CASE OF THE MONTH

Bishnu Devkota MD & Fereidoon Shafiei MD

A 40 year old African Amercian male, with a history of diabetes, presented to the emergency department with persistent diarrhea over the past few months. Soon after arrival, the patient developed respiratory failure, requiring mechanical ventilation. Labs at the time of presentation revealed severe hypokalemia (K 1.0), metabolic acidosis (HCO3 10), prerenal azotemia (BUN 150, Cr 11) and marked hypoalbuminemia (Alb 1.0). IV hydration and electrolyte supplementation were initiated, he was soon extubated and he had a relatively uneventful hospital course. A non-contrast CT of the abdomen was normal and a colonic biopsy showed only nonspecific, mild inflammation.

Two weeks after discharge, the patient presented with worsening diarrhea (up to 40 times per day) and severe weakness; he denied hematochezia or melena and had no abdominal pain. His past medical history was remarkable for diabetes mellitus, hypertension, a seizure disorder (thought to be related to alcohol use) and a long history of alcohol and tobacco abuse. Surgical history was limited to amputation of a toe due to gangrene. He admitted to noncompliance regarding his medications. Family history was also positive for hypertension and diabetes.

His admission exam revealed that he was alert and oriented to time, person and place. He was pale and his mucous membranes were dry. Orthostatic vitals revealed a BP of 132/97 and P 81 when supine, BP 87/45 and P 115 when standing. Chest was clear to auscultation. Abdomen was soft, non-tender and non-distended; bowel sounds were diffusely hyperactive. Skin turgor was decreased, generalized muscular weakness was noted but no neurologic deficits were found.

Admission labs revealed WBC 13,300 (with 63.5%N, 29.6%L, 1%Eos, 5%M), Hgb 7.8, Hct 22, and platelet count of 213,000. Chemistries returned Na 136, K 1.7, Cl 115, HCO3 14, BUN 12, Cr 2.4, Gluc 153, Ca 6.1, Alb 2.6, AST 65, ALT 34 and AlkPhos 168. His serum amylase and lipase were normal. EKG demonstrated T wave inversion and U waves, reflecting his severe hypokalemia. A CXR was normal and plain abdominal films were unremarkable.

IV hydration and electrolyte repletion were initiated. Based on the conviction that this patient may have chronic pancreatic insufficiency, he was started on pancreatic enzyme supplementation. His electrolye abnormalities and diarrhea soon resolved and he was doing well at the time of followup, 1 month later; he did report that his diarrhea would redevelop if he stopped taking the enzyme supplements for a few days. At a followup visit 2 years later, the patient has remained compliant with his medications and has had no further diarrhea.

Discussion: Pancreatic insufficiency usually causes severe protein and fat malabsorption; patients generally become symptomatic once 90% of the pancreatic exocrine function has been lost. One of the most common causes of pancreatic insufficiency is chronic pancreatitis, usually secondary to a long history of alcohol abuse.

Chronic pancreatitis is a syndrome that involves progressive inflammatory change in the pancreas, eventually resulting in permanent structural damage; this leads to impairment of endocrine and exocrine function. Patients with chronic pancreatitis often complain of epigastric pain (which may radiate to the back), weight loss and diarrhea; nausea and vomiting may also occur. Our patient, though plagued by severe diarrhea, did not experience abdominal pain; in one study, 20% of patients with chronic pancreatitis presented with endocrine or exocrine dysfunction in the absence of abdominal pain. Forty five percent of asymptomatic alcoholics have been found to have evidence of chronic pancreatitis on postmortem examination [1].

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The true prevalence of chronic pancreatitis is not known, although estimates range from .04 to 5 percent [2]. A long history of heavy alcohol consumption (at least 6-12 years) accounts for 60-70% of cases in developed countries [3]. Obstruction of the pancreatic duct can also lead to chronic pancreatitis; this is characterized by dilation of the pancreatic duct and exocrine insufficiency. Tropical pancreatitis, most often seen in Africa and Asia, appears in young persons and is characterized by pancreatic insufficiency, diabetes mellitus and recurrent abdominal pain; it is uncertain whether this condition is caused by protein malnutrition or by ingestion of toxic substances such as the cyanogens in cassava root [4]. Mutations in serine protease inhibitor SPINK1 have been identified as a cause in some patients [5-6]. Chronic pancreatitis can also occur in association with cystic fibrosis or hyperparathyroidism [3].

Autoimmune pancreatitis is most often seen in the Far East and is associated with other autoimmune disorders such as Sjogren's syndrome and SLE; these patients have autoantibodies such as ANA and increased gamma globulin in their blood and often have no or minimal symptoms [7]. Approximately 30-40% of patients with chronic pancreatitis have no apparent underlying cause and are thus classified as idiopathic chronic pancreatitis. Regardless of the cause, the pathogenesis of chronic pancreatitis, though poorly understood, has been attributed to an increased secretion of ductal protein without a compensatory increase in ductal bicarbonate; histologic examination may reveal patchy inflammatory changes within the exocrine pancreas.

Diagnostic Considerations. An accurate history and diagnostic evaluation is required to confirm the presence of chronic pancreatitis. Steatorrhea may be assessed qualitatively by looking for fat globules or by staining stool samples with Sudan red; quantitative results are obtained by fecal fat excretion (>20 grams per 24 hours). Dynamic testing, such as the secretin stimulation test and the bentiromide (chymex) test, and quantitative tests such as stool chymotrypsin are now infrequently used due to a significant improvement in imaging technology [8]. Diffuse, intraductal calcium deposition, pathognomonic of chronic pancreatitis, will be seen on plain abdominal radiographs in up to 30% of cases [9]. The diagnostic sensitivity and specificity of ultrasound is 60-70% and 80-90% respectively [10]. CT scanning has a higher sensitivity and is the imaging modality of choice to look for complications of chronic pancreatitis [11]. Endoscopic ultrasonography is becoming a popular tool for the diagnosis and ERCP remains the gold standard for confirming chronic pancreatitis secondary to ductal abnormalities [12].

When the diagnosis remains uncertain, other causes of chronic abdominal pain, such as peptic ulcer disease, gallstones, irritable bowel syndrome and endometriosis, should be considered. The possibility of pancreatic carcinoma must be kept in mind since it can mimic chronic pancreatitis and may develop against the background of pancreatitis, often delaying the diagnosis until late in the disease process [8].

Treatment Considerations. The treatment of chronic pancreatitis involves the elimination of its cause, symptomatic therapy and pancreatic enzyme supplementation. Cessation of alcohol is imperative; while this may or may not relieve pain, it does reduce mortality [2]. Dietary changes, especially the consumption of small meals with low fat content, often improves symptoms; pancreatic enzyme supplementation may also reduce pain in some patients [13]. Oral trypsin deactivates intrinsic cholecystokinin and thus decreases pancreatic stimulation of digestive peptides; this appears to be the mechanism by which they help to relieve pain [14]; however, this therapy remains controversial, has not been consistently supported in studies and is most likely to benefit women and those with mild disease. Steroid therapy has been shown to dramatically improve symptoms in patients with autoimmune pancreatitis [15].

Many anecdotal reports, including our own, have documented significant improvement in clinical symptoms with the use of pancreatic enzyme supplementation and either H2 blockers or proton pump inhibitors; pancreatic enzyme supplementation is devoid of major side effects although, very rarely, allergic reactions have been reported. Colonic stricture is a rare complication of pancreatic enzyme therapy in patients with cystic fibrosis [16].

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According to clinical trials, pancreatic enzyme supplements are most likely to relieve pain in patients with small duct disease [17]. Treatment with octreotide, a potent pancreatic enzyme secretion inhibitor, is not widely recommended. The use of antioxidants has shown some benefit but further studies are warranted. CCK receptor antagonists (MK329) and the treatment of pain with tricyclic antidepressants and gabapentin are other promising options [17]. Endoscopic ductal dilatation, in patients with mild pancreatitis, and endoscopic ultrasound or CT guided celiac plexus blockade are other modalities being used for the relief of chronic pain. Finally, surgery is reserved for the management of intractable pain.

Conclusion: The accurate diagnosis of chronic pancreatitis relies on a constellation of imaging and laboratory studies. When such studies are unavailable or contraindicated (e.g. the presence of acute renal failure), a therapeutic and diagnostic trial of pancreatic enzyme supplementation may be warranted; indeed, in our patient, this therapy completely controlled his symptoms and protected him from the potential complications of dehydration and electrolyte imbalance. When the clinical suspicion of chronic pancreatitis is high and the resources are limited, this intervention may prove to be an excellent strategy.

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