Case Report

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Sitagliptin Associated Acute Pancreatitis

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Abstract

Dipeptidyl peptidase IV (DPP-IV) inhibitors such as sitagliptin prolong the duration of active incretin hormones such as glucagon-like peptide 1 (GLP-1) in the bloodstream and thereby enhances control of type 2 diabetes. Adverse events with sitagliptin include upper respiratory tract infections, sore throat, headache and diarrhea. It has also been linked with pan creatitis in case reports, animal studies and postmarketing drug surveillance studies. We report a case of 52 year old diabetic female taking sitagliptin since 2 months presented with abdominal pain and vomiting since 2 days and was diagnosed as acute pancreatitis.

Keywords: Type II Diabetes Mellitus; Sitagliptin; Dipeptidyl Peptidase Iv Inhibitor; Acute Pancreatitis.

Introduction

Dipeptidyl peptidase IV (DPP-IV) inhibitors such as sitagliptin prolong the duration of active incretin hormones such as glucagon-like peptide 1 (GLP-1) in the bloodstream and thereby enhances control of type 2 diabetes [1,2]. These drugs are less likely to cause hypoglycemia because of the meal-dependent nature of GLP-1 secretion [3]. Adverse events with sitagliptin include upper respiratory tract infections, sore throat, headache and diarrhea. It has also been linked with pancreatitis in case reports, animal studies and postmarketing drug surveillance studies [4–7].

Case Report

A 52 year old female with diabetes mellitus (type 2) since 6 years and hypertension since 4 years presented with complains of pain abdomen and vomiting since 2 days. Pain abdomen was more in upper abdomen, dull in character and radiated to back. It was associated with multiple episodes of vomiting, non-projectile. Content of vomitus was partially digested food material and was not associated with blood.Patient had no history of headache, diarrhea, fever, peptic ulcer disease and chest pain. The patient also denied any history suggestive of hyperlipidemia, hypercalcemia, recent travel, insect bites, trauma, alcohol or drug use.

Patient was admitted to another hospital 2 months back for sudden severe headache and vomiting. She was diagnosed at that time with SAH and hydrocephalus and managed conservatively. Patient was started at that time on Tab Sitagliptin/ Metformin (50/500) and Tab Glimepiride/ Metformin (2/500) twice a day for diabetes and Tab Telmisartan/Hydrochlorothiazide (40/12.5) once a day for hypertension.

Patient also has history of pancreatitis 15 years back for which no documentation was availabe.

On admission, the patient's body mass index was 23.8 kg/m^2. Her vital signs included a temperature of 37.3°C, blood pressure of 136/82 mmHg, heart rate of 108 beats/min, and oxygen saturation of 95% on room air. On abdominal examination, tenderness was present in the epigastrium without

rebound tenderness and guarding. There was no palpable masses.

On investigations, amylase (304 U/L) and lipase (739.8 U/L) were raised more than three times the normal. Her white blood cell count was 8300/mm [3]. Liver function tests were normal. Triglyceride and Serum calcium levels were also normal. Blood glucose was 329 mg/dl. Ultrasound abdomen was done and revealed hepatomegaly and bulky pancreas with dilated main pancreatic duct suggesting acute on chronic pancreatitis. CECT abdomen was done and revealed acute odematous mild pancreatitis (balthazar score-2).

Patient was managed conservatively with fluid resuscitation and was kept nil per orally. Sitagliptin and other OHAs were discontinued, and the patient was started on an insulin regimen. By hospital day 2, the patient's abdominal pain started to improve, and she was started on a clear liquid diet. Patient improved symptomatically and was started on soft, low-residue and low-fat diet from day 3. Her amylase and lipase decreased to normal range.The patient received diabetic education and was discharged on day 6.

Discussion

The most common inciting factors for acute pancreatitis are gallstones (35-40%) and alcoholabuse (30%) [8]. Other causes of acute pancreatitis include structural abnormalities, neoplasms, metabolic disorders, drugs, trauma, iatrogenic causes, infections, vascular disorders, genetic and idiopathic conditions.

Pancreatitis is a known, although rare, side effect of DPP-IV inhibitors. It has been postulated that incretin drugs (including DPP-4 inhibitors and GLP-1 agonists) might promote pancreatitis by increasing pancreatic mass, modifying enzyme secretion, disturbing acinar architecture, promoting inflammation, or increasing ductal turnover and metaplasia [6]. DPP-IV-induced pancreatitis has previously been reported anywhere between several weeks to 8 months after initiating the medication.

GLP-1 stimulates both the synthesis of insulin and its release from pancreatic beta cells, and it also reduces release of glucagon from pancreatic alpha cells. GLP-1 is released from intestinal cells in response to food intake, and it usually has a half-life of less than 5 min due to rapid inactivation by the DPP-IV enzyme [1].

The incidence of acute pancreatitis was approximately two times higher in patients with type 2 diabetes [9]. The reasons for the higher risk of pancreatitis in such patients may be due to higher rates of known risk factors for pancreatitis, such as obesity, hypertriglyceridemia, age and the greater use of medications potentially associated with pancreatitis in such patients.

A population-based matched case–control study of 1269 casesof acute pancreatitis, showed a significantly increased oddsratio of acute pancreatitis in patients with currentor recent exenatideor sitagliptin use [10].

Conclusion

Acute pancreatitis is rare but serious condition and thus requires caution and long term monitoring of diabetic patients receiving sitagliptin. Physicians should be aware of the possibility of such side effects and evaluate patients taking sitagliptin who presents with abdominal pain and other features of pancreatitis.

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