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CASE REPORT

Recurrent Acute Pancreatitis Possibly Induced by Atorvastatin and Rosuvastatin. Is Statin Induced Pancreatitis a Class Effect?

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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. While statins are generally well tolerated they have been known to be associated with pancreatitis. Acute pancreatitis has been reported in a few cases treated with atorvastatin, fluvastatin, lovastatin, simvastatin and pravastatin.

Case report We report the case of a 77-year-old patient who developed acute pancreatitis after treatment with rosuvastatin, which resolved on withdrawal of the medication. She had a similar episode of pancreatitis a year ago precipitated by atorvastatin, which resolved on withdrawal. Extensive workup on both occasions failed to reveal any other etiology for the pancreatitis.

Conclusion To our knowledge this is the first report of rosuvastatin-induced pancreatitis. The occurrence of pancreatitis with two different statins in our patient argues that statins induced pancreatitis may be a class-effect of statins. With statin prescriptions on the rise clinicians need to be aware of this complication of statin treatment and remember that the newest statin, rosuvastatin is not dissimilar to the other statins in causing pancreatitis.

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. Statins are generally well tolerated. Acute pancreatitis has been reported in a few cases treated with atorvastatin, fluvastatin lovastatin, simvastatin and pravastatin. To our knowledge, rosuvastatin-induced pancreatitis has never been reported in the literature. We are reporting a case of rosuvastatin-induced pancreatitis in a patient who had a prior similar episode of atorvastatin-induced pancreatitis.

CASE REPORT

A 77-year-old white female presented with abdominal discomfort, nausea and vomiting for the past few days. Her medical history was significant for hypertension, hyperlipidemia, hypothyroidism, cholecystectomy 10 years ago and a pacemaker placement. She denied alcohol consumption or trauma. There was no family history of pancreatitis. Medications on admission included rosuvastatin, zolpidem, enalapril, synthroid and salsalate. She was allergic to penicillin. She had recently been started on rosuvastatin and her dose increased from 10 to 20 mg daily.

Her physical examination revealed a mildly distended abdomen with epigastric tenderness, but was otherwise normal. Laboratory data showed elevated lipase (2,036 U/L, reference range: 16-63 U/L) and amylase (1,157 U/L reference range: 20-104 U/L). ALT (34 U/L, reference range: 5-55 U/L), AST (37 U/L, reference range: 5-45), ALP (126 U/L, reference range: 30-147 U/L) and bilirubin (0.5 mg/dL, reference range: 0-1.5 mg/dL) were within normal range. Complete blood count, metabolic profile, cholesterol, triglycerides, CK, CA 19-9 and CEA were all normal. Abdominal ultrasound revealed a normal biliary tree without choledocholithiasis. Abdominal CT showed diffuse pancreatic edema without necrosis or calcifications consistent with acute pancreatitis. Drug induced pancreatitis was considered and the patient improved with conservative management and discontinuation of rosuvastatin.

Careful history revealed that she had a similar episode of pancreatitis precipitated by atorvastatin a year ago. A generalized maculopapular rash and a photosensitivity reaction accompanied that episode. Other medications included enalapril, synthroid, tramadol and venlafaxine. Lipase and amylase levels were elevated at 3,070 U/L and 655 U/L respectively. ALT (35 U/L), AST (22 U/L), alkaline phosphatse (80 U/L), bilirubin (0.5 mg/dL) and triglycerides (143 mg/dL, reference range: 50-200 mg/dL) were all within normal limits. Workup including an ultrasound and CT scan failed to reveal any obvious etiology for the pancreatitis. The possibility of drug-induced pancreatitis was considered and atorvastatin was thought to be the probable etiologic agent and discontinued. She made an uneventful recovery. She was discharged home on all her previous medications except atorvastatin. Several months later she was started on rosuvastatin and the dose-increase probably precipitated this second episode of pancreatitis.

While microlithiasis still remained a diagnostic possibility, the presence of a pacemaker precluded the use of magnetic resonance cholangiopancreatography. Normal liver enzymes and biliary tract imaging on both occasions made this less likely. Enalapril has also been known to cause pancreatitis but the patient had been stable on it for a long time and it was well tolerated - along with other medications - throughout both episodes of pancreatitis, as well as during follow-up, making it unlikely in our case. On the other hand, the occurrence of pancreatitis with atorvastatin therapy, rapid improvement on discontinuation of atorvastatin, prompt recurrence with rosuvastatin rechallenge, and improvement on discontinuation of rosuvastatin strongly implicated the statins as the etiologic agent in our case. Rosuvastatin was discontinued and she was discharged home after a complete recovery and advised to avoid all statins in the future.

DISCUSSION

Drug induced pancreatitis accounts for 1-2% of all cases pancreatitis [1]. 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. Using a recently published reporting method by Nebeker *et al*. [2] we determined rosuvastatin to be the probable cause of pancreatitis in our patient. Acute pancreatitis has been previously reported with simvastatin [3], pravastatin [4], fluvastatin [5], atorvastatin [6] and lovastatin [5]. To our knowledge there have been no published reports of pancreatitis occurring with rosuvastatin therapy, although pancreatitis occurred in less than 1% of patients on rosuvastatin in clinical trials [7].

The exact mechanism of pancreatitis with statins is uncertain but drug interaction has been proposed as a trigger mechanism in some cases. The duration of statin treatment until the onset of pancreatitis has varied [5], occurring within the first day of therapy in some cases with a delay of months in others (like our patient). Similar to previous reports [5] the clinical course in our patient was mild,

and she recovered within a few days of symptomatic therapy.

As the association between the statins and pancreatitis is based on case reports it is not known whether different statins carry different risks [5]. Although in one previous report the patient tolerated pravastatin both before and after having had atorvastatin-induced pancreatitis [8], reintroduction of statins has precipitated pancreatitis in several cases [4, 5]. In another case, the patient developed epigastric pain with simvastatin after fluvastatin induced pancreatitis [5]. Although this class effect of statins has not been proven, as clinicians will not reintroduce another drug of the same class in a patient who has had a reaction to a drug of the same class, the occurrence of pancreatitis with two different statins in our patient argues that statin induced pancreatitis may be a class-effect of statins.

With statin prescriptions on the rise clinicians need to keep the possibility of drug-induced pancreatitis with statins in mind when faced with a diagnosis of pancreatitis without an obvious etiology. They also need to be aware that this might be a class effect of statin drugs and the newest statin, rosuvastatin is as likely to be associated with pancreatitis as the other statins.

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