Clinical Report

Necrotizing pancreatitis due to hypercalcemia in a hemodialysis patient with pica

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Abstract
Pica refers to the persistent, compulsive craving for and ingestion of nonfood items and certain food items. Pica is quite common among dialysis patients. The nutrient composition of some of the substances ingested may contribute to severe metabolic and mineral disturbances and other serious medical complications. We report the first case of a hemodialysis patient with chalk pica associated hypercalcemia who developed acute necrotizing pancreatitis. Hydration, nutritional support and hemodialysis treatments with low-calcium bath led to clinical improvement and correction of his calcium. This case illustrates the dangers of pica in dialysis patients and describes modalities of treatment and detection of this high risk behavior.

Keywords: hemodialysis; hypercalcemia; pancreatitis; pica

Background
Pica refers to the persistent, compulsive craving for and ingestion of nonfood items and certain food items. End-stage renal disease (ESRD) may constitute a potent stress and stimulus for pica, which is quite common among dialysis patients [1]. The nutrient composition of some of the substances ingested may contribute to severe metabolic disturbances, mineral imbalances, poisoning, excess fluid intake, anemia and other serious medical complications [2]. To the best of our knowledge, this is the first case report of a hemodialysis patient with chalk pica-associated hypercalcemia who developed acute necrotizing pancreatitis.

Case report
A 43-year-old man with a history of hypertension and ESRD of unknown etiology presented with acute onset of severe nausea, vomiting and abdominal pain of a 1-day duration. There was no history of abdominal trauma, alcohol abuse, hepatobiliary disease, hypertriglyceridemia or intake of medications known to cause pancreatitis. He had been on hemodialysis thrice weekly for 1 year.

On presentation, the patient was afebrile, blood pressure was 156/77 mmHg and pulse 105 b.p.m. He appeared awake and in distress due to the abdominal pain. The remainder of the physical examination was significant for diffuse abdominal tenderness with mild guarding. Laboratory evaluation showed a white blood count of 12 200/mm³ with 81% neutrophils. Serum creatinine, albumin and calcium were 107 μmol/L, 41 g/L and 3.87 mmol/L, respectively. Serum amylase and lipase were 428 and 1020 U/L, respectively. Liver transaminases, total bilirubin and serum triglycerides were in normal range. Pancreatic protocol contrast-enhanced computed tomography (CECT) with a radiographic contrast agent revealed necrotizing pancreatitis. The patient was admitted to the intensive care unit and managed with empiric antibiotics, intravenous fluids and nutritional support. Intact parathyroid hormone (iPTH) was <0.3 ng/L suggestive of primary hypercalcemia. On further inquiry about particular eating habits, the patient disclosed an almost daily consumption of pieces of chalk >2 years. He reported having developed a strong craving for pieces of chalk (composed mostly of calcium carbonate (CaCO₃) with minor amounts of silt and clay), and was eating up two full boxes every day (100–150 g of CaCO₃ daily). The patient had daily hemodialysis treatments with low-calcium bath (1.25 mmol/L). Over a period of the following 10 days, his clinical status improved and his calcium had normalized to 2.55 mmol/L. CECT with intravenous contrast agent showed improvement of pancreatic necrosis. At follow-up 4 weeks later the patient was asymptomatic and his serum calcium remained normal (2.5 mmol/L).

Discussion

Pancreatitis
Necrotizing pancreatitis is associated with high morbidity and mortality. Patients with ESRD appear to have a higher incidence and prevalence of acute and chronic pancreatitis than the general population [3, 4]. Post-mortem
examination of 78 patients with ESRD revealed pancreatic fibrosis, cystic changes and calcifications in 28% [5]. Suggested mechanisms of pancreatitis in renal failure included uremic toxicity to parenchyma; recurrent volume contraction during hemodialysis, resulting in decreased pancreatic flow [4], and increased secretion of trypsin. Such underlying pathology might also predispose patients with ESRD to pancreatitis when affected by agents that interfere with the pancreatic microcirculation.

**CaCO₃ induced hypercalcemia**

Severe hypercalcemia is another metabolic condition causing acute pancreatitis through trypsin-mediated mechanisms. Persistent or recurrent hypercalcemia can result in chronic pancreatitis. Common causes of hypercalcemia include primary hyperparathyroidism, malignancy (especially lung, breast and multiple myeloma), granulomatous diseases (tuberculosis, sarcoidosis), vitamin D toxicity, drugs (thiazides, lithium) and calcium supplements. The kidney plays an important role in normal calcium homeostasis. It regulates the excretion of calcium and phosphorus, and hydroxylates calcidiol (25(OH)D) by the enzyme 1α-hydroxylase to form calcitriol (1,25(OH)₂D₃), which is the active form of vitamin D, and this metabolite is responsible for the effects of vitamin D on calcium and phosphorus metabolism, bone health, and the regulation of parathyroid function. In chronic kidney disease (CKD), production of calcitriol and excretion of phosphate are reduced, leading to hypercalcemia and secondary hyperparathyroidism (HPT). Hypocalcemia used to be a condition most commonly seen in patients with CKD and ESRD, resulting from hypophosphatemia, low vitamin D levels and skeletal resistance to PTH. Today, hypercalcemia, previously less common, has become ever more frequent, mainly as a result of treatment strategies. The most frequent causes of elevated calcium in ESRD patients are the use of vitamin D analogues in an attempt to improve secondary hyperparathyroidism, and calcium-containing phosphate binders such as calcium carbonate or calcium acetate [6, 7]. Tertiary HPT with extremely high PTH levels and hypercalcemia may develop in patients with severe secondary HPT, especially those with severe hyperphosphatemia. Adynamic bone disease and using supraphysiological dialysate calcium concentration (>1.25 mmol/L) can result in hypercalcemia, especially when used in conjunction with vitamin D analogues and calcium-containing phosphate binders [8]. In the Dialysis Outcomes and Practice Patterns Study (DOPPS), increased risk of mortality was found for calcium levels >2.5 mmol/L, phosphorus levels >2.5 mmol/L and PTH levels >600 ng/L [9]. Presence was found for calcium levels >2.5 mmol/L, phosphorus levels >3.5 mmol/L and PTH levels >800 ng/L [10]. Hypercalcemia, elevated Ca × P product, and/or the use of calcium-containing phosphate binders in dialysis patients is associated with the increased risk of vascular calcifications [11]. Hypercalcemia may also be the consequence of calcium excess in the diet, usually dairy products, which may be resolved by dietary restriction of calcium. Patients with ESRD must follow a rigid and complex diet that restricts potassium, phosphorus, sodium and fluid; however, for a variety of reasons many patients find it difficult to do. Of the many types of dietary non-adherence, one in particular is of special concern yet has received relatively little attention in the literature: pica.

The term ‘pica’ is derived from the Latin for ‘magpie bird’, known for its fickle appetite and habit of eating anything [11]. Pica refers to the persistent, compulsive craving for and ingestion of food and nonfood items, including ice (pagophagia), laundry starch, clay, chalk or soil (geophagia), grass, leaves, paint chips, cigarettes, etc. [12]. Pica is most frequently observed in pregnant women, patients of lower socioeconomic status, children and in cases of iron deficiency anemia as well as in deficiencies of other nutrients, such as zinc. Pica is quite common among dialysis patients with reported prevalence ranging from 10 to 22% [1, 2]. ESRD may create a potent stress and stimulus for pica, especially in those patients with an underlying cultural predisposition [1]. Pagophagia is the most commonly reported type of pica behavior among dialysis patients [13]. Iron deficiency anemia, common in ESRD, along with fluid restrictions, make ice and freezer frost substances that dialysis patients may be especially likely to crave [13]. The existence of pica in dialysis patients is a serious concern. Geophagia can cause severe hypercalcemia, and pagophagia presents a problem for the fluid-restricted patient. Patients who reported eating dirt, starch and flour were found to be at greater risk for interdialytic weight gain [13]. Anemia, metabolic and mineral disturbances, poisoning, nutritional concern, excess fluid intake, bowel obstructions, parasite infections and dental injuries are all potential complications that arise as the result of dialysis patients engaging in this behavior [14]. The present case illustrates a hemodialysis patient with acute necrotizing pancreatitis triggered by severe hypercalcemia due to chalk pica (geophagia). Hence, it is clear that pica in dialysis patients presents unique and serious complications.

**Pica**

Pica treatment includes different modalities such as patient education, nutritional counseling and behavior management. Interventions need to be interdisciplinary, involving the physician, nursing staff, psychologist, social worker, dietitian, patient and family members [12]. Patient and family members need to be educated about the behavior and offered alternative behaviors and skills to help the patient reduce the high risk behavior. A formal pica questionnaire would be an important resource for dialysis centers to detect this problematic conduct among patients, especially those who have been identified as being at greater risk.

**Conflict of interest statement.** None declared.

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