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Case Report

Frusemide-induced acute pancreatitis: Report of a rare case

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ABSTRACT

This paper reported a rare case of frusemide-induced acute pancreatitis in a 65-year-old female who presented to the emergency department with severe epigastric pain and vomiting for two days. Her medical history included type 2 diabetes mellitus and liver cirrhosis caused by hepatitis C virus infection, for which she was taking insulin and spironolactone. Ten days prior, she was prescribed frusemide for poorly controlled ascites. She had no history of alcoholism or gallbladder disease. However, two years ago, the patient developed acute pancreatitis. Upon reviewing her medical record, we found that her first acute pancreatitis episode occurred after she had been prescribed frusemide 40 mg daily for ascites control six days before the pancreatitis episode. Serum amylase was 1022 IU/L, and lipase was 3122 IU/L, while abdominal ultrasonography showed a contracted gallbladder without lithiasis and a normal biliary tree and liver. The patient was diagnosed with frusemide-induced acute pancreatitis. She received conservative management with analgesia, hydration, and fasting. Abdominal paracentesis was performed with an albumin replacement. In the following days, the patient remained stable and afebrile, and her symptoms improved. Consequently, she was discharged with strict instructions to avoid frusemide in the future.

1. Introduction

Alcohol and biliary tract stones are the leading causes of acute pancreatitis, accounting for approximately 60%–80% of all cases.[1] Other causes include autoimmune diseases, metabolic disorders, infections, drugs, toxins, and others.[2] Drugs are responsible for 0.1%–2% of acute pancreatitis incidents.[3] Some drugs are considered a cause of acute pancreatitis based on various evidence, including rechallenge, while other drugs are considered to cause acute pancreatitis only based on a few published case reports in which researchers found no obvious cause of acute pancreatitis.[4] This report presents a case of frusemide-induced pancreatitis proven by rechallenge. We describe the context in which the diagnosis was made and the treatment plan. Additionally, we review the literature to identify similar cases and enhance the awareness of physicians of this adverse reaction.

2. Case Presentation

A 65-year-old female presented to the emergency department with a two-day history of severe epigastric pain associated with nausea and vomiting. Her medical history included type 2 diabetes mellitus and liver cirrhosis caused by hepatitis C virus infection, for which she was taking insulin, spironolactone, and more recently, frusemide. She admitted that at her last appointment 10 days earlier, her attending physician had added frusemide tablets at 40 mg per day to control her ascites, which was

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inadequately controlled with spironolactone alone. She had no history of alcoholism or gallbladder disease. However, two years ago, the patient developed acute pancreatitis. Her first acute pancreatitis episode occurred after she had been prescribed frusemide 40 mg daily for ascites control six days before the pancreatitis episode. During the first pancreatitis episode, the patient was admitted, and ascites was controlled by abdominal paracentesis and an albumin replacement, while only spironolactone was continued upon discharge.

Upon examination, the patient appeared ill but was conscious and oriented. She was tachypneic, with a heart rate of 102/min, blood pressure of 110/70 mmHg, and a body temperature of 36.2°C. Her abdominal examination showed a distended abdomen with positive shifting dullness, but there was no lower limb edema. The rest of her examination was unremarkable.

Her white cell count was 4×10^9/L; hemoglobin was 8.2 g/dL; amylase was 1022 IU/L; lipase was 3122 IU/L; lactate dehydrogenase was 999 IU/L; aspartate aminotransferase (AST) was 135 IU/L, alanine transaminase (ALT) was 118 IU/L; and alkaline phosphatase was 333 IU/L. Her serum albumin was 2.2 g/dL, her corrected calcium was 2.33 mmol/L with a normal INR, and her lipid profile was normal. Her abdominal ultrasound demonstrated a contracted gallbladder without lithiasis and a normal bile duct. Abdominal computed tomography with contrast revealed an edematous pancreas and peripancreatic stranding consistent with acute pancreatitis without fluid collection or necrosis, in addition to moderate ascitic fluid.

Based on her medical history and abdominal CT, which ruled out gallbladder disease, the patient was diagnosed with frusemide-induced acute pancreatitis, so we discontinued frusemide. The patient received conservative management with analgesia, hydration, and fasting. Abdominal paracentesis was performed with an albumin replacement. In the following days, the patient remained stable and afebrile, and her symptoms improved. Consequently, she was discharged with strict instructions to avoid frusemide in the future.

3. Discussion

Loop diuretics such as frusemide and bumetanide are widely used to treat hypertension and edema secondary to congestive heart failure, liver cirrhosis, or chronic kidney disease. However, they can cause various side effects, including hypokalemia, hypocalcemia, hypomagnesemia, hyperuricemia, hypernatremia, dehydration, and ototoxicity. Additional side effects include dizziness, headaches, and gastrointestinal discomfort. Acute pancreatitis is a serious but rare side effect associated with loop diuretics. A review of the literature indicated a few reports[5–9] describing acute pancreatitis as a side effect of frusemide. The scarcity of cases may be attributed to the difficulty of many physicians implicating the drug as a cause of pancreatitis.

Diagnosing frusemide-induced acute pancreatitis is often difficult to establish. Badalov et al. modified the previous classification system for drug-associated pancreatitis into five categories: Ia, Ib, II, III, and IV.[6] Classifications are based on the number of case reports, available rechallenge data, consistent latency period, and the ability to exclude other causes of acute pancreatitis. Class Ia includes drugs with at least one case report, evidence of a positive rechallenge, and the exclusion of other causes of acute pancreatitis. Class Ib is similar to class Ia, but in this class, other causes of acute pancreatitis could not be ruled out. Criteria for class II drugs encompass at least four case reports with a consistent latency period for at least 75% of the cases. Class III drugs have at least two case reports but do not have rechallenge data or a consistent latency period. Finally, class IV drugs have one case report without rechallenge data. Our case is classified as Class Ia because more than two previous cases[5–9] have been reported and a positive rechallenge evidenced by the occurrence of acute pancreatitis after ingestion of frusemide tablets with recovery of symptoms after stopping the drug on two occasions. We excluded the most common causes of acute pancreatitis such as alcoholism and gallstones from the medical history and by abdominal ultrasound and contrast-enhanced abdominal computed tomography. However, we have not performed all studies to exclude other causes of acute pancreatitis, such as performing endoscopic ultrasound (EUS) and screening for viruses associated with acute pancreatitis, mainly mumps and of Coxsackie, as there was no obvious indication based on data derived from the history and/or physical examination.

The mechanism by which frusemide-induced acute pancreatitis occurs is not well understood, however, various mechanisms have been postulated. First, frusemide may damage pancreatic perfusion by decreasing intravascular volume, affecting blood flow, producing ischemia, and subsequently developing acute pancreatitis[10] Second, it may stimulate the exocrine pancreas, producing a hypersensitivity reaction[5] Third, an immunologic response against a drug-protein adduct.[9]

4. Conclusion

Acute pancreatitis is a rare complication of frusemide treatment that should not go unrecognized. Therefore, we intend to alert physicians who prescribe frusemide to monitor for acute pancreatitis symptoms and discontinue the medication as soon as pancreatitis is suspected.

4.1. Consent

Written informed consent was obtained from the patient for publication of this case report.

4.2. Authors' contribution

All authors contributed to the completion of this work. The final manuscript was read and approved by all authors.

5. Source of Funding

None.

6. Conflict of Interest

None.

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