A CASE OF PRIMARY DUODENAL CARCINOMA AND SMALL BOWEL LEIOMYOMAS IN A PATIENT WITH NEUROFIBROMATOSIS

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SYNOPSIS

A 75 year old Chinese male with neurofibromatosis presented with gastrointestinal bleeding was found to have a primary duodenal carcinoma on barium meal examination, endoscopy and biopsy. At laparotomy multiple leiomyomas were discovered on the serosa surface of jejunum and ileum. The occurrence of a primary duodenal carcinoma with small bowel leiomyomas in a patient with neurofibromatosis has not been reported before. It suggests that a defective immune surveillance may be present in this patient thereby predisposes to multiple tumour occurrence.

INTRODUCTION

Neurofibromatosis, an autosomal dominantly inherited disease occurs once in every 3,000 live births (1). The disease has varied manifestations in the skin, nervous tissue, bone and soft tissues. Gastrointestinal tract may also be involved with multiple neurofibromas giving rise to obscure gastrointestinal bleeding and obstruction (2). The severity of cutaneous lesions, however, bears no relationship to the presence of disease in other tissues (3).

An increased incidence of neoplasms is well documented in association with neurofibromatosis. Pheochromocytoma, glioma, neurinoma, nephroblastoma (4) and acute leukaemia (5) had been reported to be associated with neurofibromatosis.

Present case report describes an unusual occurrence of a primary adenocarcinoma of duodenum with small intestinal leiomyomas in a patient with neurofibromatosis. We have been unable to find any record of such an association in the literature.

CASE REPORT

A 75-year-old Chinese male was admitted to the University Department of Medicine (II), Singapore General Hospital with a history of fever, anorexia, passing tea coloured urine and slight hypochondrial discomfort for one week. Since early puberty he had developed multiple soft painless skin lesions over his face and body. There was no significant past medical history of note and no family history of similar skin lesion.

On examination, he was febrile, wasted and moderately jaundiced. He had generalised cutaneous neurofibromatosis and cafe-au-lait spots. There were clubbing of fingers. The liver was 3 cm below the right costal margin and it was smooth, firm and slightly tender. There was no evidence of hepatic failure or portal hypertension.

Investigations revealed haemoglobin of 13 gm/100 ml, a total white count of 10,300 per mm^3. The sedimentation rate was 90 mm in first hour. The blood urea and electrolytes were normal. Serum bilirubin was 7.6 mg/100 ml, serum glutamic pyrivic transaminase of 69 units (normal range 9 - 33 units), serum alkaline phosphatase of 135 international units (normal up to 100 international units), serum protein 6.9 gm/100 ml and serum albumin 3.1 gm/100 ml. Hepatitis B antigen was negative by counter-immunoelectrophoresis technique and alpha-feto protein was negative by immuno-diffusion technique. Liver biopsy confirmed the diagnosis of acute viral hepatitis.

His clinical condition improved with bed rest. He became afebrile and his appetite returned to normal.

However two weeks after admission he was noticed to be pale and he complained by passing dark stools. Haemoglobin was 10.1 gm/100 ml. Barium meal examination showed a very large fungating mass in the second part of duodenum shown in (Figure 1).

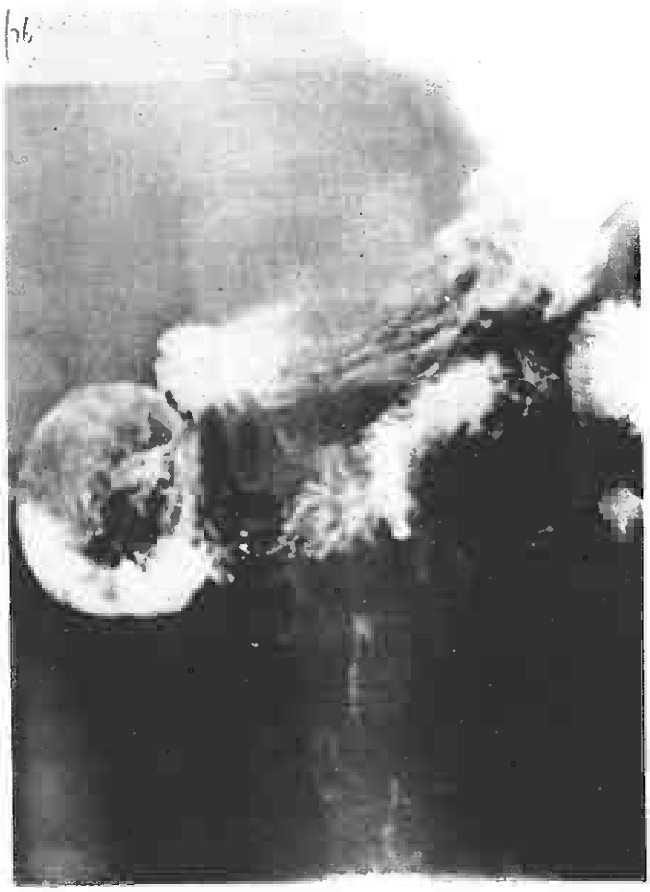

Figure 1. Barium meal examination showing presence of a large tumour in the second part of duodenum.

Oesophago gastroduodenoscopy using Olympus GIF-D_3 fiberoptic endoscopy showed a large ulcerated fungating tumour present in the intra-ampullary region of the duodenum (Figure 2). The ampulla of Vater was not obstructed by the tumour mass. The oesophagus and stomach were normal. Several biopsies were taken from the tumour mass. The histology revealed papillary adenocarcinoma of the duodenum (Figure 3).

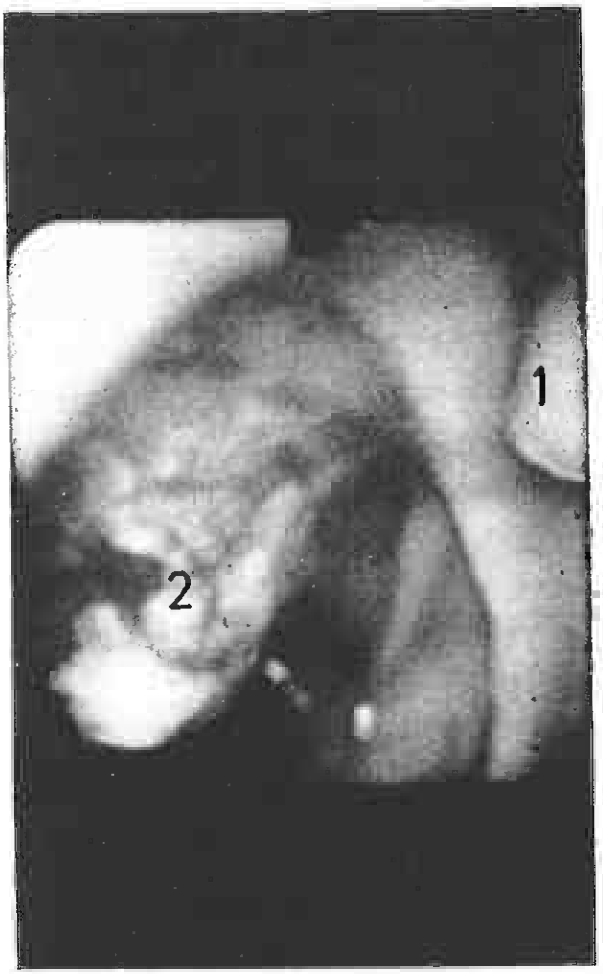

Figure 2. Endoscopic visualisation of the duodenal tumour. 1, the ampulla of Vater not obstructed by 2, the fungating haemorrhagic duodenal tumour.

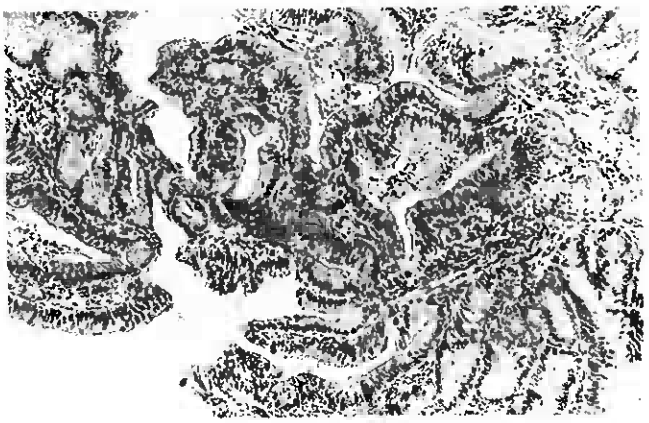

Figure 3. Photomicrograph showing primary adenocarcinoma arising in the duodenal mucosa (H & E x 100)

At operation a freely mobile approximately 4 cm in diameter duodenal tumour was found at the second part of the duodenum. There were multiple tumour deposits noted on the serosa surface of the jejunum and ileum. The liver was slightly enlarged. Multiple gallstones were present in the gall bladder and at Hartmann's porch. In view of his age, poor general condition and multiple tumour deposits, a bypass surgery of cholecystojejunostomy and gastro-jejunostomy was performed. Biopsies of the tumour revealed leiomyomas of the small intestine (Figure 4).

On the second post operative day, the patient developed bronchopneumonia with high fever, marked leukocytosis. Despite vigorous antibiotic treatment he expired on the third post-operative day. Consent for post-mortem was not obtained.

Figure 4. Photomicrograph showing a spindle-cell tumour with features of leiomyoma (H & E x 100).

DISCUSSION

Benign tumours of small bowel are uncommon, occurring in 0.1% of surgical specimens (6). Of these adenomas, leiomyomas and lipomas are three frequent tumours. The etiology of these benign tumours is unknown. Many benign tumours remain asymptomatic and are discovered incidentally at surgery or postmortem examination. Clinically, leiomyoma is probably the most important symptomatic small bowel tumour. It is found at all level of small intestine but most commonly in the subserosa and submucosa surface of jejunum. It occurs most commonly in elderly patient and appears to have no sex predilection (7). Patients may present with gastrointestinal bleeding due to central necrosis or ulceration of tumour mucosa, intestinal obstruction or even vulvulus. In the study of 1399 benign tumours of small intestine, only 14 cases were associated with neurofibromatosis (8). Hochberg (9) however found 5 cases of intestinal leiomyomas in 39 cases of neurofibromatosis with gastrointestinal involvement in a survey of literature. This suggest an increased frequency of leiomyomas in patients with neurofibromatosis than previously recognised.

Neurofibromatosis may also associate with malignant gastrointestinal neoplasms. Of these, the commonest tumour is malignant neurofibromas followed by sarcomas (9), although adenocarcinoma of colon and adenocarcinoma of pancreas in association of neuroifibromatosis had recently be reported (10).

Primary adenocarcinoma of the duodenum is a rare lesion.It accounts for only 0.03 - 0.5% of all carcinomas (11). and constitutes approximately 0.3% of all gastrointestinal tumours (12). Yet, 33 - 45% of all small bowel carcinomas are located in the duodenum (13). Since the first documented case of primary adenocarcinoma of duodenum described by Hamburger in 1976 (14), up to 1974,only 694 cases had been reported. It is a disease of elderly patients, occur mostly in the 6th to 8th decade of life (15) with slight male preponderance (13). The presenting symptoms varied with the location of tumour. Abdominal pain, malaise, anorexia, weightloss and bleeding are common presenting symptoms. Jaundice may also occur as a result of obstruction to bile duct due to involvement of ampulla of Vater. As in all small bowel tumours, considerable delay in the diagnosis is common. This is due to low index of suspicion of the existence of these tumours in the small intestine, the vague early symptoms and paucity of physical signs. Barium meal examination is the mainstay of diagnosis of duodenal carcinoma. Radiological signs include constriction, obstruction, mucosal distortion, filling defect,rigidity and proximal dilatation of the duodenum (16). With the advent of fiberoptic endoscopy, direct visualisation of the entire duodenum can be accomplished and the suspected lesion photographed and biopsied. In our patient, the duodenum tumour was diagnosed by barium meal examination and endoscopy, and histologically confirmed by endoscopic tissue biopsy.

It is a well known clinical observation that small bowel tumours are rarer than tumours of stomach and colon. Many speculations have been offered : the rapid transit time, the fluid content of small intestine reduces exposure to any potential carcinogens, and the relative sterility of small bowel as compared with the large bowel. Lowenfels (17) hypothesized that an immune surveillance system of the small bowel militates against the development of tumours. This hypothesis is supported from observation that primary and metastatic tumours occur more frequently in whom the immune response is depressed as in immunodeficiency diseases (18) and in patient receiving immunosuppressive therapy (19). Similarly, there is an increased incidence of small bowel tumour in known immunological abnormalities, such as Crohn's disease (20) and Coeliac disease (21). There is also an experimental evidence to show the tumour arises most frequently in immune suppressed experimental animals (22). The occurrence of multiple small intestinal leiomyomas and primary adenocarcinoma of duodenum in this patient with neurofibromatosis suggest a defective or deficient immune surveillance, thereby predisposing to neoplastic transformation. We are however unable to exclude the possibility of coincidence.

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