FATAL MUSHROOM POISONING CAUSED BY *AMANITA VIROSA* IN THAILAND

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Abstract. Consumption of toxic mushrooms belonging to the genus *Amanita* frequently leads to severe gastrointestinal distress followed by acute hepatic failure with a fatal outcome. In Thailand, valuable information as to the locally prevalent poisonous species, the preferred habitat and the management of suspected victims of intoxication is basically non-existent. We report here 5 cases of fatal poisoning with *Amanita virosa* having occurred in a family residing in the northeast of Thailand who as countless others had enjoyed mushroom gathering as a pastime. Within 4 to 6 days after ingestion of the mushrooms, all had succumbed to acute hepatic failure with subsequent hepatoencephalopathy. Treatment modalities exist in the form of penicillin and silibinin, or thioctic acid administration followed by plasmapheresis. In cases taking a lethal course apparent from the results of liver biochemistry, liver transplantation is clearly indicated. In order to prevent mushroom poisoning altogether, educating the general population to that end certainly presents the method of choice.

INTRODUCTION

Toxic mushroom poisoning or mycetismus, defined in Anisworth and Brisby's Dictionary of the fungi as distress resulting from the consumption of a fungal organism (Omidynia *et al*, 1997), has been identified as one of the more rarely encountered causes of fulminant hepatic failure. The underlying fatal poisoning is due to amatoxins present in some toadstools, predominantly the mushrooms belonging to the genus *Amanita*. These particular toxins constitute a family of nine cyclic octapeptides and cause cellular necrosis by binding very tightly to the enzyme RNA polymerase II and thereby inhibiting the formation of precursors of messenger ribonucleic acid (mRNA). Thus, the process of transcription of subsequent protein synthesis is interrupted with a fatal outcome ensuing in most cases (Faulstich, 1980; Piqueiras, 1989).

Most of the knowledge about mycetismus is related to *Amanita phalloides,* "the green death agaric" (Wieland *et al*, 1971; Lincoff *et al*, 1977). Yet, in some regions as for example Japan (Benedict, 1971), Mexico (Perez-Moreno *et al*, 1994), Milwaukee (Piering, 1990) and Oslo (Madsen *et al*, 1990) most cases of mystecismus are caused by some white species of *Amanita*.

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In Thailand, as almost everywhere else, mushrooms have always been considered a most nutritious and hence favored food and moreover, mushroom "hunting and gathering" represents a popular pastime, especially in the northeastern part of the country during the early rainy season. According to the data provided by the Ministry of Public Health, 3,473 cases of mushroom poisoning were reported between 1992 and 1996, 43 of which had a fatal outcome (Division of Epidemiology). MOPH, 1995, 1996.) These figures probably to some entest constitute an underrepresentation, as some cases might either have been too mild to warrant hospitalization, or might have gone unrecognized as mushroom poisoning. To make mattes worse, in most cases the exact species of the mushroom had remained unidentified due to the general lack of data available on specific types of poisonous mushrooms prevalent in any given area. Thus, *Amanita phalloides* appears to be the only member of the genus *Amanita* whose capcity for causing liver failure has been ascertained beyond doubt (Becker *et al*, 1976). Yet in 1995, a case of liver failure due to mushroom poisoning allegedly by a member of the species *Amanita verna* was reported in Maha Sarakham Province (Pongskul *et al*, 1995). Likewise, Plotzker *et al* (1982) reported the case of a patient with acute hepatic necrosis caused by *Amanita virosa*. Piering and Bratonow (1990) also have reported two such cases and furthermore, some additional ones had occurred in Europe (Piering *et al*, 1990). From Thailand, as yet no clinically recorded case of *Amanita virosa* poisoning has been reported.

We report here 5 cases of liver failure having occurred in one family as a consequence of *Amanita virosa* poisoning. Our intention is to draw attention to the fact that this type of poisonous mushroom can indeed be encounterd in Thailand and hence, that in particular the populace residing in the northeastern part of the country ought to be comprehensively educated in that regard.

CASE 1

The first case was a Thai woman, 36 years of age, who resided with her husband and two children at Ban Prong, Si That district, Udon Thani Province. Twelve hours after having ingested white capped mushrooms she had finely chopped in order to prepare that day's meal, she became nauseous and subsequently suffered from vomiting and diarrhea. For 3 days she received supportive treatment at the village hospital before she was referred to Udon Thani Provincial Hospital.

On admission she was conscious, with stable body temperature (BT 37.5°C) and vital signs. Her pupils had a diameter of 2 mm and reacted to light. She had jaundice, yet no hepatosplenomegaly. Her neurological parameters were normal.

Laboratory examination revealed the following data: CBC contained hemoglobin 11.0 g/dl; Hct 32.8 %; WBC 11,500 cells/mm^3; neutrophils 94 %; lymphocytes 5 %; monocytes 1 %; platelets 144,000 cells/mm^3. Urine was deep yellow in color, analysis showed: Sp Gr 1.018, pH 6; protein 2+, sugar negative; WBC 3-5 cells/HP; RBC 50-100 cells/HP. Biochemistry data were as follows: BUN 13 mg/dl; creatinine 1.5 mg/dl; Na 140 mEq/l; K 2.7 mEq/l; Cl 103 mEq/l; HCO_3 23 mEq/l. Liver function tests: Total bilirubin 22.0 mg/dl; directed bilirubin 7.5 g/dl; AP 183 U/l; AST 3,400 U/l; ALT 3,930 U/l Albumin 4.1 g/dl; globulin 1.7 g/dl; cholesterol 35 mg/dl; PTT (partial thromboplastin time) 165.7 seconds (control 28-51 seconds) PT (prothrombin time) extended to more than 600 seconds (normal control 10-16 seconds).

The patient was diagnosed as acute liver failure and received supportive treatment in the form of intravenous fluid and supplements of vitamin K, neomycin and lactulose, but showed no sign of clinical improvement. Upon developing hepatic encephalopathy she expired on the sixth day after having ingested the poisonous mushrooms.

CASE 2

The second case was the son of case 1, a boy of 8 years of age, who developed nausea, vomiting and diarrhea 12 hours after having ingested a white capped mushroom, At the local hospital, he was receiving intravenous fluid replacement, which did not produce any clinical improvement. Two days after the onset of symptomatic treatment he developed persistent diarrhea with mucous bloody stool, whereupon he was referred to Udon Thani Provincial Hospital.

At the physical examination performed 3 days after the onset of his symptoms he was conscious with pale complexion and raised body temperature (BT 38.1°C), but stable vital signs. His pupils were 3 mm in diameter and reacted to light. His neurological parameters were normal. He developed mild jaundice without hepatosplenomegaly.

Laboratory investigation showed the following data: Hct 33.8 %; hemoglobin 11.4 g/dl; WBC 15,400 with 77 % neutrophils, 22 % lymphocytes and 1 % atypical lymphocytes, platelets 200,000 cells/mm^3. Urine analysis showed WBC 2-4 cells/HP and RBC 10-12 cells/HP. Blood sugar 81 mg/dl; BUN 5 mg/dl; Cr 0.4 mg/dl; electrolytes: Na^+ 136 mEq/l; K^+ 4.4 mEq/l; HCO_3^- 21 mEq/l, Cl^- 108 mEq/l; LFT: TB 5 mg/dl, DB 2.4 mg/dl, ALT 1,738 U/l; AP 671 U/l; cholesterol 34 mg/dl; total protein 4.6 g/dl; albumin 3.7 g/dl; globulin 0.9 g/dl; PTT 138 seconds (control 25-51 seconds), PT above 600 seconds (control 10-16 seconds).

Six hours after admission he developed hepatic encephalopathy and remained unconscious, responding only to deep pain stimuli. Also, he was still passing watery bloody diarrhea. Fifteen hours after admission he developed convulsions, gastrointestinal bleeding and hypoglycemia (blood sugar 36 mg/dl). He died five days after having ingested the poisonous mushroom.

CASES 3-5

Case 3 : the husband of case 1, 36 years of age; case 4 : an 11-year-old brother of case 2, case 5 : a 6-year-old female cousin, developed identical gastrointestinal symptoms followed by acute liver failure and hepatic encephalopathy. They all expired 4-6 days after having ingested the poisonous mushrooms.

The relatives returned to the area from which the stricken family had previously collected the mushrooms and picked some for identification. Their gross as well as microscopic inspection performed by a botanist at Kasetsart University, Bangkok, suggested identification as *Amanita virosa*. Their

caps were kept for culturing and subsequently, some insects were found growing inside them.

DISCUSSION

In Thailand, every year lots of "toadstools" are growing during the early rainy season and the people residing in the rural areas collect the mushrooms for food. Most of the mushrooms are edible, but the poisonous ones are difficult to differentiate especially because neither has the presence of *Amanita phalloides* in Thailand ever been reported, nor is any valuable information available as to its most favorable habitat. Hence, information regarding the taxonomy of mushrooms in Thailand is urgently required in order to ascertain the presence or absence of some of the poisonous species.

Cases of *Amanita* poisoning keep being reported from different countries. For example, in southern France the poisonous *Amanita proxima* can easily be mistaken for the very common and edible *Amanita ovoidea,* and the first published cases of *Amanita proxima* poisoning with subsequent acute renal failure have been reported in 1994 by a team from Montpellier (de Haro *et al,* 1998). A group from Italy has reported a case of *Amanita phalloides* poisoning subjected to four treatments of plasmapheresis. The renal and hepatic parameters of this patient could already be stabilized after the first cycle which improved his general condition (Russo *et al,* 1997). Also from the Pacific Northwest region of the US and from southwestern Columbia, Canada, isolated cases of renal failure have occurred as a consequence of ingesting wild mushrooms. The patients's symptoms and time of onset after ingestion suggested the mushroom involved to be *Amanita smithiana,* which contains nephrotoxic compounds and which had apparently been mistaken for the edible pine mushroom (Leathem *et al,* 1997).

The cases described here occurred within one family, all of whose members developed indentical symptoms of acute gastroenteritis approximately 12 hours after having ingested the poisonous mushrooms. Since the amatoxins bind firmly to RNA polymerase II and thus inhibit messenger RNA and subsequent protein synthesis, only immediate stomach lavage followed by administration of activated charcoal in order to inhibit absorption and subsequent plasmapheresis might prevent the ensuing acute hepatic failure, which inevitable is followed by hepatic encephalopathy with a fatal outcome after 3 to 5 days.

Therefore, on the pure suspicion of *Amanita* intoxication antidote treatment with penicillin and silibinin (Carducci *et al,* 1996), or thioctic acid (Plotzker *et al,* 1982) should be administered immediately without awaiting biochemical parameters, as this therapy has been proven to prevent hapatocellular damage in tissue not yet injured. Subsequent transferral to a hepatological department with access to liver transplantation ought to be considered in cases of abnormal biochemical liver function developing (Schiodt *et al,* 1995).

As a last resort, liver transplantation is clearly indicated if the patient develops irreversible signs of poisoning. The criteria for a probably lethal course under conservative treatment are met in cases of severe liver failure with a prothrombin time below 20% over the course of several days, serum creatinine concentraion above 1.4 mg/dl even after water and electrolyte abnormalities have been corrected, serum bilirubin above 4.6 mg/dl and progressive encephalopathy (Beckurts *et al,* 1997). All these criteria had been met by the cases described above so that liver transplantation would ideally have constituted the treatment of choice in order to save their lives.

Yet, due to a combination of several limiting factors, in Thailand this most probably will not represent an alternative to be relied upon any time soon. To begin with, most victims of mushroom poisoning belong to that part of the populace that has enjoyed only rudimentary education and is therefore prone to fall for all kinds of superstitious beliefs, as for example that poisonous mushrooms change color upon cooking, that a silver spoon dipped into the mushroom soup will turn black, that rice boiled in that same mushroom soup will remain hard, or that mushrooms which show any kind of parasitic infestation or at which some amimal has nibbled cannot be poisonous. Moreover, they usually are rural folk residing in largely inaccessible areas with some rather ill equipped village hospital as the closest medical facility, in which the medical personnel may not be cognizant of the latest achievements in diagnosis and treatment. Last but not least, the communications system between the few large medical centers capable of performing an emergency liver transplantation and those remote village hospitals is insufficient if not altogerher non-existent.

Finally, the one conclusion emerging from the few conclusive data available, combined with the numerous confusing and contradictory data so frequently mingled with myths and hence thriving on superstition, is that profound and thorough eductation of the populace is the only safe way to prevent future occurrence of mushroom poisoning. Just to give one

example, as has been shown by culturing the cap of *Amanita virosa* and subsequently discovering live insects emerging from it, neither the presence of whatever parasitic infestation, nor traces of some animal having nibbled at the mushroom can be taken as a guarantee as to the edibility of any given mushroom or plant. Particularly with potentially fatal intoxication as have frequently been reported with respect to mushroom poisoning, the advice "prevention is better than cure" definitely ought to be heeded. Hence, instead of venturing into the unknown by trustingly ingesting wild mushrooms from one's own collection, it might after all be safer to eat commercially cultured mushrooms.

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REFERENCES

Becker CE, Tong TG, Boerner U, *et al.* Diagnosis and treatment of *Amanita phalloides*-type mushroom poisoning: Use of thioctic acid. *West J Med* 1976; 125: 100-9.

Beckurts KT, Holscher AH, Heidecke CD, Zilker TR, Natrath W, Siewert JR. The role of liver transplantation in the treatment of acute liver failure following *Amanita phalloides* poisoning. *Dtsch Med Wochenschr* 1997; 122: 351-5.

Benedict RG. Mushroom toxins other than *Amanita*. In: Ciegler A, Kadis C, Ajl SJ, eds. Microbial toxins, Vol 6. Fungal toxins. New York: Academic Press 1971: 281-320.

Carducci R, Armelliono MF, Volpe C, *et al.* Silibinin and acute poisoning with *Amanita phalloides*. *Minerva Anestesiol* 1996; 62: 187-93.

Division of Epidemiology, Office of the Permanent Secretary for Public Health, Ministry of Public Health, Thailand. Annual Epidemiological Surveillance Reprot, 1995.

Division of Epidemiology, Office of the Permanent Secretary for Public Health, Ministry of Public Health, Thailand. Annual Epidemiological Surviellance Report, 1996.

Faulstich H. The amatoxins. In: Hahn FE, ed. Progress in molecular and subcellular biology. New York: Springer Verlag, 1980: 88-134.

de Haro L, Jouglard J, Arditti J, David JM. Acute renal insufficiency caused by *Amanita proxima* poisoning: experience of the Poison Center of Marseille. *Nephrologie* 1998; 19: 21-4.

Leathem AM, Purssell RA, Chan VR, Kroeger PD. Renal failure caused by mushroom poisoning. *J Toxicol Clin Toxicol* 1997; 35: 67-75.

Lincoff GH, Mitchel DH. Toxic and hallucinogenic mushroom poisoning: Handbook for physicians and mushroom hunters. New York: Van Nostrand Reinhold, 1977.

Madsen S, Jenssen KM. Poisoning with deadly agaric *(Amanita virosa).* Symptoms, diagnosis and treatment. *Tiddsskr Nor Laegeforen* 1990; 110: 1828-9.

Omidynia E, Rashidpourai R, Qaderi MT, Ameri E. Mycetismus in Hamadan, of West Iran. *Southeast Asian J Trop Med Public Health* 1997; 28: 438-9.

Perez-Moreno J, Perez-Moreno A, Ferrera-Cerrato R. Multiple fatal mycetism caused by *Amanita virosa* in Mexico. *Mycopathologia* 1994; 125: 3-5.

Piering WF, Bratanow N. Role of the clinical laboratory in guiding treatment of *Amanita virosa* mushroom poisoning: report of two cases. *Clin Chem* 1990; 36: 571-4.

Piqueras J. Hepatotoxic mushroom poisoning: diagnosis and management. *Mycopathologia* 1989; 105: 99-110.

Plotzker R, Jensen DM, Payne JA. Case report. *Amanita virosa* acute hepatic necrosis: treatment with thioctic acid. *Am J Med Sci* 1982; 283: 79-82.

Pongskul C, Sirivong D, Phunmanee A. Fatal mushroom poisoning: a case report and review literatures. *Srinagarind Med J* 1995; 10: 307-10.

Russo GE, Giusti S, Maurici M, *et al.* Plasmapheresis and mushroom poisoning: report of a case of *Amanita phalloides* poisoning. *Clin Ter* 1997; 148: 277-80.

Schiodt FV, Ott P, Bondesen S. Poisoning by green and white mushrooms at a special hepatology unit, 1989-1994. *Ugeskr Laeger* 1995; 157: 4350-4.

Wieland T, Wieland D. The toxic peptides of *Amanita* species. In: Ciegler A, Kadis C, Ajl SJ, eds. Microbial toxins, Vol 6. Fungal toxin. New York: Academic Press, 1971: 249-80.