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Short Communication

Angiotensin-Converting Enzyme Inhibitor-Induced Pancreatitis

J. S. MUCHNICK, M.D., J. L. MEHTA, M.D., PH.D.

Division of Cardiology, University of Florida, College of Medicine and the VA Medical Center, Gainesville, Florida, USA

Summary: Approximately 2% of pancreatitis in adults is drug induced. Although some angiotensin-converting enzyme (ACE) inhibitors have been associated with pancreatitis, to the knowledge of the authors this is the first reported case involving benazepril. This case report presents laboratory- and image-proven pancreatitis in a noninsulin dependent 70-year-old man. The patient took benazepril at three different times and experienced the same epigastric symptoms 30 min after each dose. Possible mechanisms are reviewed. Clinicians should strongly consider discontinuing ACE inhibitors, including benazepril, in patients with pancreatitis of no identifiable source.

Introduction

Pancreatitis is a common cause of abdominal pain in American adults. More than 80% of cases are caused by alcohol or cholelithiasis.[1] The majority of the remaining cases are related to trauma, hypercalcemia, hypertriglyceridemia, infection, drugs, or are idiopathic. Some drugs cause reproducible pancreatic inflammation in animals and after patient rechallenge. Others, such as angiotensin-converting enzyme (ACE) inhibitors, are considered probable causes of pancreatitis.[2–7] The newer ACE inhibitors are not implicated in nearly as many cases of pancreatitis as are captopril and enalapril. The following is probably the first reported case of benazepril-induced pancreatitis.

Address for reprints:

J.L. Mehta, M.D., Ph.D.
Department of Medicine
University of Florida College of Medicine
1600 Archer Road
PO Box 100277 JHMHC
Gainesville, FL 32610, USA

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Case Report

A 70-year-old man with type II diabetes presented to the emergency department complaining of severe epigastric pain, nausea, and vomiting 30 min after taking 5 mg of benazepril. His primary physician had prescribed the drug for essential hypertension 1 week prior to presentation. Thirty min after taking the first dose, he experienced severe epigastric pain with cramping that lasted 6 to 8 h. On the next day he took a second dose and had the same response, only without improvement. His doctor discontinued benazepril by telephone and scheduled a follow-up appointment in 1 month. The patient had two episodes of vomiting and was unable to eat for 4 days. On the morning of presentation, he decided to take a third dose for an elevated home blood pressure measurement. The pain, which had subsided, acutely returned. The patient firmly denied alcohol use, confirmed by his spouse and by the absence of signs of alcohol use. The patient denied trauma, weight loss, or family history of pancreatic disease.

Significant physical findings included only sinus tachycardia and moderate epigastric tenderness. He had no fever or jaundice. Serum amylase was 234 U/l and serum lipase was 755 U/l. Abdominal ultrasound showed a single, mobile gallstone without sludge or gallbladder wall thickening. The common bile duct was of normal caliber and the pancreas was obscured by bowel gas. Abdominal computed tomography showed a mildly edematous, inflamed pancreas and confirmed the single nonobstructing gallstone. Biliary and hepatic enzymes were normal. Serum calcium was 9.3 mg/dl, triglycerides were 106 mg/dl, glucose was 271 mg/dl, and the white blood cell count was 15.3 K/cm^3 with 80% neutrophils. The remainder of the admission panel was normal.

The patient was placed on bowel rest and given meperidine for pain. His pain improved over 1 week and he began to tolerate food. His discharge amylase and lipase were 50 and 189 U/l, respectively, and his white blood count returned to normal. His blood pressure was controlled with a beta blocker, and he has been asymptomatic for 2 months after discharge.

Discussion

Drugs are a relatively uncommon cause of acute pancreatitis in adults. While definite associations exist for some com-

monly used drugs such as valproate, estrogen, didanosine, calcium, and aminosalicylates, ACE inhibitors have only a likely association. Most case reports of ACE inhibitor-induced pancreatitis involve enalapril, captopril, and lisinopril.[1–5] Ours may be the first documented case of benazepril-induced pancreatitis, the mechanism of which is unclear in humans. The prevailing hypothesis applies a proven ACE inhibitor side effect, angioedema, to the pancreatic duct. The bradykinin-mediated edema causes ductal obstruction. This theory explains the acute onset of symptoms common to most case reports. Other possible mechanisms include a direct toxic effect on pancreatic cells and antibody induction.[2,8]

In an attempt to define the mechanism of ACE inhibitor-induced pancreatitis, Niebergall-Roth *et al.*[9] administered 5 mg of enalapril to conscious dogs and measured secretin and caerulein-stimulated pancreatic bicarbonate and protein secretion. The hormonally stimulated bicarbonate secretion was increased 3–4 fold with enalapril administration. These investigators suggested that enalapril is capable of enhancing pancreatic secretion and this phenomenon may be causally related to the genesis of pancreatitis.

We thought it unethical to readminister benazepril to this patient because of the risk of fulminant pancreatitis.[10] Our patient clearly developed pancreatitis that was related to benazepril ingestion on three separate occasions. He had no history or signs of alcohol use and we felt that the presence of gallstones was an incidental finding. Computed tomography scan and laboratory data failed to reveal expected findings of common or pancreatic duct obstruction. Sludge that cannot be seen by current imaging techniques is well known to cause pancreatitis. We considered this to be even less likely than gallstones because of the abrupt onset of pain after ingestion of benazepril. We also excluded other causes of pancreatitis such as hypercalcemia, hypertriglyceridemia, carcinoma, infection, and trauma. Some clinicians are aware of older ACE inhibitors causing pancreatitis; we believe this report clearly adds benazepril to the list.

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