Hong Kong J Radiol. 2012;15:105-9

CASE REPORT

Primary Carcinoid Tumour of the Pancreas with Atypical Presentation

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ABSTRACT

Carcinoid tumours of the pancreas are extremely rare. We report a very unusual case of carcinoid tumour of the pancreas with extensive regional lymph node involvement and no liver metastasis in a patient with worsening jaundice; the patient was otherwise asymptomatic. Dilated intrahepatic and extrahepatic ducts with no calculi or mass within the liver or pancreas were noted on abdominal ultrasound. Enhanced abdominal computed tomography showed extensive enlarged abdominal lymph nodes, a thickened duodenal wall, and dilated biliary tree, as well as common bile duct and pancreatic duct. The pancreas appeared normal. A periampullary tumour with a distal common bile duct stricture and dilatation of the common bile duct was seen on endoscopic retrograde cholangiopancreatography. Endoscopic ultrasonography examination showed a diffusely enlarged and irregular mass at the head of the pancreas, and histology of biopsy samples was consistent with a neuroendocrine tumour.

Key Words: *Carcinoid tumor; Cholangiopancreatography, endoscopic retrograde; Endosonography; Pancreatic neoplasms; Tomography, X-ray computed*

中文摘要

胰腺原發類癌腫瘤的非典型症狀

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胰腺的類癌腫瘤非常罕見。本文報告一名胰腺類癌腫瘤患者，其淋巴結廣泛受累，但無肝轉移；病人除了有不斷惡化的黃疸病外，並無異常。腹部超聲顯示其肝內膽管和肝外膽管擴張，但肝臟和胰腺內並無發現結石或腫塊。增强腹部電腦斷層掃描顯示廣泛腹腔淋巴結脹大、十二指腸壁增厚，膽管樹、膽總管及胰管擴張。胰腺顯示正常。內窺鏡逆行胰膽管造影顯示壺腹周圍腫瘤，並有膽總管下端狹窄，膽總管擴張。內窺鏡超聲成像顯示在胰腺頭部彌漫性不規則腫塊灶，活檢組織學結果吻合胰腺神經內分泌腫瘤。

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Submitted: 2 Aug 2011; Accepted: 4 Oct 2011.

INTRODUCTION

Carcinoid tumours most commonly arise in the midgut organs (appendix and small bowel), less commonly in hindgut organs (colon and rectum), and rarely in organs derived from the embryonic foregut, i.e., bronchus, stomach, pancreas, and thyroid. Carcinoid tumour of the pancreas is a rare neuroendocrine tumour originating from the pancreatic enterochromaffin cells and mostly excretes serotonin derivatives.

We report a case of neuroendocrine tumour of the pancreas confirmed by immunohistochemical techniques, and describe the different radiological features and differential diagnosis.

CASE REPORT

A 53-year-old Malay woman presented with a history of gradually increasing jaundice for one month. She was free of abdominal symptom or other clinical symptoms. There was associated fever and tea-coloured urine but no stool pallor, change in bowel movements, or gastrointestinal bleeding. Physical examination revealed that the patient was jaundiced. No mass was palpable in the abdomen and other systems were unremarkable. One year prior to this admission, she had undergone an uneventful appendicectomy.

Laboratory examinations showed a slightly elevated white cell count of 11.6 x 10^9 /l (reference range [RR], 4-10 x 10^9 /L). Liver enzymes were deranged. The alkaline phosphatase was 361 IU/l (RR, 35-115 IU/l), alanine aminotransferase 90 IU/l (7-56 IU/l), aspartate aminotransferase 62 IU/l (5-45 IU/l), and the gamma-glutamyltransferase 386 IU/l (43-60 IU/l). Total bilirubin was 242 μmol/l (reference level, <26 μmol/l) with a conjugated bilirubin of 205 μmol/l (<7 μmol/l). Tests for serum serotonin level and urinary 5-hydroxyindoleacetic acid (5-HIAA) were negative. The other biochemical blood tests showed nil significant, as was hepatitis screening. Tumour markers were within normal limits, except for carbohydrate antigen (CA-199), which was elevated measuring 235 U/ml (reference level, <40 U/ml).

An abdominal ultrasound showed dilated intrahepatic and extrahepatic ducts. No calculi or mass was seen in the liver or pancreas, however.

An enhanced computed tomographic (CT) abdomen showed extensive enlarged lymph nodes at the porta hepatis, coeliac, and superior mesenteric artery region and also along the para-aortic and para-caval region (Figure 1).The C-loop of the duodenum appeared thickened, however, no enhancing lesion was seen. There was associated dilatation of the biliary tree distally down to the level of the pancreatic head and the common bile duct measured 2.0 cm in maximal diameter (Figure 2), and was also dilated. No intrahepatic or extrahepatic calculi were seen. Multiple small calculi were seen within the gall bladder, but the pancreas appeared normal.

Based on the CT findings of thickened duodenum with multiple abdominal lymphadenopathy and dilatation of the biliary tree and pancreatic duct, the most likely radiological diagnosis was lymphoma.

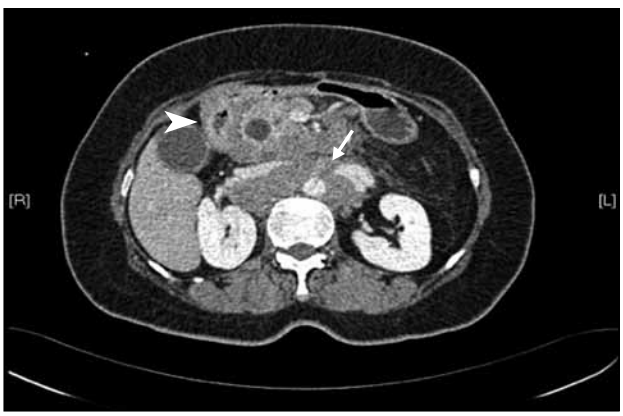

Figure 1. Computed tomographic abdomen shows thickened duodenal wall (arrowhead) and enlarged abdominal lymph nodes (arrow).

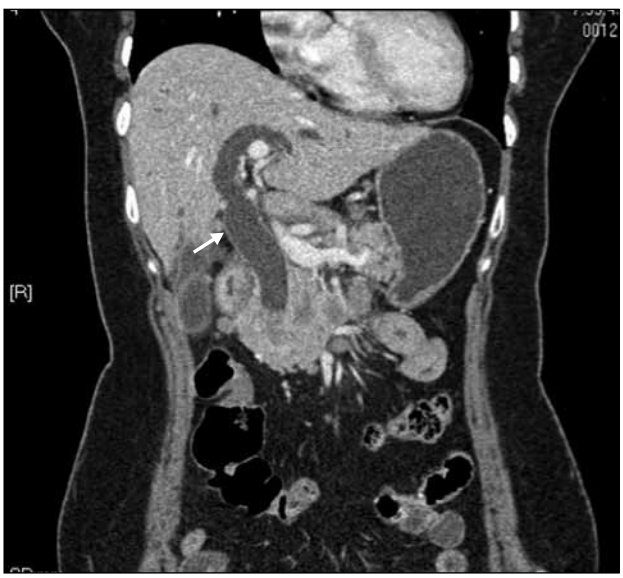

Figure 2. Computed tomographic abdomen: coronal reconstruction shows massive dilatation of the intrahepatic ducts and common bile duct (white arrow).

The other differential diagnoses to be considered were periampullary carcinoma or carcinoma of the duodenum.

Endoscopic retrograde cholangiopancreatography (ERCP) was performed and showed a periampullary tumour with a distal common bile duct stricture and dilatation of the common bile duct. A plastic biliary stent (8.0 cm x 10 Fr) was inserted and biopsy of the periampullary region was performed.

Oesophagogastroduodenoscopy showed a normal oesophagus and stomach. At the region of the ampulla of Vater, a mass was noted. Endoscopic ultrasonography (EUS) showed a diffusely enlarged and irregular mass at the head of the pancreas (Figure 3) and was biopsied.

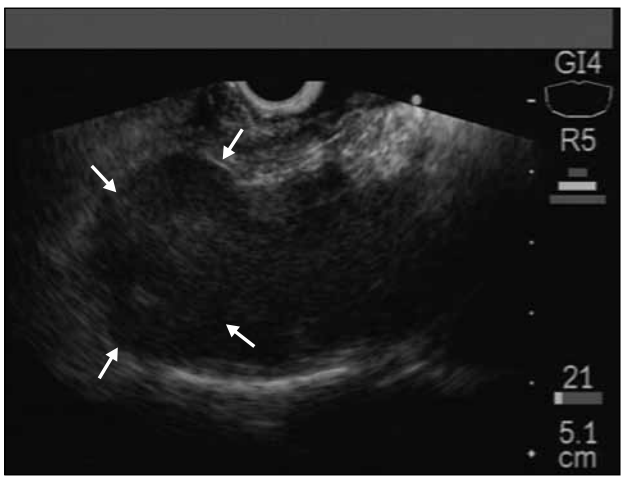

Figure 3. Endoscopic ultrasonography examination shows a diffusely enlarged and irregular mass at the head of the pancreas (white arrows).

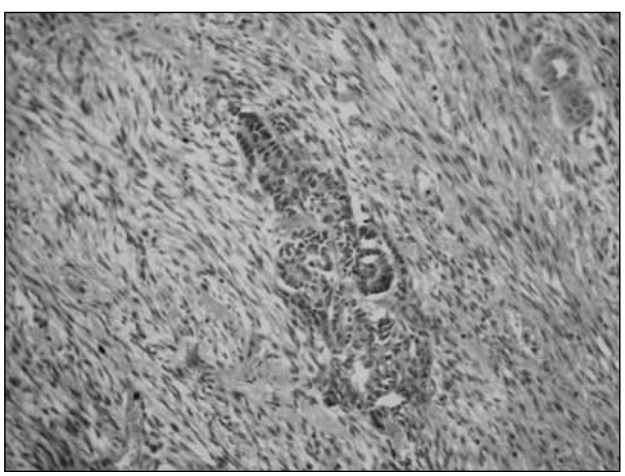

Figure 4. The tumour is stained positively with neuron-specific enolase, chromogranin, synaptophysin but negative for leukocyte common antigen and MNF 116 antibody which is consistent with a neuroendocrine tumour.

Biopsy samples obtained by the aid of ERCP and EUS showed solid nests of malignant monotonous cells with hyperchromic, irregular nuclei and mitotic figures. The stroma exhibited fibrosis in some areas. There was also positive staining for serotonin of the tumour cells and chromogranin. The neoplastic cells expressed neuron-specific enolase, chromogranin, and synaptophysin but was negative for leukocyte common antigen and MNF 116 antibody, which was consistent with a neuroendocrine tumour (Figure 4).

Post-stenting, the patient improved clinically and biochemically. Initially, tumour resection and lymph node sampling was planned. Due to the patient's fragile clinical condition, surgery was deferred and she was referred to the oncology department for chemotherapy. She was later assessed to be unfit for chemotherapy. The plan was having optimised her condition by diet and later, depending on her general health condition and progress she would receive somatostatin analogues. The patient's condition deteriorated however, and she died about two weeks later. No postmortem was performed.

DISCUSSION

Although carcinoid is the most frequently occurring neuroendocrine tumour, localisation in the pancreas is exceedingly rare and often accidental.[1] Only 13 cases have been reported in the literature since 1963.[2] Among the largest published series of 8305 cases of carcinoid tumours reported by Modlin and Sandor,[3] only 46 (0.55%) were in the pancreas. It is likely that a significant percentage of carcinoid tumours remain asymptomatic and undetected during life. The term carcinoid was first used in 1907 by Oberndorfer to describe small intestinal tumours histologically similar to but not as aggressive as adenocarcinomas.[4] Carcinoid tumours most commonly arise in the midgut organs (appendix and small bowel), less commonly in hindgut organs (colon and rectum), and rarely in organs derived from the embryonic foregut (bronchus, stomach, pancreas, and thyroid). Carcinoid tumours are mostly benign but malignant ones have been reported and are usually associated with distant metastases and carcinoid syndrome.

Carcinoid tumours are characterised by the secretion of serotonin (5-HT). This is of fundamental clinical importance and may produce the carcinoid syndrome.[5] The endocrine-secreting activity and clinical symptoms vary in different patients. The majority of patients present with abdominal symptoms. In our patient,

the clinical presentation entailed gradually increasing jaundice, which is quite rare. This presentation was due to the tumour being located in the periampullary region causing obstruction to the common bile duct. There are reports of pancreatic carcinoid tumours presenting as obstructive pancreatitis.[6] One in every nine patients with carcinoid tumours develop carcinoid syndromes.[7] Characteristic features include cutaneous flush, diarrhoea, and valvular heart disease and less commonly, telangiectasia, wheezing, and paroxysmal hypertension. Our patient did not demonstrate any of these symptoms.

Carcinoid tumour may be detected by laboratory tests revealing high levels of serum and urine 5-HIAA (a metabolite of 5-HT).[7] In our case however, the urine and serum serotonin levels were normal on two occasions. A similar case was reported in 1993, for which the diagnosis was confirmed by histopathology as the laboratory results were all negative.[1] There are insufficient data in the literature regarding any correlation between tumour markers and carcinoid tumours of the pancreas. The serum CA-199 level was elevated in our patient.

Different radiological methods have been used to diagnose carcinoid tumour, namely: ultrasonography, CT, and magnetic resonance imaging. Radiologically, pancreatic carcinoid and islet cell tumours may be indistinguishable. The sensitivity of ultrasonography is 86 to 100%,[8] if the transducer is applied directly to the pancreatic surface, where it manifests as a round or oval, well-defined and hypoechoic lesion in contrast to the surrounding pancreatic tissue. However, hyperechoic tumours with calcifications have also been described.[8] Calcification is only seen in about 2% of reported cases as compared to 22% in ductal tumours or islet cell tumours. In our case, there was no calcification seen.

CT may help detect small hypodense areas not revealed by ultrasound, which may contain calcification. Following contrast administration, there is marked enhancement of the tumour in some reported cases but this enhancement is not related to the degree of function.[9] Some tumours can appear as hypodense or isodense to the surrounding pancreatic tissue. A cystic appearance has also been reported.[9] Small tumours are likely to be homogeneous and hypervascular, whereas larger tumours are heterogeneous and hypovascular. Primary carcinoid of the pancreas therefore displays varied and non-specific imaging features. These tumours do metastasise. Metastases are noted in 33% of small bowel lesions, 60 to 70% of colonic, 18% of rectal, and only 2 to 3% of appendicular lesions (although this is the most common primary location).[4] Liver metastases are commonly associated with carcinoid of the pancreas; several cases have been reported so far.[6] The frequency of liver metastases in cases of pancreatic carcinoid tumours is not known, and is not noted in our case.

Carcinoid tumour can also involve the regional lymph nodes, as demonstrated in our case. Due to the presence of extensive regional lymph nodes, lymphoma was our first diagnosis as it can present with multiple enlarged intra-abdominal lymph nodes. This was further supported by the thickened duodenal wall and absence of any other organ involvement. The presence of enlarged lymph nodes anywhere else in the body and a lymph node biopsy can confirm the diagnosis. However, there were no enlarged lymph nodes anywhere in the body. Lymph node sampling from the abdominal region with tumour resection surgery was planned but the patient died prior to surgery.

Somatostatin receptor scintigraphy and positron emission tomography are useful confirmatory examinations in suspected cases with neuroendocrine tumours and can exclude distant metastases, but it was not available in our centre at that time. However, it offers an excellent investigation to exclude lymphoma and confirm the diagnosis of carcinoid tumour.

For our patient, another differential diagnosis was a periampullary carcinoma. Patients with periampullary carcinoma are in older age-groups and present with intermittent jaundice or a palpable right upper quadrant mass. On CT scan, the tumour usually manifests as an enhancing lesion, stricture or filling defect at the periampullary region and can obstruct the pancreatic, extrahepatic and even intrahepatic ducts. ERCP is the investigation of choice and biopsy normally confirms the diagnosis. In our case, ERCP and EUS were performed and biopsy samples obtained on both occasions confirmed the diagnosis. Carcinoid tumour can also produce sclerotic bony metastases, and a few cases with metastases in the brain, breast and orbits have also been reported.[2]

Due to marked similarity in clinical and radiological features of carcinoid and islet cell

tumour of the pancreas, definitive diagnosis requires anatomopathologic techniques based on immunohistochemistry. These reveal positive staining for serotonin, as demonstrated in our case. Immunohistochemical study disclosed the tumour cells to be positive for serotonin and chromogranin positive, which was consistent with neuroendocrine tumour. In our case the biopsy samples were obtained on two separate occasions, during ERCP and EUS, both of which confirmed the diagnosis.

Usually, carcinoid tumours are locally aggressive and slow growing. The long-term survival is frequently owing to a slow growth and effective medical treatment for the secondary bioactive effects of the tumour. Management of pancreatic carcinoid implies surgery as the first step followed by chemotherapy, and somatostatin analogues are used if the tumour is only partially removed or symptoms persist. Carcinoid tumours have a better prognosis than the common forms of pancreatic adenocarcinomas.

In conclusion, our patient had a rare pancreatic neuroendocrine tumour with extensive regional lymph node involvement, no liver metastasis and an atypical presentation, namely gradually increasing jaundice. It highlights the importance of radiological, surgical, and pathological techniques for diagnosing and management of pancreatic neuroendocrine tumours.

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