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Medication as a Cause of Acute Pancreatitis

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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Conflict of interest: None declared

Patient: Male, 74
Final Diagnosis: Acute pancreatitis
Symptoms: Epigastric pain radiating to the back
Medication: Furosemide
Clinical Procedure: —
Specialty: Gastroenterology and Hepatology

Objective: Challenging differential diagnosis

Background: Acute pancreatitis is an inflammatory condition of the pancreas characterized clinically by epigastric abdominal pain and elevated levels of pancreatic enzymes in the blood. Drug-induced pancreatitis has recently gained more attention and as a result, physicians are screening more frequently for medications as a cause of acute pancreatitis.

Case Report: We report the case of a 74-year-old man with a significant past medical history for coronary artery disease, sleep apnea, and gastroesophageal reflux disease who presented with epigastric pain radiating to the back. After a careful history was taken, it was found the patient recently started furosemide; therefore, a diagnosis of furosemide-induced acute pancreatitis was made.

Conclusions: Furosemide and other medications should be strongly considered in the differential diagnosis of patients presenting with acute pancreatitis.

MeSH Keywords: Abnormalities, Drug-Induced • Furosemide • Pancreatitis

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Background

Acute pancreatitis is an inflammatory condition of the pancreas characterized clinically by epigastric abdominal pain and elevated levels of pancreatic enzymes in the blood. In developed countries, obstruction of the common bile duct by stones (38%) and alcohol abuse (36%) are the most frequent causes of acute pancreatitis [1,2]. When they are not identified as the source, practitioners must remember to take a detailed medication history. Drug-induced pancreatitis has recently gained more attention and as a result, physicians are screening more frequently for medications as a cause of acute pancreatitis. We describe the case of a patient with a significant past medical history of coronary artery disease, sleep apnea, and gastroesophageal reflux disease, who developed acute pancreatitis after recently starting furosemide.

Case Report

A 74-year-old man with a significant past medical history for coronary artery disease, sleep apnea, and gastroesophageal reflux disease presented with epigastric pain radiating to the back. Upon admission, the pain was described as 7-out-of-10 in severity, with no relieving or exacerbating factors. The onset of pain began the morning of admission. The patient attempted to relieve the pain by going for a mile-and-half walk with his wife. The pain persisted and that prompted the patient to visit the Emergency Department. The patient was slightly nauseated with no emesis. The patient denied any palpitations, shortness of breath, constipation, diarrhea, or recent weight changes. He is a lifetime non-smoker and non-alcoholic drinker. When questioned about recent changes in medications, furosemide had been added approximately 6 weeks prior for bilateral lower-extremity swelling. The patient has never been diagnosed with congestive heart failure. Vital signs upon admission 158/80 mm Hg, heart rate of 64 beats per minute, respiratory rate 18 breaths per minute, and afebrile. Inspection of the abdomen showed no Grey Turner or Cullen sign. On auscultation, normoactive bowel sounds were present. Abdominal palpation revealed epigastric tenderness. A complete metabolic panel revealed glucose of 104 mg/dL, triglyceride level 80 mg/dL. Renal function (BUN/Cr) was within normal limits. Liver chemistry was within normal limits. Serum amylase (1022 U/L) and lipase levels (>600 U/L) were both elevated. Ultrasound showed satisfactory appearance of the liver, gallbladder, distal common bile duct, spleen, and kidneys. The pancreas was suboptimally visualized due to overlying intestinal gas. A chest x-ray with 2 views showed no acute process. We proceeded with treatment of IV fluid hydration and keeping the patient nil per os for 24 h. This case had a positive outcome with the patient regressing in symptoms 24 h after treatment and withdrawal of furosemide.

Discussion

Our patient presented with symptoms of acute pancreatitis after adding furosemide 6 weeks prior for bilateral lower-extremity swelling. The Naranjo adverse drug reaction probability scale of 5 suggests a probable medication source of his acute pancreatitis [3]. No other medication changes were present within the last few years, narrowing our differential to furosemide-induced pancreatitis. Although acid-suppressing drugs (H₂-antagonists or proton-pump inhibitors) and gastroesophageal reflux disease are risk factors for acute pancreatitis [4], we felt that the addition of a new drug (furosemide) was more likely the cause of the acute pancreatitis versus a medication that the patient had been taking consistently for many years.

We ruled out the 2 most common causes of acute pancreatitis – alcohol and gallstones – through the patient's history as a lifetime non-alcoholic drinker and ultrasound findings showing no gallstones. Our patient presented with a triglyceride level of 80 mg/dL, ruling out triglyceride as a source. According to the ACG, if triglycerides are greater than 1000 mg/dl, then it should be considered the etiology in the absence of gallstones or alcoholism [5]. In accordance with the ACG guidelines in the Management of Acute Pancreatitis, a contrast-enhanced computed tomographic and/or magnetic resonance imaging of the pancreas was not ordered because the diagnosis of acute pancreatitis was made based on the patient's clinical presentation and clinical improvement [5]. However, because these imaging modalities were not ordered, a non-functional PNET cannot be completely ruled out. The diagnosis of a nonfunctional PNET was much lower on our list of differentials because of the absence of symptoms such as jaundice, and unintentional weight loss. The diagnosis of autoimmune pancreatitis (AIP) also cannot be ruled out, but we did not order IgG4. In the absence of painless jaundice, along with lack of involvement of salivary gland and lungs, this was a diagnosis that was lower on our list of differentials.

Gallstones and chronic alcohol abuse induce the majority (>90%) of acute pancreatitis. The true incidence is unknown since there are few population-based studies available [6]. The majority of information we have on drug-induced pancreatitis is extrapolated from case reports such as this one. Idiopathic acute pancreatitis accounts for up to 20% of cases and the argument can be made that some drug-induced cases are unfortunately misclassified as idiopathic. Drug-induced pancreatitis is rare, with an estimated incidence rate of 0.1–2% [7]. In a retrospective Medline search to assess clinical outcomes of positive drug rechallenge following possible drug-induced pancreatitis, 250 cases of drug-induced pancreatitis were identified [7]. Of these, we analyzed and reviewed 183 cases with a positive rechallenge. The total number of furosemide cases was 3, which accounts for 1.6% of the total number of analyzed cases.

Furosemide-induced pancreatitis has been suggested to induce acute pancreatitis by impairing pancreatic perfusion [8] by a decrease in extracellular fluid volume [9]. The susceptibility of ischemia due to vessel atherosclerosis was increased in our patient because of the past medical history of coronary artery disease. Other proposed mechanisms are pancreatic exocrine stimulation by furosemide, hypersensitivity from an immunologic response, or a direct toxic effect to the pancreas [9].

Latency of furosemide-induced acute pancreatitis ranges from several hours up to 7 weeks [10]. Latency was categorized by Chao et al. as short (<24 h), intermediate (1 day to 1 month), and long (>1 month) term. Dosage plays a role in proposed mechanisms of furosemide-induced acute pancreatitis divided into low-dosage and high-dosage [10]. Our patient falls into the category of long-term latency (6 weeks) and low-dosage (40 mg). The proposed mechanism of acute pancreatitis suggested by Jones and Oelbaum [11] and Juang et al. [12] propose these cases are best explained by hypersensitivity reactions.

Definite proof for drug-induced pancreatitis causality is defined by the WHO classification if symptoms recur upon rechallenge. In the actual algorithm, the diagnosis is confirmed if no other cause of acute pancreatitis can be detected, and the patient is taking one of the suspected drugs [13]. Rechallenge is the only definitive way to prove drug-induced pancreatitis, but this would harm our patient if it were the cause of the pancreatitis. We chose to not rechallenge furosemide. Practitioners need to realize the importance of considering medications and taking a detailed medication history in evaluation of patients presenting with acute pancreatitis.

Conclusions

Furosemide and other medications should be strongly considered in the differential diagnosis of patients presenting with acute pancreatitis.

Conflict of interest

None.

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