

Antral gastrin cell hyperfunction associated with chronic pancreatitis

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ABSTRACT: This report describes a patient with antral gastrin cell hyperfunction who also had pancreatic pseudocysts and partial common bile duct obstruction secondary to chronic pancreatitis. A 60-year-old female had a three-month history of worsening epigastric discomfort with episodes of nausea, vomiting and weight loss. The patient had no history of peptic ulcer disease and no ulcers were demonstrated during diagnostic work-up. Baseline fasting serum gastrins were 715 and 1000 pg/mL (normal 50 to 170 pg/mL). These decreased to 515 pg/mL during an intravenous secretin test and increased up to 2155 pg/mL after a protein meal test. The patient also had chronic pancreatitis, multiple pancreatic pseudocysts and a partial common bile duct obstruction. Truncal vagotomy and antrectomy for antral gastrin cell hyperfunction, Roux-en-Y cystjejunostomy for pancreatic pseudocysts and cholecystojejunostomy for common bile duct stricture were performed. Three months after the operation, the patient was symptom-free and fasting serum gastrin levels at one week, two months and three months after the surgery were 11, 40 and 50 pg/mL, respectively. *Can J Gastroenterol* 1988;2(3):123-126.

Key Words: Antral gastrin cell hyperfunction, Chronic pancreatitis

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ANTRAL GASTRIN CELL HYPERFUNCTION resembling the Zollinger-Ellison syndrome (ZES) was first described in 1972 (1) and subsequently reported by others (2-8). Other terms such as 'ZES type 1' (2) and 'pseudo-ZES' (5), have been used for this syndrome. Since the volume density of antral G cells has been found to be both increased (2,5,7) and normal (8), and since an increased G cell density can occur in other conditions (9-11), the term antral gastrin cell hyperfunction appears to be most appropriate (12).

The incidence of this entity is unknown, but with refinements of diagnostic procedures, including serum gastrin response to protein meal and intravenous secretin, its recognition is increasing as awareness of its possibility is appreciated. The clinical significance of differentiating between various causes of hypergas-

trinemia is obvious because their managements are quite different. The clinical associations of antral gastrin cell hyperfunction include basal hypergastrinemia, an exaggerated gastrin response to a protein meal, peptic ulcer disease and the absence of gastrinoma. The purpose of this report is to present a patient with antral gastrin cell hyperfunction without peptic ulcer disease who also had pancreatic pseudocysts and a partial common bile duct obstruction secondary to chronic pancreatitis of unknown etiology.

CASE PRESENTATION

In May 1987, a 60-year-old white female was admitted to hospital after the sudden onset of acute, sharp, stabbing mid-epigastric pain. She had previously been completely asymptomatic and the present complaints had developed following a heavy meal. The patient was diagnosed as having acute pancreatitis and medical management was begun. Because of epigastric discomfort, esophagogastroduodenoscopy was performed. A 'beefy appearing gastric mucosa with edematous folds' was described. There was no ulcer or gastric outlet obstruction. Gastric aspirate pH was 1.0 by indicator paper and fasting serum gastrin concentration was 1800 pg/mL. An abdominal computerized tomography (CT) scan showed a mass in the tail of the pancreas. Seven days after admission symptoms had resolved and the patient was discharged on cimetidine 800 mg bid and antacids. A follow-up serum gastrin concentration two weeks later was above 1000 pg/mL and repeat abdominal CT scan showed persistence of the previously noted pancreatic mass. The patient was referred to Tulane University Medical Center where she was admitted on August 13, 1987 for further study and treatment.

At the time of admission the patient described post prandial epigastric distress associated with a 30 lb weight loss over the previous three months even though there had been no change in her usual good appetite. There was no vomiting or diarrhea and no history of peptic ulcer disease or pancreatic disease. She also denied alcohol and tobacco use and drug abuse. There was no family history of

peptic ulcer disease or endocrinopathy. Physical examination was unremarkable except for mid-epigastric tenderness to palpation.

The following laboratory data were reported on admission: hemoglobin 14.1 g/100 mL, hematocrit 41.3%, white blood cell count 5600/mm³ with normal differential, urinalysis normal, stool exam negative for occult blood and negative Sudan-III reaction. Blood urea nitrogen, total serum protein, albumin, liver enzymes, alkaline phosphatase, bilirubin, electrolytes, calcium concentrations and lipid profile in serum, serum and urinary amylase concentrations were within normal limits.

Stimulation tests for serum gastrin were performed by the intravenous administration of secretin 2 U/kg (Pharmacia, Inc) and by administration of a protein meal. Fasting venous blood samples were taken through an intravenous catheter 15 and 5 mins before secretin injection and then 1, 2, 5, 10, 15, 30 and 60 mins after the injection.

Immediately after completion of the secretin test, the patient ate a test meal consisting of three eggs, two slices of bacon, two slices of toast and 8 oz of milk containing 2% butterfat. The meal contained 34.5 g protein, 26.6 g fat and 41.1 g carbohydrate (5). Blood samples were taken 0, 5, 10, 15, 30 and 60 mins after starting the meal. Serum gastrin was measured in all blood samples using a radioimmunoassay technique which specifically measures physiologically active gastrin, both G-17 and G-34 (13). Ele-

vated baseline serum gastrin concentrations (715 and 1000 pg/mL) decreased (down to 515 pg/mL) after intravenous secretin; there was an exaggerated increase (up to 2155 pg/mL) after the protein meal (Figure 1). Serum concentrations of prolactin (11.2 pg/mL), pancreatic polypeptide (253 pg/mL) and parathyroid hormone (25 μ L Eq/mL) were within normal limits.

Because of the low pH value of gastric aspirate during the initial esophagogastroduodenoscopy and the patient's significant epigastric discomfort, a gastric secretory study was deferred. However, the serum group I pepsinogen concentration was 200 ng/mL (normal, 25 to 100 ng/mL) and was consistent with increased gastric secretory capacity. Endoscopic retrograde cholangiopancreatography (ERCP) showed a partial obstruction of the intrapancreatic portion of the distal common bile duct. Also noted were dilatation of the proximal common bile duct (approximately 21 mm in diameter) and intrahepatic bile ducts (Figure 2). The main pancreatic duct was diffusely narrowed and was more prominent in the body and the tail. Contrast extravasation during ERCP was interpreted as representing a pseudocyst in the tail of the pancreas.

Because of the patient's persistent symptoms, surgical exploration was performed on August 17, 1987. No intra-abdominal gastrinoma was found. The pancreas was noted to be firm and appeared chronically inflamed. There were two pseudocysts in the body and

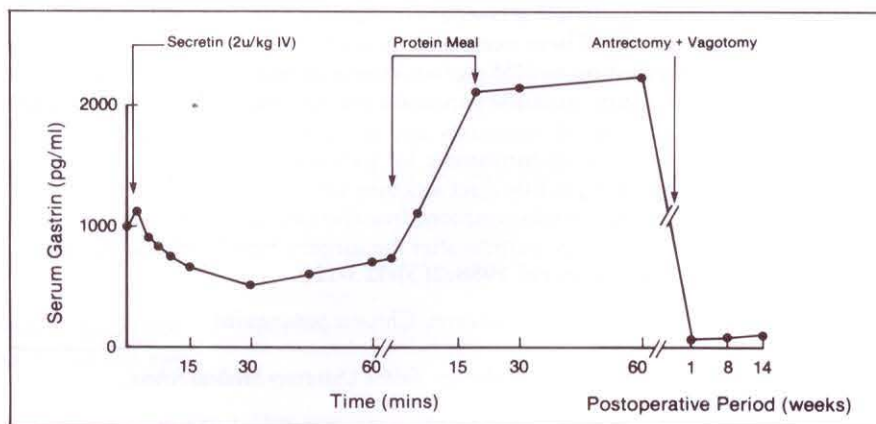


Figure 1 Serum gastrin response to the stimulation tests and after surgery. Elevated baseline serum gastrin decreased to 515 pg/mL after intravenous secretin test and increased up to 2155 pg/mL after a protein meal test. The serum gastrin levels returned to normal limits after antrectomy and vagotomy

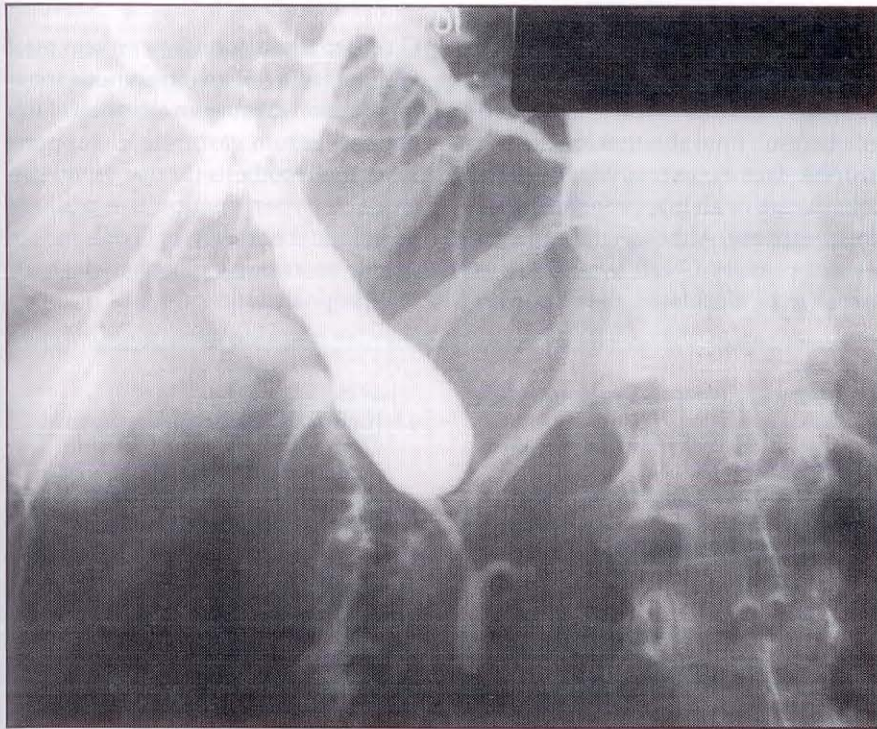


Figure 2) Endoscopic retrograde cholangiopancreatography showed a smooth partial stricture of the distal common bile duct combined with post stricture dilatation of the common bile duct and intrahepatic bile ducts. The main pancreatic duct was diffusely narrowed

tail. The following procedures were performed: pancreatic biopsy; Roux-en-Y pancreaticocystjejunostomy; cholecystectomy; Roux-en-Y choledochojejunostomy; and antrectomy and vagotomy. Pathologic exam of the pancreatic biopsy was consistent with chronic pancreatitis. The gastric antrum showed chronic hypertrophic gastritis, pancreatic acinar-type and intestinal metaplasia with G cell hyperplasia. The gallbladder showed chronic cholecystitis with cholesterosis. The patient's postoperative course was uneventful. The patient was discharged on August 26, 1987 and has remained well for at least the last five months and is now on pancreatic enzyme therapy and has gained 20 lbs. Fasting serum gastrin levels at the end of the first postoperative week, two months and three months after surgery were 11, 40 and 50 pg/mL, respectively.

DISCUSSION

Zollinger-Ellison syndrome has been classified into two types; type 1, due to antral gastrin cell hyperfunction and type 2, due to a gastrinoma (1). Characteristically, antral gastrin cell hyperfunction

patients have been mostly male, relatively young (oldest 58 years old) and have always had peptic ulcer disease with acid hypersecretion, moderate fasting hypergastrinemia with an exaggerated response to a standard test meal and a minimal gastrin response to intravenous secretin (1-8). Some of the patients in the original study (1), as well as those reported by other authors (4,5), had pre-

viously been treated by vagotomy, a condition known to result in G cell hyperplasia. The present patient had not had a prior vagotomy to account for this. The authors believe that the patient had antral gastrin cell hyperfunction with a fasting hypergastrinemia and an exaggerated gastrin response to a protein meal. Moreover, the dramatic return of hypergastrinemia to normal after antrectomy and vagotomy suggested that the antrum was the sole source of the excess serum gastrin.

This is the first reported case of antral gastrin cell hyperfunction associated with chronic pancreatitis and its complications, such as pancreatic pseudocysts and a partial common bile duct obstruction. Fasting and post prandial hypergastrinemia have been observed in patients with chronic pancreatitis (14,15). This hypergastrinemia may be secondary to chronically reduced gastric acid secretion (14). On the other hand, a more recent study indicated that patients with severe pancreatic insufficiency frequently have had gastric acid hypersecretion (15). However, none of the previous studies showed basal gastrinemia above 400 pg/mL in these patients (14,16). This association appears to be coincidental in the present case. Despite significant partial stricture of the distal common bile duct combined with dilatation of extra- and intrahepatic bile ducts, the patient's liver function tests were within normal limits.

This is the oldest patient reported with antral gastrin cell hyperfunction (1-8,12).

L'hypersécrétion de gastrine antrale associée à la pancréatite chronique

RESUME: Ce rapport décrit une patiente souffrant d'une hypersécrétion de gastrine au niveau de l'antré, chez qui on a également décelé des pseudokystes pancréatiques et une obstruction secondaire partielle des canaux biliaires suite à une pancréatite chronique. Agée de 60 ans, la patiente souffrait depuis trois mois de malaises épigastriques qui empiraient et qui s'accompagnaient de nausées, de vomissements et d'amaigrissement. Elle n'avait jamais eu d'ulcères peptiques et un examen approfondi n'en révéla aucun. La gastrinémie à jeun était de 715 et 1000 pg/mL (niveau normal de 50 à 170 pg/mL), diminuant jusqu'à 515 pg/mL durant un test de sécrétine par iv et augmentant jusqu'à 2155 pg/mL après un repas-test protéinique. Le chirurgien a effectué une vagotomie tronculaire pour corriger l'hypersécrétion de gastrine antrale, une kysto-jéjunostomie de Roux-en-Y pour les pseudo-kystes pancréatiques et une cholédocho-jéjunostomie pour l'obstruction secondaire partielle des canaux biliaires. Trois mois plus tard, tous les symptômes avaient disparu et les niveaux de gastrinémie à jeun étaient de 11, 40 et 50 pg/mL respectivement, une semaine, deux mois et trois mois après l'intervention.

Although the previously reported patients had a strong family history of peptic ulcer disease among first degree relatives and had a form of peptic ulcer that was recurrent and resistant to medical management, the present patient had neither previous nor present peptic ulcer disease nor a family history of ulcer disease. One other antral gastrin cell hyper-

function patient was reported to have had no peptic ulcer disease (5).

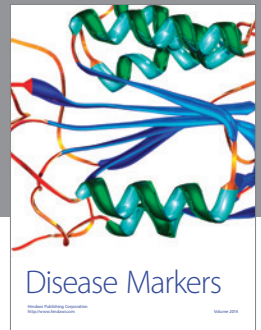
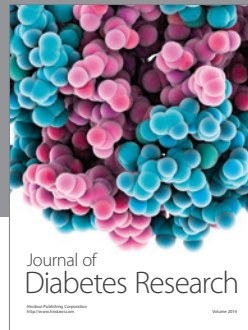
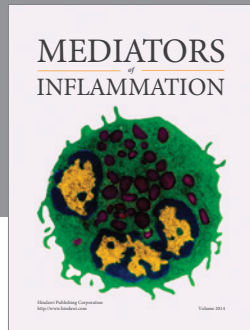
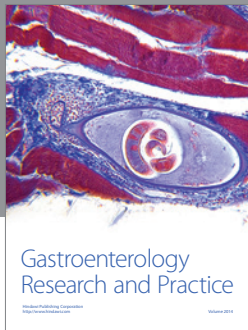
Antral gastrin cell hyperfunction might result from abnormal or excessive trophic factors, excessive neurogenic stimulation or an inappropriate physiologic response. Although the pathogenesis of primary G cell hyperplasia remains to be elucidated, the response of

G cells to stimulation by a protein meal and the failure of an intravenous secretion injection to cause an elevation of this patient's serum gastrin level supports Friesen's hypothesis (5) that antral gastrin cell hyperfunction is a primary pathologic abnormality of G cells and not merely an example of a physiologically inappropriate function.

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