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Carcinoid syndrome without liver metastasis

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Summary: The carcinoid syndrome generally occurs due to metastasis of a carcinoid tumour in the liver. A patient is presented who had carcinoid syndrome due to abdominal disease without hepatic metastasis.

Introduction

The carcinoid syndrome arises from the systemic effects of the vasoactive substances produced by the tumour and in 95% of patients is associated with extensive hepatic metastasis from the primary tumour in the gastrointestinal tract. We present a patient with features of the carcinoid syndrome in the absence of hepatic metastasis.[1]

Case report

A 31 year old male Somali presented with a 9-month history of episodic watery diarrhoea and lower abdominal pain with cramps and borborgymi. He felt warm, sweaty and profoundly weak following the diarrhoeal episodes. The frequency of the diarrhoea varied between 15 to 20 times per day. His symptoms of diarrhoea, palpitations and dizziness occurred spontaneously but could be precipitated by food. The patient had intense and generalized pruritus and had lost 10 kg in weight over the previous 9 months. Occasionally his stool was black. He denied any history of bronchial asthma or laxative abuse.

Physical examination showed him to be hyperpigmented but there was no facial flush. His tongue had a violaceous hue. The skin over his limbs and the trunk showed multiple scratch marks. He had occasional tachycardia of 120 per minute with hypotensive episodes of 90/60 mmHg. In the paraumbilical area, there was a soft tender, mobile, ill defined mass measuring about 10 cm by 10 cm. The surface was irregular and no bruit was heard over the mass. No ascites or organomegaly was detected. Rectal examination was normal.

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Initial laboratory investigations showed hypochromic microcytic anaemia (haemoglobin 10.9 g/dl) with a normal leucocyte count and erythrocyte sedimentation rate. Thyroid and liver function tests were normal.

Repeated stool examination for parasites, bacteria and stool cultures were negative. Chest X-ray was normal. Ultrasound examination of the abdomen revealed a heterogeneous solid mass in the central abdomen. Small bowel contrast study showed some thickening of the mucosa of the jejunum and the ileum. Barium enema, upper gastrointestinal endoscopy and colonoscopy examinations were normal.

A laparoscopic examination of the abdomen was normal except for mild thickening of the serosal surface of the small bowel. At this point the patient refused to undergo laparotomy for further investigations. As tuberculosis of the small intestine was considered to be a likely diagnosis, a trial with rifampicin, isoniazid and ethambutol was commenced. The frequency of diarrhoea reduced to 2–4 times per day and on discharge the patient was followed in the medical clinic at regular intervals. The patient claimed that the episodic diarrhoea had become quiescent and abdominal pain was less. The patient had gained 7 kg in weight over a 6 month period.

However, 7 months after discharge from the hospital the diarrhoea relapsed. The abdominal mass remained unchanged clinically but computed tomography of the abdomen showed enlargement of several para-aortic lymph nodes.

He was readmitted and cytological examination of specimens obtained by ultrasound guided fine needle aspiration of the enlarged para-aortic lymph nodes showed adenocarcinoma. At laparotomy a 50 cm segment of the distal jejunum and proximal ileum containing multiple yellowish nodules along with its mesentery and mass of matted lymph nodes was

excised in block. The mass of matted lymph nodes was situated in front of the aorta 1 cm above the bifurcation. This mass of lymph nodes was adherent to the aortic sheath but was removed as a whole. Palpation of the para-aortic gutter did not reveal any other palpable lymph node. Other organs including the liver, stomach, spleen, rectum and colon were normal. Section of the bowel showed multiple yellowish nodules on the serosal surface with fibrous thickening (Figure 1). Histological examination of the resected segment revealed multiple tumours arising from the muscosa, invading the submucosa and muscle layer and often reaching the serosa. The tumour nodules were composed of solid rounded groups of small regular cells with rounded nuclei and very few mitotic figures. Histology of the metastatic deposits of tumour showed that the tumour was partially replaced with fibrosis and the mesenteric mass consisted of invaded lymph nodes. A silver stain produced a strong argentaffin reaction. Electron microscopy showed epithelial tumour cells with neurosecretory granules, confirming that the patient had carcinoid tumours (Figure 2).

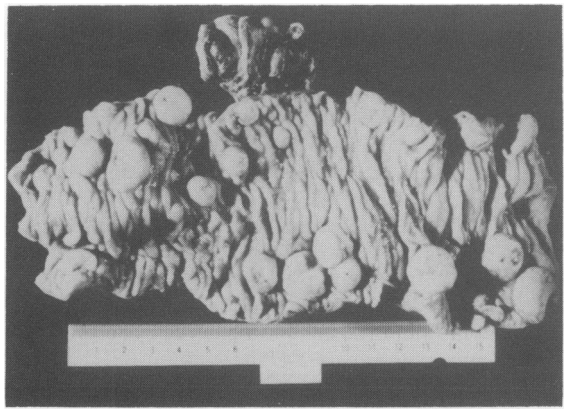

Figure 1 Section of bowel showing multiple yellowish nodules on the serosal surface with fibrous thickening.

Post-operatively 24-hour urine collection for 5-hydroxyindole acetic acid (5HIAA) estimation was negative. The patient was discharged without any medication and followed up in the clinic for 18 months. Ten months after laparotomy, a repeat ultrasound examination did not reveal any evidence of enlarged para-aortic lymph node. Further estimation of 24-hour urine for 5HIAA in the outpatient clinic was normal. He had complete remission of symptoms.

Discussion

The carcinoid syndrome comprises facial flushing, diarrhoea, wheezing and cardiac valvular lesions with right sided cardiac failure. It is a rare clinical entity and Linell & Mansson[2] stated that two new cases would occur in a population of 250,000 over 10-year period. In 95% of symptomatic cases there are hepatic metastases.[3] In the remaining 5%, the syndrome is not associated with metastasic disease of the liver.[3]

Feldman[1] has recently described three patients with gastrointestinal carcinoid who had carcinoid syndrome without liver metastasis. In one of these, the

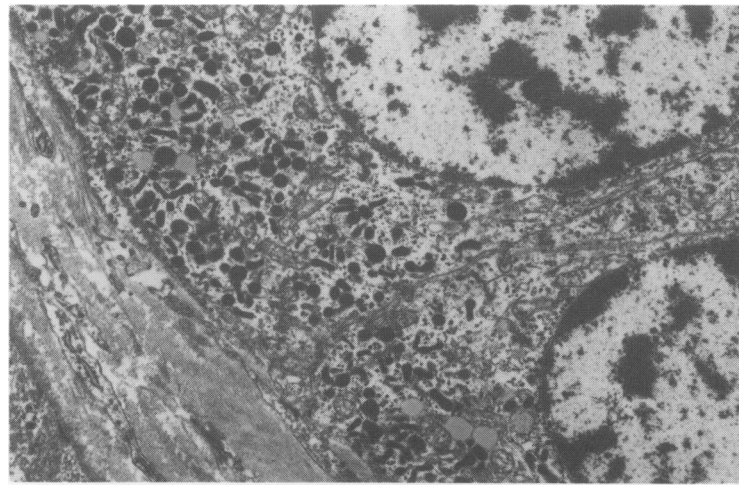

Figure 2 Electron microscopy showing cytoplasmic neurosecretory granules (× 8470 magnification).

carcinoid tumour was limited to the proximal ileum with adjacent local lymph node involvement and there were no obvious metastases draining into the systemic circulation. Our patient is similar to this since no secondary deposits were noted in the liver at operation or by imaging techniques such as ultrasonography and computed tomography of the liver and abdomen.

The mechanism of the carcinoid syndrome without hepatic involvement is not clear. It has been suggested that vasoactive products may be absorbed from the peritoneal surface or taken to the systemic circulation in lymph draining the area around the tumour nodules thus avoiding the usual metabolic degradation by the liver.[3] In cases of bronchial or ovarian carcinoids, the chemical mediators directly drain into systemic circulation.

Paroxysmal facial flushing is present in 90% patients with carcinoid syndrome.[4] This patient had no facial flushing but his tongue showed a violaceous discolouration. Grahame-Smith[5] described violaceous discolouration of the face, neck and upper trunk. It may be that in a dark skinned person, violaceous discolouration may be better observed in the mucous membrane of the tongue. In addition to the discolouration of the tongue, our patient had other skin manifestations such as generalized intense pruritus and a generalized warm feeling associated with symptoms of vasodilatation. As carcinoid syndrome was not suspected clinically in our patient 5 HIAA was not done initially to confirm the diagnosis biochemically.

In patients without the classical symptomatology there is often delay in diagnosis. This period may vary between 1–3 years and on occasion up to 10 years.[6] To diagnose the carcinoid syndrome, the clinician must have a high index of suspicion even in patients without hepatic metastasis.

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