively demonstrated in animal models that gyromitrin has a cumulative low-grade carcinogenic effect on the body. It stands to reason that consumption of this mushroom should perhaps be avoided, regardless of how expertly they are prepared.

Clinical Toxicology

The toxidrome induced by gyromitrin is initially similar to the better-known course of amatoxin poisoning. Initially there is a gastrointestinal phase marked by bloating, nausea, vomiting and diarrhea which begins within 6-12 hours of oral ingestion and as early as 2 hours after inhalation. The diarrhea is classically watery, but may contain small amounts of blood. Abdominal pain is not a major component of the syndrome, but some colicky pain may be present. Fever is more likely at this stage than it is in amatoxin poisoning, though this is not a reliable diagnostic trait. The majority of poisonings are mild enough to be limited to the gastrointestinal phase.

Liver toxicity develops at approximately 36-72 hours post-exposure. Symptoms include jaundice, liver tenderness, mild
hepatomegaly and splenomegaly, and may progress to CNS symptoms of hepatic failure.

Alternatively, terminal CNS symptoms may precede liver effects: delirium, tremulousness, muscle fasciculations or spasm, seizures, mydriasis, stupor, coma, circulatory collapse, and respiratory arrest.

Renal failure is rare, but may occur secondary to intravascular hemolysis or rhabdomyolysis. Methemoglobinemia can also complicate the clinical picture and is manifested as cyanosis despite a normal value for arterial pO₂.

There is no laboratory tissue assay to confirm the clinical diagnosis. If possible the samples of the mushroom itself should be gathered by relatives or friends of the victim and identified by an experienced mycologist. Spore analysis can confirm the morphology typical of Gyromitra.

Other laboratory assays may assist the management of the patient including liver and renal function tests, blood lactate, CPK, a complete blood count and methemoglobin.

Treatment

The important distinction to make in the treatment of gyromitrin poisoning is that one is not, in fact, dealing with amatoxin poisoning-their initial toxidromes may be similar. If a single species of mushroom were ingested and it is available for inspection, the diagnosis should be easy. If a mushroom potpourri were served, or if the offending agent is unavailable, the physician may be obliged to presume Amanita poisoning.

The management of gyromitrin poisoning is largely supportive with the exception of pyridoxine treatment that is discussed below.

If the patient arrives within an hour after a known gyromitrin ingestion, for which a poor outcome is anticipated (uncooked meal, massive overdose), consider gastric decontamination provided the unusual contraindications are not present. Frequently, the patient will facilitate treatment by vomiting spontaneously.

Repeat doses of activated charcoal and cathartics are reasonable, though unstudied. Nausea may be treated with anti-emetics though it should be mentioned that the vomiting in gyromitrin poisoning is central in origin and may prove refractory to conventional anti-emetics.

The laboratory work-up should include liver function tests, serum electrolytes, a complete blood count and blood methemoglobin levels. Urine should be checked for hemoglobinuria.

Pyridoxine is indicated to relieve GABA deficiency in the setting of neurological symptoms ranging from confusion or delirium, to seizures and coma. The dose is 25 milligrams/kilogram of body weight of pyridoxine given as an infusion over 15 to 30 minutes. Repeat doses may be administered for recurring neurologic signs, and while some authors advocate maximum total daily doses of 15 to 20 grams, some caution is advised since overzealous administration of pyridoxine may lead to profound and permanent neuropathies. An upper limit of 300 mg of pyridoxine per day may be a more prudent value. Patients with seizure activity should be treated with a benzodiazepine, such as lorazepam, in conjunction with pyridoxine. There is no evidence that pyridoxine alters the course of hepatic disease.

Methemoglobinemia, should it occur, may be safely treated with intravenous methylene blue at a dose of 1 mg/kg. Additionally, methemoglobinemia may herald the presence of hemolysis and should alert the clinician to a possible need for a diuresis to prevent renal complications.

Any symptomatic patient should be admitted to the hospital for observation with toxicologic consultation. Asymptomatic patients may be safely discharged to close observation at home.

Mert Erogul, MD
Kevin Ernsting, MD
Daniel Savitt, MD
Department of Emergency Medicine
Rhode Island Hospital
Providence, RI

Mushroom Poisoning Case Registry collected by the North American Mycological Association, 1998, obtained in personal communication from Kenneth W. Cochran.


