Editor:

Although more frequent among peritoneal dialysis (PD) recipients (1,2), acute pancreatitis (AP) is in general an infrequent inflammatory condition in the dialysis population. Diagnosis can be challenging in patients on PD in view of the broad differential diagnosis for a presentation of abdominal pain and the difficulties of biochemical testing in uremic patients secondary to impaired pancreatic enzyme clearance (3). Furthermore, use of the glucose polymer icodextrin interferes with the serum amylase assay, resulting in falsely low amylase levels (4,5). Here, we present a case of recurrent pancreatitis in a patient on PD using icodextrin.

CASE PRESENTATION

A 42-year-old African American woman with history of hypertension, type 2 diabetes, pulmonary hypertension, and end-stage renal disease presented with chief complaints of diffuse abdominal pain with associated nausea, intermittent vomiting, and decreased oral intake. Peritoneal dialysis had been started 7 months earlier, using a regimen consisting of continuous cycling PD (CCPD) alternating between 2.5% and 4.25% dextrose solution, plus a daytime long dwell using 7.5% icodextrin solution.

Laboratory data were significant only for an elevated serum lipase level of 2669 U/L. Abdominal imaging by computed tomography showed no sign of pancreatic or gastrointestinal (GI) tract abnormality, but was significant for diffuse vascular calcifications and an uncomplicated cholelithiasis.

The patient had no history of smoking, alcohol, or illicit drug abuse, and a review of her medical records revealed no history of hypercalcemia or hypertriglyceridemia. While an inpatient, she was maintained on her usual CCPD regimen, except for the daytime long dwell with 7.5% icodextrin, which was not administered because of formulary limitations. Her symptoms resolved rapidly, and the patient tolerated food intake well. She was discharged home without a change to her PD orders.

The patient was readmitted 1 week later with identical GI symptoms and a serum lipase level of 217 U/L. Although her symptoms resolved quickly during her inpatient stay (when she had no icodextrin exposure), she underwent preemptive cholecystectomy for cholelithiasis and was switched temporarily to hemodialysis. After 8 weeks of hemodialysis, she resumed CCPD, including daytime icodextrin.

Over the following 9-month period, the patient had multiple admissions with similar chief complaints of abdominal pain, nausea, and vomiting. After each

**Recurrent Acute Pancreatitis in a
Patient on Peritoneal Dialysis
Using 7.5% Icodextrin**

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admission, her GI symptoms would resolve rapidly with conservative measures, including cautious fluid resuscitations and elimination of icodextrin because of inpatient formulary limitations. Figure 1 shows the trend of her biochemical parameters, including lipase levels.

Evaluation of the patient's peritoneal fluid showed normal white blood cell counts with macrophage predominance, and all cultures remained negative. Diagnostic work-up for her symptoms, including computed tomography imaging, endoscopic retrograde cholangiopancreatography, and colonoscopy with mucosal biopsy, ruled out inflammatory or ischemic GI tract pathology. Magnetic resonance imaging of her abdomen without contrast showed a normal-sized pancreas with normal signal characteristics, but the presence of side-branch ectasia in the tail of the pancreas suggested mild chronic pancreatitis. Hence, we entertained the idea of icodextrin-induced pancreatitis. The patient was subsequently discharged home with elimination of icodextrin from her CCPD regimen. During further outpatient follow-up, she remained free of recurring symptoms of nausea, vomiting, and abdominal pain.

The clinical picture of AP in patients on PD resembles that of infectious peritonitis. The main risk factors for AP are mechanical obstruction (cholelithiasis), which can be toxic and chemically induced (by alcohol, for instance), or idiopathic. Patients on PD with AP are more likely to require hospitalization and to develop necrotizing pancreatitis (1). The reasons for that increased association are not clear, but it is possible that the composition of PD fluid, its tonicity, or the dialysis process itself is an unidentified factor that increases the risk for AP. Diffusion of dialysate through the peritoneum to the anterior surface of the pancreas could cause chemical irritation.

Figure 1 — (Left y axis) During admissions (white circles), serum lipase was significantly elevated (normal range: 10 – 60 U/L), associated with the preceding use of icodextrin peritoneal dialysis solution. During hospitalization, icodextrin was withheld, and at the time of discharge (white triangles), serum lipase had significantly declined. (Right y axis) During admissions, white blood cell (WBC) counts in peritoneal fluid were all less than 100/mm³, values not associated with peritonitis.

It is also possible that dialysate with a supraphysiologic concentration of ionized calcium could cause “local hypercalcemia” in the pancreas despite seemingly normal systemic calcium levels (2). Thus, in this special patient population, the diagnosis of otherwise unknown or “idiopathic” pancreatitis may represent the cumulative result of multiple coexisting noxious insults—that is, uremia, secondary hyperparathyroidism with hypercalcemia, hypertriglyceridemia, polypharmacy, drug abuse, or the dialysis process itself (including peritonitis).

Our patient had always used dialysate with 2.5 mEq/L calcium, and both her systemic calcium and her calcium × phosphorus product remained under excellent control. She had no episode of bacterial peritonitis diagnosed either by elevated white blood cell count in the PD effluent or by positive culture of effluent (Figure 1).

Icodextrin, first used in the late 1980s, is a relatively novel colloid osmotic agent, predominantly used for long daytime dwells in patients with low net ultrafiltration and high peritoneal transport properties. With an average molecular weight of about 17 000 Da, icodextrin shows very little diffusion across the peritoneal membrane. However, it is absorbed into the systemic circulation mainly via lymphatic transportation, reaching a steady state within 1 week of treatment initiation (6).

The general safety of icodextrin is well documented. Its major side effects, as described in the literature, are infrequent cutaneous allergic reactions (7) and metabolic derangements such as hyponatremia and decreased plasma amylase activity (6). Sporadic cases of abdominal pain and sterile peritonitis (8,9) have been described in the literature, but those episodes have been a result of manufacturing defects or microbial contamination (10).

In patients dialyzed with icodextrin, a 90% decline in measured serum amylase activity must be considered. In contrast, serum lipase is not altered (4), suggesting that lipase measurement is the biochemical method of choice for the diagnosis of pancreatitis in PD patients using icodextrin. Our patient showed a clear chronologic relationship between clinical presentation, elevated serum lipase, and preceding icodextrin exposure. The lack of major risk factors for AP, the negative imaging studies, and the rapid resolution of symptoms when this patient was effectively undergoing icodextrin withdrawal during her inpatient admissions made us consider the possibility of a chemically-induced pancreatitis and the potential for a causal link between AP and icodextrin use. Clinical uremia may have imitated some of her symptoms, but she remained free of symptoms after withdrawal of icodextrin despite unsatisfactory small-solute clearances (Kt/V urea 1.47 on PD after elimination of the icodextrin).

Our patient was subsequently switched to hemodialysis and has remained symptom-free. In the era of bundled payment for end-stage renal disease services and increasing use of home dialysis modalities, PD is expected to undergo a re-emergence in the United States. Chemically-induced pancreatitis should be considered in PD patients with recurrent unexplained pancreatitis, noncontributory imaging studies, and peritoneal fluid studies negative for infection.

The diagnosis of AP can be challenging in PD patients, particularly those using icodextrin. Although the safety and efficacy of icodextrin is well documented, clinicians should maintain vigilance about biocompatibility issues for this highly effective and useful glucose polymer.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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