and include gyromitra, orellanus and phalloides syndrome.[1]

The orellanus syndrome is produced by several species from the genus *Cortinarius* that contains toxins, orellanines, with a marked renal tropism. After a long period without any symptoms (3-17 days), the patient presents with polyuria and severe renal failure, which is often irreversible.[2-4] We present a case of mushroom poisoning with signs of orrellanus syndrome.

We present the case of an 83-year-old male patient with history of arterial hypertension (AHT), dyslipidaemia and a haemorrhagic stroke in 2006. He underwent surgery for rectal neoplasia in 2000, and received chemotherapy and adjuvant radiotherapy. The patient came to the emergency department due to vomiting and liquid bowel movements, with no other symptoms. The only event that the patient referred was having eaten wild mushrooms that he had picked 4 days before. The biochemistry found: glucose: 130 mg/dl; urea: 240 mg/dl; creatinine: 4.62 mg/dl; glutamate-pyruvate transaminase (GPT): 3903IU/l; glutamate-oxaloacetate transaminase (GOT): 868IU/l; bilirubin: 0.80mg/dl; amylase: 86IU/l, CK: 86IU/l; sodium: 134mEq/l; potassium: 5.1mEq/l; ionic calcium: 1.12mmol/l; and lactate: 1.3mmol/l. The blood gases showed a pH of 7392 and HCO_3 of 15.1mEq/l. The haemogram showed thrombocytopenia with $69x10^3/\mu l$ of platelets; the rest of the haemogram and coagulation were normal. The abdominal ultrasound did not show any changes. Given that it was suspected that the patient had mushroom poisoning, he was admitted to the intensive care unit (ICU). Intensive fluid therapy was started, with sibilin and penicillin G. The patient was haemodynamically stable throughout his hospital stay, with good diuresis forced with mannitol during the first few hours, and then spontaneously. After 48 hours in the ICU he was transferred to the medical ward, where his hepatic function continued to improve, but he had polyuria and gradual deterioration of kidney function (reaching creatinine levels of 10.6mg/dl 13 days after admission). He was therefore indicated renal replacement therapy. Kidney biopsy was not performed given that he was considered a high-risk patient. Complementary examinations were also performed, with the following results: negative antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), anti-DNA and anti-glomerular basement membrane antibodies. The serology tests for hepatitis B virus (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV) were negative. The C3 and C4 proteinogram and Ig assessment were within normal limits. Basic urine test: normal. Microalbuminuria: $36\mu g$/min. Negative Bence-Jones proteinuria.

Although the orellanus toxin is not common in our area,[5] the clinical symptoms described for delayed polyuric renal failure after wild mushroom consumption, with interstitial failure data, match with orellanus syndrome.[2,4] The patient was indicated continuous treatment with regular haemodialysis every 48 hours. No improvement in renal function was observed in the long term.

In summary, when a patient presents with clinical symptoms of liver and kidney involvement, mushroom poisoning must be considered, including orellanus syndrome, especially in regional areas with a tradition of wild mushroom picking.[3]

1. Humayor Yáñez J, Rementería Radigales J. Intoxicación por setas. En: Manual de intoxicaciones en pediatría. Madrid: Ediciones Ergón, 2003;21:209-23.
2. Wörnle M, Matthias WA, Angstwurm MD, Sitter T. Treatment of intoxication with *Cortinarius speciosissimus* using an antioxidant therapy. Am J Kidney Dis 2004;43(4):E3-6.
3. Martínez J, Losada P, Morey A, Alarcón A, Munar MA, Marco J. Fracaso renal agudo secundario a intoxicación por setas. Nefrologia 1999;19(6):560-3.
4. Saviuc P, Garon D, Danel V, Richard JM. Cortinarius poisoning. Analysis of cases in the literature. Nephrologie 2001;22:167-73.
5. Soto Bermejo E, Piqueras Carrasco J, Elizalde Fernández J. Fracaso renal agudo tras ingestión de setas: síndrome orellánico. Nefrologia 2009;29(3):273.

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Hepatotoxicity following cyclophosphamide treatment in a patient with MPO-ANCA vasculitis

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To the Editor,

Cyclophosphamide is a synthetic alkylating agent used in chemotherapy and as an immunosuppressive agent. Among its adverse effects are infections, myelosuppression, haemorrhagic cystitis, hypersensitivity reactions, digestive/hepatic, pulmonary, cardiac and neurological toxicity, sterility and syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH).[1-3]

We describe a patient with abdominal pain and an increase in hepatic and pancreatic enzymes after cyclophosphamide administration.

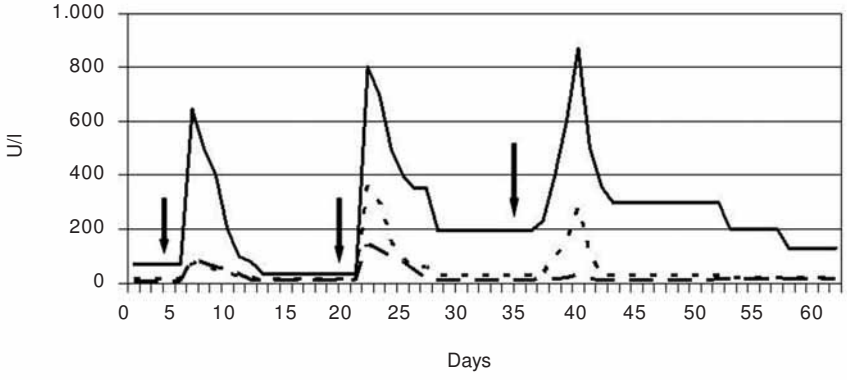
Male, 57-year-old patient, admitted for renal failure. Patient history: arthralgia and arthritis during the past 10 years,

deafness, frequent nosebleeds; pancreatitis due to cholelithiasis a month before. Physical examination: he did not have fever, blood pressure: 130/70mm Hg; lung crackles in both lungs, and remaining data were normal. The analysis showed: haemoglobin: 8.1g/dl: (13-17); creatinine: 6.44mg/dl (0.84-1.25); urea: 163mg/dl (17-43); albumin: 2.63g/dl (3.50-5.20); GOT: 5IU/l (10-39); GPT: 15IU/l (10-45); GGT: 71IU/l (10-55); alkaline phosphatase: 102IU/l (30-120); total bilirubin: 0.69mg/dl (0.3-1.2); amylase: 100IU/l (22-80); sediment: 60-100 red blood cells per field; proteinuria: 1.5g/24hr; negative urine culture. Negative c-ANCA, positive p-ANCA, negative PR3, MPO: 50.5(N<7IU/ml); negative anti-MBG antibodies, negative serology tests for hepatitis B, C and human immunodeficiency virus (HIV). Abdominal ultrasound: cholelithiasis, normal-size kidneys; pulmonary computerised tomography (CT) revealed bilateral nodes. The kidney biopsy showed focal and segmental necrotising glomerulonephritis with few deposits seen in the immunofluorescence. The patient was diagnosed with ANCA-positive vasculitis (microscopic polyangiitis/Wegener's granulomatosis).

He was treated with three 500-mg boli of methylprednisolone, continuing with 60mg of prednisone a day orally, haemodialysis and plasmapheresis. He also received omeprazole, calcium carbonate, sevelamer, furosemide and erythropoietin. The first cyclophosphamide bolus was administered (500mg) and 12 hours later the patient presented with sweating and diffuse abdominal pain, with no signs of peritoneal irritation. He presented with GOT: 90IU/l; GPT: 76IU/l; GGT: 645IU/l; alkaline phosphatase: 109IU/l; total bilirubin: 0.66mg/dl and amylase: 173IU/l. These parameters normalised in the following days. Fifteen days later the second cyclophosphamide bolus was prescribed (750mg), and 24 hours later the pain in the right hypochondrium reappeared. He presented with GOT: 144IU/l; GPT: 358IU/l; GGT: 802IU/l; alkaline phosphatase: 103IU/l; total bilirubin: 6.44mg/dl; amylase: 208IU/l; lipase: 378IU/l (21-67); which decreased in the following days. The magnetic resonance cholangiography showed cholelithiasis with no signs of complications, bile duct not dilated, free of choledocholithiasis. After 15 days he was administered 50mg/day of oral cyclophosphamide. After 4 days he presented with self-limited pain in the right hypochondrium. He had GOT: 27IU/l; GPT: 281IU/l; GGT: 871IU/l; alkaline phosphatase: 129IU/l; total bilirubin: 0.74mg/dl; amylase 97IU/l and lipase 154IU/l (Figure 1). Cyclophosphamide was withdrawn and treatment with mycophenolate mofetil was started at a dose of 500mg/8 hours. After a month, the patient was asymptomatic, normotensive, with spontaneous diuresis of 2l/day, Cr 2.59mg/dl; GPT: 9IU/l; GPT: 28IU/l; GGT: 155IU/l; alkaline phosphatase: 105IU/l; total bilirubin: 0.68mg/dl; normal amylase and lipase, weakly positive MPO-ANCA. The lung computerised tomography (CT) showed that the images had almost disappeared.

The effectiveness and toxicity of cyclophosphamide differs greatly from one patient to another, which has mainly been related to pharmacokinetic and pharmacogenetic mechanisms.[1,2,4,5] As such, Navin Pinto et al suggest that certain polymorphisms of enzymes metabolising cyclophosphamide (cytochrome P450, glutathione *S*-transferases and aldehyde-dehydrogenases) could be related to this variation.[3] A relationship has been found between high doses of cyclophosphamide and its toxic metabolites (acrolein and phosphoramide mustard) and hepatotoxicity.[2,4] Hepatotoxicity has also been related to high levels of other metabolites such as 4-hydroxycyclophosphamide[2] and *o*-carboxyethyl-phosphoramide mustard.[4] Furthermore, it has been shown that cyclophosphamide-induced adverse reactions could be due to cholinesterase inhibition.[6] Cyclophosphamide-induced hepatotoxicity is characterised by cytolysis and cholestasis, as occurred in this case. It may appear with oral or intravenous administration and seems to depend on the dosage. Three histological patterns have been described: massive hepatic necrosis, necrosis of perivenous hepatocytes and diffuse hepatocellular damage with mild steatosis.[1]

Patients with advanced renal failure can have high levels of amylase (up to three times the upper normal limit) and lipase (up to double). In this patient, after the second cyclophosphamide bolus, an increase in lipase, five times the normal level was observed, which may indicate pancreatic involvement. As far as we are aware, cyclophos-



— —: GOT; ••••: GPT; —: GGT; ↓: cyclophosphamide administration.

Figure 1. Evolution of GOT, GPT and GGT during cyclophosphamide treatment

phamide is not associated with pancreatitis, but iphosphamide, another nitrogen mustard, similar to cyclophosphamide is described to produce pancreatitis.[7]

ANCA vasculitis can affect the digestive system. Our patient's cholelithiasis was not complicated; biliary colic could cause analytical alterations similar to those that developed, but in the magnetic resonance cholangiography there were no signs of choledocholithiasis. In this case, there was a clear temporary relationship with cyclophosphamide, which supports the drug's role. According to Naranjo et al's[8] scale, hepatotoxicity and cyclophosphamide are likely to be related in this case.

This case shows that hepatic and pancreatic functions must be monitored during treatment.

1. Snyder LS, Heigh RI, Anderson ML. Cyclophosphamide-induced hepatotoxicity in a patient with Wegener's granulomatosis. Mayo Clin Proc 1993;68:1203-4.
2. Jonge ME, Huitema AD, Beijnen JH, Rodenhuis S. High exposures to bioactivated cyclophosphamide are related to the occurrence of veno-occlusive disease of the liver following high-dose chemotherapy. Br J Cancer 2006;94:1226-30.
3. Pinto N, Ludeman SM, Dolan ME. Drug focus: pharmacogenetic studies related to cyclophosphamide-based therapy. Pharmacogenomics 2009;10:1897-903.
4. McDonald GB, Slattery JT, Bouvier ME, Ren S, Batchelder AL, Kalhorn TF, et al. Cyclophosphamide metabolism, liver toxicity, and mortality following hematopoietic stem cell transplantation. Blood 2003;101:2043-8.
5. Akay H, Akay T, Secilmis S, Kocak Z, Donderici O. Hepatotoxicity after low-dose cyclophosphamide therapy. South Med J 2006;99:1399-400.
6. Imai H, Kodama T, Yasuda T, Nakamoto Y, Miura AB. Inverse relationship between serum cholinesterase activity and the administration of cyclophosphamide: an index of cyclophosphamide therapy. Nephrol Dial Transplant 1994;9:1240-9.
7. Garg R, Agarwala S, Bhatnagar V. Acute pancreatitis induced by ifosfamide therapy. J Pediatr Surg 2010;10:2071-3.
8. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981;2:239-45.

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Syndrome of inappropriate antidiuretic hormone hypersecretion associated with Guillain-Barré syndrome

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To the Editor,

Hydroelectrolytic disorders are frequently associated with severe neurological problems, being involved in their pathogenesis or being a consequence of it. Hyponatraemia is the most prevalent hydroelectrolytic disorder in clinical practice and is triggered by several causes. One of them is the syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH) which can also be triggered by several types of neurological diseases.

We present the case of a 63-year-old man who told us that he had fever and diarrhoea, which stopped spontaneously, for two weeks. Later, he started with paraesthesia in his hands and feet, alterations in mobility and instability when walking. He therefore came to the emergency department where his gait instability became worse and stopped him from being able to walk at all. He also presented with paresis in his four limbs and facial muscles. He is hypertensive but is not treated or monitored and drinks 20g of alcohol daily. The neurological examination showed: facial diplegia with hypophonia, absence of patellar and Achilles reflex and decreased biceps and triceps reflex with no loss of strength, absence of the vibration sensitivity and bilateral reduction in tactile and pain sensitivity with ataxic gait.

Complementary tests showed: 10 100 leukocytes with normal formula; haemoglobin: 16g/dl; creatinine: 0.6mg/dl; uric acid: 2.8mg/dl; sodium: 120mmol/l; potassium: 4.3mmol/l; chlorine: 87mmol/l; bicarbonate: 16mEq/l; total cholesterol: 232mg/dl, glucose: 110 mg/dl; and serum osmolarity: 259mOsm/kg. Sodium urine test: 144mmol/l and osmolarity in urine: 719mOsm/kg. Urinary sediment was within normal levels. The cranial tomography did not show any alterations. The cerebrospinal fluid test showed red blood cells: 1/μl; leukocytes: 1/μl; proteins: 141mg/dl; and glucose: 78mg/dl. Lastly, the electromyogram showed a diffuse peripheral and distal demyelinating neuropathy, mainly involving sensitivity. The clinical symptoms and results from the analyses and electromyogram suggested that the patient had Guillain-Barré syndrome (GBS) with SIADH.

Hyponatraemia is often associated with SIADH or salt wasting syndrome in patients with central nervous system disorders. These two conditions are the most important causes of non-iatrogenic hyponatraemia.[1] GBS is a neurological disease in which the immunological system attacks the pe-