

ACUTE RENAL FAILURE FROM INTOXICATION BY MUSHROOMS

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Keywords: intoxication, renal failure, mushrooms intake

Abstract: Intoxication caused by the consumption of wild mushrooms is still a serious public health problem, with the most severe consequences. As part of their clinical picture, renal failure occurs in late stages of intoxication with hepatotoxic mycotoxins, that of hepatorenal failure, or as an independent clinical entity, in case of toxins' ingestion with direct nephrotoxic action, such as orellanin (orellanian paraphalloidian syndrome). This paper presents a review of the toxicological issues related to mycotoxins with renal tropism, describing the clinical features, physiopathology and treatment of acute renal failure caused by the ingestion of poisonous mushrooms.

Cuvinte cheie: intoxicație, infecție renală, consum ciuperci

Rezumat: Intoxicațiile provocate de consumul de ciuperci sălbatice reprezintă în continuare o gravă problemă de sănătate publică, cu consecințe dintre cele mai severe. În cadrul tabloului clinic al acestora, insuficiența renală apare în stadiile tardive ale intoxicațiilor cu micotoxine hepatotoxice, acela al insuficienței hepato-renale, sau ca și entitate clinică independentă, în cazul ingestiei de toxine cu acțiune nefrototoxică directă, cum este orellanina (sindromul paraphalloidian, orellanian). Lucrarea de față prezintă o trecere în revistă a aspectelor toxicologice legate de micotoxinele cu tropism renal, descrierea particularităților clinice, fiziopatologice și de tratament a insuficienței renale acute provocată de ingestia de ciuperci otrăvitoare.

INTRODUCTION

The first mention of what will be called orellanian or paraphalloidian syndrome dates from 1950, when it was observed in Poland a sequence of about 100 poisoning cases with similar symptoms, without being able to identify a common causative agent. The causal link between the type of intoxication and mushroom ingestion of Cortinarius species was observed by the physicist Orellanus Gryzmala Stanislaw.(1) The responsible toxin was isolated in 1962, and caused the same symptoms with those of the ingestion registered in humans made on animal experiments.

Insufficient acute renal failure after intoxication with Cortinarius mushrooms was later reported in Finland (2), Scotland (3), Sweden (4), Norway (5) and France.(6)

Paraphalloidian syndrome includes severe clinical manifestations, with fatal consequences. It is due to the consumption of mushrooms from Cortinarius species - horseradish forest (picture no. 1) and Lepiota - sponge snakes (picture no. 2).(7)

Figure no. 1 Cortinarius odorifer



Figure no. 2. Lepiota roseifolia



Figure no. 3. Cortinarius orellanus



Cortinarius species that contain orellanian may include:

- Cortinarius orellanus,
- Cortinarius speciosissimus,
- Cortinarius rainierensis,

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Article received on 28.10.2011 and accepted for publication on 31.01.2012

ACTA MEDICA TRANSILVANICA March 2012;2(1):208-210

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- Cortinarius callisteus,
- Cortinarius gentilis Cortinarius splendens,
- Cortinarius cinnamomeus group,
- Cortinarius semisanguineus group.

Cortinarius orellanus presents the following characteristics:(8)

The cap, at first globular, convex and then gradually becoming flat, rusty colour, with red shades, soft and dry due to the numerous scales that cover it; the central part is provided with a little nipple not very prominent, but very broad and deep in the middle and with a diameter of 3-9cm, of cinnamon colour. At full maturity, the **edge** tends to crack deeply.

The stem is very smooth, dense and thick in the inside, cylindrical or curved and less thin at the basis, with a height of 4,5 cm and of rusty colour.

There is much space between **the gills**, which are rather fleshy.

The flesh is yellow-brown, with a low characteristic odour of radish and of sweet taste.

VARIABILITY. Cap colour varies from red-orange to reddish brown. The stem is initially yellow and gradually turns in rust shades.

HABITAT. It is a rare species found in deciduous forests, on rich silicon soil.

PERIOD OF GROWTH. Late summer-autumn.

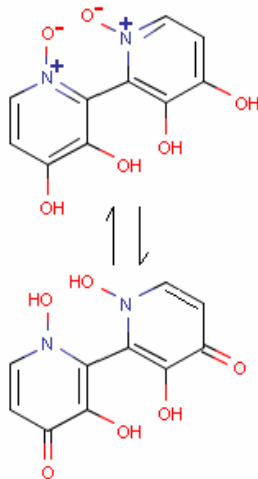
RELATED SPECIES. It can be easily confused with other species of Cortinariaceae of reddish color: Cortinarius bolaris, Cortinarius Cortinarius sanguineus and speciosissimus, all of them being totally suspect.

SYNONYM. Cortinarius rutilans.

ORELLANIN

Orellanin is the main toxin present in the mushrooms belonging to this family. This, 3,3',4,4'-tetrahydroxi-2, 2'-bipiridino-1, 1'-dioxide) is a crystalline compound, colourless, with important nephrotoxic features.(9)

Figure no. 4. Orellanin structure



Molecular formula: $C_{10}H_8N_2O_6$

Molecular weight: 252.17 g/mol

Physiopathological features

The patients who have ingested mushrooms from the Cortinarius family may early experience gastrointestinal symptoms due to other toxic components thereof. Orellanin is strictly nephrotoxic with a long latency period of 30 hours-21 days. The inhibition of alkaline phosphatase decreased ATP production and compromises the cellular metabolism. The reaction is specific at the level of proximal tubular cells, without having a noticeable effect at glomerular level. The result is tubulointerstitial nephritis and renal failure, with their specific

symptoms and complications.

Anamnesis

Determining the ingestion of the consumed poisonous mushrooms is the most important factor in supporting the diagnosis of poisoning. For orellanin, the moment of ingestion may be long before the presentation, due to the long latency until the onset of the nephrotoxic effects. The early digestive manifestations may unnoticeably pass, or they may be of low amplitude, which does not require the patients' presentation to the emergency room. Patients with renal symptoms may have a free symptoms period of up to 1-3 weeks from the time of ingestion.

The emergency physician must take into account and request information about a possible mushroom ingestion in cases of gastroenteritis. A short period of time between ingestion and the occurrence of symptoms suggests a higher dose or the intake of a more aggressive toxin, with a high probability of acute renal failure installation. Its magnitude may vary from reversible damage, with the recovery of the renal function in several weeks or months, to the need for hemodialysis or chronic renal transplantation.

Important historical data for mushroom poisoning:

- time between ingestion and the onset of symptoms;
- mushrooms eaten quantity, aspect, species of mushrooms if they are known;
- if it is the case, other mushrooms species that have been consumed;
- whether other people also consumed the mushrooms and in this case, their symptoms;
- mushrooms' gathering place.

Gastrointestinal symptoms:

- nausea, vomiting,
- abdominal pain,
- diarrhoea or constipation.

The symptoms occur early, upon 24-48 hours from ingestion and are of low intensity.

Renal symptoms:

- back, flank pain,
- severe thirst (described as burning),
- polyuria or oliguria,
- anuria (rarely).

Acute renal failure may occur at any interval between 36 hours-14 days

General symptoms:

- anorexia,
- chills,
- myalgia,
- rashes.

Neurological symptoms:

- sleepiness,
- headaches,
- parenthesis,
- tinnitus,
- loss of consciousness.

Objective examination

The patients with acute renal failure induced by the ingestion of orellanin presents a low number of symptoms upon the physical examination.

- Volemic status – Signs suggesting hypovolemia may be induced by the anorexic or polyuria syndrome, while hypervolemia occurs in anuric renal failure.
- Neurologically – in the incipient or less severe stages

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of the acute renal failure, the mental status remain unaltered. In severe renal failure, confusion, space temporal disorientation or even coma may also occur. In this stage, myoclonus or asterix suggests the presence of uremia.

- Gastrointestinally – the digestive symptoms may already be absent upon presentation.
- Renally- a certain sensibility at the level of kidneys can be observed.
- Others– signs of uremia (pericarditis, pleuritis, hypervolemia)

Differential diagnosis

- Botulism,
- Gastritis, ulcer,
- Gastroenteritis,
- Giardiasis,
- Acute glomerulonephritis,
- Intoxication from the ingestion of poisonous plants,
- Renal colic,
- Renal failure due to other causes,
- Rhabdomyolysis,
- Ethylene glycol poisoning,
- Intoxication from the ingestion of other species.
- Infections of the urinary tract.

TREATMENT

Laboratory samples:

- Electrolytes, urea, creatinine, glycaemia,
- Testing the hepatic function,
- Haemoleucogram, coagulograma may be normal or it may present an anaemic syndrome after a prolonged renal insufficiency, coagulopathy in uremia stage.
- Urine sample – microscopic haematuria, leucocyturia, sometimes albuminuria.

Other investigations

Electrocardiogram may be useful in detecting hyperpotassemia.

It is important to consult a botanist, forester or any other person with experience in identifying and knowing the effects of ingestion of poisonous mushrooms. The existence of a regional or national poison centre can be useful. If there is any rest of the food ingested and a specialized laboratory, orellanine can be easily identified. Because the period between ingestion and occurrence of the renal symptoms is high, the collection of food samples is unlikely. The existence of raw mushrooms collected in the same day is yet possible, as well as the identification of the geographical area where it was gathered.

Prehospital therapy

Evaluation, stabilization of symptoms with fatal potential, initiation of the specific therapy if the diagnosis is certain.

Therapy in the Emergency Room

- fluid and electrolyte resuscitation, monitoring,
- because patients come to hospital a few days after ingestion, gastric decontamination (gastric lavage, activated charcoal) are quite inefficient,
- if ingestion is recent, administration of activated charcoal may be effective, with the exception of recent emetic syndrome or the alteration of the consciousness,
- correction of dehydration and shock treatment,
- diuresis monitoring,
- administration of antiemetics to treat nausea and possible vomiting,
- benzodiazepines for seizures followed by phenytoin,

- hemodialysis may be required in emergency cases with fulminant renal failure or severe diselectrolemias. Haemoperfusion or early hemodialysis was proposed in the treatment scheme and early after ingestion, although there are no signs of kidney damage, but there are no concrete data to support their effectiveness.

Specific treatment

Although there is no specific antidote to counteract the effect of orellanine, hospitalization and the aggressive treatment early instituted can prevent the installation of serious and irreversible kidney damage. In addition to the above general measures, N-acetylcysteine with antioxidant role and glutathione provider or corticosteroids has been proposed as well as the classical agents in treating tubulointerstitial nephritis.(11)

Check-upsThe nephrologist decides the opportunity for the emergency haemodialysis or for the acute renal failure management.

- If existed, the regional toxicological centre may offer specific data related to the toxin.
- External sources for the accurate identification of the ingested mushroom species.

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