Management of Maternal *Amanita phalloïdes* Poisoning during the First Trimester of Pregnancy: A Case Report and Review of the Literature

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**Background:** *Amanita phalloïdes* poisoning produces acute liver failure and often death. Maternal poisonings are rare, and medical decisions of abortion or liver transplantation in this critical situation frequently are based on laboratory data. We report here the case of a 22-year-old-woman in the 11th week of pregnancy, who ingested mushrooms.

**Case Report:** The patient’s clinical symptoms (e.g., vomiting and diarrhea) and blood chemistry data (persistent increases of aspartate aminotransferase and alanine aminotransferase and severe decreases in prothrombin, factor V, factor II, factor VII, and factor X) indicated poisoning of medium severity. The management consisted of intravenous hydration, and administration of silymarine and *N*-acetylcysteine. No fetal damage was observed, and birth and development of the infant (now 2 years of age) proceeded without incident.

**Conclusion:** Abortion is not necessarily indicated in maternal poisoning by *A. phalloïdes*, even in the first trimester of pregnancy.

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The diagnosis of suspected poisoning by *Amanita phalloïdes* remains a challenge to emergency physicians. This mushroom intoxication starts as gastroenteritis, progressing to liver failure and death as a result of hepatic coma. The mature *A. phalloïdes*, despite its distinctive green cap and white gills, can be mistaken, even by mycologists, for similar-appearing edible mushrooms (1). Unfortunately, these mushrooms have no unique smell or taste characteristics, and cooking does not destroy the two types of cyclic oligopeptide toxins, the amatoxin and the phallotoxins.

Phalloïdin, which constitutes the main agent of phallotoxins, is a cyclic thermostable and easily dialyzable octapeptide, with a molecular mass of ~900 Da (2). The sulfur atom of this compound, which is engaged in a thioamide bond with the indole ring, is responsible for a weak part of the toxicity of *Amanita* (e.g., only the initial symptoms of gastroenteritis). After formation of this latter bond, the polymerization of G-actin to F-actin is interrupted, leading to disorganization of the cytoskeleton and cell death.

Amatoxins, which constitute the second group of *Amanita* toxins, are cyclic octapeptides that interfere with DNA transcription (3). They bind to a 140-kDa subunit of RNA polymerase II in the nuclei of liver cells with consequent blockade of protein synthesis and finally cell necrosis (4). Cells that maintain a high rate of protein synthesis (e.g., in the gastrointestinal tract and liver) are more sensitive to injury. This agent is thus responsible for the severe liver damage and for the brain and kidney deterioration that lead to death.

Since the 1960s, intoxication by *A. phalloïdes* has been reported with increasing frequency in Europe, although mortality has decreased during the last decade with improved supportive care (5, 6). However, little is known about the management of *A. phalloïdes* poisoning during pregnancy. We describe the case of a 22-year-old woman in the 11th week of pregnancy who had *A. phalloïdes* poisoning and whose fetus developed normally.

**Case Report**

A 22-year-old woman in her second month of pregnancy ate a few wild mushrooms, which had been harvested and briefly cooked by friends. Her husband, an amateur mycologist, seemed to recognize some edible mushrooms, e.g., *Agaricus campestris* and *A. citrina*. Two hours after...
ingestion of the mushrooms, the woman experienced diffuse abdominal pain. The next day (10 h later), she developed nausea, vomiting, and profuse watery diarrhea. Thirteen hours after ingestion, she was admitted to our emergency department.

At the time of admission, the clinical examination was normal. The hemoglobin was 145 g/L, blood platelets were 178 000/μL, and erythrocytes were 4 450 000/μL. The Quick time was within reference values at 100%, cephalin kaolin time (CKT), 34 s. Electrolytes and transaminase activities were within reference values (Table 1). Initial hospital management consisted of intravenous hydration and antiemetic and antidiarreheal drugs.

By 36 h after ingestion, the patient’s aspartate aminotransferase (AST) and alanine aminotransferase (ALT) had increased, from 17 and 10 U/L to 663 and 607 U/L, respectively. We examined a specimen of the wild mushrooms eaten. Among the intact remaining mushrooms we identified A. phalloïdes. The patient received silymarine (Legalon®, 20 mg/kg four times per day). To remove any remaining mushroom particles from the stomach, the patient was given activated charcoal orally. Simultaneously, N-acetylcysteine (150 mg/kg at 30 min, 50 mg/kg at 4 h, and finally 100 mg/kg at 16 h) was recommended by the Poison Center, Strasbourg, France.

With progressive hepatic damage indicated by persistent increases of AST and ALT to 2091 and 2211 U/L, respectively, the pregnant woman was transferred to the Edouart Herriot Hospital Center (Lyon, France) for liver transplantation. On arrival in this center, her ALT activity reached its maximum value (4127 U/L), whereas her AST remained stable (2903 U/L). The patient’s prothrombin, factor V, factor II, factor VII, and factor X had decreased by 20%, 24%, 23%, and 13%, respectively. Her neurologic status was normal, without clinical symptoms or biochemical evidence of encephalopathy; moreover, no clinical features of biliary obstruction or ascites were observed. Abdominal ultrasound showed no abnormal size of her liver nor any abnormalities of the biliary canaliculi. Fetal movements and cardiac activity were recorded.

Clinical management consisted of intravenous hydration, administration of vitamins and trace elements, and oral N-acetylcysteine regimen. Neomycin and Fungizone were given prophylactically for digestive decontamination. Despite the persistence of vomiting and diarrhea, her biochemical values normalized. Because her prothrombin and factor V values reached 100% again and her blood chemistry revealed hepatic normalization, hepatic transplantation was not performed. The patient was discharged from the Edouart Herriot Hospital Center and transferred back to our emergency department on the ninth day.

On day 10, an obstetric examination revealed no fetal abnormalities. Pregnancy was accompanied by the development of a gestational diabetes, and at 38 weeks, the patient gave birth to a healthy baby, weighing 3060 g without sign of hepatic damage. The condition of the young mother was good 2 years later, and the baby is demonstrating undisturbed development.

**Discussion**

In southern France, some wild mushrooms are usually gathered in the late summer. Unfortunately, this has led to frequent episodes of poisoning, with several fatalities reported annually (7). The majority of fatal poisoning have been attributed to the species *Amanita*, and *A. phalloïdes* has been held accountable for >90% of the fatalities (8).

The lethal dose of the *α*-amanitin component is 0.1–0.3 mg/kg (8), and phalloitoxins seem to exacerbate the action of amatoxins. *α*-Amanitin represents 0.2–0.4 mg of the amatoxins, which can reach concentrations as high as 5 mg/g of dry mass in *A. phalloïdes*. Approximately 85% of these toxins are eliminated in urine within 6 h of ingestion. After 36–48 h, toxins disappear from the plasma, although toxins are detectable in the urine as long as 96 h after ingestion (9). Hepatic uptake occurs via the enterohepatic recirculation. This must be considered in the management of this poisoning.

No correlation exists between the plasma amatoxin concentration and clinical outcome, nor does the amount of liver-bound toxin correlate with the plasma concentration. Furthermore, during pregnancy, amatoxins do not cross the placental barrier, even during the acute phase of intoxication (10). Their deleterious effects on fetal nucleic acid and proteins therefore could not occur, which explains the absence of fetal damage. This is consistent with the relevant data in the literature (10–13): the prevalences of both major and minor anomalies were similar to the prevalences of such developmental failures during pregnancy not complicated by exposure to the toxins. Thus, no fetal blood sampling (which is dangerous for the fetus) was performed, to avoid further complications. However, because of teratogenic risk during the first 3 months, no conclusion can be drawn (13). In our observation, no fetal damage occurred with maternal exposure during the first 3 months of pregnancy to moderate *A. phalloïdes* poisoning [according to the scale developed by Floersheim et al. (5)]. However, this should be balanced by a German case

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<th>Table 1. Blood chemistry values observed during the treatment of maternal <em>A. phalloïdes</em> poisoning.</th>
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<td><strong>Glucose, mmol/L</strong></td>
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<tr>
<td>Initial value</td>
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<td>4.8</td>
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<td>112</td>
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<td>21.7</td>
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*a* LDH, lactate dehydrogenase.

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report during the first trimester (14). In this latter report, the pregnancy was interrupted because they speculated fetal toxicity. Histologic analysis of the fetal liver revealed a few microscopic abnormalities, such as loss of lobular architecture and edema. The authors did not indicate the management of this poisoning.

Patients who have consumed A. phalloı¨des mushrooms exhibit typical symptoms and signs (1) that occur during three stages after a quiescent period, as summarized below. Phalloidin toxin may explain the first stage, with digestive disorders 24–48 h after ingestion. The second stage often is clinically asymptomatic. However, the laboratory data may reveal hepatic or renal deterioration, and poisoned patients typically have increased transaminase and bilirubin and decreased prothrombin and factor V. Increases of both serum creatinine and urea reflect the renal damage. This stage of poisoning may lead to underestimation of the magnitude of the liver damage. The third stage (48–96 h after ingestion) can occur suddenly, with hepatorenal syndrome, a severe oliguria or anuria, and a severe hepatic necrosis with encephalopathy.

In light of this background, we can further analyze our observations. Concerning blood chemistry data, the only signs of hepatic damage that the woman exhibited were increases in aminotransferase and lactate dehydrogenase activity in serum (Table 2). Floersheim et al. (5) noted that among patients with aminotransferase >1000 U/L, mortality rates were 30–50%. Although bilirubin at its peak could bring more evidence on the degree of hepatocyte dysfunction, it is of little prognostic value for the management of this poisoning (15).

With evidence of the progressive hepatic deterioration, our thinking consisted of a search of coagulopathy and encephalopathy secondary to liver failure. The young woman exhibited no sign of neurotoxicity and was totally coherent in her responses and actions. A putative encephalopathy reflected by the course of ammonemia was not evidenced in our case. However, the severity of the coagulopathy was confirmed by laboratory findings (decreased prothrombin activity and factor V), which suggested a high risk of death for this young woman. Indeed, the severity of the poisoning has been found to be reflected best by the degree of lowest plasma prothrombin activity (5), i.e., a lowest prothrombin activity <10% indicates mostly fatal poisoning, prothrombin activity of 10–40% indicates moderate severity, and prothrombin activity >40% indicates light toxicity. Concerning the renal status for this pregnant woman, the chemistry data did not reveal any renal failure; we noted only serum creatinine of 40–50 μmol/L (Table 2). Serum creatinine often increases only late in the course of fatal poisoning and is of little prognostic value (16). This was confirmed from a clinical point of view: diuresis was conserved (3000 mL/24 h) after simple intravenous hydration without use of osmotic or diuretic agents.

The mainstay in the management of poisoned patients is aggressive therapy to correct fluid and electrolyte disturbances and to support the patient in the face of fulminant hepatic failure. Some well-known therapeutic rules have been established, such as gastric evacuation or administration of activated charcoal (30–60 g every 4 h) to avoid enterohepatic recirculation of toxins (17). Hemoperfusion and dialysis are not recommended as elimination procedures because they should be performed very quickly after ingestion (<36 h). Silymarine (from the milk thistle Silibum marianum) exerts its protective effect after intravenous administration in various ways: (a) by interrupting the enterohepatic recirculation of amanitin;
(b) by inhibiting the binding of toxins to hepatocyte membranes; (c) by competing with amatoxin for transmembrane transport; and (d) by inhibiting the penetration of amanitin into liver cells (1). At doses of 20–50 mg · kg⁻¹ · day⁻¹, silymarine could be administered during pregnancy without being harmful to the fetus.

High doses of intravenous penicillin G (300 000–1 000 000 units · kg⁻¹ · day⁻¹) may also be useful, although the mechanism of action of this agent is not clearly defined. Penicillin is a well-known antibiotic used without restriction during pregnancy, but it does exhibit some adverse allergic effects.

Other chemotherapeutic agents, such as acetylcysteine, could be used in Amanita poisoning. Acetylcysteine is the antidote of choice after ingestion of toxic amounts of acetaminophen. The drug enhances glutathione stores, is a common antidote of choice after ingestion of toxic amounts of acetaminophen. The drug enhances glutathione stores, and when present, hypoglycemia. Pregnancy should not be considered as a contraindication to transplantation (19), although after the operation an increased risk of hypertension, anemia, hyperbilirubinemia, and preterm cesarean delivery exists. In addition, it should be emphasized that the search for compatible donors lasts ~48 h, so that liver transplantation is not always possible.

In conclusion, our pregnant patient did not differ from other nonpregnant adults with medium severity poisoning. From a therapeutic point of view, the patient and the fetus did well after acetylcysteine was administered as a protective agent in the management of A. phalloides poisoning. This therapy may have been of benefit. Finally, based on a review of the literature and after this last experience, we recommend that during the first trimester of pregnancy, invasive prenatal tests should be avoided and abortion not recommended. However, monitoring of such poisoning must be intensified.

References