
CASE REPORT

Pancreatic Neuroendocrine Tumour Causing Chronic Diarrhoea: Radiological-Pathological Correlations

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ABSTRACT

This report is of an unusual case of chronic diarrhoea due to a pancreatic neuroendocrine neoplasm. A 57-year-old man presented to Kwong Wah Hospital, Hong Kong with chronic diarrhoea for more than 1 year. A wide spectrum of investigations was performed, including complete blood counts, liver and renal function tests, thyroid function test, stool culture, and colonoscopy, which showed no abnormalities. Contrast computed tomography of the abdomen and pelvis subsequently showed a 5-cm well-circumscribed hypoenhancing pancreatic tail mass. In view of the clinical presentation, a pancreatic neuroendocrine tumour was diagnosed. Octreotide scan showed strong tracer uptake at the pancreatic tail tumour, with no other tracer uptake focus. Positron-emission tomography-computed tomography scan showed a solitary hypermetabolic pancreatic tail tumour with no evidence of distant metastases. Endoscopic ultrasound-guided fine-needle aspiration cytology showed features of pancreatic neuroendocrine tumour. Pancreatic neuroendocrine neoplasms are rare tumours. Clinical, biochemical, and radiological correlations are essential in making an accurate preoperative diagnosis. Imaging played a central role in detection, localisation, and subtype differentiation of this tumour. Knowledge of the features of the various imaging techniques could aid in diagnosis, treatment planning, prognosis, and disease monitoring.

Key Words: Neuroendocrine tumors; Octreotide; Pancreatic neoplasms; Positron-emission tomography and computed tomography

中文摘要

因胰腺神經內分泌腫瘤引致的慢性腹瀉：放射病理的相關性

卓元怡、盧偉強、陳紹騏、黃鎮威

本文報告一個由胰腺神經內分泌腫瘤引致罕見的慢性腹瀉。一名到香港廣華醫院求診的57歲男性患有慢性腹瀉一年多。包括全血球計數、肝腎功能檢查、甲狀腺功能檢查、大便細菌培植和大腸鏡的各種檢查結果均未有發現異常。及後，病人被安排進行腹盆對比電腦斷層造影，發現一個5 cm的胰尾腫瘤。在綜合病人的臨床表徵後，診斷出胰腺神經內分泌腫瘤。奧曲肽掃描顯示這胰尾腫瘤表現出較強的吸收，而腫瘤沒有擴散跡象。正電子—電腦斷層掃描亦顯示腫瘤無遠處轉移的證據。內鏡超聲引導針吸細胞學印證了腫瘤具神經內分泌腫瘤的特徵。胰腺神經內分泌腫瘤是一種罕見的腫

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瘤。準確的術前診斷須結合臨床、生化和醫學影像特徵。醫學影像在腫瘤檢測、定位和亞型分類中起着核心的作用。熟悉胰腺神經內分泌腫瘤在各種醫學影像的特徵有助術前診斷、治療計劃、預後判斷和疾病監測。

INTRODUCTION

Pancreatic neuroendocrine neoplasms (PNEs) arise from pluripotent cells of the pancreatic duct as opposed to the islets of Langerhans. The use of the term 'islet cell tumour' would therefore be imprecise, and PNE is a more accurate term that has become widely used in recent years. PNEs have an incidence of 1 in 100,000 population.¹ Most sporadic PNEs occur in the fourth to sixth decades of life, and have no significant sex predilection.

Clinically, PNEs have been classified into functioning and non-functioning on the basis of clinical and laboratory findings. Functioning PNEs could produce a variety of hormones such as insulin, glucagon, and gastrin. Terms reflecting the clinical syndromes such as insulinoma, glucagonoma, and gastrinoma are usually applied to these PNEs.²

This report is of a patient with a serotonin-secreting PNE who presented with chronic diarrhoea. The histological and imaging features are discussed.

CASE REPORT

In June 2011, a 57-year-old man presented to Kwong Wah Hospital, Hong Kong with chronic diarrhoea for more than 1 year. A wide spectrum of investigations was performed, including complete blood counts, liver and renal function tests, thyroid function test, stool culture, and colonoscopy. No abnormalities were detected.

Contrast computed tomography (CT) of the abdomen and pelvis subsequently showed a 5-cm well-circumscribed hypoenhancing pancreatic tail mass (Figure 1). In view of the clinical presentation, a pancreatic neuroendocrine tumour was diagnosed. 24-Hour urine collection to test for 5-hydroxyindoleacetic acid, a serotonin metabolite, showed marked elevation (115 $\mu\text{mol/d}$; reference range, <50 $\mu\text{mol/d}$). Octreotide scintigraphy with single-photon emission CT showed strong tracer uptake by the pancreatic tail tumour with no other tracer uptake focus (Figure 2). Positron-emission tomography (PET)-CT scan showed a solitary hypermetabolic pancreatic tail tumour with no

evidence of distant metastases. Endoscopic ultrasound-guided fine-needle aspiration cytology (FNAC) showed features of PNE. Therefore, a preoperative diagnosis of pancreatic neuroendocrine tumour was made.

The patient underwent distal pancreatectomy and splenectomy. Pathological examination confirmed the diagnosis of pancreatic neuroendocrine tumour (Figure 3). The patient's diarrhoea resolved completely after operation.

DISCUSSION

PNEs are rare tumours. They can be classified into functioning and non-functioning tumours on the basis of the clinical and laboratory findings. Functioning PNEs produce signs and symptoms related to the associated clinical and biochemical endocrinopathy such as Whipple's triad for insulinoma and Zollinger-Ellison syndrome for gastrinoma.

Histologically, well-differentiated tumours are composed of uniform polygonal cells that resemble normal islet cells on microscopic examination.

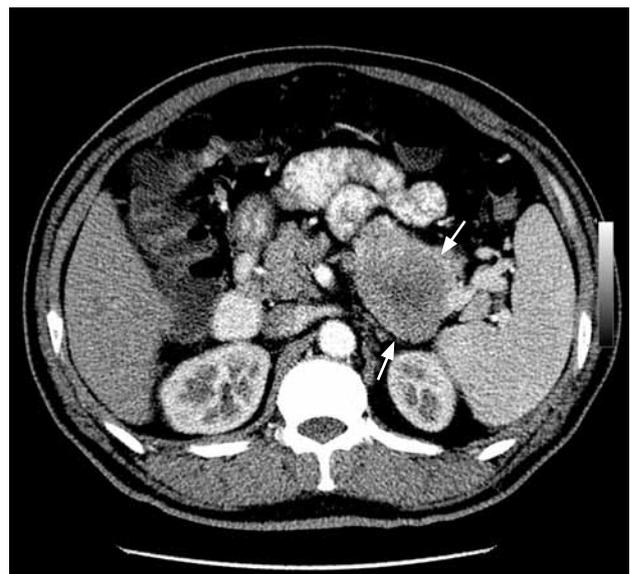


Figure 1. An arterial-phase contrast computed tomography image of the abdomen and pelvis shows a well-circumscribed hypoenhancing mass at the pancreatic tail (arrows).

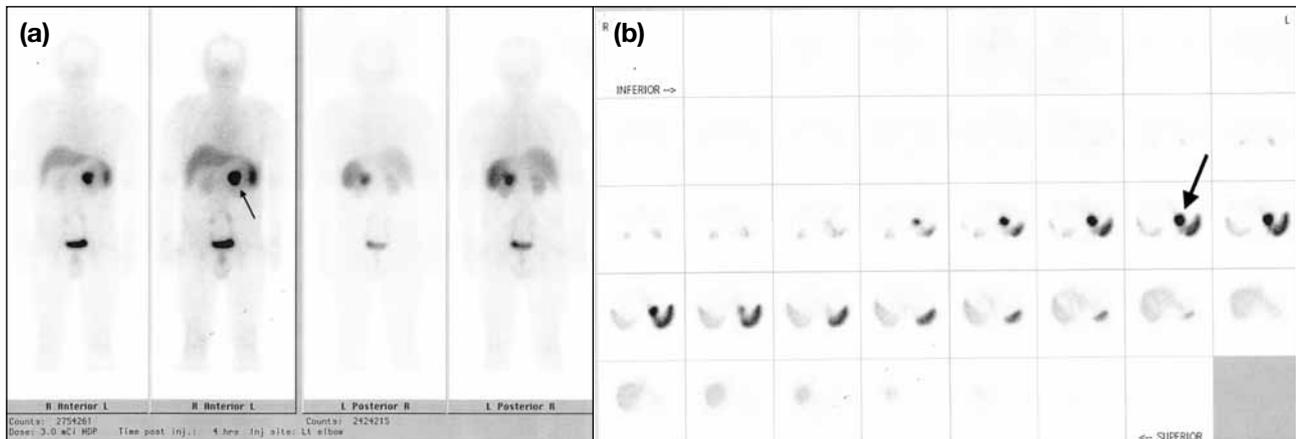


Figure 2. Octreotide scan: (a) planar scintigraphy image shows a solitary increased tracer uptake focus at the region of the pancreatic tail (arrow); and (b) single-photon emission computed tomography image confirms the hot spot at the pancreatic tail (arrow).

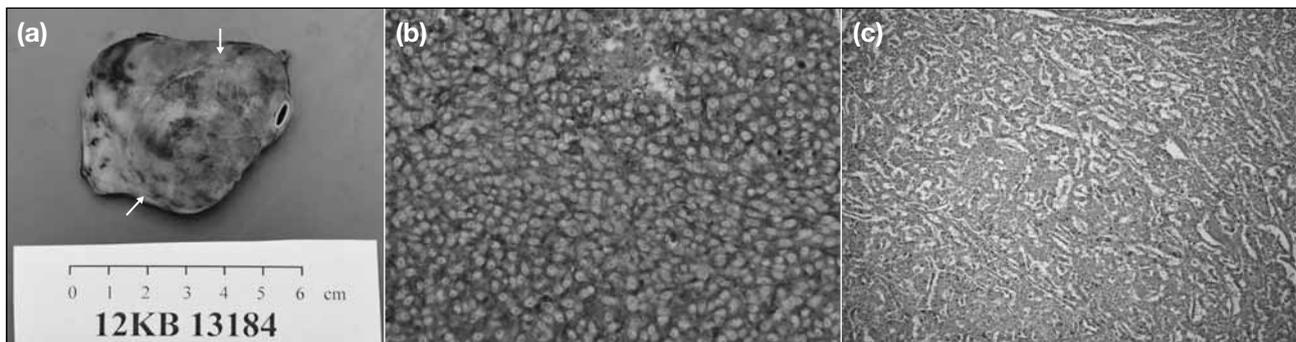


Figure 3. Pancreatic neuroendocrine tumour. (a) Gross specimen shows a section of the well-circumscribed pancreatic tail mass (arrows); (b) synaptophysin stain of the cells shows diffuse cytoplasmic immunoreactivity for synaptophysin (original magnification, x 200); and (c) haematoxylin and eosin stain shows the neoplasm is composed of polygonal cells in trabecular, gyriform, and glandular patterns of growth with delicate vasculature (original magnification, x 100).

The tumours usually have characteristic organoid arrangement of the tumour cells, with nesting, trabecular, or gyriform patterns. The cells are relatively uniform and produce abundant neurosecretory granules, reflected in the strong and diffuse immunorexpression of neuroendocrine markers such as chromogranin A and synaptophysin. Poorly differentiated tumours less closely resemble non-neoplastic neuroendocrine cells and have a more sheet-like or diffuse architecture, irregular nuclei, and less cytoplasmic granularity.² Although the functional hormone can usually be identified on immunohistochemical staining, the histological features do not correlate with the functional state.¹

Imaging plays an important role in the diagnosis of PNENs. Multiphasic multidetector CT achieves a sensitivity of more than 80% and specificity of more

than 90% in most studies. The enhancement pattern depends on the histological microvascular density.³ While classically hyperenhancing in the arterial and portovenous phases, some PNENs can be iso- or hypoenhancing, as in this patient. Tumour enhancement at the pancreatic phase has been shown to correlate with a degree of differentiation. Hypoenhancing tumours correlate with poorly differentiated PNENs and, consequently, a decrease in overall survival.⁴

Small PNENs such as insulinoma typically demonstrate homogeneous hyperenhancement. Larger PNENs may show heterogeneous enhancement due to areas of cystic degeneration, necrosis, and calcification, which are prognostic of poor outcome.⁵ Involvement of the major vessels and gross invasion of other organs (T4 disease) can be readily discerned in the corresponding

phases, and preclude surgical resection in most patients. Hepatic metastases also show hyperenhancement in the arterial phase, and may be accompanied by portovenous washout.

Sensitivity and specificity for magnetic resonance imaging (MRI) in detection of PNENs are variable in different studies, but MRI is at least comparable, if not superior, to CT.⁶ On MRI, PNENs are usually of low signal intensity in T1-weighted images and intermediate-to-high signal intensity in T2-weighted images. The pancreatic duct and the common duct can be seen on T2-weighted images. As for CT, the primary tumour can be homogeneously enhancing when small and heterogeneously enhancing when large.

Restricted diffusion has been observed in PNENs. Neuroendocrine tumour and neuroendocrine carcinoma have a statistically different apparent diffusion coefficient (ADC) value. An inverse relationship has been demonstrated between the ADC value and proliferative activity (Ki-67 index), which may help predict the growth of the tumour.⁷

Octreotide is a synthetic analogue of somatostatin. Octreotide binds primarily to the somatostatin receptor (SSTR) subtypes 2 and 5. The drug is very useful for detection of metastases and recurrences, localisation of the disease in a patient with known clinical syndrome, and differential diagnosis of a pancreatic mass. The sensitivity of octreotide scan depends on the tumour subtype. Most PNENs express a high level of SSTR-2 and are effectively imaged with indium-111-labelled octreotide scan. However, insulinoma typically expresses SSTR-3 and, therefore, often cannot be effectively imaged.

The sensitivity of octreotide scan has been reported to be at least 80%, depending on the tumour size and subtype.¹ PNENs do not usually demonstrate increased uptake on fluorodeoxyglucose (FDG) PET scan unless they are poorly differentiated. FDG PET has been shown to detect octreotide-negative tumours, thereby providing additional diagnostic information.⁸

Endoscopic ultrasound (EUS) could localise PNENs and guide FNAC. A previous report has shown that tumours smaller than 10 mm can be detected, although

limitations were noted.⁹ EUS is complementary to other imaging modalities in the management of PNENs. EUS-guided FNAC may be useful for cytological diagnosis of a non-functioning tumour.

Treatment of PNENs requires a multimodality approach. Surgery remains the only curative treatment, and ranges from enucleation for a small benign tumour to total pancreatectomy for more advanced disease.

CONCLUSION

PNENs are rare tumours. Clinical, biochemical, and radiological correlations are essential for making an accurate preoperative diagnosis. Imaging plays a central role in tumour detection, localisation, and subtype differentiation. Knowledge of the imaging features of various tumours could aid in diagnosis, treatment planning, prognosis, and disease monitoring.

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