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Acute renal injury cause by confirmed *Psilocybe cubensis* mushroom ingestion

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ABSTRACT

Psilocybe mushrooms are consumed for their hallucinogenic properties. Fortunately, there are relatively few adverse effects associated with their consumption. This is the first reported case of acute kidney injury (AKI) secondary to confirmed ingestion of *Psilocybe cubensis* mushroom.

A 15-year-old male developed symptomatic AKI 36 h post-ingestion of *Psilocybe cubensis* mushrooms. He was admitted to hospital with hypertension, nausea and abdominal pain and a creatinine of 450 mmol/L. A sample of the crop of mushrooms was confirmed by mass spectrometry to contain psilocin. On day 5 post-admission, he was discharged home. Outpatient follow-up confirmed complete resolution of his renal function.

1. Introduction

Psilocybe mushrooms are often consumed for their hallucinogenic properties. Despite the apparent popularity of these mushrooms, relatively few adverse effects are have been reported from their use, with most being benign and self-limited [1]. Here, we report on a patient who developed symptomatic acute kidney injury (AKI) after ingesting *Psilocybe cubenesis* mushrooms.

2. Case

A 15-year-old male bought a “grow kit” for *Psilocybe cubensis* mushrooms from an online website. He germinated the spores into mushrooms and ate his “harvest” with three of his friends. All boys experienced hallucinatory effects, which resolved completely over a 6-h period.

36 h after ingestion, the patient developed nausea, abdominal discomfort and low back pain. He did not experience vomiting, diarrhea, or fevers. Initial bloodwork ordered by his primary care provider showed a creatinine of 207 micromoles/L.

After two days, the patient's symptoms persisted. Repeat bloodwork showed worsening of his renal function with a creatinine of 444 micromoles/L (reference range 65–121 micromoles/L) and a urea of 13.5 mmol/L (reference range 3.0–7.0 mmol/L). He was referred to a pediatric tertiary care hospital, where he was admitted with further evaluation by the nephrology team. On the day of admission (day zero) he was hypertensive with a blood pressure of 144/85. Admission bloodwork included a CBC, LFTs, electrolytes, calcium panel, blood cultures and a CK. All were within the normal ranges, with the exception of an elevated phosphate (1.98 mmol/L, reference range 0.90–1.50 mmol/L). Urine microscopy revealed 5–10 red blood cells per high power field (RBC/HPF), and no protein, leukocytes, or casts. A renal ultrasound showed normal-sized kidneys bilaterally and enhanced cortical echogenicity. Additional investigations included normal complement levels, negative antistreptolysin O titres, negative urine cultures and two sets of negative blood cultures.

Prior to definitive identification of the ingested mushrooms, the initial clinical presentation appeared consistent with possible ingestion of an orellanine-containing mushroom. During his hospital stay, he received supportive care with IV fluids, hydralazine for hypertension, and IV N-acetyl cysteine based on case reports of benefit for orellanine-induced renal injury. On day 5 post-admission, he was discharged home. Serum creatinine and phosphate levels were resolving at 108 micromoles/L and 1.68 mmol/L respectively. Having ruled out infectious and rheumatologic causes, the discharge diagnosis was presumed AKI from mushroom ingestion.

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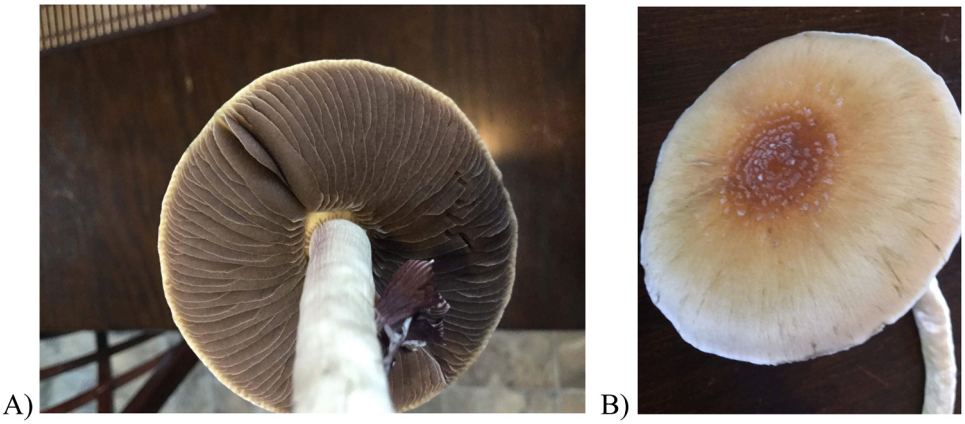

Fig. 1. Sample of crop of *Psilocybe cubensis* mushroom ingested by our patient.

At a 3-month follow up visit, the patient remained asymptomatic, with normal blood pressure and full recovery of his renal function. His creatinine was 80 micromoles/L, with a urea of 4.7 mmol/L, and normal electrolytes. Urinalysis was normal.

A sample of the crop of mushrooms yielding the ingested specimens (Fig. 1) was sent to a mycologist who identified the species as *Psilocybe cubensis* [2]. The identification of the mushroom sample was based on shared characteristics with published descriptions of the *Psilocybe cubensis* mushroom, including the overall stature of the basidome, the presence of a prominent annulus derived from a partial veil, a blue-staining reaction of tissues, coloring of the pileus and the stipe, the concentric arrangement of the scales, and the lamellae bearing purple-brown basidiospores with germ pores. A sample of the mushroom crop was further analyzed by mass spectrometry (LC-MS/MS). Briefly, 5–10 µL of extracted mushroom (in methanol) was injected and separated using a ToxTyper (Bruker) triple quadrupole liquid chromatography coupled to mass spectrometer (LC-MS/MS). The sample was analyzed in alternating polarity mode using the Toxtyper system equipped with an electrospray ionization source. Full scan MS, MS^2 and MS^3 spectra were acquired in data dependent MS/MS mode. The Toxtyper system identifies compounds based on retention time, MS, MS^2, and if necessary, MS^3 information. A peak was identified with a retention time of 2.5 min, corresponding to psilosin. No other peaks were identified, including for orellanine or amatoxin.

The three other boys who ingested the patient's 'crop' at the same time also presented to their physicians for evaluation on the advice of the medical team. They all remained asymptomatic and had normal renal function.

3. Discussion

Humans have been consuming hallucinogenic mushrooms for centuries [3]. The *Psilocybe cubensis* mushroom is one of the more commonly sought species by people using hallucinogenic mushrooms recreationally.

The hallucinogenic compound in *Psilocybe* mushrooms is the tryptamine molecule, psilocybin. Once ingested, psilocybin is dephosphorylated by the alkaline phosphatase enzyme to the active metabolite, psilocin [4,5]. Both psilocin and psilocybin resemble the chemical structure of the serotonin molecule, and, not surprisingly, have affinity for several serotonergic receptors, including 5-HT2A, 5HT2C, 5-HT1A, and 5-HT1D [4]. Agonism at the 5-HT2A receptor is believed to account for most of the hallucinatory properties of these molecules [1,5].

Signs and symptoms of *Psilocybe* mushroom ingestion include perceptual distortions (including visual hallucinations), euphoria, anxiety, agitation, mydriasis, tachycardia, hypertension and flushing. Symptoms occur within 20–60 min of ingestion and generally resolve within 4–6 h [6,7].

Ingestion of *Psilocybe* mushrooms is regarded as having a low potential for harm. The most commonly reported adverse effects are negative sensory experiences, where people present severely agitated, confused and anxious, with impaired concentration and judgment. The rare fatalities associated with *Psilocybe* ingestion seem related to co-ingestion with another drug (often alcohol) or trauma [8].

Nephrotoxicity has been described following ingestion of a number of mushrooms types, most commonly *Cortinarius* species, as well as some species of *Amanita*.

Mushrooms of the *Cortinarius* genus contain the toxin orellanine [9]. Reported cases of orellanine poisoning describe a delayed onset of renal injury (~3–20 days) after mushroom ingestion. Orellanine toxin has been demonstrated in in vitro studies to cause inhibition of protein, RNA and DNA synthesis, and has also been shown to produce an *ortho*-semiquinone radical that can lead to oxidative stress, suggesting that the observed renal injury occurs through direct toxicity to the renal tubular epithelium causing tubular necrosis, interstitial nephritis and fibrosis [10]. Case cohorts of exposures are reported, with a high proportion of patients developing irreversible renal failure requiring dialysis and even transplant [11,12].

An "Amanita nephrotoxic syndrome" is well recognized following exposure to *Amanita smithiana and A. proxima* [12]. Although the chemical structures of the toxins responsible have not been isolated, a toxin similar to *A. smithiana* has been identified in other *Amanita* species including *A. boudieri, A. gracilior and A. echinocephala*. These patients typically present with nausea and vomiting 2–12 h after mushroom ingestion. Renal injury develops after 2–6 days, associated with mild hepatitis. Renal biopsies in these cases demonstrate acute tubular necrosis and interstitial nephritis with recovery of renal function after supportive care and occasionally hemodialysis [12].

Other mushrooms such as *A. phalloides, A. virosa, and A. bisporigera* containing amatoxin produce a clinical picture that is distinct from other nephrotoxic mushroom ingestions with severe gastrointestinal symptoms (nausea, vomiting, diarrhea) developing 6–24 h post ingestion, followed by fulminant hepatotoxicity associated with AKI. The renal injury is presumed secondary hepatorenal syndrome or direct renal toxicity from amatoxin [13].

There are two case reports in the literature describing possible association of "magic mushroom" ingestion and renal injury. The first was of a 28-year-old man who presented with renal failure and required dialysis [11]. He had mistakenly eaten a *Cortinarius* mushroom, instead of a hallucinogenic mushroom. On renal biopsy, orellanine toxin was detected, confirming the exposure.

The second case was a 20-year-old woman who presented with symptomatic renal failure 5 days after ingesting what she believed to be "magic mushrooms" [14]. Her symptoms resolved with supportive treatment, and she did not require renal replacement therapies. Of note,

she denied experiencing the expected hallucinations or altered sensorium after ingesting the mushrooms. The authors suspected that this patient's renal failure was in fact due to consumption of a *Cortinarius* mushroom, however the identity of the mushroom she ate was never confirmed, and the patient was lost to follow-up.

Here, we report a case of a patient with evidence of AKI on day 2 post-ingestion of confirmed *Psilocybe cubensis* mushroom. Based on the temporal association of exposure to the mushrooms in the absence of any other possible cause, we have hypothesized that the AKI was related to *Psilocybe cubensis* ingestion. Although renal biopsy was not done, other features of his clinical presentation were consistent with acute tubular necrosis (ATN) including the sudden rise in creatinine, microscopic hematuria, and no leukocytes or casts in the urine. While the psilocybin and psilocin molecules are not known to cause ATN, in theory, their affinity for serotonergic receptors may have some vasoconstricting effects that could alter renal hemodynamics, a known risk factor for ATN [1].

We considered the possibility that the spores purchased on the internet were contaminated with another nephrotoxic substance; however, the other people who ingested the mushrooms from the same crop did not become ill, which would be expected if there were a toxic contaminant. Another possibility is that there may have been significant intra-batch variability, and that our patient was exposed to a greater amount of a yet-unidentified toxic contaminant or a greater amount of psilocybin leading to increased serotonergic activity. There may also be unidentified predisposing factors that contribute to the development of ATN following *Psilocybe* mushroom ingestion. For example, the case of the 20-year-old female who developed AKI after the ingestion of “magic mushrooms” shares similarities to our case. Unfortunately, the identity of that mushroom is not known.

This case identifies that there may be potential for reversible nephrotoxicity following exposure to *Psilocybe* mushrooms. With supportive care, the AKI in our patient resolved without sequelae.

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Conflict of interest

There are none.

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