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Exenatide (Exendin-4)-Induced Pancreatitis

A case report

Exenatide is a 39–amino acid peptide approved for the 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 β -cells, restoration of first-phase insulin response, suppression of glucagon secretion, and delay of gastric emptying. Kendall et al. (1) found no evidence of cardiovascular, pulmonary, hepatic, or renal toxicities with exenatide. Nausea (39–48%) and hypoglycemia (19–27%) were the most common side effects reported.

A 69-year-old man with type 2 diabetes of 15 years' duration presented for follow-up. He had known diabetic neuropathy and retinopathy. His medical history was remarkable for coronary artery disease, gastroesophageal reflux dis-

ease, rheumatoid arthritis, and colonic polyposis. He was taking metformin at 500 mg p.o., a.c., b.i.d.; pioglitazone at 30 mg p.o. daily; NPH insulin at 45 units s.q., a.c., in the morning, and 20 units s.q., a.c., in the evening; insulin aspart on a sliding scale; metoprolol at 50 mg p.o. daily; gabapentin at 1,200 mg p.o. daily; lovastatin at 40 mg p.o. daily; irbesartan at 150 mg p.o. at bedtime; clopidogrel at 75 mg p.o. daily; infliximab at 3 mg/kg i.v. every 8 weeks; ezetimibe 10 mg p.o. daily; and esomeprazole at 40 mg p.o. daily. Remarkable findings on examination were exogenous obesity, bilateral retinal dot hemorrhages, trace pitting bipedal edema, hyperpigmentation of the legs, and a symmetric distal stocking polyneuropathy. The patient was 6 ft tall and weighed 268 lb. HbA_{1c} level was 10.5%.

Treatment options were discussed, and exenatide at 5 mg s.q. b.i.d. was initiated. The pioglitazone and the metformin were discontinued. Within 24 h of initiating the exenatide, the patient developed a midepigastic abdominal pain that radiated through to the back. As he continued with the exenatide therapy the pain intensified. There was no fever or chills. He denied alcohol use or exposure to new medication. There was no previous history of pancreatitis or gallstones.

The patient presented to the emergency room on the 5th day of therapy. He was noted to have a glucose level of 309 mg/dl, creatinine of 1.0 mg/dl, and CO₂ of 27, and ketones were negative. Aspartate aminotransferase was 25 IU/l and alanine aminotransferase 25 IU/l. Serum triglycerides were 150 mg/dl, serum calcium was 8.6 mg/dl, white blood cell count was 11,000, and hemoglobin was 13.8 g/l. Serum amylase was 384 IU/l and serum lipase 346 IU/l. Computed axial tomography scan of the abdomen revealed no evidence of cholelithiasis. The presumptive diagnosis of acute pancreatitis was made. Intravenous fluids along with intravenous pantoprazole were started. He was made NPO (nothing to eat), and a gastroenterologic consultation was obtained. The NPH and the exenatide were withheld. A weight-based sliding scale of insulin was started using aspart.

On subsequent days the lipase was 106, 27, and 17 IU/l. The abdominal pain resolved by day 3. Clear fluids were started, and the diet was advanced without difficulty. The patient was discharged home without sequelae.

We report a case of acute pancreatitis

in which exenatide appears to be the etiologic agent. A review of the literature failed to reveal any previously reported cases of exenatide-induced acute pancreatitis. An occult etiology for the pancreatitis cannot be completely discounted. Pancreatitis has been reported with mevacor, infliximab, and gabapentin, but their protracted use without change in dose mitigates their being the etiologic agent. The temporal relation of the symptoms to the onset and cessation of therapy along with the normalization of laboratory parameters on drug withdrawal implicates exenatide as the cause. Caution should be exercised when prescribing exenatide with agents known to cause pancreatitis and in patients at high risk.

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The Use of Insulin Glargine With Gestational Diabetes Mellitus

We agree with the recent letter by Woolderink et al. (1) that insulin glargine use during pregnancy may be appropriate. In contrast to that letter, which described the use of insulin glargine in pregnant women with type 1 diabetes, we detail the use of insulin glargine in four patients with gestational diabetes mellitus (GDM). Target blood glucose levels set by the American College of Obstetricians and Gynecologists for women with GDM include fasting glucose ≤ 95 mg/dl and 1-h postprandial glucose ≤ 130 –140 mg/dl or 2-h postprandial glucose ≤ 120 mg/dl (2). These criteria are used by the Maternal-Fetal Medicine

