The patient was a 67-year-old white man with a history of coronary artery disease, metabolic syndrome, and benign prostatic hypertrophy who presented with asymptomatic hyperamylasemia but developed nonspecific abdominal symptoms during the course of the following year. Colonoscopy was consistent with Crohn's disease. The patient's Crohn's disease was treated medically, however, his amylase levels remained elevated. An endoscopic ultrasound showed changes consistent with chronic pancreatitis. Although not especially common from a symptomatic standpoint, a substantial number of patients with chronic pancreatitis exhibit asymptomatic involvement, either through elevated enzymes or abnormal imaging. A handful of reports document evidence of pancreatitis before diagnosis of Crohn's disease.

The patient was a 67-year-old white man with a history of coronary artery disease, metabolic syndrome, and benign prostatic hypertrophy who, upon routine laboratory testing, was found to have an elevated serum amylase level. At that time, the patient was completely asymptomatic with an unremarkable physical examination. Coincidentally, he also had an elevated gamma-glutamyltransferase level of approximately 4× normal (normal, 25–125 U/L) and a borderline elevated alanine aminotransferase. The elevated amylase level was of pancreatic origin, confirmed by the presence of elevated lipase, elevated trypsin, and amylase isoenzymes. A gallbladder ultrasound and abdominal computed tomography scan revealed no pancreatic abnormalities and no evidence of gallstones. The patient had been a lifelong social drinker but ceased alcohol consumption after the discovery of his elevated amylase. However, his amylase levels remained consistently elevated to 3× normal on repeat screening during the next year; his liver enzymes did return to within normal limits.

The following year, the patient developed episodic abdominal symptoms associated with malaise. These would begin with a vague headache followed by upper abdominal discomfort. He then would experience diaphoresis and abdominal cramping followed by diarrhea. Acute symptoms would last approximately 2 hours, but fatigue and weakness lasted for 2 to 3 days afterward. Episodes were accompanied by acute elevations of serum amylase to approximately 4× normal, but without leukocytosis.

The patient also experienced intermittent episodes of bright red blood in the stool. He underwent a colonoscopy with biopsy that showed histologic evidence of indeterminate inflammatory bowel disease (IBD), with a gross distribution consistent with Crohn's disease. The patient was treated with mesalamine, but continued to have episodic abdominal symptoms and elevated amylase levels. A magnetic resonance cholangiopancreatogram (MRCP) showed normal pancreatic and biliary ductal architecture. An endoscopic ultrasound (US) showed hyperechoic changes of the pancreatic head consistent with chronic pancreatitis (Figure).

It was concluded that the patient's elevated amylase levels were due to chronic pancreatitis as an extraintestinal manifestation of Crohn's disease. Common etiologies of chronic pancreatitis were ruled out; the patient was a social drinker with only mild to moderate occasional alcohol intake. Imaging repeatedly showed no evidence of gallstones or ductal obstruction. The patient had no evidence of autoimmune disease other than Crohn's disease. His medications with potentially associated side effects of pancreatitis had been stopped previously with no effect on amylase levels. Normal immunoglobulin G (IgG) levels on serum electrophoresis were not suggestive of primary autoimmune pancreatitis (though a test for the IgG4 subtype was not performed). The patient did not have electrolyte abnormalities and his lipids were within acceptable ranges.

Figure. Endoscopic Ultrasound

This endoscopic ultrasound image shows lobularity and hyperechoic strands in the head of the pancreas consistent with chronic pancreatitis of the pancreatic head.
DISCUSSION

Chronic pancreatitis is one of several known extraintestinal manifestations of Crohn's disease and ulcerative colitis. Other more common manifestations include primary sclerosing cholangitis, uveitis/iritis, sacroiliitis, pyoderma gangrenosum, and erythema nodosum. The incidence of chronic pancreatitis as a true extraintestinal manifestation has proved difficult to determine, as it is relatively rare (at least symptomatically) and several drugs used to treat IBD cause pancreatitis, including: 5-ASA, sulfasalazine, corticosteroids, azathioprine, and 6-mercaptopurine. Barther et al found a 1.2% incidence of chronic pancreatitis by following all cases of IBD reported at a handful of French hospitals in a 15-year span. Seyrig et al similarly found an incidence of 1.5%. These studies may in fact substantially underestimate the prevalence of pancreatic involvement in the IBD population, since they evaluate only symptomatic patients, and some evidence suggests that most pancreatic involvement in the setting of IBD may indeed be asymptomatic.  

The most intriguing aspect of this case is its temporal presentation. The patient presented with evidence of chronic pancreatitis (ie, chronically elevated serum amylase) months before the appearance of symptoms and prior to the diagnosis of Crohn's disease. Even though pancreatic imaging was not confirmed abnormal until after the diagnosis of IBD, the patient's chronically elevated amylase levels suggested that pancreatic involvement had existed prediagnosis. Extraintestinal manifestations of IBD generally present post-diagnosis, however, a handful of case reports in the literature describe chronic pancreatitis as the sentinel presentation of Crohn's disease and ulcerative colitis.  

This patient presented with asymptomatic hyperamylasemia and was diagnosed with chronic pancreatitis radiographically. It is questionable whether he was ever truly symptomatic from a pancreatic standpoint, given the atypical symptomatology consisting of brief episodes of vague abdominal discomfort. Apart from pancreatitis, these symptoms could be accounted for by other causes, such as active IBD. In any case, the patient was largely asymptomatic while concurrently hyperamylasemic. The presentation of asymptomatic pancreatic findings in the setting of IBD might be somewhat common. In a cross-sectional study of pancreatic enzymes in an unselected regional population of IBD patients, Heikus et al found the prevalence of hyperamylasemia and hyperlipasemia in the setting of Crohn's disease to be 17% and 9%, respectively. The findings for ulcerative colitis were 9% and 7%, respectively. However, only 3% of the entire IBD study population had ever been diagnosed with acute pancreatitis. Incidentally, 2 patients in the study were diagnosed with acute pancreatitis before the onset of IBD. Oishi et al found the prevalence of hyperamylasemia in patients with Crohn's disease to be 16%. All hyperamylasemic patients then underwent pancreatic imaging, mostly via transabdominal US, but some were further evaluated with endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT), and MRCP. The cumulative incidence of abnormal pancreatic imaging among the entire population was estimated to be 5.2% at 5 years and 6.3% at 10 years following diagnosis of Crohn's disease. Whereas there was no characteristic pattern of imaging abnormalities, 69% displayed intrapancreatic coarseness on US and 81% displayed "pancreatic deformity with irregular contour" on CT and US. A substantial number of patients displayed ductal abnormalities on ERCP and MRCP, as well.  

The mechanism of pancreatic involvement in IBD is unclear. It has been suggested that inflammatory involvement of the duodenal papilla in Crohn's disease may cause pancreatic obstruction and subsequent pancreatitis. However, Barther et al found only 1 case of periampullary involvement; Oishi et al found none. A minority of patients displayed histologic evidence of intrapancreatic granulomatous inflammation. In addition, Heikus et al found no correlation between use of medication and levels of pancreatic enzymes. Interestingly, pancreatic autoantibodies (PAB) have been found to be a specific marker for Crohn's disease, albeit present only in around 27% of patients. To our knowledge, there have been no studies conducted to evaluate a possible correlation between PAB and pancreatic enzyme levels. Thus, more work needs to be done to ascertain the mechanisms for pancreatic involvement.  

CONCLUSION

Pancreatic involvement is an important extraintestinal manifestation of Crohn's disease and ulcerative colitis. Though not especially common from a symptomatic standpoint, a substantial minority of patients exhibit asymptomatic involvement—either through elevated enzymes or abnormal imaging. It remains unclear how pancreatic involvement correlates with the long-term prognosis of IBD. In addition, more research is needed to ascertain the mechanism of injury. It is worth noting that in a handful of reports pancreatic involvement precedes diagnosis of IBD. Clinically, this knowledge might lower the threshold at which an IBD workup is pursued in the setting of hyperamylasemia (or symptomatic pancreatitis) without clear etiology.

References