Case report

Successful living related kidney transplantation for end-stage renal failure caused by orellanine syndrome

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A 43-year-old previously healthy man presented with a 10-day history of feeling unwell, nausea, vomiting, diarrhoea, myalgia and fever. He had not passed urine for 2 days. He was not taking any medications and denied taking recreational or ‘over the counter’ drugs.

On examination, he was dehydrated. Blood pressure was 150/90 mmHg. Systemic examination was otherwise normal. Initial blood/serum tests were as follows: creatinine 2650 μmol/l, urea 50 mmol/l, potassium 6.7 mmol/l, sodium 128 mmol/l, C-reactive protein 30 mg/l, normal liver function tests and haemoglobin 14.4 g/dl. Urine microscopy revealed haematuria and leukocyturia but no proteinuria or casts. Chest X-ray showed congested lung fields. Renal ultrasound showed echogenic but normal sized kidneys with no evidence of obstruction. Anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, extractable nuclear antibodies, anti-glomerular basement membrane antibodies and myeloma screen were negative. Kidney biopsy performed 3 days after admission showed normal glomeruli, severe interstitial nephritis with a predominantly lymphocytic infiltrate and moderate degree of tubular necrosis. Staining for immunoglobulins and complement was negative. Electron microscopy showed no glomerular deposits.

The patient was commenced on haemodialysis from the day of admission. As the aetiology of this patient’s acute kidney injury (AKI) was still unknown, history was revisited. He accepted eating raw wild mushrooms whilst on a backpacking trip in the mountains of north Wales in the UK, 4 days before onset of symptoms. He showed the medical team photographs of the mushrooms (Figure 1a and b) and presented dried uncooked samples of the mushrooms. He was unaware whether these mushrooms were poisonous. Based on the photographs and analysis of the samples, the mushroom was identified as Cortinarius rubellus (Cortinarius speciosissimus), which is known to contain a nephrotoxin (orellanine). The main reasons for this identification were the composition of cells of the cap skin and the ornamentation and shape of the spores. The diagnosis was now almost certainly orellanine syndrome from toxic mushroom poisoning.

To treat the interstitial nephritis, he was given methylprednisolone 500 mg intravenously for 3 days, followed by prednisolone 60 mg orally daily. This was tapered and stopped after 6 weeks as he continued to remain anuric and developed side effects of steroid therapy. As the renal function did not recover, he continued on dialysis for 20 months and then received a kidney transplant donated by his brother. Twelve months after transplantation, S. creatinine was 110 μmol/l with no significant proteinuria.

Discussion

Our patient presented with dialysis-requiring AKI which evolved into end-stage renal failure (ESRF) and was ultimately treated with kidney transplantation. The diagnosis was almost certainly toxicity by ingestion of the poisonous mushroom, C. rubellus Cooke. We made this diagnosis based on the...
To our knowledge, this is only one of three reported cases of renal transplantation in the UK undertaken to treat ESRF secondary to poisoning by *Cortinarius* mushrooms.\(^1\) Poisoning by *Cortinarius* is itself very rare with only five cases being reported from the British Isles.\(^1,2\) Worldwide, there have been 13 cases reported where renal transplantation has been performed for a similar indication.\(^1,3,4\)

There have been several case reports of AKI and ESRF resulting from *Cortinarius* mushroom poisoning, primarily from continental Europe.\(^3–7\) The clinical presentation includes a latent phase (which can vary from 12 h to 14 days; median 3 days), followed by a pre-renal phase with systemic symptoms which can include burning sensation in the mouth, polyuria and polydipsia, night sweats and paresthesiae and a renal phase with flank pain and oliguria.\(^8\) Some patients may become asymptomatic and the renal injury is only identified by biochemical tests. Approximately, 70% of all reported cases of *Cortinarius* poisoning had evidence of renal injury and several required dialysis. About half of those patients requiring dialysis did not recover kidney function.\(^8\)

The mushroom consumed by our patient, *C. rubellus* (*C. speciosissimus*), is an orange coloured mushroom found in the mountains of Europe and North America. It has been shown to contain a high content of orellanine.\(^9\) The other species known to contain this toxin and implicated in cases of AKI is *Cortinarius orellanus*.\(^9\) Orellanine is a tetrahydroxylated di-N-oxidized bipyridine. It is a tubular toxin and causes severe interstitial nephritis and tubular necrosis. *In vitro*, orellanine has been shown to be oxidized to an ortho-semiquinone radical, which depletes glutathione.\(^10\) In one animal study, orellanine caused a dose-dependent decrease in glomerular filtration rate and increased levels of free radicals and oxidative protein damage.\(^11\) In suspected cases where there are no mushroom samples available, orellanine can be detected in renal biopsy tissue using a thin-layer chromatography technique but this is not widely available.\(^12\)

There is no specific antidote to orellanine and, hence, treatment is mainly supportive. Haemodialysis, haemoperfusion and plasma exchange have all been used with the intention of removing the toxin from circulation but not with much success.\(^13,14\) The lack of efficacy of these techniques is probably because the toxin is highly concentrated in renal tissues quite early on and undetectable in plasma by the time renal failure develops.\(^12\) N-acetylcysteine has been used in association with corticosteroids and selenium in isolated cases with encouraging results when started early.\(^2,15\) Evidence for the efficacy of steroids on their own to improve kidney function is inconsistent.\(^6\) Orellanine can be detected in renal tissues even 6 months after the poisoning and it is released very slowly from renal cells.\(^16\) This raises concern regarding potential harm to a renal allograft from toxin released from native kidneys, but no actual harm has been shown to date.\(^3\)

In summary, we have presented a rare case of *Cortinarius* mushroom poisoning which led to ESRF. Renal transplantation was performed 20 months later with good outcome up to 12 months after transplantation. This case highlights the poor renal outcome after *Cortinarius* mushroom poisoning and, hence, the extreme care that needs to be taken whilst engaging in wild mushroom picking. The case also adds evidence to the suitability of renal transplantation for ESRF caused by orellanine syndrome. Last but not least, it demonstrates the importance of a thorough and systematic history in identifying the aetiology of AKI, to initiate appropriate management.

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References


