Atorvastatin Induced Acute Pancreatitis: A Case Report

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Abstract

Few data exist on the incidence of drug-induced pancreatitis in the general population. Drugs are linked to the aetiology of pancreatitis in about 1.4-2 percent of all instances of acute pancreatitis. While statins are usually well tolerated, acute pancreatitis has been documented in a few cases involving atorvastatin, Fluvastatin and simvastatin. The literature on statin-induced pancreatitis comprises mostly of sporadic case reports and the precise prevalence and cause of this condition remains unclear. We note a case of a 63-year-old patient who developed AP following treatment with atorvastatin monotherapy and resolved after withdrawing of the medication. Continued coverage of such an unusual adverse effect of atorvastatin is required to raise understanding and to control and prevent the same.

Keywords

Acute pancreatitis, atorvastatin, adverse drug reaction, case report

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INTRODUCTION:

Acute pancreatitis (AP) is a clinical condition characterised by inflammation of the pancreas. The two most common causes of acute pancreatitis are bile stones and alcohol. Nevertheless, drug-induced pancreatitis is relatively rare and should be considered if there are no other appropriate causes of pancreatitis. Drug-induced pancreatitis occurs in the general population at a rate of around 1.4-2% of all cases of acute pancreatitis [1].

A wide variety of drugs have been reported to cause pancreatitis [2-5]. Often statins are commonly used for the treatment of hyperlipidaemia. Atorvastatin is a most frequently prescribed agent among them and have been reported to cause this side effect. The exact mechanism of disease progression remains idiopathic; however, pancreatitis is reported with multiple statins.

Most drug-induced pancreatitis studies are case reports which are intended to act as a signpost for other clinicians. That is the case with respect to statins, which have been recently quoted as culprit in isolated cases of acute pancreatitis. We present a case of acute pancreatitis in which atorvastatin was considered responsible after exclusion of other known and possible causes of acute pancreatitis.

Case Report:

A 63 years old male presented with complaints of severe abdominal pain and vomiting for 10 days. The patient is a known case of hypertension, Diabetes mellitus type-2 for 15 years and recently diagnosed with hyperlipidaemia. He was on the following medications such as tablet metformin 500mg once in every 12h , tablet glimepiride 1mg once in every 24 hour, tablet amlodipine 5mg once in every 12h and tablet atorvastatin 20mg once in 24h only during night time.

He denied habitual or occasional alcohol ingestion and had no previous history of abdominal trauma and no family history of pancreatitis. The patient is not allergic to any other medications.

On admission, patient was in distress, ill-looking, and dehydrated. He denied other symptoms. On physical examination, there was tenderness throughout and increased tenderness along the middle epigastrium. His vitals on admission were as follows; Blood pressure- 138/ 75mm Hg, Heart rate- 84 beats per minute, and respiratory rate – 21 breaths per minute.

His laboratory data on admission were as per Table 1. A blood test showed neutrophilic leucocytosis. Ultrasonography (USG) abdomen revealed that the pancreas volume is globally increased and the anteroposterior diameter at the level of the pancreas head, body, and tail is increased. The CT scan workout revealed, pancreatic margins owing to inflammation. Based on the clinical findings, laboratory data, USG, and CT scan patient was diagnosed as a case of Acute Pancreatitis.

Atorvastatin was stopped and the patient was treated with the following medications.

Sl. No	Name of the Medication	Dose of medication	Frequency of Administration	Route of administration
1	Inj.Human Actrapid	25U-25U-25U	1-1-1	SC
2	Inj. Ceftriaxone	1g	1-0-1	IV
3	Inj. Ondansetron	4mg	1-0-0	IV
4	Tab. Amlodipine	5mg	1-0-1	PO
5	Tab. Pantoprazole	40mg	1-0-0	PO
6	Tab. Paracetamol + Tramadol	325mg 37.5mg	SOS	PO
7	IVF. Normal saline Ringer Lactate	1pint 2pint	10ml/hour	IV

Table 1: Laboratory data of the patient on the day of admission.

Parameters	Observed Value	Reference Value
Hb	12g/dl	14-18g/dl
Platelets	210,000/ mm^3	150,000–400,000/mm^3
Leucocytes	12,400/mm^3	4,500-11,000 /mm3
Neutrophils	89.4%	45-75%
Serum lipase	153 U/L	16-63U/L
Serum amylase	427 U/L	25-115U/L
Calcium	9.0mg/dl	8.4- 10.2 mg/dl
Total Bilirubin	0.7mg/dl	0-1.5mg/dl
AST	28U/L	5-45U/L
ALT	18U/L	5-55U/L
ALP	73U/L	30-147U/L
Total Cholesterol	208mg/dl	120-220mg/dl
LDL	110mg/dl	60-160mg/dl
HDL	72mg/dl	30-65mg/dl
Triglycerides	172mg/dl	40-140mg/dl
RBS	147 mg/dl	70–140mg/dl

After discontinuation of atorvastatin, he made an uneventful recovery and serum levels of amylase and lipase became normal. He was cautioned not to take atorvastatin and discharged with following medications: Tablet metformin 500mg once in every 12h , tablet glimepiride 1mg once in every 24 hour, tablet amlodipine 5mg once in every 12h and tablet Rosuvastatin 10mg once in 24h only during night time and the patient was scheduled for follow-up after 2 weeks.

After 2 months patient was again hospitalized with the complaints of abdominal pain and diagnosed with drug-induced pancreatitis. Other drugs in her regimen on that admission were metformin, glimepiride, amlodipine, and calcium. Rosuvastatin was discontinued. The patient recovered completely and was cautioned to avoid all statins in the future. At present, the patient is treated with bezafibrate, metformin, glimepiride, pantoprazole, and amlodipine, which are well tolerated.

DISCUSSION:

Statins are frequently used for several conditions, including diabetes mellitus, ischemic heart disease, stroke, etc. Statins are generally well tolerated, and statin induced pancreatitis is exceedingly rare, with estimated annual incidence varying up to 80 per 100000 population [6]. Bergholm et al. [7] searched the World Health Organization database of adverse drug reactions, and 72 reports of lovastatin-induced pancreatitis were found during 1968 through 1993.

Atorvastatin was shown to induce AP in a few recently reported cases that were either as monotherapy or in conjunction with other medications [8-10]. The exact initiation mechanism of pancreatitis due to statins is uncertain. Several scholars proposed interaction with medications as a trigger mechanism. The period of statin treatment before the onset of pancreatitis is also unpredictable, arising in some cases during the first day of therapy and in others after several months. Outcome findings on a potential process are missing after re-challenge of the same or other statins, useful observational results or confirmation from laboratory studies.

With no history of abdominal trauma or surgery, no weight loss, no personal or family history of pancreatitis, all such causes for pancreatitis other than atorvastatin may be omitted here. Adverse reactions to drugs cause significant morbidity and mortality yet remain underrated and misunderstood. By definition, an adverse drug reaction is a reaction to a drug that is harmful and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis , or treatment of disease, or for the modification of physiological functions [12]. Assessing causal connections between drugs and disease is important for safe practice of medicine. The pharmacovigilance of these aspects requires tools for describing adverse drug reactions, using the following criteria: time relationship between the drug use and the adverse reaction, the pathophysiology of the adverse reaction, response to dechallenge (discontinuation of therapy with the drug or dose reduction), and response to rechallenge (drug readministration). These criteria can be organised to assess the causal relationship between the drug and the adverse reaction in terms of 4 discrete levels of certainty (some, probable / likely, possible, and unlikely) [13,14]. The difference between the certain and the probable/likely grades is that the latter grade does not include a rechallenge procedure.

Most cases of drug-induced or drug-associated acute pancreatitis follow a mild course and resolve shortly after discontinuation of the causative drug. However, one report describes a severe case of simvastatin-associated acute pancreatitis that resulted in death [15].

Though there is low incidence of drug induced pancreatitis, patients with acute pancreatitis of unknown aetiology should be questioned about the drug that may be inducing the disease. As the use of statins increases, physicians should consider the diagnosis of drug induced pancreatitis in patients taking these medications who then develop abdominal pain not explained by any other process. In this case, the aetiology of acute pancreatitis was attributed to atorvastatin, which had been prescribed for hyperlipidaemia, and the patient was taking atorvastatin for 7 months without any laboratory data monitoring.

As the correlation between statin use and pancreatitis is concentrated on case reports, it is still not known if different statins bear different risks [16] , or if the reintroduction of another statin or the same type of statin previously associated with another drug, will cause recurrence of pancreatitis. Meanwhile it is advisable that clinicians do not reintroduce any statin, unless necessary [16]. There is a need for further research to identify the exact mechanism of statin-induced pancreatic injury.

Conflicts of interest:

The author declares that there is no conflict of interest to disclose.

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