

## A CASE OF ACUTE PANCREATITIS ASSOCIATED WITH CROHN'S DISEASE

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Pancreatitis related to Crohn's disease (CD) has rarely been reported.<sup>1</sup> In many cases, no etiological factors were found besides CD itself. This supports a direct association between CD and pancreatitis.<sup>2-5</sup> The present report describes a patient with CD who developed acute pancreatitis. Clinical and laboratory evaluation excluded other causes of acute pancreatitis, confirming a direct association of the latter with CD.

### Case Report

An 18-year-old Caucasian male was admitted to hospital due to epigastric and periumbilical pain with back irradiation, nausea and vomiting of three days' duration. Four months previously, the patient had experienced mucous/bloody diarrhea and a weight loss of 10 kg. On admission, colonoscopy had been performed and extensive CD involving the large bowel and the terminal ileum had been diagnosed, based on endoscopic and pathologic findings. The patient had been treated with 5-aminosalicylic acid (5-ASA) and prednisone for 1 month and initially did well. Medication with 5-ASA and prednisone had been discontinued.

Three months later, the patient reported epigastric and periumbilical pain radiating to the lower thoracic vertebral region, which worsened in the supine position, accompanied by nausea and vomiting of three days' duration. He also reported a relapse of diarrhea (4-5 episodes per day). The patient denied any history of gallbladder disease, alcoholism, abdominal trauma, familial pancreatitis or hypertriglyceridemia, and was on no medication at the time of admission. He had a 20-pack-per-year history of tobacco smoking. On clinical examination, his body mass index was 20.8 kg/m<sup>2</sup> (height 1.70 m and weight 60 kg) and his temperature was 37.8°C. Vital signs were normal. He was anicteric. The bowel sounds were

decreased in intensity and there was epigastric and periumbilical tenderness, but no rebound or guarding. Rectal examination was normal.

Routine laboratory values included a hematocrit of 36% and hemoglobin of 11.8 g/dL. White blood count was 10,300/mm<sup>3</sup> (72% neutrophils, 25% lymphocytes, and 3% monocytes), platelets were 538,000/mm<sup>3</sup> and the erythrocyte sedimentation rate was 58 mm/h. Coagulation studies were normal. Serum amylase was 390 U/L (normal, 0-90), while a simultaneous urine amylase was 2186 U/L (normal, 10-490). Serum lipase was 732 U/L (normal, 10-140). Other blood chemistry results, including calcium levels, liver function tests, cholesterol and triglycerides, were normal. Serum autoantibodies to the exocrine pancreas were negative and urinalysis was normal. Stool was negative for occult blood, pus, parasites and bacteria.

ECG was unrevealing, chest and abdominal x-rays were normal, and abdominal ultrasonography demonstrated a normal liver, spleen, gallbladder and biliary tree. No gallstones or sludge were visualized. The pancreas was also normal. CT scan of the abdomen and the pelvis, as well as abdominal magnetic nuclear resonance imaging, revealed wall thickening in segments of the jejunum and of the terminal ileum. All other abdominal organs, including the liver and the pancreas, were normal. Magnetic retrograde cholangiopancreatography (MRCP) demonstrated normal pancreatic and bile ducts, without signs of anatomic abnormalities.

Upper gastrointestinal endoscopy was performed, revealing erosive gastritis and inflammation of the duodenum without involvement of the ampulla (Figure 1A). Biopsies taken from the ampullary area were also normal. Duodenoscopy for examination of the periampullary area with a side-viewing duodenoscope demonstrated sites of duodenal inflammation. However, the ampulla was normal (Figure 1B). Prednisone and omeprazole were initiated and symptoms resolved. The pain started to resolve and finally disappeared within 3-4 days. The nausea and vomiting ceased in the same period. Diarrheal episodes decreased to 2-3 per day within 7 days. Pancreatic enzyme levels began declining and the patient was discharged. Serum lipase, serum and urine amylase gradually decreased to normal levels within the following 15 days. The patient has remained free of symptoms of acute pancreatitis and with

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FIGURE 1. Upper gastrointestinal endoscopy demonstrating sites of duodenal inflammation (A). Note that the ampulla is normal (side-viewing duodenoscope) (B).

normal pancreatic enzyme levels during a 6-month follow-up period. Repeat upper and lower gastrointestinal endoscopy confirmed remission of CD.

## Discussion

Pancreatitis associated with CD has rarely been reported.<sup>1</sup> In numerous cases, no etiological factors for the manifestation of acute or chronic pancreatitis were found besides CD itself.<sup>2-7</sup> These cases seem to support a direct association between CD and pancreatitis. However, pancreatitis (especially acute pancreatitis) is usually referred to as a complication of therapeutic agents used for the treatment of CD (such as azathioprine, 6-mercaptopurine, sulfasalazine or metronidazole), or is ascribed to co-existing biliary tract disease.<sup>2,3,7,8</sup> The incidence of this uncommon complication remains unknown, and reported frequencies vary between 1.2% -4% of patients with CD for acute pancreatitis and 1.2% -1.5% for chronic pancreatitis.<sup>6,7</sup> Interestingly, autopsy studies have shown pancreatic lesions (macroscopic or histological) in 38% of CD patients who had no clinical evidence of pancreatic disease.<sup>7</sup>

The pathogenesis of pancreatitis remains unexplained. The possibility of reflux of duodenal contents into the pancreatic ducts (due to ampullary or mucosal damage), as well as the presence of duodenal-pancreatic duct fistulas or flow obstruction (due to ampullary involvement) has been reasoned to account for the pancreatitis in cases with duodenal CD.<sup>3,5</sup> An immunologic basis, supported by increased titers of serum autoantibodies to the exocrine pancreas, has been suggested to explain the occurrence of pancreatitis in cases without duodenal involvement.<sup>3,5,7</sup> The rarity of pancreatitis occurring in this setting (absence of involvement of the ampulla while not on culprit medication) has led to speculations on the possible role of these autoantibodies in the pathogenesis of pancreatitis (as well as limitations of this role). According to these speculations, pancreatitis does not manifest as common as other extraintestinal complications of CD, due to the fact that the majority of the responsible autoantigens contact the immune system outside the pancreas.<sup>3</sup> Other possible causes of pancreatitis without ampullary involvement in CD include gallstones or sludge undetected by ultrasonography. However, these possible mechanisms are clearly speculative and lack firm supporting data.<sup>3</sup>

The reported patient presented with clinical and laboratory manifestations of acute pancreatitis (abdominal pain radiating to the lower thoracic vertebral region, nausea, emesis, leukocytosis and elevated amylase and lipase) four months after the initial presentation of an

extensive CD involving the large bowel, the terminal ileum, segments of the jejunum and the duodenum. However, the ampulla was macroscopically and histologically normal, and MRCP revealed normal pancreatic and bile ducts. On the other hand, in spite of the disagreement on their pathogenetic role in pancreatitis related to inflammatory bowel disease (IBD), the fact that autoantibodies to the exocrine pancreas were negative might permit one to speculate that another mechanism, perhaps other immunologic pathways not involving these autoantibodies, pancreatic effects of circulating inflammatory mediators or possible fistulas between the duodenum and the pancreas, as well as motility disorders, could be responsible for the presentation of pancreatitis in the reported case, as reported in other studies.<sup>3,5,6</sup> The presence of sites of duodenal inflammation might, therefore, have played a role in the pathogenesis of pancreatitis, despite the macroscopically and histologically normal appearance of the ampulla. The presentation of pancreatitis in a patient with extensive CD is in accordance with the observation made by Heikius et al.<sup>6</sup> that elevation of pancreatic enzymes (with or without clinical symptoms of pancreatitis) is associated with extensive endoscopic large bowel disease.

Other possible causes of acute pancreatitis were excluded, based on the patient's history and on clinical and laboratory evaluation which followed. Use of 5-ASA and prednisone was ruled out as being the cause, because administration of these agents had ceased months before the onset of symptoms. On the other hand, the role of drugs in inducing an elevation of pancreatic enzymes has recently been questioned.<sup>6</sup> Attribution of acute pancreatitis to presence of gallstones or sludge was ruled out due to failure of demonstration of the latter in all imaging procedures, in combination with the patient's negative history of lithiasis, as well as the fact that there was no recurrence of these symptoms over a long follow-up period. On the other hand, another interesting aspect in favor of attribution of acute pancreatitis to CD was the time association between the presentation of the latter and manifestation of the former, as well as the fact that symptoms and laboratory findings of acute pancreatitis gradually resolved after initiation of CD therapy and in concurrence with remission of CD. Heikius et al.<sup>6</sup> noted a trend in pancreatic enzyme levels to follow histological disease extent of IBD, which, however, failed to reach statistical significance.

The clinical significance of pancreatitis (or the asymptomatic elevation of pancreatic enzymes) as an indicator of pancreatic involvement in CD or as a premalignant state remains under speculation.<sup>2,6</sup> However, the fact that pancreatitis may mimic the manifestations of CD and be misinterpreted with an exacerbation of the latter, makes awareness of this uncommon complication mandatory in clinical practice.

In conclusion, pancreatitis is an uncommon complication of CD. Nevertheless, it should be considered in differential diagnoses of abdominal pain or other atypical clinical manifestations in patients with CD.

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