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Kidney transplant patient with a decreased level of consciousness of unusual aetiology: A case report☆

Paciente trasplantado renal con disminución del nivel de conciencia de etiología poco frecuente: a propósito de un caso

Introduction

Hypophosphataemia is defined as a phosphorus level below 2.5 mg/dL.[1] Its incidence in hospitalised patients is high, especially in septic, malnourished, or alcoholic patients, in whom it is associated with higher morbidity and mortality rates. Clinical manifestations present with phosphorus levels below 1 mg/dL, although these manifestations are highly diverse and unspecific, which may delay diagnosis.[2]

Our patient is a 69-year-old man who had kidney failure following kidney transplant from a deceased donor, and transient episodes of loss of consciousness due to severe hypophosphataemia.

Clinical case

Our patient had a personal history of smoking, arterial hypertension, dyslipidaemia, ischaemic heart disease with percutaneous transluminal coronary angioplasty (PTCA) and stenting of the anterior descending artery, diagonal branch, and right coronary artery with subsequent restenosis and new PTCA-stent, stenosis, moderate aortic insufficiency, mild mitral regurgitation, mild-moderate tricuspid insufficiency, ischaemic dilated cardiomyopathy, atrial flutter, nephrectomy due to papillary kidney cancer, and chronic kidney disease stage 5-D secondary to ischaemic kidney disease treated with haemodialysis from February 2009 and kidney transplant from a deceased donor in March 2013. He also presented surgically treated colonic diverticulitis due to colonic perforation after colonoscopy, duodenal ulcus, avascular necrosis of the head and patella of the femur, brucellosis, and boutonneuse fever. He was receiving tacrolimus, mycophenolic acid, furosemide, prednisone, acenocoumarol, ramipril, lansoprazole, acetylsalicylic acid, eplerenone, allopurinol, metoprolol, solifenacin, and nitroglycerin.

The patient was admitted to the intensive care unit due to septic shock secondary to acute cholecystitis after undergoing open cholecystectomy. He was on a nil-by-mouth diet for several days. Clinical outcomes were positive and inotropes and steroids were progressively discontinued (they were prescribed at high doses due to suspicion of relative adrenal insufficiency: hydrocortisone at 100 mg/8 hours). However, the patient presented pronounced anorexia; recurrent episodes of diarrhoea due to antibiotic treatment, exacerbating kidney failure and secondary metabolic acidosis, which was treated with bicarbonate; and progressive malnutrition (Fig. 1). He was transferred to the general surgery department on day 21 after admission due to slow healing of the surgical wound, and continued treatment with antibiotics and underwent surgical debridement and daily curettage. Progressive malnutrition was treated with nutritional support consisting of a lipid, amino-acid, and glucose emulsion containing 24 mmol of phosphate (744 mg). Treatment also included insulin, which had to be discontinued due to increased diarrhoea. On day 38, the patient experienced a transient episode of low level of consciousness with disorientation and fluctuating disconnection,

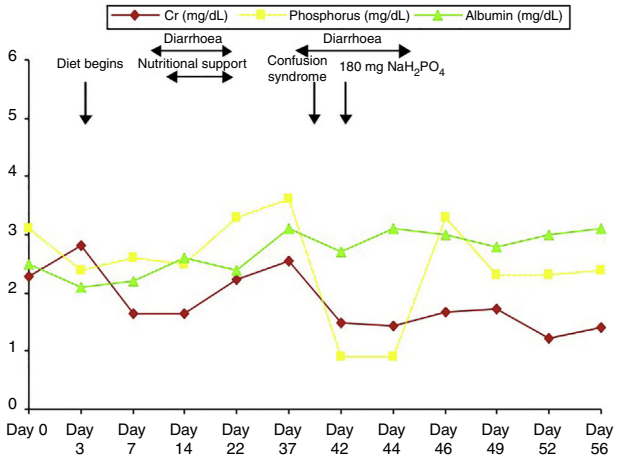

Figure 1 Changes in the patient's Cr (mg/dL), phosphorus (mg/dL), and albumin (g/dL) levels during admission, and the main clinical events causing hypophosphataemia.

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and did not respond to verbal or painful stimuli. Clinical symptoms recurred at 24 hours; given suspicion of benzodiazepine poisoning, 1/2 vial of flumazenil was administered and alprazolam was discontinued; this achieved no clinical improvement. On day 45, we were alerted to a new clinical event similar to the episode reported above. The physical examination revealed blood pressure of 110/80 mmHg, heart rate of 90 bpm, and oxygen saturation of 98%; the patient was dazed (Glasgow Coma Scale score of 9/15), disoriented in time and place, unable to follow simple instructions, and displayed echolalia. The results from an examination of the cranial nerves and reflexes were normal; the patient could move all 4 limbs, despite weakness and tremor in all 4. Assessment of sensory deficit was hindered by the patient's lack of cooperation. Laboratory blood testing revealed urea at 51 mg/dL, Cr 1.43 mg/dL, Ca 10.3 mg/dL, P 0.9 mg/dL, Na 136 mmol/L, K 3.6 mmol/L, Cl 99 mmol/L, with normal results for CK and CK-MB; venous blood gas analysis showed pH of 7.46, PCO_2 of 43 mmHg, and actual bicarbonate of 30.6 mmol/L. A brain CT scan showed no sign of ischaemia. Given suspicion of neurological impairment secondary to severe hypophosphataemia, we started treatment with 180 mg of monosodium phosphate every 8 hours, with progressive improvement of symptoms and disappearance of clinical manifestations (Fig. 1); the patient was discharged on day 56 after admission.

Discussion

Hypophosphataemia is defined by abnormally low serum or plasma phosphorus levels.[1] A serum concentration between 1 and 2.5 mg/dL is considered moderate hypophosphataemia, which typically does not lead to any clinical sign or symptom; however, severe hypophosphataemia, with a phosphorus level below 1 mg/dL, does cause symptoms.[2]

Moderate hypophosphataemia is observed in 5% of hospitalised patients, with severe hypophosphataemia being less frequent (0.1% to 0.2%).[1,2] Nevertheless, in certain risk groups such as alcoholic or septic patients, prevalence may reach 30% or even 80%, respectively. Its presence is associated with a higher rate of mortality in both hospitalised and dialysis patients.

Hypophosphataemia may be caused by 4 mechanisms[2,3]: *1)* redistribution of phosphorus from the extracellular to the intracellular space, *2)* a decrease in intestinal absorption, *3)* an increase in urinary excretion, and *4)* decreased phosphorus levels due to replacement therapy.

Clinical manifestations present with values below 1-1.5 mg/dL and in cases of chronic phosphorus depletion. The pathogenic basis of these manifestations is a decrease in levels of intraerythrocytic 2,3-bisphosphoglycerate (2,3-BPG) and intracellular ATP. Hypercalciuria and osteomalacia are frequent; patients may also present a decrease in cardiac output, which may cause congestive heart failure and respiratory failure due to muscle involvement. Proximal myopathy, and even rhabdomyolysis, are frequent in the skeletal muscle. At the nervous system level, the presence of metabolic encephalopathy has been associated with seizures and coma in patients with phosphorus levels below 0.5 mg/dL and haemolysis.[1,2] Treatment is not necessary for mild hypophosphataemia. In moderate cases, in addition to treating the cause, oral supplements should be administered. Intravenous administration should be used in severe, life-threatening cases of hypophosphataemia with respiratory failure, seizures, or coma, or in cases in which oral administration is not possible.[4] Depending on the remaining ion concentration, administration of monosodium or monopotassium phosphate may be started at a dose of 2.5-5 mg/kg body weight, depending on severity.[5] Prevention is the best treatment for hypophosphataemia. Patients with total parenteral nutrition should receive phosphorus at 1000 mg/day.

Cardiovascular disease is the leading cause of death after kidney transplantation. The current risk of mortality due to cardiovascular disease is 50 times higher in these patients than in the general population, due to the accumulation of vascular risk factors. Almost half of deaths of cardiovascular cause following transplants are due to cerebrovascular disease secondary to stroke, with cerebrovascular atheromatosis being more frequent in kidney transplant patients. However, symptoms suggesting cerebrovascular accident may be secondary to severe electrolyte imbalances, which should be considered when performing differential diagnosis.

Our patient was a kidney transplant recipient with many cardiovascular risk factors and normal baseline phosphorus levels, who presented severe hypophosphataemia secondary to progressive malnutrition caused by sepsis, diarrhoea, prolonged hospitalisation with limited food intake, and prescribed nutritional support with limited phosphorus intake. Furthermore, the patient was prescribed treatment with corticosteroids, bicarbonate, insulin, and diuretics, all of which can cause hypophosphataemia. Absence of phosphorus level determination in routine (almost daily) laboratory testing delayed both diagnosis and treatment.

In summary, despite the fact that kidney transplant patients present high cardiovascular morbidity and mortality rates, very frequently secondary to cerebrovascular disease, such electrolyte imbalances as severe hypophosphataemia may mimic cerebrovascular accidents, which should be considered in differential diagnosis. We should include phosphorus level determination in serial laboratory analyses of patients who are critical or undergoing long-term hospitalisation, in order to establish an early diagnosis and implement the appropriate nutritional preventive measures.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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Anti-NMDA receptor encephalitis in an elderly patient: A case report☆,☆☆

Encefalitis anti-NMDA en mujer anciana. A propósito de un caso

Dear Editor:

We present the case of a 74-year-old woman with no relevant history who visited the emergency department due to a 2-week history of progressive symptoms of behavioural alterations associated with asthenia and hyporexia. She was initially seen by psychiatrists and was diagnosed with depressive disorder, which was treated with desvenlafaxine at 50 mg/day. Two weeks later, symptoms intensified and she returned to the emergency department, where she was administered haloperidol intravenously; mechanical restraint was used due to psychomotor agitation.

The patient was admitted for examination and sedative medication was suspended; during the neurological examination, the patient presented stupor and could only utter incoherent phrases when strongly stimulated. No other significant alterations were observed.

A complete blood count, coagulation study, kidney and liver function studies, total protein test, thyroid hormone measurement, rheumatoid factor tests, antineuronal and anti-thyroid antibody studies, tumour markers, urine sediment, and serology test for HIV and syphilis all returned negative results.

The cerebrospinal fluid study showed no cellularity, with protein and glucose levels within normal ranges. A brain MRI scan (FLAIR) (Fig. 1) revealed a bilateral medial temporal hyperintensity, predominantly on the left side. Chest, abdomen, and pelvis CT (Fig. 2) showed a peripancreatic tumour, for which differential diagnosis between adenocarcinoma and lymphoma was considered due to its appearance.

Given suspicion of paraneoplastic limbic encephalitis,[1—3] we started treatment with immunoglobulins dosed at 0.4 g/kg/day.[4] A subsequent screening for onconeural antibodies in the cerebrospinal fluid yielded positive results for NMDA-receptor antibodies. The anatomical pathology study confirmed small-cell neuroendocrine carcinoma of the pancreas, with a proliferation index of 70%. Given the lack of response to the initial treatment, we decided to administer rituximab,[4] which improved the patient's level of consciousness and cognitive processing in the following weeks.

The tumour was localised (T3), did not invade adjacent organs, and was not associated with adenopathy. First-line treatment with carboplatin and etoposide achieved partial response after 6 cycles, with significant cognitive

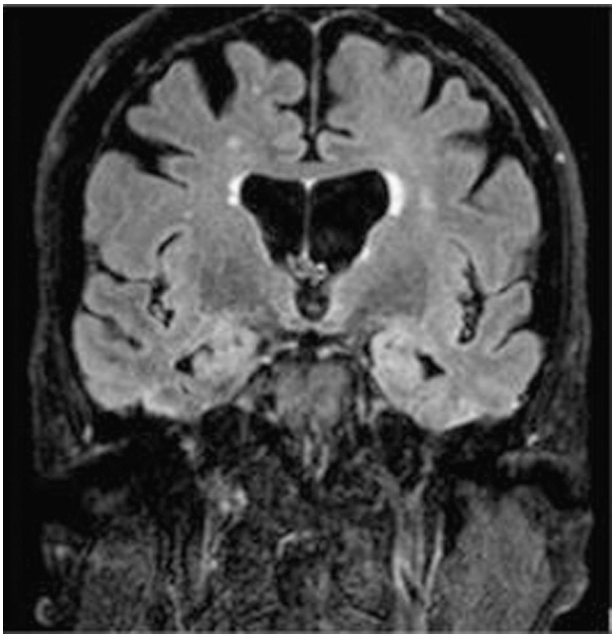

Figure 1 Brain MRI (FLAIR) scan: coronal section showing hyperintensity in both temporal lobes.

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☆☆ This study was presented in poster format at the 33rd Annual Meeting of the Valencian Society of Neurology.