The Zollinger-Ellison Syndrome

CASE REPORT

P. PANNALL, W. P. J. VAN DEN BERG

SUMMARY

Gastric acid hypersecretion and raised plasma gastrin levels were found in a young Black patient who presented with a perforated duodenal ulcer. The clinical and laboratory features are described and discussed. Although no tumour was found at laparotomy, the persistence of hypergastrinaemia after total gastrectomy confirmed the diagnosis of the Zollinger-Ellison syndrome.

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The Zollinger-Ellison syndrome is characterised by marked gastric hypersecretion secondary to a gastrin-producing tumour. Such tumours may be benign or malignant, are frequently multiple and usually occur in the pancreas or duodenum. Since plasma gastrin estimation has become available, it is apparent that the typical patient with recurrent intractable ulceration represents only part of the clinical spectrum of the disorder. Many patients present initially with symptoms of an ordinary peptic ulcer. Most patients with a gastrin-producing tumour can now be diagnosed before operation and the surgical approach modified accordingly. This report presents the clinical and laboratory findings in such a patient.

LABORATORY METHODS

Gastric acid secretion was studied in the course of a standard augmented histamine test. Specimens were collected by nasogastric tube at 15-minute intervals. The volume and pH of each was recorded and the acid content measured by titration to pH 8,0. The peak acid secretion is calculated on the two consecutive highest post-stimulation values.[1]

Plasma gastrin was estimated by radio-immunoassay. The standard used was synthetic gastrin I (ICI) and the antibody did not cross-react with secretin, glucagon or cholecystokinin. Blood from the fasting patient was taken into chilled tubes containing heparin, and was immediately centrifuged and the plasma frozen until estimation. The normal values for both White and Black patients established in our laboratory agree with those found elsewhere. Most fasting patients have values less than 100 ng/litre; a few have values between 100 and 200 ng/litre. Levels above 200 ng/litre are considered elevated.

Departments of Chemical Pathology and Surgery, Bloemfontein Academic Hospitals and University of the Orange Free State, Bloemfontein

P. PANNALL, F.F. PATH. (S.A.), M.R.C. PATH.
W. P. J. VAN DEN BERG, M.MED. (CHIR.)

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CASE REPORT

First Admission (20 August 1972)

The patient, a 37-year-old Black male was admitted to the surgical wards at Pelonomi Hospital with a 1-month history of epigastric pain and dyspepsia after meals. During this period he had vomited several times (not blood-stained) and had noted the passage of melaena stools. He had also lost weight. On examination he was anaemic and apyrexial. There was clubbing of the fingers and diminished air entry at the base of the right lung. An ill-defined mass was noted in the epigastrium.

Special Investigations

He had a normochromic, normocytic anaemia with a haemoglobin concentration of 8,6 g/100 ml and a leucocyte count of 16 700/μl. The erythrocyte sedimentation rate (Westergren) was 102 mm/h. Plain X-ray films showed free air under the right diaphragm. Since the patient refused surgery, he was given blood transfusions and managed conservatively.

A barium meal 2 weeks later revealed a penetrating ulcer in the first part of the duodenum. At gastroscopy no gastric pathology was found. The duodenoscope could not be passed through the pylorus. The diagnosis of a sealed-off perforation of a duodenal ulcer, with bleeding from the ulcer, was made.

The results of the gastric acid tests on two occasions are shown in Table I. The very high basal secretion with little increase after histamine stimulation suggested the possibility of the Zollinger-Ellison syndrome.

The fasting plasma gastrin level was raised (580 ng/litre) and failed to respond to food intake (Fig. 1). These findings were again strongly in favour of the Zollinger-Ellison syndrome.

Since a gastrin-secreting tumour may be part of multiple endocrine adenomatosis, the following tests were done, with results all within normal limits: serum calcium 10,2 mg/100 ml (N 8,6 - 10,5); urinary 11-hydroxycorticosteroids 282 μg/24 hours (N 80 - 400); urinary 17-oxosteroids 5,4 mg/24 hours and total 17-oxogenic steroids 12,1 mg/24 hours.

Since the patient still refused surgery, he was discharged on 15 November 1972 on conservative ulcer treatment.

TABLE I. RESULTS OF THE AUGMENTED HISTAMINE TEST OF GASTRIC ACID SECRETION

	Basal			Post-histamine		
	Volume (ml/h)	pH	Acid content (mEq/h)	Volume (ml/h)	pH	Peak secretion (mEq/h)
1st test (11 October 1972)	136	1,5	20,5	81	1,0	11,2
2nd test (18 October 1972)	106	1,0	15,3	97	1,0	16,0

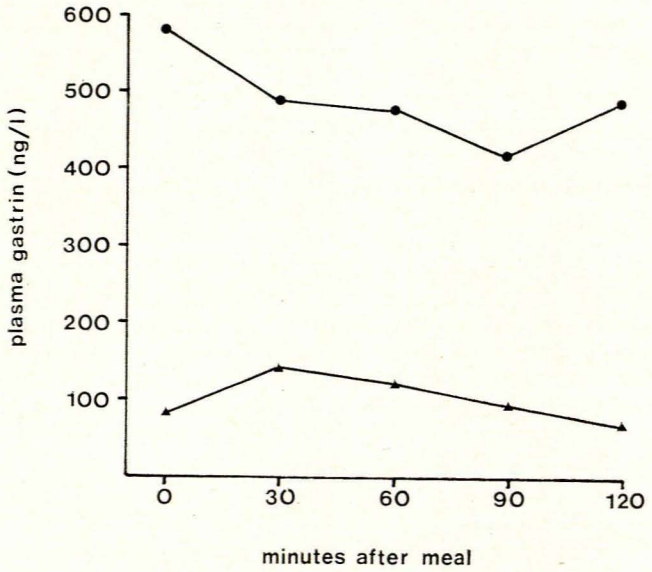

Fig. 1. Plasma gastrin levels in patient (•——•) and normal control (▲——▲) after a meal.

Second Admission (27 December 1972)

Six weeks later he was readmitted after 5 days of severe epigastric pain not alleviated by antacids. This was associated with coffee-ground vomitus and melaena stools. He denied recent ingestion of salicylates or alcohol. On examination he was again anaemic and slightly dehydrated. The blood pressure was 100/70 mmHg and the pulse rate 120/minute. There was slight epigastric tenderness.

Special Investigations

There was again a normochromic, normocytic anaemia (haemoglobin 8,6 g/100 ml), a leucocytosis (27 600/mm^3) and thrombocytosis (520 000/μl). The serum electrolyte concentrations were normal and the results of relevant serum tests were as follows: total protein 5,7 g/100 ml; albumin 3,5 g/100 ml; alkaline phosphatase 33 IU/litre (N 25 - 100); urea 107 mg/100 ml; amylase 208 IU/litre (N less than 350). The fasting plasma gastrin level was again raised at 520 ng/litre. X-ray examination showed poor movement of the right dome of the diaphragm, but no free air was seen.

The patient received 5 units of blood and was intensively prepared for surgery.

Operation (7 January 1973)

The abdomen was explored through a transverse incision halfway between the umbilicus and the xiphisternum. Dense adhesions due to the previous perforation were found between the stomach and duodenum and the liver, head of the pancreas and the spleen. These were freed and the lesser sac entered by division of the gastrocolic omentum. The body and tail of the pancreas were mobilised and inspected. Two suspicious nodules proved, on frozen section, to be lymph nodes with reactive hyperplasia and haemosiderosis. After Kocher's manoeuvre the head of the pancreas was inspected and found to form the base of the penetrating duodenal ulcer. Because of this, and oedema of the area, effective evaluation of the head of the pancreas for a gastrin-producing tumour was impossible.

A total gastrectomy was performed. Luminal palpation of the second part of the duodenum revealed no ectopic pancreatic tissue. The duodenum was closed and a Hunt-Lawrence pouch reconstruction performed (Fig. 2). No hepatic secondaries nor other intra-abdominal pathology were found. The incision was closed with two drainage tubes.

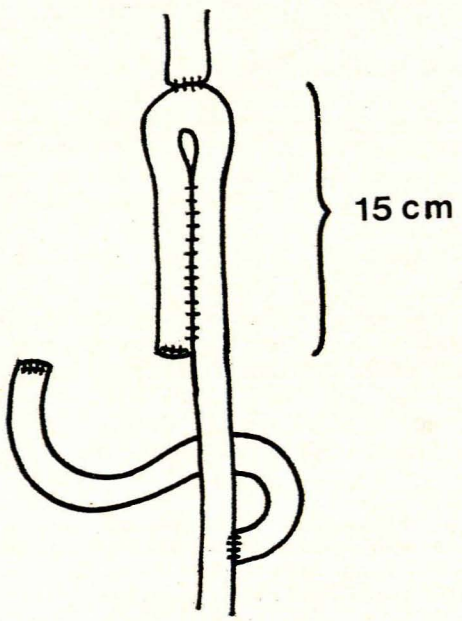

Fig. 2. See text.

The postoperative course was uneventful and the patient was discharged 12 days after operation. The elevated serum urea had returned to normal.

Histological examination of the stomach showed mild chronic gastritis. No parietal cell hyperplasia was noted.

The plasma gastrin level 6 weeks after total gastrectomy was 800 ng/litre.

DISCUSSION

The features of the Zollinger-Ellison syndrome have recently been fully reviewed.[2,3] Some of the findings of the more than 800 cases collected in the Zollinger-Ellison Tumor Registry[2] are outlined below with the corresponding findings in our patient in parentheses. The mean age at onset was 38 years (37 years) with a male to female ratio of 3 : 2 (male). Only 20% had had symptoms for less than one year (1 month). Epigastric pain was the most common feature (present) and about 30% had diarrhoea (not a feature). In almost 30% there was evidence of other endocrine adenomas (not found).

The condition is suggested by gastric acid studies. A high basal acid secretion (greater than 15 mEq/hour) is not diagnostic, but relatively poor increase after stimulation indicates an already almost maximally stimulated parietal cell mass. Patients with peptic ulcers and an increased parietal cell mass usually show a marked increase in acid secretion after histamine stimulation. In the Tumor Registry series, the basal acid secretion was more than 60% of the maximal acid output (as in our case) in 70% of cases. This finding is not diagnostic, but hypersecretion indicates the need for further studies.

The diagnosis should be confirmed by plasma gastrin estimation. Levels of greater than 500 ng/litre are usually found. Such values are also seen in some patients with achlorhydria and in patients with an isolated pyloric antrum after Bilroth II gastrectomy. In both these instances, gastrin secretion from the pyloric antrum is not under the inhibitory influence of gastric acid. For this reason, plasma gastrin values can only be properly interpreted if gastric acid secretion is known. High levels may also occur in patients with severe renal failure.

Moderately elevated gastrin levels may present a problem. Berson and Yalow[4] used the response to a standard meal to evaluate such patients (Fig. 1). Where the hypergastrinaemia is of antral origin, such a meal is followed (as in normals) by a rise in plasma gastrin. In the Zollinger-Ellison syndrome, the gastrin-secreting tumour is not affected by the meal and there is no rise. It is presumed that the normal gastrin-producing antral cells are suppressed by the high acid secretion of the stomach. The response to calcium infusion and secretin has also been used,[2] but these tests were not done in our patient.

Other causes of hypergastrinaemia in patients with peptic ulceration include pyloric obstruction and presumed primary hyperplasia of antral gastrin-producing cells.[2] In our patient, the persistence of high plasma gastrin values after total gastrectomy excludes an antral origin, and illustrates the value of this estimation in confirming the diagnosis when no tumour can be found.

REFERENCES

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