

Subsequent upper and lower gastrointestinal endoscopic surveillance has shown recurrent benign fundic and rectal polyps which were amenable to local resections. Three years after the original laparotomy she remains well with no evidence of carcinoma recurrence and the desmoid tumours remain fairly constant in size. Since there is a high risk of further polyps and cancers growing in the rectal stump, she has been advised to undergo lifelong endoscopic surveillance.

COMMENT

Familial adenomatous polyposis is characterized by the presence of hundreds to thousands of adenomatous polyps throughout the colon and rectum. Some of the tumours will undergo malignant transformation if left and the only effective treatment is prophylactic colectomy. The offspring of a patient with familial adenomatous polyposis has a 50% chance of inheriting the gene defect and, until recently, screening for symptom-free individuals has consisted of regular colonic examinations³. This would typically begin around puberty and continue for about 20 years.

With the localization of the adenomatous polyposis coli (APC) gene to chromosome 5q21 and its subsequent characterization, it has become feasible to screen at-risk individuals with a one-off genetic test instead of repeated colonic examinations. Many different mutations have been identified by molecular analysis of the APC gene but each mutation seems to be unique to that family.

Zollinger–Ellison syndrome with fasting hypoglycaemia

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For a neuroendocrine tumour to secrete multiple peptides is not unusual. For more than one of these peptides to be functional is uncommon. We report such a case.

CASE HISTORY

A 71-year-old woman was brought to casualty after an episode of syncope. She had been fasting in preparation for

The family screening process is typically initiated when a patient is diagnosed with polyposis. All first-degree relatives would be traced and screened, and, if found positive, their offspring would also be investigated. With the use of a regional polyposis register, both the age at diagnosis of familial adenomatous polyposis and the incidence of cancer are reduced⁴.

In this unusual case it was the offspring who was found incidentally to have a disruption of chromosome five around the site of the APC gene; and the death of the patient's father from colonic carcinoma at the unusually early age of 29 years was another pointer to the possibility of an underlying genetic cancer syndrome. With the family history, the previous history of multiple cysts and an osteoma, the diagnosis of Gardner's syndrome was suspected and later confirmed in the patient. The child himself will be at risk of polyposis in later life and requires long-term follow-up.

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a barium enema, which had been arranged because of a six-week history of profuse diarrhoea and associated weight loss of about 5 kg in three months. The patient also complained of episodes of epigastric discomfort. The only relevant medical history was the recent diagnosis of hypothyroidism, based on a plasma thyroxine of 39 nmol/L (normal 50–150) and thyroid stimulating hormone of 90 mU/L (0.5–5.0). The only medication on admission was eltroxin; in particular, she was not taking a non-steroidal anti-inflammatory drug.

On initial examination she was thin, pale and clammy with a sinus tachycardia of 120 beats per minute. A four-finger non-tender hepatomegaly was palpable and she was faecal occult blood positive.

Glucose was 1.1 mmol/L (normal 0.8–8.3), erythrocyte sedimentation rate 60 mm/h, lactate dehydrogenase 890 IU/L (240–450), aspartate aminotransferase 57 IU/L (7–40), albumin 30 g/L (35–50). Abdominal ultrasound showed multiple echogenic lesions scattered throughout the liver. A computerized tomographic scan confirmed the presence of these lesions, which were consistent with liver metastases. Gastroscopy revealed grade three oesophagitis,

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antral erosions and multiple deep bulbar and post-bulbar duodenal ulcers. A negative urease test and histological and microbiological studies from antral biopsies and corpus biopsies indicated the absence of *Helicobacter pylori* infection. There was no evidence of recent bleeding and a barium enema was reported as normal.

In view of the severity of ulceration revealed endoscopically, the patient was started immediately on omeprazole 20 mg twice daily. An ultrasound guided liver biopsy was then performed, yielding a sample with strong chromogranin staining, indicating the presence of a peptide secreting tumour. Electron microscopy showed numerous tumour cells with large secretory granules that stained immunohistochemically for gastrin and thyroid stimulating hormone. Blood taken earlier showed a fasting serum gastrin 1000 ng/mL (<100), insulin 1.5 ng/mL (0.5–1.0), calcitonin >1000 ng/mL (<150) and thyroid stimulating hormone of 103 mU/L. Other laboratory tests including cortisol, adrenocorticotrophic hormone, parathyroid hormone, and urine screen were normal. A repeat gastroscopy after four weeks showed complete resolution of all peptic ulceration. She remained well one year later, on maintenance omeprazole together with a long-acting somatostatin analogue to control hypoglycaemic episodes and diarrhoea.

COMMENT

In this patient the symptoms were due to two peptides—gastrin and an insulin-like peptide. Neuroendocrine tumours (NETs) represent 2% of all gastrointestinal malignancy and the clinical syndromes include carcinoid, Zollinger–Ellison and hypoglycaemia¹. In a study from Austria, 6% of all NETs were gastrinomas². The incidence of Zollinger–Ellison syndrome is estimated at 1 per million.

One-third of gastrinomas occur in association with multiple endocrine neoplasia type 1: 60% are malignant and over 98% arise from the pancreas. A high fasting gastrin

together with high basal gastric acid output is diagnostic. In the case reported here we did not measure basal acid output because we already had histological and immunohistochemical confirmation of a gastrin secreting NET. Serum gastrin can be raised by achlorhydria, so it is important to note that our specimens were taken before treatment with a proton pump inhibitor.

The management of gastrinomas and other NETs is mainly symptomatic. In Zollinger–Ellison syndrome the mainstay is a proton pump inhibitor such as omeprazole 80–120 mg/day, which will offer complete resolution in 98% of cases at two weeks and 100% at one month. Of interest in this case is the complete resolution of severe peptic ulceration on a lower dosage of omeprazole, which was begun before full diagnosis. Despite developments in therapy, the prognosis in cases unsuitable for resection (the majority) remains poor. In patients with liver metastases 5-year survival is about 25%.

This case highlights the need for extensive investigation of patients in whom peptic ulceration is not associated with *H. pylori* infection or use of non-steroidal anti-inflammatory drugs. Peptic ulceration may result from increased gastric acid secretion, stimulated by raised calcium levels (as seen with parathyroid hormone secreting tumours and renal failure), or raised histamine levels (as in the rare disorder systemic mastocytosis). Ulcer formation may also result from decreased secretion of bicarbonate into the duodenum, as happens in liver cirrhosis and chronic pancreatitis. Other rare causes are varicella-zoster virus and Crohn's disease.

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