The Puzzling Association of Pancreatitis and Crohn’s Disease

I have seen pancreatitis associated with Crohn’s duodenitis and jejunitis which I have always assumed was by direct extension from the small bowel into the pancreas, but the case of a young girl with pancreatitis associated with Crohn’s disease at a distance from the pancreas was clinically puzzling and served to remind me that such an association, though rare, does occur.

Through the courtesy of my office colleague, Doctor Sam Meyers, I was privileged to see a 23-year-old Caucasian woman with a two-year history of Crohn’s disease, after she was admitted to The Mount Sinai Hospital in New York City. She had complained for eight weeks of epigastric and right lower quadrant abdominal pain, frequent loose bowel movements, fever of up to 104°F, nausea, vomiting, anorexia, and a ten-pound weight loss. There was no improvement despite two weeks of therapy with oral metronidazole and sulfamethoxazole-trimethoprim, which were both discontinued one week prior to hospital admission. She had recurrent perianal abscesses and fistulas during the two years of her illness but was well otherwise. There was no personal or family history of biliary tract disease and alcohol use was nil. There were no symptoms suggesting an intercurrent infection with infectious mononucleosis, hepatitis, mycoplasma pneumonia, intestinal parasites, or venereal disease. She had mumps as a child. Her last menstrual period was two weeks prior to the present hospitalization. There was no history of allergy or immunologic disease and no medication use other than the antibiotics noted. She had no history of familial pancreatitis or recent trauma.

Physically, she was thin and had a body temperature of 103°F. There were no skin abnormalities or evidence of jaundice. The abdomen was tender in the right lower quadrant and especially in the epigastrium. There were no abdominal masses, organomegaly, or evidence of ascites. Bowel sounds were normal and two draining perianal fistulas were present.

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Routine laboratory data were normal. Serum liver function tests, antinuclear antibodies, human chorionic gonadotropin (beta-subunit), antibody determinations for Coxsackie B, ECHO, and Epstein-Barr viruses, cold agglutinins, calcium, cholesterol, triglycerides, multiple blood and urine cultures, as well as stool examinations for bacteria and parasites were also normal. The serum amylase was 186 U/L (normal, 42–200 U/L) upon admission. The ileocolitis was treated with intravenous clindamycin, ampicillin, and gentamicin for ten days. At the completion of this therapeutic period she was improved symptomatically. Within 24 hours of discontinuing therapy, however, there was a severe exacerbation of nausea, vomiting, diarrhea, fever, epigastric and right lower quadrant abdominal pain, and the serum total amylase was found to be increased (1700 U/L). Reinstitution of antibiotic therapy resulted in partial improvement and a modest reduction of the serum amylase level. Amylase isoenzyme determination by electrophoresis and chromatography revealed the elevated levels to be comprised of pancreatic isoenzyme. The salivary component was normal with no macroamylase present. The urine analysis was 1794 (U/2h), while a simultaneous serum amylase was 319 U/L.

Concurrent with the clinical exacerbation, chest and abdominal x-rays were normal. A gallium scan showed increased uptake in the right lower quadrant of the abdomen and epigastrium. Sonogram and computed tomography, utilizing both oral and intravenous contrast, demonstrated a slightly enlarged but swollen pancreas, most marked in the tail. The liver, spleen, gallbladder, and biliary tree were normal. An upper gastrointestinal endoscopy showed only a small erosion in the duodenal bulb. The stomach and descending duodenum were normal. Barium contrast x-ray confirmed a normal upper small bowel and demonstrated no enteric or pancreatic fistula. Colonoscopy with biopsies showed multiple aphthous ulcers, consistent with mild Crohn’s disease, through the colon and rectum.

Lack of sufficient clinical improvement necessitated surgery on the 32nd hospital day. One foot of very severe Crohn’s disease was found in the terminal ileum. An ileocolic resection, and ileoascending colostomy was carried out. At surgery the pancreas was edematous and indurated without evidence of bacterial infection or abscess. There was some free ascitic fluid but no fat necrosis. The gallbladder and biliary tree were normal, as were the duodenum and upper small bowel. There was no direct extension of the Crohn’s disease into the pancreas. Pathologic examination of the resected specimen of terminal ileum and proximal colon confirmed transmural inflammation.

The postoperative recovery was uneventful. An abdominal sonogram two weeks after surgery showed the pancreas had returned to normal. However, mild epigastric tenderness and a slightly elevated serum and urine amylase could be detected for six months without further symptoms of either Crohn’s disease or pancreatitis. She has remained well with normal amylase determinations for the past two years of available follow-up.

So my colleagues could find no other reason for the pancreatitis except the Crohn’s disease and a few other similar cases had been reported. I had not noticed any similar cases in our review of 700 patients with Crohn’s disease or ulcerative colitis, and there were none in the patient material in the National Cooperative Crohn’s Disease Study and its reports of extraintestinal manifestations. So this association must be rare but probably is a true one. There is no known mechanism at present to account for this. However, high titers of serum auto-antibodies to the exocrine pancreas have been reported in many patients with Crohn’s disease by Stöcker, Otte, Ulrich, Norman, Stöcker and Jantschek in “Auto-antibodies against exocrine pancreas and against intestinal goblet cells in the diagnosis of Crohn’s disease and ulcerative colitis” (Deutsch Med Wochenschr, 1984, 109, 1963–1969).

The recent demonstration that the genetic alterations in family pancreatitis may occur occasionally in sporadic pancreatitis, raises the possibility that some genetic linkage is involved in these familial disorders. However, the finding of granulomas in some cases of rare acute or chronic pancreatitis should not lead to the diagnosis of isolated Crohn’s disease nor sarcoidosis as has been reported in the literature.

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