

## Acute Pancreatitis Due to Pravastatin Therapy

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### ABSTRACT

**Context** Few data exist about the incidence of drug-induced pancreatitis in the general population. Drugs are related to the etiology of pancreatitis in about 1.4-2% of cases. Statins are generally well tolerated. Acute pancreatitis has been reported in a few cases treated with atorvastatin, fluvastatin, lovastatin and simvastatin.

**Case Report** We report the case of a 56-year-old patient who, after 6 months of treatment with pravastatin 20 mg once daily for hypercholesterolemia, presented with acute pancreatitis. Other causes of the disease were ruled out. Five months later, the patient, on his own initiative, reintroduced pravastatin and acute pancreatitis recurred after 3 days.

**Conclusion** To our knowledge this is the first report of pravastatin-induced pancreatitis and further strengthens the fact that statins may cause acute pancreatitis.

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### INTRODUCTION

Few data exist about the incidence of drug-induced pancreatitis in the general population. Drugs are related to the etiology of pancreatitis in around 1.4-2% of cases [1, 2]. Many drugs have been reported to be associated with acute pancreatitis but a lack of rechallenge evidence, consistent statistical data or evidence from experimental studies on

a possible mechanism prohibit definitive conclusions about most of them. Statins are generally well-tolerated. Acute pancreatitis has been reported in a few cases treated with atorvastatin [3, 4], fluvastatin [5, 6], lovastatin [7, 8, 9] and simvastatin [10, 11, 12, 13]. To our knowledge, pravastatin-induced pancreatitis has never been reported in the literature. We are reporting a case of pravastatin-induced pancreatitis. The literature concerning statin-induced acute pancreatitis is reviewed.

### CASE REPORT

A 56-year-old man presented at the Emergency Room of our hospital complaining that he had had epigastric pain radiating to the back for the previous two days. The pain was accompanied by nausea and vomiting. There was no history of alcohol ingestion or previous abdominal surgery. The patient had been treated for the previous 6 months with pravastatin 20 mg once daily for hypercholesterolemia. No other medication was regularly used.

On physical examination, the abdomen was distended with hypoactive bowel sounds and diffuse tenderness which was maximal in the epigastrium. No rebound tenderness was present and rectal examination for occult blood was negative. Laboratory data on admission showed increased serum levels of amylase (1,615 U/L; reference values: 25-115 U/L). Serum values of urea, creatinine, AST, ALT, alkaline phosphatase, triglycerides,

cholesterol, calcium and bilirubin were normal. Abdominal ultrasound revealed that the head of the pancreas was edematous and hypoechoic. The biliary tree was not dilated and no gallstones were seen. Pravastatin was discontinued and the patient received symptomatic medical treatment. The patient underwent magnetic resonance cholangiopancreatography which had no abnormal findings. Serum amylase became normal three days after admission and the patient was discharged from the hospital 5 days later.

Five months after this episode, the patient reintroduced pravastatin 40 mg once daily, on his own initiative. Three days later, the patient felt epigastric pain radiating to the back. Laboratory examination revealed an increased serum amylase level (2,334 U/L). Pravastatin was discontinued and the patient was discharged 6 days later. The patient is now being treated with bezafibrate which is well tolerated.

## DISCUSSION

Statin induced pancreatitis is very rare and only a few cases have been reported in the literature. Atorvastatin [3, 4], fluvastatin [5, 6], lovastatin [7, 8, 9], and simvastatin [10, 11, 12, 13] were the only statins reported to have caused this side-effect prior to our study (Table 1).

No data exist about the potential mechanism of statin-induced pancreatitis. In four previous case reports, drug interaction had been suggested as the triggering factor for the development of pancreatitis. Wong *et al.* [8] described a patient who had been taking lovastatin for 7 years. After the administration of erythromycin for a dental procedure, the patient developed multiple organ toxicity including pancreatitis. Lovastatin was later reintroduced without further side effects. Abdhul-Ghaffar and el-Sonbaty [9] reported that the combination of lovastatin and gemfibrozil resulted in rhabdomyolysis and

**Table 1.** Previous reports on statin-induced pancreatitis.

Author	Age, gender	Drug	Duration of treatment	Reintroduction	Outcome
Pluhar <i>et al.</i> 1989 [7]	46, male	Lovastatin 20mg bid	1 wk	Yes: recurrence	Well
Rhamdani <i>et al.</i> 1991 [11]	40, male	Simvastatin 10 mg od	8 mo	Yes: recurrence	Well
Couderc <i>et al.</i> 1991 [12]	55, female	Simvastatin 10 mg od	3 mo	No	Well
Lons <i>et al.</i> 1991 [13]	50, male	Simvastatin 20 mg od	12 h	No	Well
Abdhul-Ghaffar, el-Sonbaty 1995 [9]	55, female	Lovastatin 20 mg bid; gemfibrozil 300 mg bid	2 mo	No	Well
Hunninghake <i>et al.</i> 1998 [6]	NS	Fluvastatin	NS	NS	NS
Wong <i>et al.</i> 1998 [8]	73, male	Lovastatin 20 mg od; erythromycin	7 yr	Yes: no recurrence	Well
Belaiche <i>et al.</i> 2000 [4]	63, male	Atorvastatin 10 mg od	8 h	No	Well
Tysk <i>et al.</i> 2002 [5]	36, male	Fluvastatin 40 mg od	3 mo	Yes: recurrence	Well
Mc Donald <i>et al.</i> 2002 [10]	70, male	Simvastatin 10 mg od; fenofibrate	6 mo	No	Fatal
Miltiados <i>et al.</i> 2003 [3]	60, male	Atorvastatin 40 mg od; salicylate	5 yr	No	Well
Current report	56, male	Pravastatin 40 mg od	6 mo	Yes: recurrence	Well

bid: twice daily  
od: once daily  
NS: not stated

pancreatitis. Miltiadous *et al.* [3] suggested a possible interaction mechanism between atorvastatin and salicylates while McDonald *et al.* [10] described a case of pancreatitis associated with the synchronous administration of simvastatin and fenofibrate. The reported length of statin treatment until the onset of pancreatitis varies considerably in the previously reported cases. In two cases [4, 13], pancreatitis occurred during the first day of the therapy, while in other cases, the patients had been using the statin for years before the development of this side effect [3, 8]. Only in three cases [5, 7, 11], had the statin been reintroduced resulting in recurrence of pancreatitis. The clinical course of pancreatitis in the reported cases was, for the most part, mild. In two cases [8, 9], rhabdomyolysis complicated the course of acute pancreatitis and, in one of these patients, renal failure developed [8]. Only in the case described by McDonald *et al.* [10], was the co-administration of simvastatin and fenofibrate associated with severe pancreatitis having a fatal outcome. In the case described by Abdhul-Ghaffar and el-Sonbaty [9], pancreatitis was induced by combination therapy of lovastatin and gemfibrozil, and was complicated by pseudocyst formation. In our case, all other causes of pancreatitis were ruled out. There was no history of alcohol use and no family history of pancreatitis. There was no evidence of gallstone disease and serum values of calcium and triglycerides were normal. The patient was not taking any other medication. Our patient had been taking pravastatin for 6 months before the onset of acute pancreatitis. The reintroduction of pravastatin therapy resulted in the recurrence of pancreatitis and this strongly supports the association. In conclusion, we have described a case of pravastatin-induced pancreatitis. This is the first report in the literature about pancreatitis caused by pravastatin and it further reinforces the fact that statins may cause acute pancreatitis. Despite the low incidence of drug-induced pancreatitis, all patients with acute pancreatitis of an unknown etiology should be carefully questioned about drugs

possibly responsible for the induction of the disease. As the use of statins increases, physicians should consider the diagnosis of acute pancreatitis in patients taking these medications who then develop abdominal pain not explained by any other process. If pancreatitis is suspected, the drug should be stopped and replaced to reduce the possibility of further episodes of pancreatitis.

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**Key Words** Case Report; Chemicals and Drugs Category; Gemfibrozil; Naphthalenes; Pancreatitis; Pharmaceutical Preparations; Polycyclic Hydrocarbons; Polycyclic Hydrocarbons, Aromatic; Pravastatin

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