THE ZOLLINGER-ELLISON SYNDROME

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by
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THE ORIGINAL PAPER of Zollinger and Ellison in 1955 called attention to a syndrome characterized by peptic ulceration of the jejunum associated with a non-beta islet cell pancreatic tumour. Since that date some 300 papers upon the subject have been published, and it has become clear that the syndrome should now be re-defined.

In the majority of cases the peptic ulceration is normally situated in the stomach or the first part of the duodenum, and in only about 25 per cent of cases is the ulceration at unusual sites. Gastric hypersecretion is present in well over 90 per cent of cases, and it can usually be shown that this is caused by a hormone, indistinguishable from gastrin, secreted by the pancreatic tumour tissue. The tumour itself in the pancreas is malignant in some 60 per cent of cases and, even when benign, is likely to be present at more than one site. The cells of the tumour are not beta cells but either alpha cells or agranular cells. Diarrhoea is a common accompaniment of the syndrome and this may be caused by the severe jejunitis consequent upon the gastric hypersecretion or by the direct effect upon the intestine of some additional hormone other than gastrin. In a small number of cases very severe diarrhoea is present without gastric hypersecretion or peptic ulceration.

When we consider treatment of this syndrome it must be accepted that the effect of resection of the tumour is not likely to be as successful as resection of a beta cell tumour because the tumour is more likely to be malignant, sometimes with functioning metastases, and when benign is more likely to be multiple. In addition it has to be remembered that patients dying of this syndrome usually die from the complications of peptic ulceration, i.e. of haemorrhage, perforation or peritonitis. For this reason it has sometimes been suggested that, even if it appears possible to remove the pancreatic tumour, total gastrectomy should still be the surgical procedure of choice.

Seven cases of the Zollinger-Ellison syndrome have been encountered and these will be briefly summarized with particular reference to whether or not total gastrectomy appeared to be indicated.

1. A lady of 49 first attended St. George's Hospital in 1942 when a nodular goitre was removed. In 1954 a gastrectomy was performed for a large stenosing duodenal ulcer and a distal pancreatectomy and splenec-

tomy was carried out at the same time for what proved to be a malignant non-beta islet cell tumour. She remained well for two years, but between 1956 and 1957 she had several operations for recurrent stomal ulceration. She was seen by the writer for the first time in December 1957 and underwent a laparotomy at which a large recurrent islet cell carcinoma was found and considered to be inoperable. She died on 31st January 1958.

2. A man born in 1919, operated upon in March 1951 by Mr. Norman Tanner, had a gastrectomy for a large duodenal ulcer (Fig. 1). Repeated operations for stomal ulceration followed and in June 1958 a non-beta cell tumour was removed from his pancreas, the pathology report suggesting

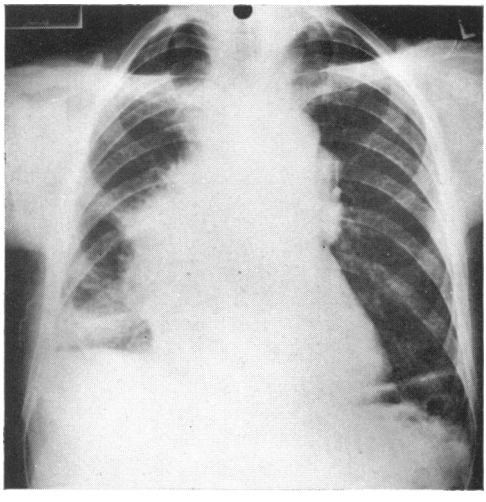

Fig. 1. Chest X-ray from a man (Case 2) treated by multiple surgical operations, including distal pancreatectomy and total gastrectomy. Death finally resulted from this massive metastatic carcinoma in the chest.

that the tumour was benign. At the time of removal of the tumour he also had a total gastrectomy. In October 1963 a huge mass appeared in the mediastinum and a biopsy of this showed it to be a recurrence of the original tumour, which was now realized to be malignant. In December 1964 he died from the effects of this mediastinal mass.

The daughter of this patient had already had a beta islet cell tumour removed from her pancreas.

The patient himself, before he died, developed hyper-parathyroidism and an adenomatous enlargement of his prostate.

3. A lady aged 38 in 1956 had a laparotomy for a huge duodenal ulcer and marked gastric hypersecretion (12-hour gastric secretion over 4 litres

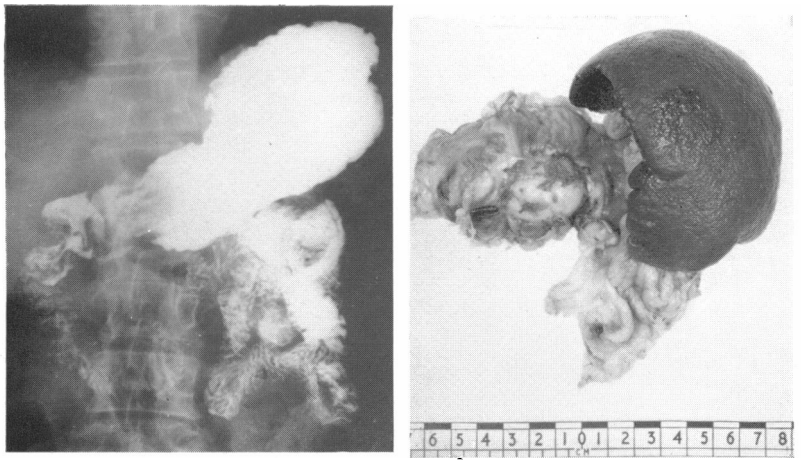

Fig. 2. (*a*) Barium meal showing a large benign duodenal ulcer (Case 3). (*b*) Distal pancreatectomy specimen showing the large malignant non-beta islet cell tumour, removal of which resulted in healing of the ulcer, the patient being well nine years later.

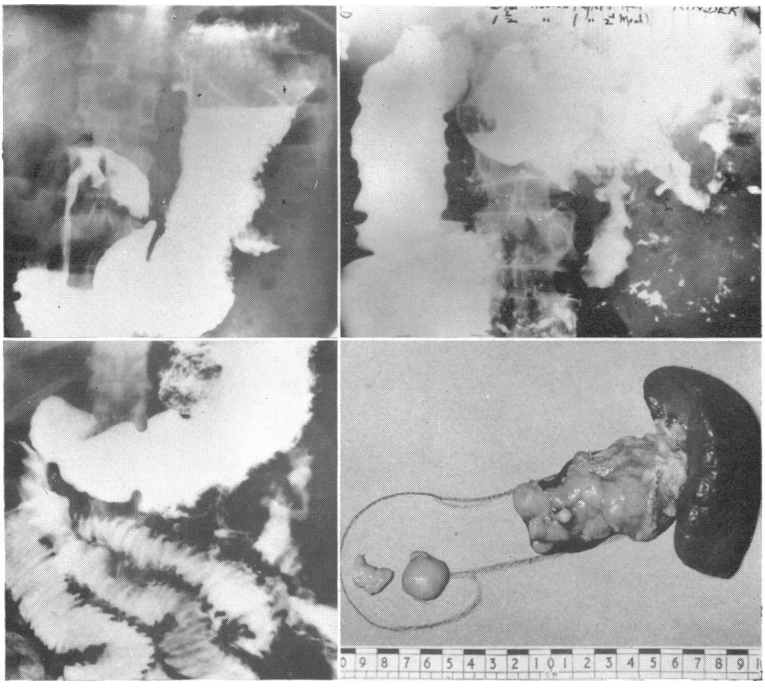

Fig. 3. (*a*) Barium meal showing gross ulceration and distortion of stomach and duodenum (Case 4). (*b*) Several deep jejunal ulcers present in the same case. (*c*) Appearance of the small intestine. (*d*) Distal pancreatectomy and enucleation of two adenomas from the head of the pancreas removed in all nine individual benign adenomas of the pancreas, each being a non-beta islet cell tumour. The same patient later had three parathyroid tumours removed. She is well eight years later.

with 425 mEq. HCl) (Fig. 2). At her operation a tumour in the distal pancreas was found and this was treated by distal pancreatectomy. The tumour was shown to be a malignant non-beta islet cell tumour with one

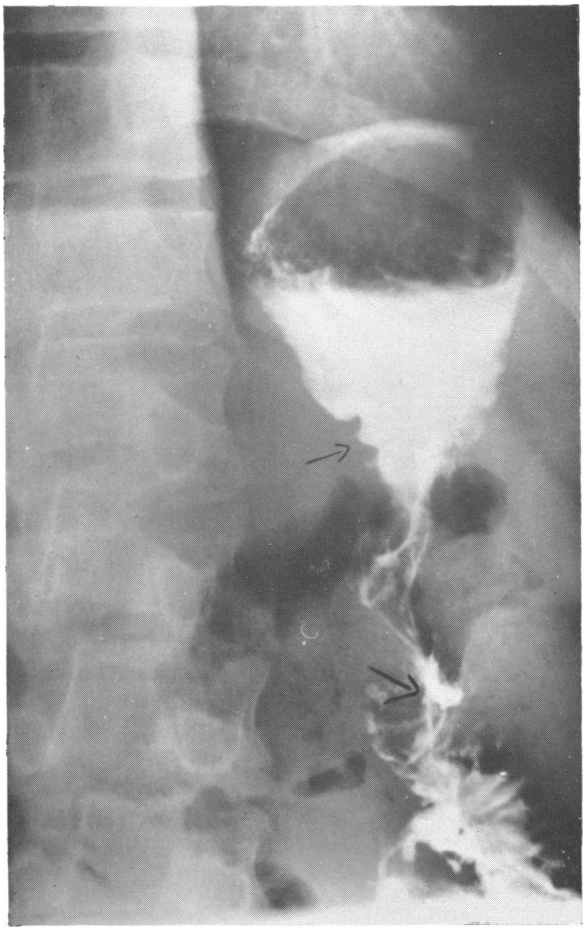

Fig. 4. (*a*) Barium meal five weeks after an emergency gastrectomy for haemorrhage in a young man (Case 6). Already two new ulcers are present.

lymph node in the hilum of the spleen containing metastatic tumour. The stomach was not removed. The patient has remained well.

4. A lady of 30 in 1957 was found to have multiple peptic ulcers with severe gastric hypersecretion (12-hour secretion 7½ litres containing 750 mEq. HCl). Subtotal pancreatectomy was carried out for multiple benign adenomas. Later the demonstration of hyper-parathyroidism led

to the removal of three parathyroid adenomas. The stomach was not removed and the patient remains well (Fig. 3).

5. A lady of 35 in 1962 had, at another hospital, a cholecystojejunostomy for obstructive jaundice caused by a tumour in the head of the pancreas. Repeated severe gastric haemorrhages followed. In 1963 she was referred to the writer and underwent a radical pancreato-duodenectomy together with removal of three-quarters of the stomach. The portal vein appeared to contain a thrombus, but when this was removed by venotomy it was found to be tumour tissue. Histologically the tumour

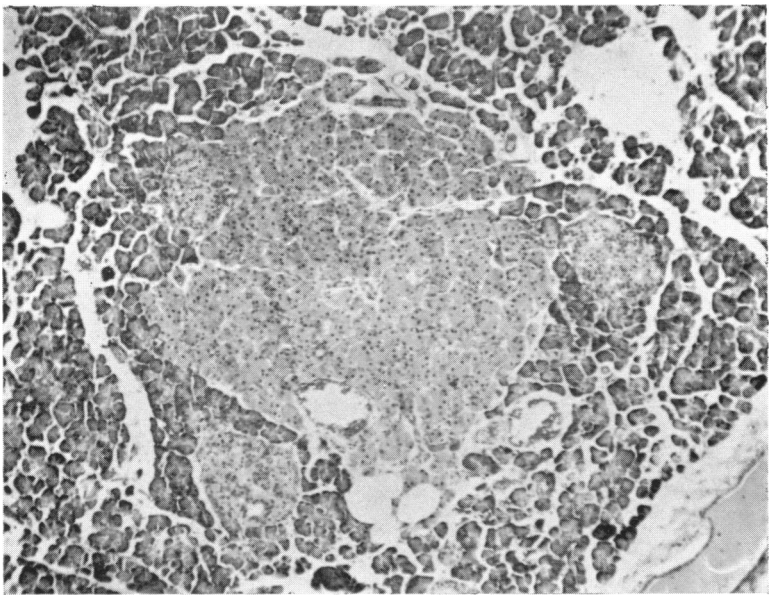

Fig. 4. (*b*) Subtotal distal pancreatectomy in Case 6 has shown the pancreas to be the site of micro-adenosis.

was shown to be a non-beta islet cell carcinoma and the source of the bleeding was a huge peptic ulcer of the duodenum.

The patient is still alive but in poor health, the main symptom being diarrhoea.

6. A man of 27 in 1964 underwent an emergency gastrectomy for haemorrhage, the bleeding coming from a very large duodenal ulcer. Within six weeks two new ulcers had appeared (Fig. 4*a*), one above and one below the anastomosis. Exploration was undertaken with a diagnosis of a possible Zollinger-Ellison syndrome. The pancreas was grossly normal. Subtotal gastrectomy and vagotomy was carried out, together with distal

pancreatectomy. The histology of the pancreas showed clearly micro-adenosis of a non-beta cell pattern affecting particularly the tail of the pancreas (Fig. 4*b*). The patient remains well one year later.

7. A lady of 65 in 1963 was admitted to hospital with very severe diarrhoea, losing per rectum more than 10 litres of fluid daily. She had no peptic ulceration or gastric hypersecretion. Investigation suggested that this was a variant of the Zollinger-Ellison syndrome. In November 1963 exploration of the abdomen was undertaken and two tumours were enucleated from the head of the pancreas. On histological study one of

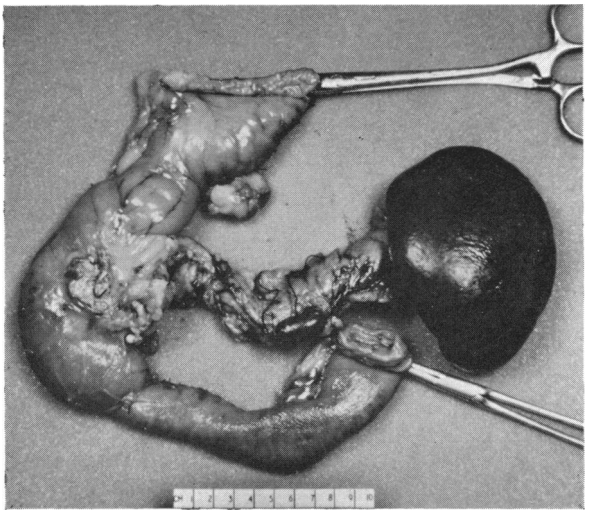

Fig. 5. Total pancreatectomy specimen from a patient (Case 7) with severe diarrhoea caused by a multi-focal non-beta islet cell carcinoma of the pancreas.

these was seen to be a malignant non-beta islet cell tumour, the other a metastatic lymph node. This operation had no useful effect in checking the diarrhoea. Two weeks later a total pancreatectomy was performed and the pancreas was shown to contain multiple deposits of non-beta islet cell carcinoma (Fig. 5). The patient remains well, though her diarrhoea recurs if she is not maintained still on steroid therapy.

From this series of cases it appears that in some circumstances it is logical to treat the Zollinger-Ellison syndrome by resection of the pancreatic tumour or tumours without recourse to total gastrectomy.

REFERENCE

ZOLLINGER, R. M., and ELLISON, E. H. (1955) *Ann. Surg.* **142,** 709.