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Epigastric pain in a patient with neurofibromatosis type 1

於1型神經纖維瘤病患者身上的上腹疼痛症狀

Patients with neurofibromatosis type 1 are at increased risk of developing carcinoid tumours of the duodenum, particularly in the ampulla of Vater. Aggressive surgery with pancreatoduodenectomy is recommended for all ampullary carcinoid tumours because of their propensity to metastasise. We report a case of a 43-year-old woman with neurofibromatosis type 1, who presented with recurrent epigastric pain for 15 months. Evaluation using magnetic resonance cholangiopancreatography and side-viewing duodenoscopy revealed a submucosal tumour at the ampulla of Vater causing pancreatobiliary ductal obstruction and dilation. The ampullary tumour was overlooked initially by forward-viewing endoscopy. The patient subsequently underwent pancreatoduodenectomy. Histological examination of the surgically resected specimen confirmed the presence of a carcinoid tumour, with metastasis to peri-pancreatic lymph nodes. She remained asymptomatic 10 months after surgery.

1型神經纖維瘤病患者的十二指腸，特別是在法特氏壺腹的位置，會有較高生成類癌瘤的機會。基於壺腹部類癌瘤具有轉移性，我們建議施行胰十二指腸切除術。本病例報告的1型神經纖維瘤病，患者是一位43歲的女性，她出現反復性上腹疼痛達15個月。以磁共振胰膽管造影、側視十二指腸鏡檢查診斷後，發現在法特氏壺腹有一黏膜下腫瘤，引致胰膽管阻塞和擴張。之前進行的前視內窺鏡檢查並未能發現該壺腹部腫瘤。患者隨後接受胰十二指腸切除術；手術切除物樣本經組織檢測後證實為類癌瘤，並已擴散至胰臟周邊的淋巴結。患者在手術後10個月仍然沒有任何復發症狀。

Key words:
Ampullar of Vater;
Carcinoid tumor;
Neurofibromatosis 1

關鍵詞：
法特氏壺腹；
類癌瘤；
1型神經纖維瘤病

Hong Kong Med J 2005;11:213-5

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Introduction

Neurofibromatosis type 1 (NF-1; also known as von Recklinghausen's neurofibromatosis) is an inherited autosomal disorder characterised by multiple cutaneous neurofibromas, café-au-lait spots, and axillary and/or inguinal freckling. Gastrointestinal involvement is seen in 10% to 25% of patients with NF-1 and causes symptoms in fewer than 5%.[1] The gastrointestinal manifestations of NF-1 occur in three forms:

(1) Hyperplasia of the submucosal and myenteric nerve plexuses and mucosal ganglioneuromatosis, which typically occur in a patchy distribution and may appear as discrete neurofibromas or plexiform neurofibromas;
(2) Gastrointestinal stromal tumours that are mostly located in the stomach and jejunum, and are usually benign; and
(3) A distinctive glandular, somatostatin-rich carcinoid tumour of the peri-ampullary region of the duodenum that contains psammoma bodies.

We report a case of a patient with NF-1 who presented with recur-

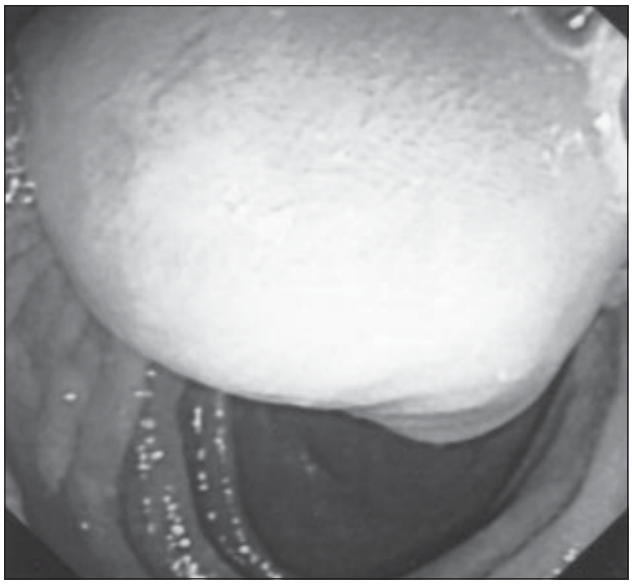

Fig 1. A submucosal mass at the ampulla of Vater is detected by side-viewing duodenoscopy

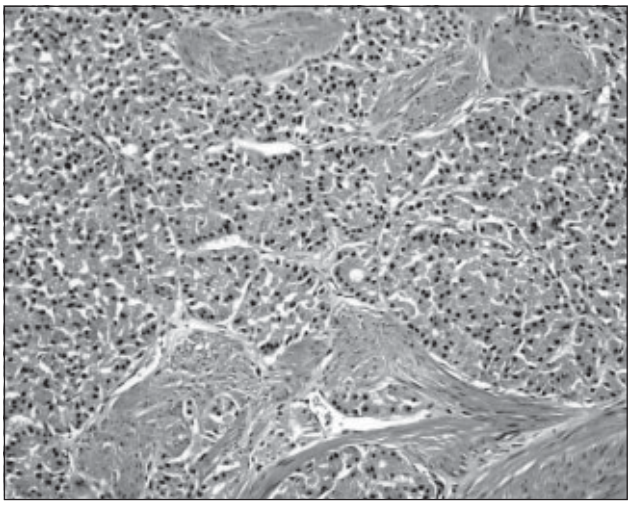

Fig 2. Photomicrograph of the ampulla showing tumour cells with monotonous nuclei arranged in solid pattern (H&E, x40)
Immunostaining revealed the tumour cells were positive for synaptophysin and chromogranin

rent epigastric pain, which was attributed to an ampullary carcinoid tumour causing pancreatobiliary obstruction.

Case report

A 43-year-old Chinese woman was referred to United Christian Hospital in July 2003 because of non-ulcer dyspepsia. She complained of recurrent epigastric pain over previous 15 months, which was worse after meals. Upper endoscopy had previously been performed and reported as normal. Physical examination revealed multiple café-au-lait spots and numerous cutaneous and subcutaneous neurofibromas, suggesting the diagnosis of NF-1. Blood tests including liver function tests were normal. Transabdominal ultrasonography showed the biliary tree was dilated, and endoscopic retrograde cholangiopancreatography was arranged. The side-viewing duodenoscope revealed a 1.5-cm submucosal mass in the ampulla of Vater (Fig 1); however, cannulation of the common bile duct was unsuccessful. Subsequent magnetic resonance cholangiopancreatography showed a suspicious, rounded mass lesion in the region of the ampulla of Vater. The lesion was causing obstruction and dilation of the common and intrahepatic bile ducts, as well as the pancreatic duct.

In light of the association between NF-1 and ampullary carcinoid tumour, the patient was referred for pancreatoduodenectomy (Whipple procedure). A 1.8-cm submucosal ampullary tumour was identified at surgery. Histological examination of the resected ampullary tumour showed that the tumour cells were arranged in a solid pattern, with monotonous nuclei and no atypia or mitotic activity (Fig 2). Immunostaining revealed that the tumour cells were strongly positive for synaptophysin, weakly positive for chromogranin, and negative for S100 protein. These findings confirmed the diagnosis of carcinoid tumour. One of seven peri-pancreatic lymph nodes was positive for metastatic carcinoid tumour, but no evidence of tumour was found in the pancreas. The patient's epigastric pain ceased after the operation, and she remained asymptomatic 10 months after surgery. A computed tomographic scan of the abdomen at 9 months after surgery did not reveal any evidence of recurrence.

Discussion

Neurofibromatosis type 1 is one of the most common genetic disorders, with a frequency of nearly 1 in 2500 live births in the United Kingdom.[2] In comparison, ampullary carcinoid tumour is extremely rare and accounts for less than 2% of all ampullary tumours and less than 1% of all gastrointestinal carcinoid tumours.[3] A particular association has been noted between NF-1 and the occurrence of ampullary carcinoid tumours, with up to 25% of these tumours being associated with NF-1.[3,4] Typically, ampullary carcinoid tumours occurring in patients with NF-1 are somatostatin-rich (hence these tumours may also be referred to as ampullary somatostatinomas in the literature) and contain psammoma bodies. To our knowledge, fewer than 60 ampullary carcinoid tumours in patients with NF-1 have been reported to date.[5,6]

The most common presenting symptoms of ampullary carcinoid tumours are jaundice (59%) and abdominal pain (37%).[7] Less common symptoms include weight loss (10%), upper gastrointestinal bleeding (3%), and acute pancreatitis (3%).[7] The occurrence of carcinoid syndrome is rare.[7] Somatostatin syndrome is likewise rare even though ampullary carcinoid tumours associated with NF-1 are typically somatostatin-rich. Psammoma bodies, present on histology in more than two thirds of ampullary carcinoid tumours,[8] were not evident in this case. Immunostaining for somatostatin was not performed.

There appears to be no correlation between the size of ampullary carcinoid tumours and presence of metastasis at the time of surgery. This is in contrast to carcinoid tumours of the duodenum where tumour size greater than 2 cm predicts metastasis.[4] Metastatic disease may be present in even small (<1 cm) ampullary carcinoid tumours. Although endoscopic or transduodenal resection is appropriate for treating duodenal carcinoid tumours of less than 2 cm in size, aggressive surgery with pancreatoduodenectomy is warranted for all ampullary carcinoids irrespective of size.[4,7,9] The prognosis is good even in the presence of metastatic disease, as ampullary carcinoids are usually slow growing. A 5-year survival rate approaching 90% can generally be expected.[3]

Patients with NF-1 presenting with abdominal pain should undergo careful examination of the duodenum with endoscopy to rule out the presence of an ampullary tumour. As illustrated by the present case, visualisation of the major papilla may not be adequate with regular forward-viewing endoscopy. In cases where there is a high index of suspicion, side-viewing duodenoscopy should be utilised for optimal examination of the peri-ampullary region.

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