Lansoprazole induced pancreatitis

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Abstract

Drug-induced pancreatitis is a rare and sometimes fatal cause of pancreatitis which is often difficult to diagnose. Acid suppressing medications include histamine-2 receptor antagonists and proton pump inhibitors have been linked to acute pancreatitis in several case-reports and recent systematic reviews. However, only one case of lansoprazole induced pancreatitis has been described in literature until date. A 67-year-old female presented with complaints of abdominal pain, nausea, vomiting and worsening generalized weakness for the past 1 week. She had recently been started on lansoprazole therapy for gastroesophageal reflux with no other change in medications. She denied any trauma, recent viral infection, alcohol intake, over-the-counter or herbal medication use. On presentation, she had abdominal distension with tenderness and epigastric guarding. Laboratory investigations were significant for leukocytosis and elevated amylase and lipase with normal triglyceride levels. Computed tomography of the abdomen and pelvis with contrast revealed features of acute interstitial pancreatitis with retroperitoneal lymphadenopathy and no other abnormality. She was diagnosed to have acute pancreatitis secondary to lansoprazole therapy and was managed conservatively. Her symptoms resolved after 3 days of discontinuation of the drug. There have been several cases reporting a potential link between acute pancreatitis and acid suppressing medications. However, drug-induced pancreatitis still remains a diagnosis of exclusion as it is difficult to establish causality. Almost all the acid suppressing medications have been linked to pancreatitis, but a case associated with lansoprazole has only been described once. Further studies are needed to establish causation.

Keywords: drug induced pancreatitis; lansoprazole; lansoprazole induced pancreatitis; adverse drug reaction; interstitial pancreatitis.

Introduction

Acute pancreatitis is an inflammatory condition of the pancreas characterized by abdominal pain and elevated levels of pancreatic enzymes in the blood, along with impairment of the underlying microcirculatory system. It is caused by various factors, including alcohol, gallstones, viral infections, autoimmune causes, hypertriglyceridemia, and drugs.[1][2] In the

United States, more than 300,000 cases are reported annually, leading to hospitalization and significant healthcare costs.[3] The prevalence of drug-induced pancreatitis remains uncertain as most cases have been documented only in isolated reports. The overall incidence is estimated to range between 0.1% and 2% of all cases of pancreatitis and can sometimes be life-threatening.[4]

Among medications, acid-suppressing drugs such as histamine-2 receptor antagonists and proton pump inhibitors are commonly used for managing peptic ulcer disease and reflux esophagitis. These medications have potential adverse effects on various systems including the central nervous system, renal system, hematological system, and cardiovascular system.[5] Case reports have linked cimetidine and ranitidine to acute pancreatitis.[6][7] While a retrospective cohort study in 2000 did not find a significant increased risk of acute pancreatitis with the use of acid-suppressing drugs[8], recent systematic reviews have identified cimetidine and ranitidine (class Ia), omeprazole (class Ib), and pantoprazole (class Ic) as potential culprits based on the modified Badalov classification.[9][10] The Badalov classification system initially consisted of five classes (Ia, Ib, II, III, and IV), and the modified classification added a class Ic. This classification system categorizes drug-induced pancreatitis cases based on the number of published cases, re-challenge information, and latency period.[11]

Class Ia includes drugs that have been clearly implicated in causing pancreatitis, supported by numerous published cases and positive re-challenge tests. Class Ib and Ic encompass drugs with fewer published cases, limited re-challenge data, or conflicting evidence regarding their association with pancreatitis, with or without ruling out other causative factors. Class II consists of drugs with isolated case reports of pancreatitis but lacking substantial evidence to establish a definitive causal relationship. Class III includes medications that have been reported to cause pancreatitis in certain situations or patient populations, but the evidence is limited. Class IV encompasses drugs that have been suspected to cause pancreatitis based on theoretical considerations or anecdotal reports, but the evidence is insufficient to establish a conclusive link.[10][11]

Continuous use of proton pump inhibitors can lead to hypergastrinemia, which in turn stimulates pancreatic enzyme secretion and can eventually result in pancreatitis. Numerous case reports have associated various proton pump inhibitors with pancreatitis.[12][13] However, to date, only one case of lansoprazole-induced pancreatitis has been described in the literature.[14] A recent systematic review identified 213 different drugs and classified them into different classes based on the modified Badalov classification regarding their propensity to cause drug-induced pancreatitis.[15] However, lansoprazole was not identified as a causative agent. Through this case report, we aim to highlight lansoprazole as another potential proton pump inhibitor that can cause drug-induced pancreatitis.

Case Presentation

A 67-year-old female presented with complaints of abdominal pain, nausea, vomiting and worsening generalized weakness for the past one week. She had a past medical history significant for paroxysmal atrial fibrillation on anticoagulation with apixaban; coronary artery disease managed with percutaneous coronary intervention and drug-

eluting stent placement on aspirin and metoprolol succinate; hypertension on lisinopril; dyslipidemia on atorvastatin and recently diagnosed spondylolisthesis, which was being managed conservatively. She also had ongoing symptoms of gastroesophageal reflux including heartburn, indigestion and postprandial bloating for the past one month, for which she was started on lansoprazole 30mg once daily by her primary care physician. She started taking the lansoprazole 27 days prior to her symptom onset, and was compliant to it, diligently taking one tablet a day before lunch until the day of presentation. She did not have any change in her existing medications and denied any over-the-counter pain-relief or herbal medication use. She had not undergone any endoscopy or other medical or surgical intervention in the recent past. She was post-menopausal, was not on any hormone replacement therapy, had a normal body mass index, and had no recent weight changes. She also did not have any history of autoimmune disease or any symptoms suggestive of inflammatory bowel disease. On presentation, she complained of significant persistent abdominal pain localized mostly in the epigastric region with occasional radiation to the back. Her vital signs revealed a pulse rate of 108/min in sinus rhythm, blood pressure 144/70 mm Hg, respiratory rate of 18/min, saturating 97% on room air and a body mass index (BMI) of 28.2 kg/m$^{[2]}$. Physical examination was significant for a mildly distended abdomen with tenderness and some guarding in the epigastric region but no rebound tenderness, guarding or rigidity. She had sluggish bowel sounds present in all 4 quadrants. There were no obvious skin changes over the abdominal wall. Laboratory investigations were significant for an elevated white blood cell count with neutrophilic predominance, normal electrolytes, kidney and renal function tests, normal liver function tests, elevated amylase to 1085 U/L and lipase to 177 U/L, and normal triglyceride levels (Table 1).

Table 1. Laboratory investigations at presentation

Laboratory Test	Value	Normal range
CBC		
Hemoglobin	13.1 g/dL	12.0-15.5 g/dL
WBC's	26,500 cells/mcL	4,500-11,000 cells/mcL
Platelets	418,000 cells/mcL	150,000-450,000 cells/mcL
BMP		
Sodium	142 mmol/L	135-145 mmol/L
Potassium	4.1 mmol/L	3.5-5.0 mmol/L
Chloride	102 mmol/L	96-106 mmol/L
Bicarbonate	26 mmol/L	22-28 mmol/L
Blood Urea Nitrogen	18 mmol/L	8-20 mg/dL
Creatinine	0.9 mmol/L	0.5-1.1 mg/dL
LFT		
Total Bilirubin	0.8 mg/dL	0.1-1.2 mg/dL
Direct Bilirubin	0.2 mg/dL	0.0-0.4 mg/dL
Alanine Aminotransferase	48 U/L	7-56 U/L
Aspartate Aminotransferase	34 U/L	10-40 U/L
Alkaline Phosphatase	96 U/L	30-120 U/L
Gamma Glutamyl transpeptidase	21 U/L	5-40 U/L
Total Protein	6.4 g/dL	6.0-8.3 g/dL
Albumin	4.1 g/dL	3.5-5.0 g/dL
Amylase	1085 U/L	25-125 U/L
Lipase	177 U/L	0-160 U/L
Triglycerides	102 mg/dL	<150 mg/dL

Computed tomography of the abdomen and pelvis with contrast revealed features of acute interstitial pancreatitis with peripancreatic fat stranding but no focal lesion or ductal dilatation. There were multiple soft tissue densities in the bilateral peritoneum along the retroperitoneal lining suggestive of reactive lymphadenopathy (Figure 1,2). There was also a non-obstructive calculus in the gall bladder with some biliary sludge, but no intra or extra-hepatic biliary dilatation.

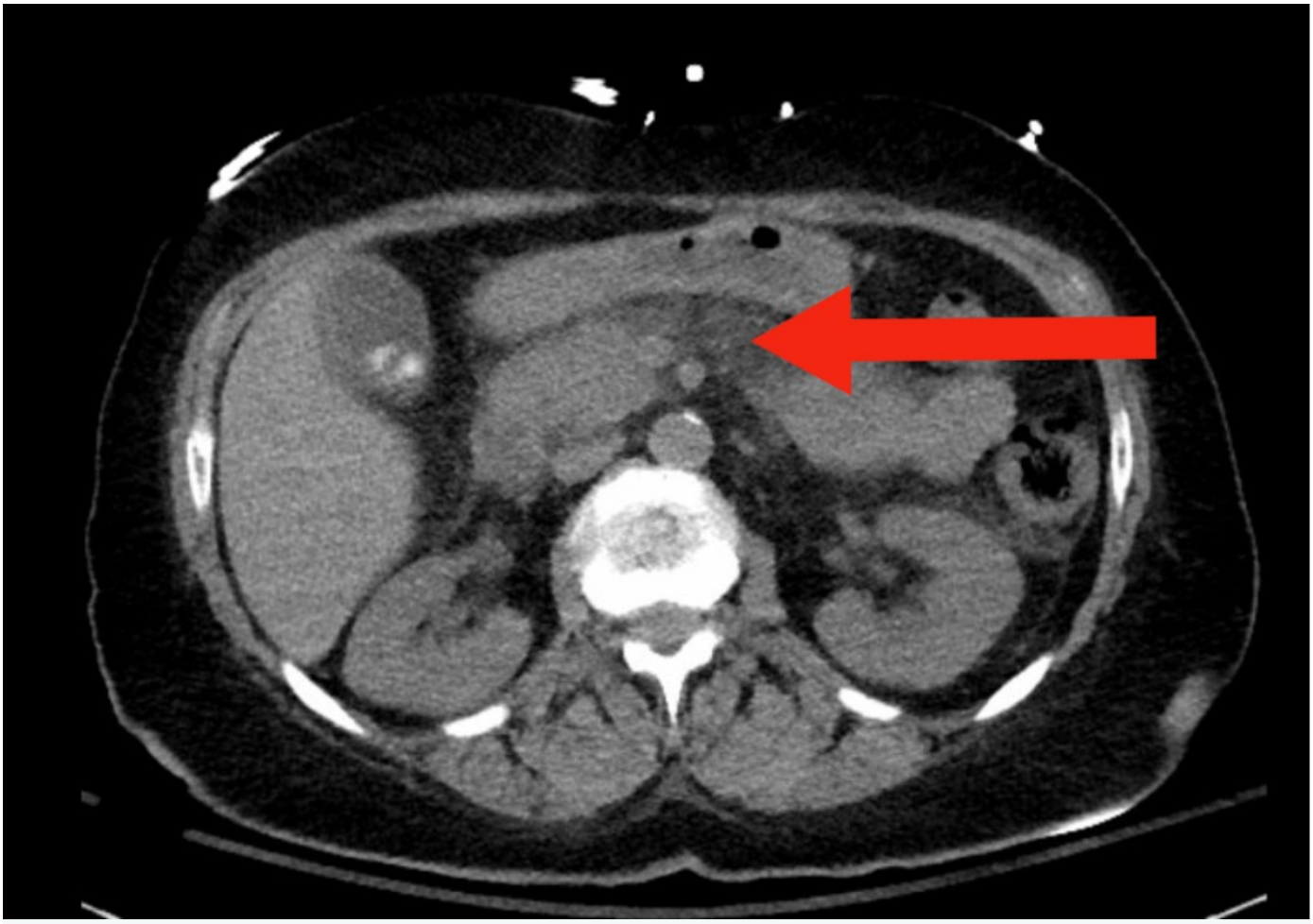

Figure 1. CT Abdomen Pelvis with contrast demonstrating inflammation of the pancreas with peri-pancreatic fat stranding. Also a non-obstructed biliary calculus with biliary sludge.

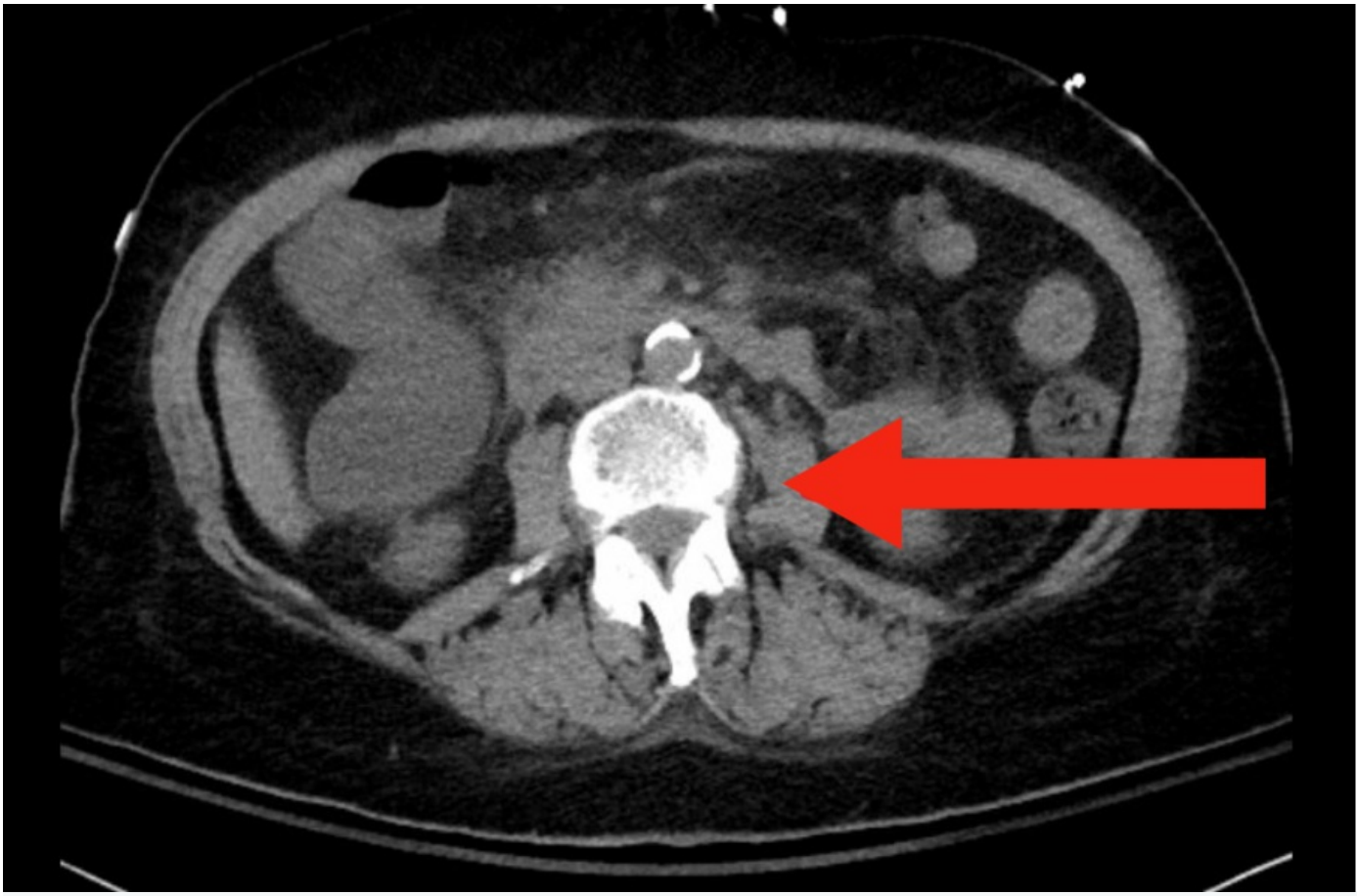

Figure 2. CT Abdomen Pelvis with contrast demonstrating soft tissue densities along the bilateral retroperitoneal lining, suggestive of reactive lymphadenopathy.

She was diagnosed to have acute pancreatitis based on clinical, radiological and laboratory criteria and was admitted for further management. The patient denied any history of alcohol consumption. She was on her regular medications except the newly started lansoprazole almost 4 weeks ago, to which she was compliant and was taking a pill daily. She did not have any recent illness, any symptoms suggestive of a viral infection, any history of abdominal trauma, any history of over the counter or recreational drug use. Her urine tox screen was also negative. She was managed with IV hydration, bowel rest and pain control along with broad-spectrum antibiotic therapy. As all other common etiologies were ruled out, drug-induced pancreatitis was diagnosed and was attributed to the lansoprazole use, which was discontinued. After 3 days of admission, her symptoms improved. Her laboratory parameters normalized and she started tolerating a normal diet. Her lansoprazole was completely discontinued at discharge without any rechallenge, and she was planned for follow-up on outpatient basis.

Discussion

There have been several cases reporting a potential link between acute pancreatitis and acid-suppressing medications.[8][9][15] An experimental model for omeprazole-induced pancreatitis was studied, which demonstrated that intraperitoneal administration of omeprazole could induce inflammation in peri-pancreatic fatty tissue and elevate

pancreatic enzyme levels.[16] However, drug-induced pancreatitis still remains a diagnosis of exclusion as establishing causality is challenging. A recent review has linked almost all acid-suppressing medications to pancreatitis, but there has been only one reported case associated with lansoprazole.[14]

Potential mechanisms contributing to drug-induced acute pancreatitis include constriction of the pancreatic duct, which impairs pancreatic enzyme flow and leads to inflammation. Certain drugs can also exert cytotoxic and metabolic effects on pancreatic cells. The accumulation of toxic metabolites or intermediaries resulting from drug metabolism can trigger pancreatic inflammation, although this typically occurs over time. Furthermore, drugs may induce acute pancreatitis through hypersensitivity reactions, where the body's immune system reacts adversely to the medication. Hypertriglyceridemia and chronic hypercalcemia caused by drugs can also contribute to drug-induced acute pancreatitis. Other causes include localized angioedema in the pancreas, leading to inflammation, and arteriolar thrombosis, which involves the formation of blood clots in the small arteries supplying the pancreas.[9][10][11]

In our case, the patient did not have any other identifiable causes for acute pancreatitis apart from the newly started medication, lansoprazole. Although she was on other medications that have the potential to cause pancreatitis, such as lisinopril and atorvastatin, she had been tolerating them well for the past few years. She did not have any other risk factors, including tobacco or alcohol exposure, abdominal trauma, or autoimmune diseases such as inflammatory bowel disease. Additionally, she was not obese, was post-menopausal, and was not on hormone replacement therapy, which overall puts her at low risk for gallstone induced pancreatitis. The CT scan showed a single non-obstructive biliary calculus with gallbladder sludge, but there was no cholestatic pattern of liver injury or pancreatic duct dilatation, ruling out the gallbladder stone as a potential etiology. This finding may have been incidental on the CT scan and could not explain the development of her pancreatitis. Her condition improved with conservative management and discontinuation of the drug. According to the Naranjo algorithm, this was a possible adverse drug reaction with a score of 3. As per the Badalov classification, this case was classified as class IV, with one case report without rechallenge, and according to the modified Badalov classification, it was classified as class Ic, with one case report without rechallenge and other causes ruled out.[10][11] The exact causation could not be established as the patient was not re-challenged with the drug. The risks and benefits were explained, but she opted for alternative therapy, and the reintroduction of the potential culprit drug was deferred.

Conclusion

Lansoprazole, commonly used in the treatment of gastroesophageal reflux disease, may have the potential to cause acute pancreatitis. However, recent studies have not identified lansoprazole as a potential culprit yet. As the second reported case of lansoprazole-induced pancreatitis in the literature, determining exact causation is challenging. Analyzing subsequently reported cases and potential rechallenge will help strengthen the evidence base and provide further insight into establishing or refuting this causation.

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