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CASE REPORT

Pravastatin: A potential cause for acute pancreatitis

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Abstract

Acute pancreatitis (AP) secondary to drugs is uncommon, with an incidence ranging from 0.3% to 2.0% of AP cases. Drug-induced AP due to statins is rare, and only 12 cases have thus far been reported. In this case report, we report a case of a 50-year-old female on pravastatin therapy for 3 d prior to developing symptoms of AP. The common etiological factors for AP were all excluded. The patient was admitted to the intensive care unit secondary to respiratory distress, though she subsequently improved and was discharged 14 d after admission. Although the incidence of drug-induced AP is low, clinicians should have a high index of suspicion for it in patients with AP due to an unknown etiology. Clinicians should be aware of the association of statins with AP. If a patient taking a statin develops abdominal pain, clinicians should consider the diagnosis of AP and conduct the appropriate laboratory and diagnostic evaluation if indicated.

Key words: Drug-induced pancreatitis; Acute pancreatitis; Statins; Pravastatin.

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INTRODUCTION

Acute pancreatitis (AP) secondary to drugs is uncommon, with an incidence ranging from 0.3% to 2.0% of AP cases[1]. The literature on drug-induced AP consists mostly of case reports, though there have been reviews analyzing the association of various drugs with AP[1-3]. The following drugs have been definitely associated with AP in many of the reviews: azathioprine, chlorothiazide, hydrochlorothiazide, estrogens, furosemide, sulfonamides, tetracycline, L-asparaginase, sulindac, valproic acid, didanosine, salicylates, aminosalicylates (mesalamine, sulfasalazine), calcium, sodium stibogluconate, pentamidine, vinka alkaloids, and metronidazole. There are many other drugs which have been implicated as having probable or possible associations with AP, including 6-mercaptopurine, methyldopa, ACE inhibitors, clozapine, rifampicin, cyclosporine, and many other drugs.

There have been 12 cases of AP associated with statins described thus far[4-14]. In four of the cases presented, reintroduction of the statin led to a recurrent attack of AP[4-6,12]. In this case report, we report a case of AP associated with pravastatin therapy. In view of the magnitude of use of statins in prevention of coronary artery disease, even an infrequent occurrence is worth reporting.

CASE REPORT

A 50-year-old female presented to our hospital with right upper quadrant abdominal pain, nausea, and vomiting for 1 d. Four days prior to admission, she was started on 10 mg pravastatin by mouth daily, though the patient stopped this medication the day prior to admission as she attributed her symptoms to the new medication. Her lipid panel one month prior to admission showed a total cholesterol level of 262 mg/dL, triglyceride level of 268 mg/dL, high-density lipoprotein (HDL) level of 52 mg/dL, and low-density lipoprotein (LDL) level of 156 mg/dL. She was also treated for hypertension with 10 mg enalapril by mouth daily for the past 18 mo, and 25 mg hydrochlorothiazide by mouth daily for 6 years. She took 2.5 mg olanzapine by mouth daily for the past year for severe anxiety, and a combination of 500 mg/1 mg metformin and rosiglitazone (Avandamet™) in the past year for type Ⅱ diabetes mellitus. She had osteoarthritis of both knees, and took 325 mg/37.5 mg one to two tablets of acetaminophen/tramadol (Ultracet™) as needed for pain. Of note, she was on atorvastatin 2 years prior to admission for a period of 3 d, though this was discontinued secondary to generalized body pain. Laboratory tests were not performed at that time. She had a cholecystectomy 16 years prior to admission. The common etiological factors for AP such as alcoholism, trauma to the abdomen, HIV disease, hypertriglyceridemia, and hypercalcemia were all excluded.

Table 1 Laboratory values

	Admission	48 h
Amylase (U/L)	914	280
Lipase (U/L)	1613	261
WBC (mm^3)	26300	21500
HCT (%)	53.9	42.4
LDH (IU/L)	389	645
Glucose (mg/dL)	495	
AST (IU/L)	18	
ALT (IU/L)	28	
Calcium (mg/dL)	10.2	6.5
PO_2 (mmHg)		76
BUN (mg/dL)		17
Base deficit		-1
Fluid sequestration (L)		2.8
Total cholesterol (mg/dL)	202	
Triglycerides (mg/dL)	118	

On physical examination, her blood pressure was 158/104 mmHg, heart rate was 131 beats per minute, respiratory rate was 30/min, temperature was 98 degrees Fahrenheit, and SpO_2 was 93% breathing room air. Her abdominal examination revealed hypoactive bowel sounds, with diffuse tenderness without rebound tenderness or guarding.

Laboratory values are included in Table 1. Three out of five Ranson criteria were fulfilled on admission, and two out of six criteria were fulfilled after forty-eight hours.

She was admitted to the intensive care unit, and given isotonic intravenous fluids and meperidine for pain control. CT scan of the abdomen showed inflammatory changes within the pancreas, though no discrete peripancreatic fluid collections were noted. Abdominal ultrasound did not show biliary ductal dilatation. Magnetic resonance cholangiopancreatography showed a normal pancreatico-biliary system. She developed respiratory distress, though this resolved after support with BIPAP and diuretic therapy. She improved significantly following this, and was discharged 14 d after admission.

Of note, she was restarted on enalapril during the admission and continued to take enalapril without any adverse effects. She was not restarted on pravachol or hydrochlorothiazide. Olanzapine and metformin/rosiglitazone were also restarted without any adverse effects. The patient was last seen 4 mo after discharge, and her hypertension and diabetes were well controlled on enalapril, metformin, rosiglitazone, atenolol, and glipizide. She also continued to take olanzapine without any adverse effects.

DISCUSSION

Statin-induced AP is rare and only 12 cases have thus far been reported in the literature[4-14]. Although AP is a rare side effect of statin therapy, there seems to be a strong association between statins and AP, as there have been four cases where reintroduction of the statin has led to a recurrence of AP[4-6,12]. In our case report, the patient was on pravastatin for three days prior to symptom onset, and the outcome was favorable. A rechallenge test involving documenting AP development during treatment with a drug, its disappearance after stopping the drug, and recurrence after reintroduction of the drug, was not performed in this patient due to ethical issues. This would be the most reliable evidence that pravastatin caused AP in this patient.

No data about a potential mechanism for statin-induced AP are available at this time. In previously published cases of statin-induced pancreatitis, the duration of statin treatment until the onset of AP varied from 8 h to 7 years, though the vast majority of patients presented within 6 mo of introduction of the statin[4-14]. Generally, the outcome is favorable in statin-induced AP, though there was a fatality in one case after a four-month hospital stay[13].

A number of medications that our patient took are known to be associated with AP. Thiazide diuretics[15], ACE inhibitors[16], atypical antipsychotics[17], biguanides[18], and acetaminophen[19] have been associated with AP. However, continuation of all of the above medications, with the exception of the thiazide diuretic, did not precipitate AP.

In conclusion, though the incidence of drug-induced AP is low, clinicians should have a high index of suspicion for it in patients with AP due to an unknown etiology. A diligent review of medications should be performed, focusing on drugs that have been associated with drug-induced AP[1-3]. Clinicians should be aware of the association of statins with AP. If a patient taking a statin develops abdominal pain, clinicians should consider the diagnosis of AP and conduct the appropriate laboratory and diagnostic evaluation if indicated.

REFERENCES

1 **Lankisch PG**, Dröge M, Gottesleben F. Drug induced acute pancreatitis: incidence and severity. *Gut* 1995; **37**: 565-567
2 **Mallory A**, Kern F. Drug-induced pancreatitis. *Baillieres Clin Gastroenterol* 1988; **2**: 293-307
3 **Rünzi M**, Layer P. Drug-associated pancreatitis: facts and fiction. *Pancreas* 1996; **13**: 100-109
4 **Anagnostopoulos GK**, Tsiakos S, Margantinis G, Kostopoulos P, Arvanitidis D. Acute pancreatitis due to pravastatin therapy. *JOP* 2003; **4**: 129-132
5 **Pluhar W**. [A case of possible lovastatin-induced pancreatitis in concomitant Gilbert syndrome]. *Wien Klin Wochenschr* 1989; **101**: 551-554
6 **Ramdani M**, Schmitt AM, Liautard J, Duhamel O, Legroux P, Gislon J, Pariente EA, Agay D, Faure D. [Simvastatin-induced acute pancreatitis: two cases]. *Gastroenterol Clin Biol* 1991; **15**: 986
7 **Lons T**, Chousterman M. [Simvastatin: a new drug responsible for acute pancreatitis?]. *Gastroenterol Clin Biol* 1991; **15**: 93-94
8 **Abdul-Ghaffar NU**, el-Sonbaty MR. Pancreatitis and rhabdomyolysis associated with lovastatin-gemfibrozil therapy. *J Clin Gastroenterol* 1995; **21**: 340-341
9 **Hunninghake D**, Bakker-Arkema RG, Wigand JP, Drehobl M, Schrott H, Early JL, Abdallah P, McBride S, Black DM. Treating to meet NCEP-recommended LDL cholesterol concentrations with atorvastatin, fluvastatin, lovastatin, or simvastatin in patients with risk factors for coronary heart disease. *J Fam Pract* 1998; **47**: 349-356
10 **Wong PW**, Dillard TA, Kroenke K. Multiple organ toxicity from addition of erythromycin to long-term lovastatin therapy. *South Med J* 1998; **91**: 202-205
11 Belaïche **G**, Ley G, Slama JL. [Acute pancreatitis associated

with atorvastatine therapy]. *Gastroenterol Clin Biol* 2000; **24**: 471-472
12 **Tysk C**, Al-Eryani AY, Shawabkeh AA. Acute pancreatitis induced by fluvastatin therapy. *J Clin Gastroenterol* 2002; **35**: 406-408
13 **McDonald KB**, Garber BG, Perreault MM. Pancreatitis associated with simvastatin plus fenofibrate. *Ann Pharmacother* 2002; **36**: 275-279
14 **Miltiadous G**, Anthopoulou A, Elisaf M. Acute pancreatitis possibly associated with combined salicylate and atorvastatin therapy. *JOP* 2003; **4**: 20-21
15 **Eckhauser ML**, Dokler M, Imbembo AL. Diuretic-associated pancreatitis: a collective review and illustrative cases. *Am J Gastroenterol* 1987; **82**: 865-870
16 **Maringhini A**, Termini A, Patti R, Ciambra M, Biffarella P, Pagliaro L. Enalapril-associated acute pancreatitis: recurrence after rechallenge. *Am J Gastroenterol* 1997; **92**: 166-167
17 **Koller EA**, Cross JT, Doraiswamy PM, Malozowski SN. Pancreatitis associated with atypical antipsychotics: from the Food and Drug Administration's MedWatch surveillance system and published reports. *Pharmacotherapy* 2003; **23**: 1123-1130
18 **Ben MH**, Thabet H, Zaghdoudi I, Amamou M. Metformin associated acute pancreatitis. *Vet Hum Toxicol* 2002; **44**: 47-48
19 **Mofenson HC**, Caraccio TR, Nawaz H, Steckler G. Acetaminophen induced pancreatitis. *J Toxicol Clin Toxicol* 1991; **29**: 223-230

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