Sitagliptin induced acute pancreatitis: Case report and a brief review of the literature

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ABSTRACT Background: Sitagliptin phosphate is a dipeptidyl peptidase IV (DPP-IV) inhibitor used as an oral hypoglycemic agent in the treatment of type 2 Diabetes Mellitus. Features of drug-induced pancreatitis are a temporal sequence, known response pattern and reversible when the drug is withdrawn. Acute pancreatitis is a rare known complication of sitagliptin, which can occur at any time after initiation of the drug therapy. **Case Summary:** A 32-year old man was presented in medical casualty with acute pain in the abdomen. He was a case of a T2DM taking tablet of sitagliptin 100 mg/day since last one year. The patient was obese, nonsmoker and not alcoholic. Diagnostic laboratory workup showed glycosylated haemoglobin 6.7%, raised levels of serum amylase (109 u/l Normal range 28-90 U/L) and Lipase (174 U/L Normal range- 0-64 U/L), which favoured the diagnosis of acute pancreatitis. We stopped his tablet sitagliptin and shifted him to insulin and metformin. Symptomatic treatment was offered, and he improved clinically and discharged from the hospital. **Conclusion:** Acute pancreatitis among patients receiving sitagliptin is a rare entity. But physicians should always keep the possibility of sitagliptin-induced pancreatitis during follow up of the patients. Cautious monitoring for development of signs and symptoms of acute pancreatitis in patients receiving sitagliptin is essential in long-term management.

KEYWORDS sitagliptin, Diabetes Mellitus, acute pancreatitis.

Background:

Drug-induced pancreatitis (DIP) is a relatively uncommon condition with an estimated incidence of 0.1-2%. (1) Most common causes of acute pancreatitis are alcoholism, hypertriglyceridemia, gallstones, obesity, and advanced age. When no other etiological factors are present besides the use of pancreatitis associated drug, then it is considered as a DIP. Sitagliptin phosphate is a dipeptidyl peptidase IV (DPP-IV) inhibitor used as an oral hypoglycemic agent in the treatment of type 2 Diabetes Mellitus (T2DM). It prolongs the duration of active incretin hormones like glucagon-like peptide 1 (GLP-1) in circulation, which results in increased synthesis, and release of Insulin from beta cells of the pancreas in response to a meal. It is a potent and effective anti-diabetic drug. Common side effects of sitagliptin are nausea, headache, pharyngitis and sore throat. Acute pancreatitis is a rare known complication of sitagliptin, which can occur at any time after initiation of the drug therapy. (2) But physicians should always keep the possibility of sitagliptin-induced pancreatitis during follow up of the patients.

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Case presentation:

A 32-year old man was presented in medical casualty with acute pain in abdomen since two days. There was no history of fever, nausea, vomiting, loose motions and any other gastrointestinal symptoms. On acquiring history, he was a case of a T2DM taking tablet of sitagliptin 100 mg/day since last one year. The patient was obese (BMI- 30 Kg/m2), non-smoker and not alcoholic. On arrival, his random blood sugar was 199 mg%.

On physical examination, he was afebrile with normal vital parameters pulse rate, respiratory rate, heart rate and blood pressure. On abdominal palpation, tenderness was present in the right hypochondriac region was present. There was no evidence

of hepatomegaly, splenomegaly, and ascites. Findings of systemic examination were unremarkable. Diagnostic laboratory workup showed glycosylated haemoglobin 6.7%, raised levels of serum amylase (109 u/l Normal range 28-90 U/L) and Lipase (174 U/L Normal range- 0-64 U/L), which favoured the diagnosis of acute pancreatitis. Rest of the parameters of complete blood examination, liver, kidney function tests, urine analysis, coagulation and lipid profile were within stipulated range. Ultrasound examination of the abdomen showed evidence of grade II fatty liver while excluding other causes of acute abdomen. He was shifted to intensive care unit. We stopped tablet sitagliptin and shifted him to insulin and metformin. Symptomatic treatment was offered, and he improved clinically. His glycemic status was monitored every 4 hourly by estimating blood glucose. The course during the hospitable stay was favourable; hence he was discharged on the third day. Informed written consent was obtained from the patient for publication of present case report.

DISCUSSION

Our patient had an episode of acute pancreatitis without any obvious etiological factor other than the administration of sitagliptin. He was receiving sitagliptin since last one year for glycemic control. Hence we believed this case as sitagliptin-induced pancreatitis about symptoms, pancreatic enzymes levels and exposure to the drug. Several case reports have been published about sitagliptin-induced pancreatitis with the varying interval from initiation of the drug and occurrence of pancreatitis. Mathew et al. reported a case of sitagliptin-induced pancreatitis in a 57-year-old lady who had been receiving it for more than three years. She had been shifted to Insulin regimen after discontinuation of sitagliptin. [2] In a case report by Mariko sue and associates patient on sitagliptin from 8 months developed severe acute necrotising pancreatitis with extensive inflammation and necrosis with evidence of pancreatic cyst. [3] One report from Kuwait reported pancreatitis within one month after starting the drug in the uncontrolled T2DM patient. [4]

Patients with T2DM have approximately two times more risk for acute pancreatitis because of insulin resistance and hyperglycemia compared to non-diabetic persons. [5] Inconsistent results have been documented about the association of sitagliptin with acute pancreatitis. A population-based matched case-control study observed an association of increased odds of acute pancreatitis among T2DM patients treated with sitagliptin and exenatide. The study reported statistically significantly higher odds of acute pancreatitis after adjusting for available confounders like metformin use, current use within 30 days and recent use. [6] One of the cross-sectional studies analysed spontaneous adverse events among users of sitagliptin or exenatide observed the 6-fold increased risk of acute pancreatitis compared to other oral hypoglycemic drugs. Also, they reported an increased risk of carcinoma of the pancreas in their study population. [7] But contradictory results also have been documented in the literature. Garg et al. did not find any association between acute pancreatitis with Exenatide and sitagliptin in their study. They observed acute pancreatitis in 1.9, 5.6, 5.7 and 5.6 per 1000 patients yearly among four studied groups-nondiabetics, diabetics receiving other therapy, exenatide and sitagliptin respectively. [8] Dore et al. observed extremely low 0.12% incidence of acute pancreatitis with sitagliptin in comparison with metformin. They studied the risk of acute pancreatitis among patients using incretin-based drugs and found risk with exenatide as RR 1.0 CI 95% (0.6-1.7) and with sitagliptin RR 1 CI 95% (0.5-2). [9]

Although the prevalence of DIP is low, practising physicians must be aware of this condition for the differential diagnosis of cases with acute abdomen. Features of DIP are a temporal sequence, known response pattern and reversible when the drug is withdrawn. [10] Our patient improved clinically shortly after cessation of sitagliptin. 88 cases of sitagliptin induced acute pancreatitis were reported to FDA out of which two were hemorrhagic and necrotizing. Other drugs like statins, fenofibrate, angiotensin converting enzymes agonists and inhibitors may cause a DIP in T2DM patients. [11,12] But our patient was young 32 year male with no history of such pancreatotoxic medication, nonalcoholic and nonsmoker. So we diagnosed him as a case of sitagliptin induced pancreatitis.

Previous case reports, studies and post-marketing surveillance warrants the judicious use of this drug judiciously and need of monitoring the patients for signs and symptoms of acute pancreatitis. As soon as clinician suspect acute pancreatitis in these patients even with the mild clinical presentation, the drug should be immediately withdrawn, and the patient should be shifted to an alternative drug.

CONCLUSION

Sitagliptin is an effective oral hypoglycemic agent to improve glycemic control in patients with T2DM. But physician should always weigh its benefits against risk of acute pancreatitis after initiation of therapy. Cautious monitoring for development of signs and symptoms of acute pancreatitis in patients receiving sitagliptin is important in long-term management.

AUTHORS' STATEMENTS

COMPETING INTERESTS

The authors declare no conflict of interest.

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