

Case series of *Chlorophyllum molybdites* intoxication in Sicily: an “alien” mushroom species in Europe

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Abstract

Introduction. Mushroom poisoning is an important cause of intoxication worldwide. The toxic mechanism remains frequently unknown and the diffusion of non-endemic species may cause the emergence of new syndromes. An example is the widespread of *Chlorophyllum molybdites* in Sicily.

Case series. Pavia Poison Centre was recently involved in the management of 10 intoxications caused by the ingestion of *Chlorophyllum molybdites*, which was not considered part of the Italian mycological species. The clinical syndrome was characterized by severe gastrointestinal symptoms. In paediatric or vulnerable patients, it may bring to hypovolemic shock that necessitate intensive support. The possibly confusion with amatoxins-containing mushrooms may complicate the management.

Conclusions. *Chlorophyllum molybdites* is widespread on the oriental coast of Sicily and it could be confused with “parasol mushrooms”. Cooperation between emergency physicians, clinical toxicologist and mycologist, supported by improving of laboratory tests, is essential for the appropriate clinical management. Climate changes and migration flows can interfere with the diffusion of new species and the development of novel syndromes.

Key words

- mushrooms
- gastrointestinal syndrome
- new syndrome
- alien

INTRODUCTION

Mushroom poisoning is an important cause of intoxication worldwide. The real annual global fatality is unknown and underreported, but is estimated that the consumption of wild mushrooms causes every year an approximated number of 100 death/year in Europe alone [1].

New poisoning syndromes continue to emerge and being characterized from a clinical point of view. The toxic mechanism of many mushrooms species remains unknown. In some cases, mushrooms considered before as edible are now listed as potentially toxic, so it may result difficult to distinguish between edible and poisonous species; moreover, their toxicity may be different considering various factors such as the stage of growth, quantities ingested, cooking procedures or environmental conditions. Valid examples are the rhabdomyolysis

following the ingestion of large quantities of *Tricholoma equestre* [2] or gastroenteric syndromes from *Armillaria mellea* consumed without the correct caution of boiling and throwing the cooking water away [3]. Another important bias is that the same species could be considered edible in some part of the world and non-edible in others, this because the same mushroom may develop different toxin content and consequently causes or not clinical manifestations. A representative member of this class is *Chlorophyllum molybdites* [4].

Chlorophyllum molybdites is a mushroom that can cause severe, short-onset gastrointestinal syndrome, also known as “Morganic syndrome”. It may be confused with edible species, such as *Macrolepiota procera* (parasol mushroom) due to its aspect or *Agaricus guadalupensis*, because their habitat of growth (lawns and grassy fields) [5] (Figure 1). In some cases, the

**Figure 1**

Macroscopic comparison between *Chlorophyllum molybdites* (A, B) and *Macrolepiota procera* (C, D).

symptoms, in particular watery diarrhoea, may persist over 12-24 hours, which may hide the onset of a long latency syndrome mainly due to amatoxin containing mushrooms. From a clinical point of view, the similarity between *Macrolepiota procera* and *Chlorophyllum molybdites* is particularly important because the edibility of the former mushroom brings the consumer, even an expert one, to understate the importance of the mycological recognition to avoid eating a non-edible mushroom. Moreover, a naïve collector could mistake and pick up toadstool containing amatoxins, with the subsequent risk of severe hepatotoxic damages if not correctly framed and treated.

To date, the syndrome related to *Chlorophyllum molybdites* has been reported in medical and botanical literature since the beginning of 20th century in tropical and subtropical areas, in particular USA, Tahiti, Philippines, New Guinea, Australia, India, Africa, West Indies, South America (where in some countries was considered edible), Japan, China and Israel. In Europe this species is not considered part of the endemic mushroom flora; it was first identified in Scotland and The Netherlands at the beginning of 1990's, in association with exotic ornamental plants [4]. In Italy, *Chlorophyllum molybdites* was first spotted in 2005, on the Ionian coast of Sicily by mycologist, but during the last two years it became widespread. The mycologists of Azienda Sanitaria Provinciale (ASP Catania, Sicily, Italy) involved for territorial competency, due to the huge amount of intoxications in which *Chlorophyllum molybdites* was recognized as responsible of the characteristic clinical syndrome, sent a specific warning to the Italian Ministry of Health, that developed and spread an alert on October 26th 2021 [6, 7].

We describe ten cases of *Chlorophyllum molybdites* in-

toxication registered in the last 2 years (2020-2021) by Pavia Poison Centre (Pavia-PC).

CASE SERIES

Ten patients were studied, 2 females and 8 males (age ranging from 10 to 58 years old). Demographic data, clinical manifestation and treatment details are summarized in Table 1.

All the patients had in common the consumption of mushrooms considered as *Macrolepiota procera*, prepared with different cooking procedures or consumed raw, but after a latency between 30 minutes and 7 hours, they developed severe gastrointestinal syndrome, characterized by abdominal cramps, vomiting, and diarrhoea. All of them were taken to the local Emergency Department (ED), where they received fluids and gastrointestinal decontamination.

In particular, three patients (a family cluster of 2 adults and a child) were treated with the Pavia Protocol in the suspect of intoxication from mushroom containing amatoxins, because of the persistence of gastrointestinal syndrome after 12-24 hours since ingestion and in a case of late onset of symptoms (more than 6 hours). The treatment consists in gastric lavage, activated charcoal (AC), 30 g in adults and 10 g in child, followed by multiple doses activated charcoal (MDAC) 5 g every 2 hours, N-acetyl cysteine (NAC: 150 mg/kg in 90 minutes, then 300 mg/kg/day – i.v.), cathartics and fluids to force diuresis [8]. All the patients reached fully recovery and they were discharged from hospital within two days.

DISCUSSION

Chlorophyllum molybdites, also known as *Lepiota morgani* and commonly named “false parasol” or “green-

spored lepiota", is a mushroom that belongs to the *Agaricaceae* family, considered non-edible in many countries. Mature specimens are recognized by green spores and gills, the flesh is firm and white, the cap measures 7-30 cm, is broad, convex, knobbed or flat usually white and brown spotted, the stalk is 10-25 cm long and 10-25 mm thick. Younger specimens are usually white and the cap is button shaped. Colonies assume a ring-configuration and characteristically found in meadows and lawns, typically at the end of summer and autumn [4].

Currently the toxic mechanism remains unknown. In the past, authors agreed to consider at the base of the *Chlorophyllum molybdites* toxicity a polymeric protein with a molecular weight greater than 400 kDa and a monomer size between 40-60 kDa; specifically, the experiment from Eilers and Nelson evidenced that this polymer was thermolabile and degraded from pepsin and acid [9]. In 2012 Yamada *et al.* discovered a small protein, homologue of metalloendopeptidase, named "Molybdophyllysin" (23 kDa), that may correspond to the monomer reported by Eilers and Nelson, that seems to be responsible of the toxicity in animal model, in particular it was evidenced lethal in mice. It is able to develop its proteolytic activity in a pH range between 4.0-11.0 and maintain thermostability after heating for 10 minutes at various temperatures between 30-70 °C (86-158 °F) [10]. In the majority of the cases followed by Pavia-PC, the gastrointestinal symptoms broke out after a meal with cooked mushrooms, prepared with different cooking times, so it is likely that a thermo-

stable toxin is responsible of the human gastroenteric syndrome.

Often the mycologists have to recognize mushrooms from cooked residues or the spores in digestive samples. Recently, Wang and co-authors described a loop-mediated isothermal amplification (LAMP) assay to help in the visual identification of *Chlorophyllum molybdites*: a set of specific primers were designed and tested against the target and other 43 different mushroom species to define specificity; LAMP method is able to identify the presence of traces of *Chlorophyllum molybdites* in boiled and digested samples with high specificity and sensibility [11].

From a clinical point of view, *Chlorophyllum molybdites* is classified as a gastrointestinal irritant mushroom [1]. The primary symptoms seen are gastrointestinal discomfort, characterized by abdominal pain, cramps, nausea, vomiting, and severe diarrhoea (initially watery, then may become bloody), accompanied by profuse sweating. In isolated cases, autonomic nervous system effects can cause altered perception, dilated/pinpoint pupils, blurred vision, dizziness, lacrimation, salivation, hypotension and tachycardia. ECG abnormalities and T-wave inversion have occurred. Hematologic abnormalities can also be present with bleeding and a condition similar to disseminated intravascular coagulation (DIC). Prolonged dehydration following gastrointestinal symptoms may lead to acute renal insufficiency and electrolyte imbalance [1, 4]. The clinical manifestation may cause also hypovolemic shock, requiring intensive support with fluids resuscitation, endotracheal intuba-

Table 1
Summary of case series from Pavia Poison Centre, in which *Chlorophyllum molybdites* was identified

Age Sex	Cooking method	Latency a: meal - symptoms b: symptoms - hospital	GI symptoms	FL	GL	AC	MDAC	WBI	NAC	Hospital stay
28, M	Risotto	a: 2 hours b: 6 hours	+	✓						5 h Self-discharged
52, M	Grilled	a: 2 hours b: 6 hours	++	✓	✓	✓		✓		1 day
50, M	Raw	a: 2.5 hours b: 6 hours	++	✓	✓	✓		✓		2 days
56, M	Pan cooked	a: 5 hours b: 9 hours	+++	✓		✓		✓		2 days
58, M	Pan cooked	a: 5 hours b: 9 hours	++	✓		✓		✓		2 days
47, F*	Pasta sauce, baked	a: 4 hours b: 7 hours	+++	✓	✓	✓	✓	✓	✓	2 days
10, M*	Pasta sauce, baked	a: 4 hours b: 7 hours	+++	✓	✓	✓	✓	✓	✓	2 days
47, M*	Pasta sauce, baked	a: 7 hours b: 7 hours (long latency)	+++	✓	✓	✓	✓	✓	✓	2 days
42, M	Pasta sauce	a: 3 hours b: 8 hours	++	✓	✓	✓		✓		1 day
38, F	Pasta sauce	a: 3 hours b: 8 hours	++	✓	✓	✓		✓		1 day

*: family cluster.

GI symptoms: abdominal pain, nausea, vomiting, diarrhoea; +: mild; ++: moderate; +++: severe.

FL: fluids; GL: gastric lavage; AC: activated charcoal; MDAC: multiple doses activated charcoal; WBI: whole bowel irrigation; NAC: N-acetyl cysteine.

tion and dopamine drip, especially in paediatric population [12]. The onset of symptoms typically varies within 30 minutes and 2 hours. In some cases, symptoms may not appear for up to 4 hours, which may hide a delayed onset syndrome. Generally, symptoms resolve spontaneously in 6-24 hours, only with supportive care [1, 4, 5].

The cases in which Pavia-PC was involved, had in common the consumption of mushrooms, considered *Macrolepiota procera*, but after a variable latency (30 minutes - 7 hours) they developed severe gastrointestinal syndrome, characterized by abdominal cramps, vomiting, and diarrhoea. All of them were taken to the local Emergency Department, where they received fluids and gastrointestinal decontamination. Three patients underwent the Pavia Protocol in the suspect of ingestion of mushroom containing amatoxins: a prompt mycologist identification of *Chlorophyllum molybdites* permitted the hospital discharge in day 2. A complete recovery followed. The correct identification of the mushroom involved is crucial to evaluate the severity of the clinical hallmark and subsequently to apply the appropriate medical treatment. As general advice, mycological identification before the consumption of picked mushrooms should be always carried out, even if they are collected by expert picker, to avoid the ingestion of non-edible species. Additional problem in the management of suspected mushroom poisoning for long latency was the fact that in whole Sicily, but also in other Italian regions, it is difficult to determine urinary alfa-amanitin because, currently, only a few laboratories are able to test it. This test is essential to confirm intoxication but result more useful to exclude the potential intoxication due to lesional toxins such as alfa-amanitin.

CONCLUSIONS

Chlorophyllum molybdites is an “alien” widespread mushroom in Eastern Sicily, that may even disseminate in Europe. It could be confused with both edible and poisonous species. It is responsible of a severe gastrointestinal syndrome with abdominal pain, nausea, vomit and diarrhoea; secondary dehydration could cause renal failure, electrolytes imbalance and hypovolemic shock in paediatric and fragile patients. It is important to consider the presence of *Chlorophyllum molybdites*, especially when patient referred the ingestion of single “para-

sol mushroom”, to frame and treat the gastrointestinal syndrome in the right way. Cooperation between ED physician, clinical toxicologist and mycologist is fundamental for this purpose.

It should be important to improve the availability of laboratory tests over the national territory to permit to diagnose the presence of amatoxins and distinguish even in early stages, where is necessary to extend therapy over the symptomatic treatment.

Climate changes may seriously influence the spread of non-endemic species, currently considered tropical or subtropical, also in Mediterranean areas of Europe, a valid example of this is what is happening in Sicily with *Chlorophyllum molybdites*. In addition, migration flows may introduce different food customs. So, in front of a mushroom intoxication physicians should always contact mycological department to reach the correct identification and not consider only the old known illnesses, but also be alert on these emerging syndromes.

At the same time, it is fundamental to made aware the population about the risk correlated to the consumption of unknown mushrooms, improving local information about the kind of species diffused on the territory and the mycological services available.

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Author's contribution

VMN, DL, AS, VMP, LB, BB and CG patient management, data collection and article drafting; AP and EA mycological data collection; CL article review. All Authors approved the manuscript.

Conflict of interest statement

The Authors do not have any financial or professional interest in the commercial products mentioned in the manuscript, nor in companies involved in their manufacturing, distribution, and sales. No grant or honorarium was given to anyone to produce the manuscript.

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