



Exenatide and Acute Pancreatitis

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Abstract

For a female, type 2 diabetic patient, with 4 years duration of diabetes, Exenatide (Byetta) was prescribed as glycaemic control was not satisfactory along with Glimepiride and Metformin. She had gastrointestinal disturbances, since the first day of the injection. From the eighth day she developed signs of acute pancreatitis which was confirmed with CT-Scan and biochemical investigations. Byetta was withdrawn, the patient was treated for acute pancreatitis and the symptoms subsided. ©

INTRODUCTION

Exenatide is a 39 – amino acid peptide approved for adjunctive treatment of type 2 diabetes. It is an incretin mimetic agent that is consistent in activity with the actions of glucagon-like peptide 1. Proposed mechanisms of action include enhanced glucose dependent insulin secretion from pancreatic beta cells, restoration of first-phase insulin response, suppression of glucagon secretion, and delay of gastric emptying.

It was originally identified in the saliva of the poisonous Gila monster lizard. Pancreatitis has been reported with envenomation with gilamonster saliva due to over stimulation of pancreas. It is administered by subcutaneous injections, in 5 mcg dose before morning and evening meals, which can be increased to 10mcg two times a day if necessary. One of the advantages of Exenatide is that it results in substantial weight loss, hence is more useful in obese type 2 diabetic patients.

CASE STUDY

A 52 year, obese female of high socioeconomic status with type 2 diabetes of 4 years duration, came to the hospital with complaints of uncontrolled diabetes. She is a known case of diabetic neuropathy, hypothyroidism, dyslipidemia and hypertension. She was taking tab. Thyroxine (100 mcg) p.o. once daily, atorvastatin (10 mg), losartan potassium (50 mg) + hydrochlorthiazide (12.5 mg) p.o. once daily.

For treatment of diabetes she was started with metformin (500 mg). BID. She was not adherent to the dietary and exercise advice. Her post prandial blood glucose ranged between (250-300 mg) and HbA1c was (10.9%). Gradually, other oral hypoglycemic agents were also added. The drugs used were metformin with sulphonylurea, glitazones and alpha glucosidase inhibitors. She had wide fluctuations

in her blood glucose, including several episodes of hypoglycemia. She consulted her diabetologist in February 2008 and was prescribed exenatide (5 mcg) s.c.bid., plus glimepiride (2 mg) and metformin (500 mg) p.o. bid.

On the day after starting exenatide she had disturbed sleep due to non-specific uneasiness followed by nausea, vomiting and generalized weakness in early morning. Eight days later she had episodes of mild abdominal pain associated with vomiting and loose stools. She was treated as a case of acute gastroenteritis and with oral antibiotics and the symptoms subsided. Two days later she complained of intolerable abdominal pain in epigastrium and hypochondrium which was diffuse and progressive in nature. It was associated with low grade fever, redness and flushing of face. She was hospitalized and was investigated for the cause of her presenting symptoms. Ultrasound abdomen showed no significant abnormality. The pain was increasing continuously which was colicky in nature. At that time she had RBS – 280 mg/dl with HbA_{1c} -9.9%.

Significant laboratory findings were : Leucocytosis - 12900 cells/cmm, Serum Lipase - 417 IU/l, Serum Amylase - 534 IU/l.

Spiral computerized tomography of abdomen showed peripancreatic peritoneum slightly congested, suggestive of acute pancreatitis.

The diagnosis of acute pancreatitis was made and patient was managed NPO with intensive antibiotic therapy and IV fluids along with supportive and symptomatic management. Exenatide was withdrawn and rapid acting insulin was given based on sliding scale.

The abdominal pain was relieved within 4 days. Serum lipase was 29 IU/L and amylase was 52 IU/L. She had no past history of alcohol intake. There was history of cholecystectomy done 8 years back for blunt abdominal trauma. She was on intermittent course of fluconazole for vaginal candidiasis 150 mg p.o. which she was well tolerating. The illness was not preceded by viral or parasitic infestation. At discharge from our hospital, the patient was

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Received : 11.7.2008; Accepted : 29.10.2008

receiving Inj. Rapid acting insulin analogue and mixtard, a glucosidase inhibitors, pancreatic enzyme supplements, PPIs Losartan (50 mg), hydrochlorothiazide (12.5 mg). She had no abdominal discomfort.

DISCUSSION

The symptoms of acute pancreatitis started soon after introduction of Exenatide and it worsened with each day with every dose. The symptoms disappeared on withdrawal of the drug. The symptom and clinical presentations were thus typical of an adverse reaction due to the drug. The case is reported for the typical case history and supportive laboratory findings of acute pancreatitis produced by short-term use of Exenatide.

Medscape Medical News (October 17, 2007), had reported that use of exenatide may be limited due to a risk of pancreatitis. Data on 30 post marketing reports of acute pancreatitis in exenatide-treated patients were available. Many had at least 1 additional risk factor for acute pancreatitis and in seven, the symptoms started with

increase in daily dose from 5 to 10 micrograms. In 3 patients the symptoms returned on resumption of therapy. Therefore the US food and drug administration warned that the use of the drug may be linked to risk for pancreatitis and if the use of the drug causes symptoms of the disease it should be discontinued.

FDA warns of potential link between Exenatide and Pancreatitis. Medscape Alerts Medscape Medical News, Oct 17, 2007. LHP // www.fda.gov/medwatch.

REFERENCE

1. US Food and Drug Administration. Centre for Drug Evaluation and Research. Post Marketing Reviews. FDA Drug Safety Newsletter. Exenatide (marked as Byetta) : Acute Pancreatitis. 1 : 2, 2008.

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