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Hypercalcemia-Induced Pancreatitis in a 4-Year-Old

Authors:
Karl Eckberg, MD; Christian Hanna, MD; Rahul Kaila, MD; and Jonathan Strutt, MD
Department of Pediatrics, University of Minnesota Masonic Children's Hospital, Minneapolis, Minnesota

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A 4-year-old boy with a history of chronic kidney disease (CKD) presented to the pediatric emergency department (ED) with a 4-hour history of sudden onset of pain in his right lower quadrant, which was associated with anorexia and fatigue.

History. The patient had stage 5 CKD secondary to steroid-resistant nephrotic syndrome from focal segmental glomerulosclerosis. He had normal bowel and bladder movements and had no fever. His current medication list included daily cyclosporine, vitamin D, calcitriol, ranitidine, and calcium carbonate providing 1000 mg elemental calcium 3 times daily. His only recent change to medication dosing was his calcium supplementation, which 4 days prior had been increased from 500 mg elemental calcium 3 times daily for hyperphosphatemia (phosphate level, 8.4 mg/dL 1 week prior). His parathyroid hormone measured 1 week prior had been high at 144 pg/mL (reference range, 12-72 pg/mL). There had been no recent vitamin D level tests. There had been no recent exposures to steroids or nonsteroidal anti-inflammatory drugs.

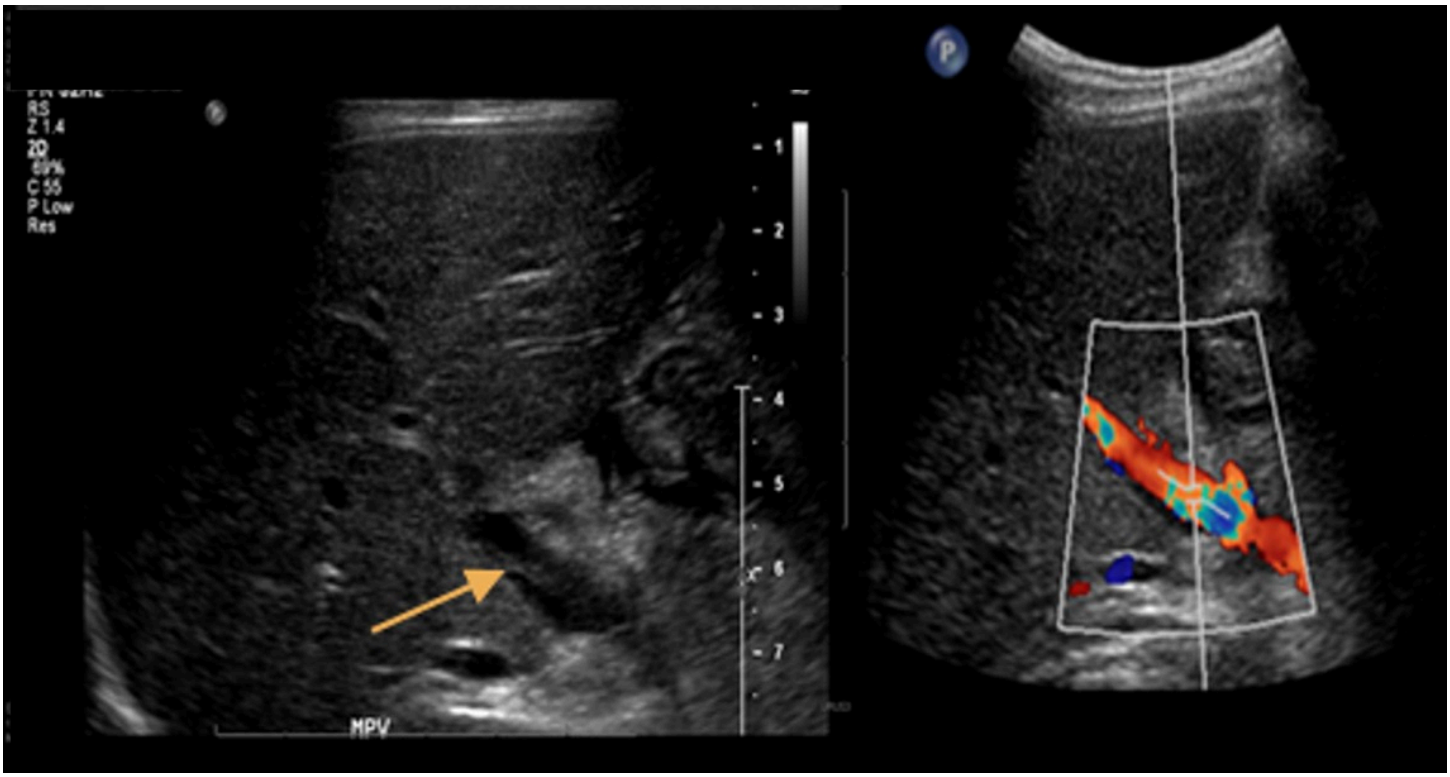
Physical examination. In the ED, the patient was sleepy but easily arousable. Vital signs included a temperature of 36.6°C, heart rate of 104 beats/min, blood pressure of 98/62 mm Hg, and respiratory rate of 26 breaths/min. Pertinent examination findings included slightly cracked lips with slightly dry mucous membranes, absence of his usual nephrotic syndrome edema, voluntary guarding upon palpation in all 4 quadrants, and brisk patellar reflexes, with otherwise normal complete examination findings.

Diagnostic tests. Initial workup was focused on a working differential diagnosis of appendicitis, urinary tract infection, renal stone, and spontaneous bacterial peritonitis (SBP). Initial blood tests revealed the following values (with reference ranges in parentheses): white blood cell count, 3080/μL (5500-15,500/μL) with an absolute neutrophil count of 2330/μL (800-7700/μL); albumin, 1.0 g/dL (3.4-5.0 g/dL); total calcium, 11.7 mg/dL (9.1-10.3 mg/dL); ionized calcium, 6.8 mg/dL (4.4-5.2 mg/dL); total carbon dioxide, 15 mEq/L (20-32 mEq/L); urea nitrogen, 76 mg/dL (9-22 mg/dL); creatinine, 4.96 mg/dL (0.15-0.53 mg/dL); total bilirubin, 0.2 mg/dL (0.2-1.3 mg/dL); albumin, 1.0 g/dL (3.4-5.0 g/dL); total protein, 5.6 g/dL (6.5-8.4 g/dL); alkaline phosphatase, 171 U/L (150-420 U/L); alanine aminotransferase, 15 U/L (0-50 U/L); aspartate aminotransferase, 41 U/L (0-50 U/L); lipase, 27875 U/L (0-194 U/L); amylase, 1767 U/L (30-110 U/L); and lactate, 4.1 mmol/L (0.7-2.1 mmol/L). The C-reactive protein level was less than 2.9 mg/L (reference value, <8.0 mg/L).

Abdominal ultrasonography findings were unremarkable including a normal pancreas, appendix, gallbladder, and liver, and no renal stones.

Empiric antibiotic administration for possible SBP and intravenous (IV) rehydration with albumin for clinically diagnosed dehydration were initiated in the ED. The patient had evidence of pancreatitis based on his elevated lipase and associated abdominal pain. An ED nurse noted that on the initial IV attempt, the patient's blood clotted immediately and looked like "thick snot." Due to the nursing report of blood clotting, D-dimer and coagulation studies were added to the second blood draw attempt. The D-dimer level was elevated at 17.0 μg/mL (reference value, <0.5 μg/mL), the international normalized ratio was 0.92 (reference range, 0.86-1.14), and the prothrombin time was 35 seconds (reference range, 22-37 seconds).

Another abdominal ultrasonography scan, now with duplex studies, was performed to assess for thrombosis, findings of which again showed a normal-appearing pancreas and gallbladder but also a newly discovered nonocclusive thrombosis along the wall of the main portal vein (**Figure**).



Discussion. The patient met the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition diagnostic criteria for acute pancreatitis (AP) with at least 2 of the following: abdominal pain compatible with AP, serum amylase and/or lipase values 3 times the upper limit of normal, and/or imaging findings consistent with AP.[1] Additional laboratory tests and imaging studies should be directed at possible etiologies for AP (eg, hypertriglyceridemia, hypercalcemia, gallstones/biliary disease, anatomic abnormalities) and to evaluate for complications (eg, pancreatic necrosis, fluid collections). The evaluation in this patient's case identified hypercalcemia as the likely cause of pancreatitis and thrombosis.

Hypercalcemia as an etiology of pancreatitis has been described in the literature, but most cases have been reported in the adult population.[2] It not only causes direct pancreatic injury but also leads to polyuria and resultant intravascular volume depletion, which in turn can lead to pancreatitis.[3] Treatment of hypercalcemia centers on increasing the urinary excretion of calcium, mostly through IV fluid administration, which has been shown to decrease mortality in patients with pancreatitis.[4] Although loop diuretics can increase urinary excretion of calcium, they should be used with caution, because they can cause excessive diuresis and dehydration.[5]

We identified one previous case of a 12-year-old with CKD and hypercalcemia-induced pancreatitis that was also associated with splenic vein thrombosis detected by computed tomography.[6] Vascular complications are noted in up to 15% of adult patients with pancreatitis, with the splenic and portal veins most commonly thrombosed.[7,8] Direct inflammatory processes exacerbated by underlying hypercoagulable states, such as nephrotic syndrome, and

intravascular volume depletion can lead to thrombosis.[6]

Our case demonstrates the importance of obtaining coagulation studies and vascular imaging in patients with hypercalcemia-induced pancreatitis due to the risk of thrombosis. Our patient appears to be the youngest patient reported to have develop pancreatitis related to hypercalcemia, which is exceedingly rare in the pediatric population. In addition, it is also unusual for pediatric patients to develop pancreatitis-related portal vein thrombosis, which in our case was diagnosed in part thanks to an astute ED nurse, who brought to our attention that the blood appeared to be “as thick as snot.” Based on our experience and one previously described case report, we recommend having a low threshold for obtaining a coagulation workup and vascular imaging to diagnosis an associated thrombosis in these patients.

Outcome of the case. Our patient successfully underwent anticoagulation for 2 weeks with resolution of his thrombosis seen on follow-up ultrasonography.

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