Case report

Accidental mushroom poisoning mimicking stroke. A case report and literature review

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Abstract. We describe here a paradigmatic case of mushroom poisoning mimicking a stroke. A 64-year old male was referred to the emergency department (ED) for a car accident. He was found diaphoretic, hypotensive, bradycardic, and slightly confused at presentation. No signs of trauma were observed on physical examination. The patient had weakness of the right limbs and bilateral severe myosis. The lab tests were normal, except for leukocytosis, mild hyperglycemia, mild hyperazotemia and moderate hypokalemia. The clinical picture, with the exception of miosis, was thereby suggestive for a stroke, which was also considered the cause of the car accident. The patients' wife, who was brought later to the ED, reported that the husband had suffered a stroke 4 years earlier, with residual right hemiparesis. She also referred that the patient showed signs of diaphoresis and confusion, and the car was intentionally driven into the ditch. Among other details, she referred that the husband ate mushrooms that she had personally collected 2 hours before taking the drive. Two mg of atropine, intravenous rehydration and potassium were hence administered in the suspicion of a cholinergic toxydrome, and complete clinical remission was rapidly obtained. Among the mixture of mushrooms eaten by the patient, a mycologist identified Armillaria Mellea (an edible mushroom) and notably Inocybe Fastigiata, a toxic muscarine-containing mushroom, easily confounded with Armillaria. After observation and oral rehydration, the patient was discharged. (www.actabiomedica.it)

Key words: Mushrooms; poisoning; Armillaria; Inocybe; stroke.

Introduction

There is consolidated evidence that rapid triage and treatment are effective to improve the outcome after stroke or transitory ischemic attack (TIA). The current Guidelines recommend that patients who are admitted to the Emergency Department (ED) with a suspected cerebral ischemia should undergo diagnosis by a validated tool, such as ROSIER (Recognition of Stroke in the Emergency Room), and all those with symptoms of acute stroke should have urgent brain scanning, electrocardiography, as well as assessment of blood glucose, coagulation profile, renal function, and hematological testing (1). The differential diagnosis at ED admission include hypoglycaemia, brain neoplasm or infection, epilepsy, complicated migraine, syncope of various origin, convulsions with Todd's paralysis, severe labyrinth disorders, vasospasm, severe hyponatremia (2). We describe here a paradigmatic case of a patient with suspected stroke, which was further diagnosed as an acute mushroom poisoning.

Case presentation

A 64-year old male, involved in a car accident while he was driving, was referred to the ED of the Academic Hospital of Parma (Italy) by the Emergency Medical Service. The car went out of the route and was found in a ditch. The man was diaphoretic, hypotensive (95/55 mmHg), bradycardic (54 bpm), not hypoxic (spO2 = 97% in ambient air) and slightly confused (Glasgow Coma Scale 14, being verbal response -1) at presentation. No signs of head, neck, chest, abdomen or limbs injuries were found at physical examination. A slight but clear weakness of the right arm, a less clear weakness of the right leg, and a bilateral severe myosis were present, however, rising the suspicion of a stroke as a cause of the car accident. The electrocardiography showed a sinus bradycardia (54 bpm) and a right bundle branch block. The lab tests were normal, except for leukocytosis (18 x 10^9/L), mild hyperglycemia (179 mg/dL), mild hyperazotemia (BUN 59 mg/dL, creatinine 1.7 mg/dL) and moderate hypokalemia (2.9 mmol/L). The clinical picture, with the exception of miosis, was thereby suggestive for a stroke, which was hence considered the main reason for the car accident. Nearly 30 min after patient's admission, while he was waiting for head CT-scan, the wife was also brought to the ED, since she was in the same car with the husband.

She reported that the husband had suffered a stroke 4 years earlier, with residual right hemiparesis. She also referred that the husband suffered from severe diaphoresis and confusion while driving, and that he drove intentionally the car into the ditch, after several attempts. Even more interestingly, she reported that the husband ate mushrooms, that she had personally collected, nearly two hours before taking the drive. The mushrooms were found close to a tree in the patient's garden, where they had already been collected for years without causing health problems. In the meanwhile, the patient presented several diarrheal discharges along with worsening of diaphoresis and appearance of bloody stools. The patient's wife was hence asked to bring the remaining mushroom to the ED and a mycologist was contextually alerted. Two mg of atropine in slow infusion, intravenous rehydration and potassium supplementation were administered in the suspicion of a cholinergic toxydrome, and a complete clinical remission was rapidly obtained. Upon mycologist arrival to the ED, the mushrooms were identified as a mixture of Armillaria Mellea (an edible mushroom, very common and very appreciated in Italy, where it is called "*chiodino*", meaning "little nail" or "little pin") and Inocybe Fastigiata (synonymous of Inocybe Rimosa) a toxic mushroom, easily confused with Armillaria spp. The patients was kept in observation, was administered oral rehydration, and was discharged upon complete clinical recovery and normalization of blood tests, after 36 hours.

Discussion

The cholinergic or muscarinic syndrome is one of the most frequent short-incubation toxydromes caused by mushrooms (3,4,5). In Europe, the species most frequently involved belong to the genera Inocybe and Clitocybe. The ingestion of mushrooms of these genera typically causes a sudden cholinergic syndrome caused by the toxin amine muscarine. Muscarine, L-(+)-muscarine, or muscarin, is a natural product found in certain mushrooms, particularly in Inocybe and Clitocybe species, but also in the genera Entoloma and Mycena. Muscarine has also been identified in harmless concentration in Boletus, Hygrocybe, Lactarius and Russula. Surprisingly, muscarine is only a trace compound (usually around 300 ppm) in the fly agaric Amanita Muscaria, whereas muscimol is the more relevant compound. Inocybe and Clitocybe contain muscarine concentrations up to 1.6% (6). Muscarine was first isolated from Amanita Muscaria by Oswald Schmiedeberg in 1869. It was hence the very first parasympathomimetic substance ever studied, and its discovery paved the way for further research on the biology of the parasympathetic system, as well as on the potential pharmacological applications of this intriguing molecule. Muscarine, a quaternary amine, is readily soluble in water and is less completely absorbed from the gastrointestinal tract than tertiary amines, although it may still permeate the brain barrier when present at high concentrations in blood (7). Muscarine avidly binds to muscarinic acetylcholine receptors, which are present in five different types

(i.e., M1 to M5). Most tissues express a mixture of these subtypes. The M2 and M3 mediate muscarinic responses at peripheral autonomic tissues, whereas M1 and M4 are more represented in brain and autonomic ganglia (8). Muscarine, as the vast majority of other agonists, does not exert a selective activity on the muscarinic receptor, while mimicking the function of the natural neurotransmitter acetylcholine in the muscarinic part of the cholinergic nervous system. Only a few studies exist on the metabolism of muscarine in humans. Although acetylcholine metabolism is strongly dependent upon the enzyme acetylcholinesterase, muscarine is not metabolized through this pathway, which partially explains its high toxicity. Renal filtration is thereby the most probable elimination mechanisms (9). Muscarine poisoning is typically characterized by miosis, blurred vision, increased salivation, excessive sweating, lacrimation, bronchial secretions, bronchoconstriction, bradycardia, abdominal cramping, increased gastric acid secretion, diarrhoea and polyuria. When muscarine crosses the blood-brain barrier and reaches the brain, it triggers tremor, convulsions and hypothermia. Cardiac ventricles, which are also enriched of muscarinic receptors, respond to muscarine with a fall in the strength of contractions, which causes a decreased cardiac output. After intravenous administration, muscarine can elicit acute circulatory failure and cardiac arrest (6). The symptoms of intoxication with muscarine-enriched mushrooms (i.e., especially Inocybe and Clitocybe), are highly suggestive and are synthetized by the acronym SLUD (i.e., Salivation and Sweating, Lacrimation, Urination, Defecation). The poisoning syndrome starts early - after 15 to 120 min from ingestion - with headache, nausea, vomiting, and pharynx constriction, which are then followed by salivation, lacrimation, and diaphoresis, associated with miosis, disturbed accommodation and reduced vision. Gastric and small bowel colic causes diarrhea, and a painful urge for urination may be frequently present. Bronchoconstriction can trigger asthmatic attacks and severe dyspnea, whereas bradycardia combined with marked hypotension and vasodilation can culminate in circulatory shock. In mild and moderate cases, spontaneous recovery usually occurs within 12 to 16 hours, but death after 8 to 9 hours has been reported in nearly 5% of untreated cases. The toxin is characterized by a lethal dose 50% (LD50) is not precisely known, ranging from 40 to 490 mg (i.e. approx 100-150 of muscarine - containing mushrooms) and is thermostable, and thereby mushrooms cooking does not produce significant inactivation (10,11).

The muscarinic syndrome is the only mushroom poisoning for which a specific and effective remedy is available so far. Atropine, an alkaloid that inhibits binding and displaces both acetylcholine and muscarine from its specific receptors, is the antidote used for this type of intoxication. Other muscarinic antagonists include scopolamine and pirenzepine. Atropine should be administered intravenously, at doses of 1-2 mg, titrated on the basis of the clinical response. The clinical recovery is usually rapid and complete.

Considering that muscarine only rarely crosses the blood-brain barrier, the present case report has some unusual features, namely the appearance of severe neurological symptoms. Several species of mushrooms, as is the case for Inocybe spp., also contain other and less characterized toxic substances. Toxins belonging to the isoxazolic group, in particolar ibotenic acid and its decarbossilated derivative muscimol may be present in Inocybe spp. These compunds, more typically involved in poisoning from Amanita Muscaria and Amanita Pantherina, acts through interaction with GABA-ergic receptors, thus causing a neurotoxic syndrome characterized by visual perception disturbances and true visual allucinations (3,10-12). A specific antidote for ibotenic acid/muscimol poisoning is currently lacking.

Mushroom poisoning represents a large and challenging area of medical toxicology, due to to the extreme biological heterogeneity of mushrooms, which frequently depends on geoclimatic and seasonal variables and leads to substantial differences in the concentration of toxins (13,14). A few syndromes are well characterized, and several forms are caused by a mixture of various toxins present simultaneously in the ingested mushrooms. It is estimated that nearly one hundred mushroom species are toxic for humans, 15 to 20% of which are potentially lethal. Nine syndrome have been classically defined, according to the toxin mainly involved (3,4,5):

- **Group I: cyclopeptides**, in particular amatoxins and

phalloidins, contained in Amanita Phalloides, A.Virosa, A.Verna, Galerina spp., Lepiota spp. High mortality: 50-60%.

- **Group II: gyromitrin**, the most toxic between the 9 hydrazones isolated from the mushroom Gyromitra Esculenta. Rarely lethal. Gyromitrin represents the only volatile mycotoxin, sometimes inhaled during cooking process.
- **Group III: muscarine**, previously discussed in this article.
- **Group IV: coprine**, a toxin capable to interact with ethanol, determining a disulfiram-like syndrome. Contained in the mushroom Coprinus Atramentarius.
- **Group V: ibotenic acid and muscimol**, previously discussed in this article.
- **Group VI: psylocin and psylocibin**, indolic, triptamin-like, toxins with hallucinogens LSD-like effects. Contained in variable amounts in several species belonging to genera Psilocybe, Panaeolus, Gymnophilus, Copelandia, Conocybe, Psathyrella.
- **Gruoup VII: gastroenteric toxins**, represented by a large family of substances, most of which still unidentified, contained in several species belonging to genera Boletus, Lactarius, Tricholoma, Entoloma, Russula. These toxins are often associated with other toxins of different groups. Many gastroenteric toxins are thermolabile and thus inactivated by cooking.
- **Group VIII: orelline and orellanine**, bipiridinic toxins that produce an irreversible injury to the kidneys (15). Contained in species Cortinarius Orellanus, C. Speciosissimus, C. Venenosus. Lethal if not treated, often requiring dyalisis or renal transplantation.
- **Group IX: involutin,** toxin causing a classic gastroenteritic syndrome followed by hemolytic anemia and acute kidney injury (16). Contained in species Paxillus Involutus.

This list is likely destined to enlarge in the forthcoming years. Only a few years ago, for example, a severe rhabdomyolysis caused by ingestion of the previously considered edible mushroom Tricholoma Equestre has been described (17).

Mushroom poisoning is still a major healthcare problem, since the general population is poorly informed, at least in part due to poor-quality literature data. In 1934 the French mycologist Josserand wrote an article titled "*Responsabilité de la Presse dans les empoisonnement par le champignons*" (Press responsability in mushroom poisoning)(18), which contained warnings about the misleading and dangerous information that is commonly available in the vast majority of publications on edibility of mushrooms.

In conclusion, the Emergency Physician is challenged by the need to distinguish trivial from severe mushroom poisonings when the history of a mushroom-based meal is obvious (13,14). Nevertheless, several cases may be attributable to mix-mushrooms-meals, either due to "gastronomic" reasons or to failure of recognizing the toxic species (as in the case described), and this represent a challenging issue. In our ED we benefit of an excellent collaboration with a group of on-call mycologists, who are able to rapidly identify the involved species, at least when some meal remnants, or gastric content, are available. It is also important to further emphasize the need of rapid access to valid scientific information, through enhanced availability of highly specialized and updated websites (19,20), reliable documents with clear pictures (21,22), and a good collaboration with specialized laboratories for dosing the most common and lethal toxins (23).

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