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A RARE CASE OF ATORVASTATIN-INDUCED PANCREATITIS

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ABSTRACT

Atorvastatin is a highly efficacious and most commonly used statin drug for patients with dyslipidemia. Its common side effects are Nausea, vomiting, headache, and muscle aches. Pancreatitis is an uncommon or rare adverse reaction seen with atorvastatin. A 56-year-old male patient presented with complaints of abdominal pain and vomiting with no history of any past abdominal surgery or trauma. No Comorbidities were present. He was not an alcoholic and did not have a significant family history of pancreatitis. He was diagnosed 2 months back with dyslipidemia by altered lipid profile measures and was put on atorvastatin 20 mg OD. His vitals were normal. Blood investigations were suggestive of pancreatic disturbance. Thus, his USG abdomen and CECT abdomen were done which confirmed the diagnosis of acute pancreatitis. Atorvastatin was suspected as the cause and was discontinued. The patient was admitted and treated symptomatically. The patient showed recovery in 5 days and was discharged. Rosuvastatin 20 mg OD was started as an alternative. On his one-week follow up all tests were within normal limits. There is no chance of drug interaction in this case because the patient was on atorvastatin monotherapy, and this mechanism for Acute Pancreatitis may be suspected to be ruled out, but more studies are needed to confirm this causal association. This case study adds to the evidence that statins can induce pancreatitis. There is a need for continuing reporting of such a rare atorvastatin adverse effect in order to raise awareness and manage and avoid it.

KEYWORDS: Adverse drug reaction, Atorvastatin, Pancreatitis, Statins.

INTRODUCTION

Atorvastatin is one of the most commonly prescribed drugs for dyslipidemia or hyperlipidemia. It is effective in lowering the serum total cholesterol, serum triglyceride, and LDL cholesterol levels. It has wide utilization around the globe and is on WHO's EML (Essential Medicines List) also.[1]

Atorvastatin is usually well tolerated. Muscle pain, weakness, and liver dysfunction may be seen in 1 to 2% of patients.[2] On prolonged use, it may cause rhabdomyolysis. But, very few cases of acute pancreatitis have been reported after using atorvastatin.[3] We report the case of acute pancreatitis following prolonged use of atorvastatin.

CASE REPORT

In this case, a 56-year-old male patient was presented to the outpatient department of our hospital with symptoms of abdominal pain and vomiting for 3 days. The patient had no co-morbidities like hypertension, diabetes mellitus, tuberculosis or asthma. The patient was non-alcoholic. He had no history of any abdominal trauma or abdominal surgery in the past. His family history was insignificant. His past history revealed that before 20 days, on a routine health check-up, he was diagnosed with dyslipidemia. He had elevated levels of serum total cholesterol (398 mg/dl), serum triglyceride (190 mg/dl), and serum LDL cholesterol (202 mg/dl). For that, he was prescribed with atorvastatin 10 mg/day. He was regularly taking the prescribed medication. After 20 days, he developed acute abdominal pain and vomiting. Thus, the patient visited the hospital. The patient had no history of taking any other medications for the last 3 months.

On general examination, his vitals were normal with blood pressure- 126/62 mm Hg, pulse rate- 80/minute, and respiratory rate- 15 breath/minute except body temperature which was 100.4 ^{O}F. Initial lab investigations were done, which showed elevated serum amylase (1076 U/L), serum lipase (3028 U/L), and serum SGPT (58 U/L) levels. His WBC count on CBC was normal (8000/µL). His Renal function tests were all within normal limits. The values were S. creatinine 0.8 mg/dl, S. sodium 141 mmol/L, and S. potassium 4.4 mmol/dL. (table 1).

Table 1: lab investigations of the patient.

Laboratory test	Values on presentation	Values on follow-up	Normal range
Total S. Cholesterol	398 mg/dl	256 mg/dl	120-220 mg/dl
S. Triglyceride	190 mg/dl	176 mg/dl	40-140 mg/dl
HDL Cholesterol	42 mg/dl	46 mg/dl	30-65 mg/dl
LDL Cholesterol	202 mg/dl	190 mg/dl	60-160 mg/dl
S. Amylase	1076 U/L	102 U/L	20-104 U/L
S. Lipase	3028 U/L	62 U/L	16-63 U/L
SGPT	58 U/L	38 U/L	5-55 U/L
SGOT	38 U/L	26 U/L	5-45 U/L

A CECT scan abdomen was done which showed peripancreatic fat standing and thickening of the left Gerota's fascia. It confirmed the diagnosis of acute pancreatitis. Atorvastatin was suspected as the cause of the patient's condition. (figure 1)

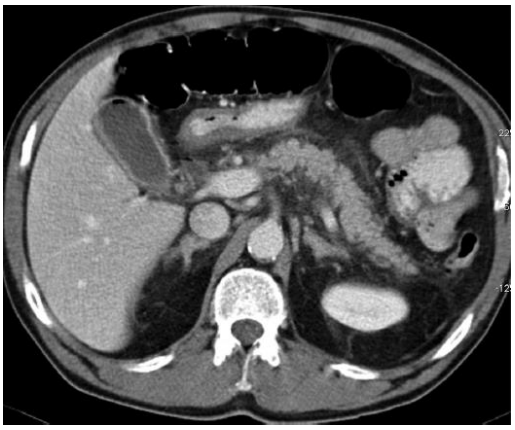

Figure I: Contrast enhanced CT scan abdomen.

The suspected medication was discontinued immediately, and the patient was admitted to the hospital. He was treated symptomatically with IV fluids; Analgesics and Anti-emetics given parenterally. No antibiotics were given, as there was no infection present. The patient showed improvement after the withdrawal of atorvastatin. He was fully recovered in 5 days. Thus, he was discharged in stable condition and with no symptoms. He was prescribed the alternative medicine Rosuvastatin 20 mg/day for his dyslipidemia.

On a follow-up visit, all necessary lab investigations were done. All were within normal limits. The lipid profile was also improving. Serum values on presentation and on follow-up are presented below in this table.

DISCUSSION

Ethical considerations were followed. Informed consent from patient was taken and necessary

confidentiality of data was maintained.

Numerous drugs have been implicated in the pathogenesis of acute pancreatitis, however, statins rarely cause pancreatitis.[4] Drug-induced pancreatitis is a clinical entity for which a causal relationship is difficult to establish. The obvious mechanism by which atorvastatin can induce pancreatitis is still unclear. Few reports are also there showing pancreatitis as a result of other statins. In a study done by Gagnon A. et al[5], It was observed that 13% of cases of acute pancreatitis were due to lipid modifying agents.

In this case, a 56-year-old male without any co-morbidities was on 10 mg/day of atorvastatin alone. When compared to another case reported by Kanbay M. et al[6], an 86 years old male with hypertension since long, was on atorvastatin 20 mg/day along with lisinopril 10 mg/day. As per the literature search, Lisinopril has not been associated with acute pancreatitis. Acute pancreatitis was reported in both of these cases.

The duration of statin treatment until the onset of pancreatitis is also variable, occurring within the first day of therapy in some cases and after several months in others.[7] In this case, this period was 20 days.

CT scan findings are useful to confirm the diagnosis. Typical CT findings in acute pancreatitis as per recent literature are focal or diffuse enlargement of pancreas, irregular margins, blurring of peripancreatic fat planes with soft tissue standing densities and thickening of fascial planes. In our study, the CECT scan abdomen showed Peripancreatic fat standing, and thickening of the left Gerota's fascia. By this the diagnosis of acute pancreatitis was confirmed.

So, in the present case, the USG and CECT scan of abdomen ruled out the possibility of a surgical cause of pancreatitis. The patient was nonalcoholic, and there was no past history of pancreatic disease or any abdominal trauma. The patient improved after dechallenge (withdrawal of the suspected drug). These factors raise a suspicion about causal relationship between atorvastatin and pancreatitis in this patient.

A similar case reported by Deshpande R. et al[8], showed the ADR as 'Probable'(Naranjo score 7). In this case, we calculated Causality assessment for this ADR using Naranjo scale; value was 7, indicative of Probable ADR. We also used WHO-UMC scale for causality assessment, which showed probable/likely ADR. ADR form (version 1.4) was filled up and

this ADR was reported to nearest ADR Monitoring Center using Vigiflow software with unique number of: IN-IPC300640732. The Rechallenge study was not done in our case.

After discontinuing atorvastatin, the patient was treated symptomatically. He was recovered in 5 days and discharged with alternative Rosuvastatin 20 mg/day. On follow-up, all the lab investigations were done which were within normal limits. Follow-up USG and CT scan were not required.

Statins are frequently prescribed for a variety of indications such as ischemic heart diseases, cerebrovascular diseases, etc. Hence, the prescriber should, therefore, be aware of this ADR while evaluating patients suffering from pancreatitis. Further research studies are needed to identify the exact mechanism of statin-induced pancreatic injury.

CONCLUSION

Atorvastatin is generally safe, when used in appropriate dosage for appropriate duration. This case study adds to the evidence that statins can induce pancreatitis. For definitive diagnosis, USG and CT scan abdomen should be performed. After diagnosis, other causes of pancreatitis should be ruled out. Atorvastatin should be discontinued immediately. In the majority of cases, conditions improve in few days. There is a need for continuing reporting of such a rare atorvastatin adverse effect in order to raise awareness and manage and avoid it.

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