

Thiazide-Induced Pancreatitis

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INTRODUCTION

Acute pancreatitis (AP) is an acute inflammatory disease of the pancreas and is associated with a wide spectrum of clinical manifestations, ranging from mild disease to more severe forms, even requiring intensive care unit hospitalization.¹ The reported annual incidence of acute pancreatitis in the United States ranges from 4.9 to 35 per 100,000 population.² Pancreatitis due to medications is rare (< 5%).³ Published reports have identified about 50 drugs that definitely or possibly may be held responsible for inducing acute pancreatitis.⁴ Also, the global prevalence of hypertension is high, and among nonpregnant adults in the United States, treatment of hypertension is the most common reason for office visits and the use of chronic prescription medications.⁵

Drug-induced pancreatitis remains a challenge for physicians. It needs further consideration when a patient has a clinical presentation suggestive of acute pancreatitis without a significant cause. This report involved a case of hydrochlorothiazide-induced pancreatitis in a patient who recently had started this medication for blood pressure control. We aimed to determine the association of thiazide drugs with the incidence of pancreatitis and add to the literature this rare case.

CASE REPORT

A 48-year-old white man was referred to a cardiology practice for management of uncontrolled hypertension. He reported a history of hypertension for more than 20 years that was never well controlled. In addition, he was mildly obese and was compliant with continuous positive airway pressure ventilation for his obstructive sleep apnea. He was asymptomatic and denied any headache, chest pain, shortness of breath, orthopnea, leg swelling, or paroxysmal nocturnal dyspnea. With regards to family history, his father had early-onset hypertension and died of a massive myocardial infarction at age 47. On initial encounter, blood pressure markedly was elevated at 170/100 mmHg. Physical examination was unremarkable.

The patient reported that he had been on amlodipine, but this was stopped due to a side effect of bilateral leg swelling. He was continued on metoprolol succinate 200 mg day and newly started on losartan-hydrochlorothiazide 100-25 mg tablets once per day.

Secondary hypertension work-up was unremarkable. A 2-D echocardiogram for the evaluation of cardiac function revealed normal left ventricular (LV) systolic function, estimated ejection fraction 55 to 60%, mild concentric LV hypertrophy, and no significant valvular disease. The patient was counseled on weight loss, exercise, and following a “Dietary Approaches to Stop Hypertension (DASH)” diet.

Four weeks later, the patient presented to the emergency depart-

ment with severe abdominal pain. The pain was in the mid-epigastric abdominal area, qualified as “burning and tearing” in nature, briefly relieved with positional changes, and mildly relieved with pain medications. The patient denied nausea, vomiting, chest pain, or shortness of breath.

The patient was hemodynamically stable and afebrile. Physical examination was remarkable for mild epigastric tenderness. Labs showed leukocytosis of 12,000 cells/mm³, an elevated lipase level of 134 units per liter, and a mild transaminitis (AST was 42 U/L, ALT was 69 U/L). Triglycerides were elevated slightly at 177 mg/dL.

Abdominal computed tomography showed acute interstitial pancreatitis (Figure 1). Gallbladder imaging was unremarkable, and the patient did not have any history of excessive alcohol use. He was admitted, treated with IV fluids and analgesics, and provided supportive care. Thiazide-induced pancreatitis was suspected and thus losartan-hydrochlorothiazide was stopped resulting in improvement of symptoms and no recurrent episodes. Repeat amylase level was normal, as well as liver function enzymes. The patient was started on spironolactone 50 mg and losartan 100 mg once per day with improved blood pressure control.

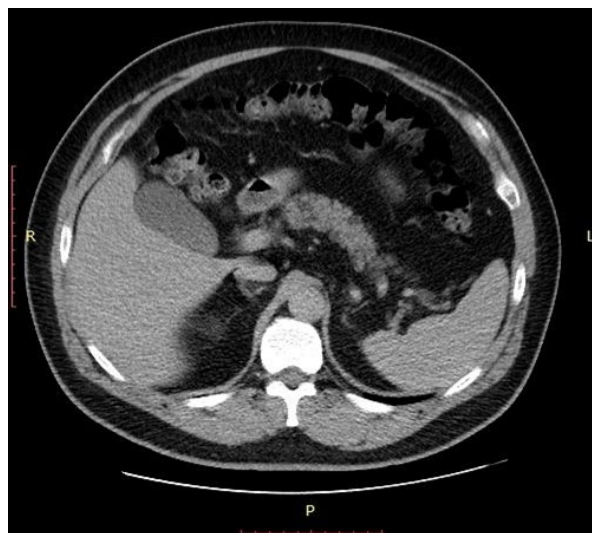


Figure 1. Computed tomography of the abdomen and pelvis with contrast showing acute interstitial pancreatitis involving the uncinate process of the pancreas.

DISCUSSION

Hypertension is a major and modifiable risk factor for cardiovascular disease and stroke.⁶ The staging system of hypertension diagnosis is very crucial as it guides the appropriate management. Normal blood pressure is defined as less than 120/80 mmHg; elevated blood pressure 120-129 or less than 80 mmHg; hypertension stage 1 is 130-139 or 80-89 mmHg; and hypertension stage 2 is greater than 140/90 mmHg.⁷ However, once an individual with hypertension qualifies for pharmacological treatment, including patients with masked hypertension, prescription of drug therapy is recommended to come from one of four drug classes (usual first-line therapy), thiazide diuretics, calcium antagonists, angiotensin-converting enzyme (ACE) inhibitors, or angiotensin receptor blockers (ARBs), unless there is a comorbidity consideration favoring the use of a different drug class. Our patient was diagnosed with stage 2 hypertension and prescribed a thiazide diuretic.

Pancreatitis is acute inflammation of the pancreas.⁸ Its severity

ranges from a benign course to life-threatening with increased mortality, one requiring hospitalization. The major causes of acute pancreatitis are gallstones (30 - 60%) and heavy alcohol use (15 - 30%) in addition to other common causes, such as hypertriglyceridemia, hyperparathyroidism, endoscopic retrograde cholangiopancreatography, trauma, pancreatic tumors, surgery, infections, and medications. Agents reported to have a definite association with pancreatitis are asparaginase, azathioprine, didanosine, estrogens, furosemide, mercaptopurine, pentamidine, sulfonamides, sulindac, tetracyclines, thiazides, and valproic acid.⁹ In our case, all other causes of pancreatitis were excluded, and drug-induced pancreatitis was suspected.

Thiazide-induced pancreatitis was first described in 1959 by Johnston et al.¹⁰ in four patients who developed pancreatitis while receiving chlorothiazide. The possible mechanisms for drug-induced pancreatitis include pancreatic duct constriction, cytotoxic and metabolic effects, hypersensitivity reactions, drug-induced hypercalcemia, and drug-induced hypertriglyceridemia.¹¹

Accurate diagnosis of acute pancreatitis requires at least two of the following three diagnostic features: abdominal pain consistent with acute pancreatitis, serum lipase or amylase levels that are at least three times the upper limit of the normal range, and findings of acute pancreatitis on cross-sectional imaging (computed tomography or magnetic resonance imaging).¹² Definite proof that a drug causes pancreatitis requires that pancreatitis develops during treatment with the drug, that other likely causes of pancreatitis are not present, that pancreatitis resolves upon discontinuing the drug, and that pancreatitis usually recurs upon re-administration of the drug.¹³

Early aggressive intravenous hydration remains the gold standard of management of acute pancreatitis. Early aggressive intravenous fluid resuscitation provides micro- and macro- circulatory support to prevent serious complications such as pancreatic necrosis.¹⁴ The cause of acute pancreatitis must be assessed and treated. For drug-induced pancreatitis etiology, practitioners should eliminate the suspected drug to prevent future episodes.

CONCLUSIONS

A prompt diagnosis of drug-induced pancreatitis may lead to early withdrawal of the offending drug, thus, improving outcomes and reducing hospital stay. In the end, practitioners need to identify common as well as uncommon potential triggers for pancreatitis, including medications such as thiazide diuretics. Our case was challenging in terms of the suspected thiazide drug, which was the etiology of acute pancreatitis. The fact that most of his clinical symptoms and labs have normalized after stopping this medication has shown evidence that the pancreatitis was related to the drug.

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