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CASE REPORT

Loss of Consciousness and Prolonged Convulsions Due to *Amanita Pantherina* Intoxication

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Abstract

Loss of consciousness ranks among very common causes for emergency medical service actions and is common occurrence in the emergency department. Its differential diagnosis is very broad and includes many possible causes, not in the least an intoxication. The same applies to convulsive states. Clinical course of mushroom poisoning varies depending on the particular fungal species, with some of the species causing loss of consciousness. One typical representative of such species is panther cap (*Amanita pantherina*). This case report introduces panther cap poisoning, initially presenting in given patient as coma and protracted generalized convulsions. Complex treatment led to withdrawal of neurologic symptoms, circulatory and metabolic stabilisation and subsequent discharge without signs of permanent organ damage.

INTRODUCTION

Loss of consciousness ranks among very common causes of Emergency Medical Service actions and occur in 1 to 10 % of patients treated in Emergency departments (Xiao *et al.* 2012). Differential diagnosis for loss of consciousness is very broad, encompassing various aetiologies, such as stroke or other anatomical brain pathologies, head injuries, hypoxia and hypoglycaemia, ketoacidosis or osmolar disorders, hypothermia and hyperthermia, reaction to medicaments, hypertensive encephalopathy, infection and sepsis, and not in the least an intoxication. Intoxications are common occurrence in patients with loss of consciousness managed at entry level of hospital care. They represent 6 to 21 % of loss of consciousness cases in various studies, reaching even 38 % in one study at the Emergency Department (Schmidt *et al.* 2019).

Mushroom poisoning from certain fungal species rank among the intoxications causing loss of consciousness, their prevalence being on the rise recently. Panther cap (*Amanita pantherina*) belongs to agaric mushrooms (*Basidiomycetes*) from order Agaricales (Figure 1). It grows mainly

in warmer deciduous woods, but in mixed and coniferous woods as well. Its scent and taste is inconspicuous, slightly raddish-like. Panther cap is highly poisonous, containing thermostable toxins ibotenic acid, muscimol and muscazon, which affect the nervous system. Panther cap is highly prevalent in Europe, North America, Asia and some regions of Southern Hemisphere. It is easily mistakable for the blusher (*Amanita rubescens*).

CASE REPORT

Emergency Medical Service (EMS) was called to a 51-year-old woman with an unspecified loss of consciousness. Closest crew with physician was dispatched. While the crew was underway to the patient, presence of continuous convulsions were reported in the patient by the dispatch centre, based on new information obtained from the site of the incident.

Upon EMS arrival on the scene, the patient was found in the living room in the presence of her daughter, who was fully conscious, communicative, and cooperative. The patient was lying on her back on the floor below low sofa, with no sharp edges or objects, blood, empty bottles, remaining medicines, or other indices in her vicinity, that would suggest trauma or intoxication. She was in deep coma with no reaction to painful stimuli, breathing spontaneously, but with generalized clonic convulsions of all limbs. There was foam at her lips, yet no traces of vomiting. She had wetted herself prior to EMS arrival.

Patient's brief medical history was obtained from her daughter, who stated that the patient had no allergies and suffered only from thyroid gland dysfunction, being healthy otherwise, without any prior neurologic disorder or head trauma. Precise pharmacotherapy was not known to the daughter. The patient had not underwent any major surgery, had not suffered from any mental disorder, was not treated by psychiatrist and had no suicidal thoughts. They shared a bit of wine together the previous evening, but only one bottle. This morning the daughter found the patient lying on the floor unconscious and called the emergency telephone line immediately. Prior to EMS arrival, the patient developed generalised convulsions of all limbs.

On the scene the physician performed physical examination per ABCDE protocol, by which patent airway and normal respiratory rate of 14 breaths per minutes with symmetrical clear alveolar breathing was determined. Oxygen saturation of blood was mildly decreased to 90 %, capillary refill time was slightly prolonged, heart rate regular 80 beats per minute, blood pressure 135 over 85 mmHg. ECG was registered with sinus rhythm without any pathologic finding. The patient remained comatose, with generalized predominantly clonic convulsions of all extremities, without apparent signs topical neurologic deficit. Eyeballs were in middle position, with isometric pupils without reaction to light. There was saliva foam at the mouth orifice, no bite marks on the tongue, abdomen soft, body temperature and hydration within norm, slightly increased glycaemia.

An intravenous line was secured and diazepam 10 mg was administered intravenously. The convulsive activity receded shortly thereafter, but there was no improvement in the level of consciousness. The patient continued breathing spontaneously with good oxygenation, was haemodynamically stable with no rhythm disturbances. However, the airway patency gradually

Fig. 1. Panther cap *(Amanita pantherina)*.

became insufficient due to persisting coma, necessitating application of manual jaw thrust manoeuvre and definite airway management by tracheal intubation protocol initiation.

At that moment patient's daughter went to the bathroom, where she began to vomit the gastric content, without any pathologic addition, but containing visible traces of mushrooms. Traces of previous intensive vomiting were then found in the bedroom also, whereof the daughter had not been aware, and which obviously took place during the night. Now the daughter confirmed that she drank the wine with the patient the previous evening, and consumed mushrooms as well, supposedly the blusher (*Amanita rubescens*) picked up by the patient's mother. The daughter was immediately assessed and found to be fully conscious, without any neurologic disorder, with her circulation and respiration stable with all vital signs within norm. Her infant was also present but had not been nursed since the time of mushroom ingestion.

Given the circumstances, another paramedic crew was summoned via dispatch centre to transport the daughter and her child to the hospital for a control assessment. Simultaneously, with all preparations completed, tracheal intubation of the patient was performed utilising midazolam and suxamethonium. Tracheal tube size 7,5 was inserted without any complications and its correct placement was verified by direct sight, bilateral auscultation, and capnography. The patient was then put on positive pressure ventilation with appropriate tidal volume and mild positive end-expiratory pressure. Sedation and analgesia were maintained by gradual administration of titrated doses of propofol, midazolam and sufentanil in combination, while muscle relaxation was maintained using rocuronium.

Throughout the whole initial phase, the patient remained haemodynamically stable, with normal blood pressure value, without any heart rhythm disturbance. Once patient's daughter along with her child were taken over by the summoned paramedic crew, anaesthesiology department of the regional hospital was notified and transport of the patient was initiated. 1000 ml of balanced crystalloid solution was administered intravenously throughout the whole prehospital treatment, both on the scene and during transport. The patient was subsequently handed over to the anaesthesiology ward, sedated, on positive pressure ventilation, with stable parameters of circulation and ventilation, without heart rhythm disturbances. A sample of gastric content with mushroom scraps obtained on the scene was handed over along the patient, for the purpose of further analysis.

In the hospital, several examinations were carried out as part of the differential diagnostic workup. Computer tomography of the brain was performed, revealing no intracranial pathology. Toxicological examination of the gastric content sample subsequently confirmed panther cap poisoning. Blood analysis at the admission was without any severe pathologies (Table 1). Routine invasive monitoring and access routes were obtained and symptomatic therapy was initiated, including activated charcoal administered via nasogastric tube. Vasopressor circulatory support by norepinephrine was initiated due to development of haemodynamic instability.

On the second day after admission the patient woke up to good contact, her condition was however complicated by the mimic muscle fasciculations. Pharmacologic sedation was therefore resumed, with continuous intravenous valproate administration added. Positive pressure ventilation and circulatory support with norepinephrine were maintained. Subsequently, extension posture in wrists and ankles along with muscle spasticity developed. Therefore another computer tomography was carried out, with the finding consistent with the previous, without any newly developed intracranial pathology. Valproate saturation was continued and central myorelaxant administration was introduced, as per recommendation of the neurologist.

Empirical antibiotic treatment with amoxicillin clavulanate was commenced due to inflammation markers elevation. Only mild elevation of liver enzymes was observed, regressing spontaneously. Renal function parameters were within norm. It was possible to decrease the vasopressor circulatory support over next few days. Pulmonary X-ray was obtained, with normal finding, inflammation markers regressed gradually. After repeated sedation weaning, patient regained consciousness and was in full contact, able to obey commands, although with somewhat slowed psychomotor tempo. No muscle fasciculations were present.

The patient was extubated without complications on the fourth day after admission to the resuscitation care ward. She then remained fully conscious, mildly disoriented, in fully stabilized condition otherwise, with adequate spontaneous ventilation supported by oxygenotherapy via a non-rebreather mask, non-febrile, with sinus rhythm, normotensive without the need for vasopressor support. She was transferred to intensive care unit on the fifth day, where the antibiotic treatment and normalization of metabolic parameters was completed. Disorientation slowly receded and the neurologic condition got back to normal. The patient was subsequently discharged home on eleventh day without any neurologic deficit and with circulation and ventilation fully stabilized.

DISCUSSION

Mushroom poisoning is quite a common occurrence, mainly due to confusing toxic species for edible ones (Satora *et al.* 2006). Vast majority of fatal intoxications is caused by the death cap (*Amanita phalloides*). However, death cap poisoning constitutes only small percentage

Tab. 1. Laboratory findings at admission and on 6th day of hospitalization

	admission to hospital	6th day of hospitalization
Arterial Astrup		
pH (normal value 7.36-7.43)	7.378	**7.441**
pCO_2 (kPa; normal value 4.8-5.8)	4.92	4.86
pO_2 (kPa; normal value 10.0-13.0)	12.81	**9.58**
Base excess (mmol / l; normal value -3.0-3.0)	-3.3	0.4
Lactate (mmol / l; normal value 0.6-2.4)	0.6	0.66
Blood count		
Leukocytes (x 109 / l; normal value 4.0-10.0)	9.2	9.4
Platelets (x 109 / l; normal value 150.0-400.0)	271	275
Erythrocytes (x 1012 / l; normal value 3.8-5.2)	4.96	4.37
Hemoglobin (g / l; normal value 120.0-160.0)	145	124
Biochemistry		
Total bilirubin (µmol / l; normal value 0-25.0)	15.5	8.7
Alanine aminotransferase (ukat / l; normal value 0-1.0)	0.64	0.78
Aspartate aminotransferase (ukat / l; normal value 0-0.8)	**1.47**	**1.17**
Gamma-glutamyl transferase (ukat / l; normal value 0-1.9)	0.31	0.50
Urea (mmol / l; normal value 3.0-8.0)	3.5	**1.5**
Creatinine (µmol / l; normal value 62.0-106.0)	**61.2**	**53.1**
Sodium (mmol / l; normal value 137-145)	135	142
Potassium (mmol / l; normal value 3.6-4.8)	3.8	4
Chlorides (mmol / l; normal value 98-109)	108	**111**
Calcium (mmol / l; normal value 2.1-2.6)	**2.06**	**2**
Magnesium (mmol / l; normal value 0.8-1.1)	0.89	0.8
Phosphates (mmol / l; normal value 0.6-1.5)	1.21	1.08
Amylase (ukat / l; normal value 0.4-1.4)	0.55	0.78
Lipase (ukat / l; normal value 0-2.6)	0.53	0.88
Glucose (mmol / l; normal value 3.6-5.6)	**6.3**	5.2
Hemocoagulation		
Activated parcial thromboplastin time (s; normal value 25.9-40.0)	27.5	27.8
Prothrombin test (s; normal value 12.0-15.0)	12.9	13.4
Fibrinogen (g / l; normal value 1.8-4.5)	3.0	2.4
Markers of inflammation		
C-reactive protein (mg / l; normal value 0-5.0)	1.3	**185.4**
Procalcitonin (ug / l; normal value 0-0.1)	0.03	0.06

of total number of mushroom intoxications. According to their typical clinical manifestation, poisonings can be categorized into several syndromes.

Similar to fly agaric, main toxins in panther cap are ibotenoic acid and muscimol, to which the ibotenoic acid is metabolized within the body. Both substances cross the blood-brain barrier and directly affect the central nervous system (CNS) by acting as neurotransmitter receptor agonists (Satora *et al.* 2005). Ibotenoic acid mimics excitatory amino acid glutamic acid and acts on N-methyl-D- aspartic acid (NMDA) receptors. Muscimol is a potent agonist of gamma-Aminobutyric acid (GABA) type A ($GABA_A$) receptors and also exerts effects on CNS (Garcia *et al.* 2015). Glutamic acid belongs to main excitatory neurotransmitters and plays a role in pathophysiology of epilepsy. Ibotenoic acid affects certain glutamate receptors, whereas muscimol drives GABA out of the bond to its

receptor and has a suppressive effect. Panther cap contains other substances affecting the brain, such as muscazon, that induces fuzziness and somnolence, and other substances affecting NMDA receptors and thus excitability.

Compared to death cap, panther cap poisoning is generally less severe and usually does not lead to death or permanent organ damage. However, the symptom severity is variable according to the quantity of ingested mushrooms and individual sensitivity to the toxins present. While panther cap and fly agaric contain similar toxins, their relative proportion varies in both species, with panther cap containing much larger amount of muscimol with sedative effect and less excitatory ibotenoic acid. That was clinically determined in retrospective analysis of 32 cases of fly agaric intoxication and 17 poisoning cases caused by panther cap, wherein coma was significantly more common in patients with panther cap poisoning (Vendramin *et al.* 2014). On the other hand, there are cases described in literature with positive EEG finding of „burst-suppression" pattern observed following panther cap intoxication (Ogawa *et al.* 2015).

Herein referred patient ingested the mushrooms together with limited amount of alcohol. The main manifestation was quantitative loss of consciousness accompanied by miosis and generalized tonic-clonic convulsions. Broad differential diagnostic workup for causes of loss of consciousness and seizures was considered initially, which was then focused on intoxication, once the history of mushroom ingestion was detected. Referred clinical signs were convincingly corresponding to panther cap poisoning syndrome. It was impossible to determine, whether hallucinations or other qualitative changes of consciousness preceded the loss of consciousness. The history of assumed ingestion of the blusher (*Amanita rubescens*), most commonly mistaken for panther cap, was very indicative indeed. The toxicological analysis of the mushroom sample obtained on the scene provided the final confirmation. This is a crucial step in any suspected mushroom poisoning.

Generalized convulsions as part of the initial presentation belongs to the clinical picture of the panther cap intoxication (Satora *et al.* 2006). In reported case, the hospitalisation was little prolonged, with presence of muscle fasciculations, necessitating administration of anti-epileptic drug. Restoration of consciousness after cessation of sedative medication was also slower, with temporary disorientation. All these factors suggest rather more severe intoxication, or higher individual sensitivity to panther cap toxins. Despite this serious course of the intoxication, the patient is now completely all right regarding her mental and neurological status. The contrast of severe clinical condition of the patient and only mild symptoms of her daughter was caused by the fact, that the daughter vomited most of the ingested mushrooms, whereas the patient did not.

The therapy in this case fully reflected standard guidelines, especially securing basic vital functions, temporary vasopressor circulatory support to manage the hypotension, and electrolyte normalisation. In majority of the patients, adequate ventilation is maintained during convulsions, unless the airway is compromised otherwise (Betjemann *et al.* 2015), therefore the oxygen administration in necessary only in case of more pronounced hyposaturation, and ventilatory support is warranted for longer apnoeic pauses. In our case, invasive airway management with tracheal intubation was necessary though, due to limited ability to keep the airway patent and longer transport time to receiving hospital.

With the vital functions secured, first-line treatment within first 10 minutes in adults is mainly diazepam 10 mg intravenously. It is possible to repeat this dose, up to the total dose of 30 mg (Šarbochová *et al.* 2017). If the convulsive state persists for more than 30 minutes, it is recommended to secure the airway by tracheal intubation using propofol intravenously with initial dose of 2 mg kg^{-1} and then 2 to 5 mg kg^{-1} h-1 by continuous infusion. Should the convulsive state persist, usually over 90 minutes, it is necessary to administer phenobarbital intravenously initial bolus of 5 mg kg^{-1} and then as continuous infusion with rate per the patient response, usually in the range of 1 to 5 mg kg^{-1} h^{-1}. The therapy should include thiamine 500 mg, to prevent depletion of thiamine reserves during the longer-lasting convulsive state and subsequent onset of acute Wernicke Korsakoff syndrome (Sechi *et al.* 2007).

The loss of consciousness and protracted convulsions considered the initial differential diagnostic workup was very broad. Consumption of one bottle of wine by two adult women was not indicative of severe alcohol intoxication. In the household environment medical drug intoxication might be considered. Neurologic or psychiatric disorder medication is the most common source of intoxication, eventually antiarrhythmic drugs. Even neurotoxic effects of certain antibiotics or antiviral drugs have recently been described. As an example, severe acyclovir intoxication might be quite surprising (Paluch *et al.* 2021). With repeated stays in the open environment and forests, neuro-infection might also have been considered, as various consciousness impairments including loss of consciousness and convulsions may be the signs of bacterial meningitis (Šín *et al.* 2022). Taking the patient's age into account, stroke could not be ruled out. However, the panther cap intoxication was determined to be the sole cause of the clinical condition.

CONCLUSION

Panther cap intoxication may be a life-threatening condition due to effects of ibotenoic acid, that is metabolized to muscimol in the organism after ingestion. Toxins cross blood-brain barrier and directly affects

central nervous system by exerting their agonistic properties on neurotransmitter receptors. Securing all the vital functions is crucial for patient survival in pre-hospital emergency care, foremost maintenance of patent airway and adequate ventilation. Need for circulatory support is common, as well as management of generalized convulsions, as in our referred case. In the European continent setting, mushroom poisoning must be considered among potential causes of loss of consciousness and convulsions during the mushrooming season.

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