Grand Rounds Vol 9 pages 14–17
Speciality: Endocrinology, Oncology
Article Type: Case Report
DOI: 10.1102/1470-5206.2009.0004

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Late metastases to the pancreas from resected renal cell carcinoma masquerading as multiple endocrine neoplasia

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Date accepted for publication 9 March 2009

Abstract

We report the case of 58-year-old gentleman with pancreatic masses, possibly of neuroendocrine origin, with the history of renal carcinoma, primary hyperparathyroidism and pituitary cyst. Histological analysis after pancreatectomy revealed metastases from renal cancer. This unusual case illustrates the challenging differential diagnosis between multiple endocrine neoplasia (MEN) syndrome and metastatic renal cell cancer.

Keywords

Renal cell cancer; metastases; pancreas; MEN 1.

Introduction

The differential diagnosis of pancreatic masses includes benign lesions, pancreatic adenocarcinoma, lymphoma and islet cell tumour, presenting usually as solitary mass, and metastases from the other primaries, which are often multiple.

Two percent of all malignant pancreatic tumours are metastases from the other primaries, with small cell lung cancer, colorectal cancer, breast cancer, melanoma and haematological neoplasm being the most common[1].

Renal cell cancer accounts (RCC) for 3% of adult malignancies. The most common sites of metastasis in RCC are the lung and lymph nodes followed by the bones and liver[2].

Pancreatic tumors are one of the presentations of the syndrome of multiple endocrine neoplasia type 1 (MEN 1 or Wermer syndrome), an inherited autosomal dominant trait with estimated prevalence of 2–20 per 100,000 in the general population. Approximately 10% of MEN 1 mutations arise de novo. The syndrome is caused by inactivating mutation in tumour suppressor gene called *menin* located on the long arm of chromosome 11q13. Clinical manifestations of MEN 1 are hyperparathyroidism, enteropancreatic tumours that can be multicentric, pituitary adenomas, carcinoid tumours, adrenal adenomas, subcutaneous lipomas and facial angiofibromas[3].

No association between MEN 1 syndrome and clear cell renal carcinoma has been described previously.

Case report

A 58-year-old gentleman presented with haematuria following an earlier urinary tract infection. An ex-smoker with a previous medical history of diet-controlled type 2 diabetes, he had an unremarkable family history.

Investigation revealed a tumour of the lower pole of the right kidney. He underwent a nephrectomy and the tumour was staged as PT 3B NO MX clear cell carcinoma involving the renal vein, but not breaching the capsule. Shortly after discharge, after good postoperative recovery, he was readmitted with pleuritic chest pain and mild hypercalcaemia. He was found to have small pneumothorax secondary to the operation, which was spontaneously resolving and did not need intervention. However, computerised tomography (CT) of the chest revealed two small lesions in the left lung base and right lower lobe suggestive of metastatic disease. On repeated scan within 1 month, the left base nodule had disappeared, but the lesion in the right lung was still present. The patient underwent thoracotomy and histology revealed a benign lymph node. A bone scan undertaken for investigation of hypercalcaemia, which subsequently settled, was negative.

Four years after his initial presentation, he represented with increased thirst and polyuria. Blood tests revealed hypercalcaemia with raised parathyroid hormone. A Sestamibi scan showed high uptake near the left upper pole of the thyroid (Fig. 1). The patient underwent parathyroidectomy, which confirmed a parathyroid adenoma.

Abdominal and chest CT scans showed two lesions in the body of the pancreas and one small nodule in the right upper lobe lung. Gut hormone profile (gastrin, vasoactive-intestinal-peptide, pancreatic-polypeptide, glucagons and neurotensin) was negative. However, it was suspected that the patient could have MEN 1 syndrome. This assumption was supported by endoscopic ultrasound and fine needle aspiration (FNA) of pancreatic masses, which showed atypical

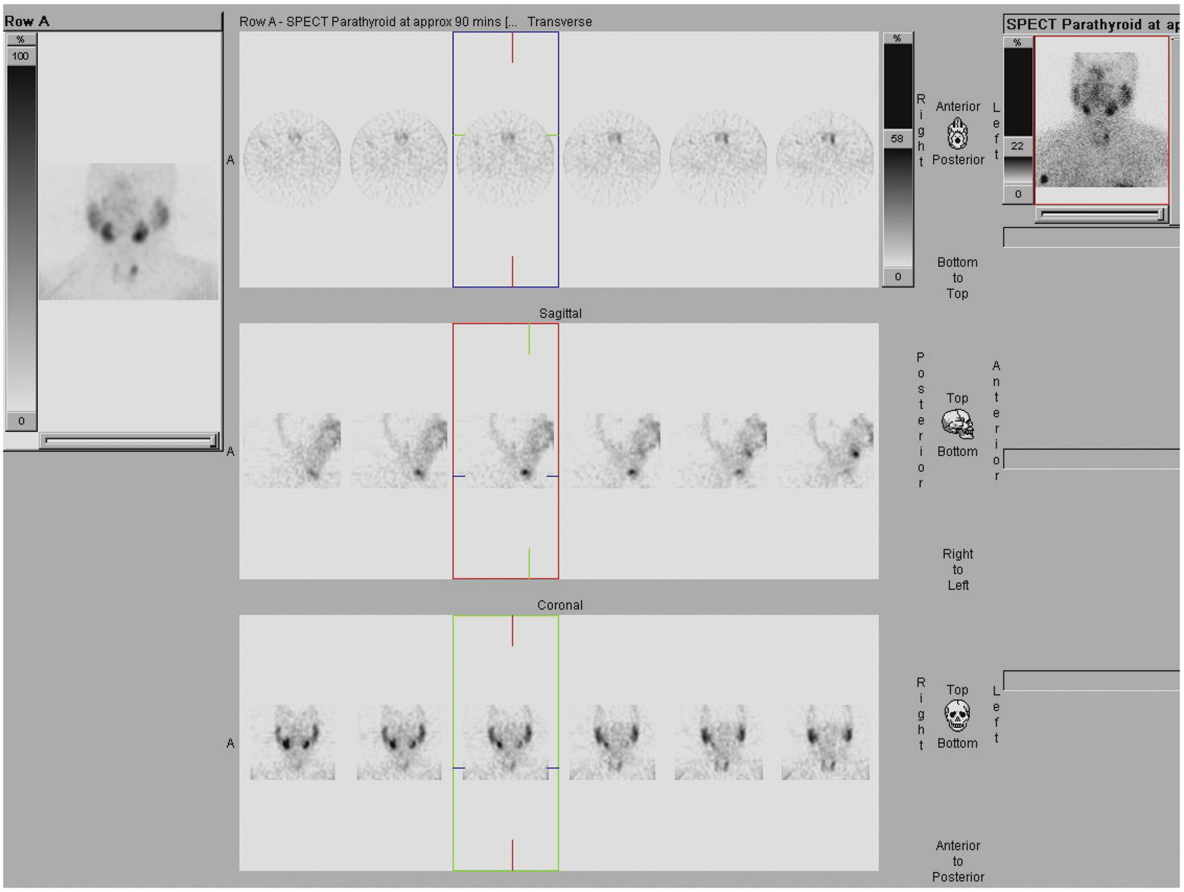

Fig. 1. Parathyroid Sestamibi scan.

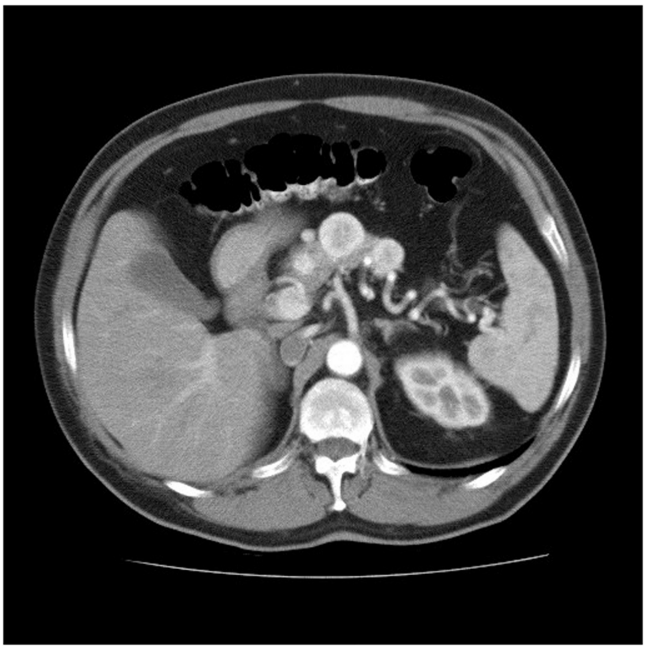

Fig. 2. Computerised tomography scan of the pancreas.

epithelial cells, suggestive of neuroendocrine lesions. Pituitary magnetic resonance imaging (MRI) showed a cyst.

A CT scan 4 months later showed at least ten lesions in the pancreas but no change elsewhere including a small nodule in the right upper lobe lung (Fig. 2). He was referred to the regional hepato-biliary centre where, in view of his previous medical history and the latest findings, it was felt that total pancreatectomy was the most appropriate management.

Histology revealed 15 tumours in the pancreatic parenchyma (5–35 mm) all of which were metastatic deposits of clear cell carcinoma with features fully consistent with the kidney as the primary site. The largest tumour in the head of the pancreas invaded a large vein; lymph nodes were not affected. Genetic testing for MEN 1 was negative.

This is an unusual case of renal cell carcinoma with metastatic spread only to the pancreas. Following surgery, the patient is well and at his last follow-up, 5 months after surgery, there was no evidence of recurrence.

Discussion

Differential diagnosis of pancreatic masses in this particular patient was challenging. On the one hand, multiple pancreatic lesions in a patient with known primary tumour are suggestive of metastatic spread. However, renal cell cancer metastasizing to the pancreas is rare and occurs in 2.8% of patients with metastatic RCC; metastases often present many years after nephrectomy (median time of 8 years). On the other hand, the presence of a functional parathyroid adenoma and pancreatic lesions raise the possibility of MEN 1.

Watchful waiting of hormonally inactive pancraeatic nodules in MEN 1 is an acceptable strategy[4], but the significant increase in the number of pancreatic lesions only 4 months later required further investigations.

In order to differentiate the nature of the mass, endoscopic ultrasound and FNA was performed, which are known to be useful procedures in establishing the origin of pancreatic lesions[5]. Cytological examination was suggestive of neuroendocrine lesions. However, it is known that differentiating between clear cell neuroendocrine tumour of the pancreas and renal cell carcinoma can be problematic[6] and would require an adequate tissue sample through biopsy for immunocytochemical analysis[7]. Endoscopic ultrasound (EUS)-guided FNA can correctly diagnose pancreatic neuroendocrine tumours if adequate aspirate is obtained[8].

Surgical intervention is a reasonable approach in both neuroendocrine pancreatic tumours and metastatic renal cell cancer in the absence of more widespread disease[9]. Contrary to expectations, the histology revealed metastasic deposits of clear cell carcinoma with features fully

in keeping with the kidney as the primary site. Only later was it revealed that the genetic test for MEN 1 was negative.

Teaching point

Renal carcinoma metastasising only to the pancreas is rare, but should be borne in mind in patients with resected renal carcinoma, even after many years. CT imaging is not helpful in differentiating between pancreatic metastasis from renal cell carcinoma and neuroendocrine tumor of the pancreas because both lesions show rapid enhancement during the early phases of helical CT scan and MRI. Endoscopic ultrasound-guided FNA is a good diagnostic tool for differentiating pancreatic tumours, but only if an adequate sample is obtained for satisfactory immunocytochemical analysis. That should be taken into consideration in the interpretation of the results and the decision about further management: surgical intervention versus watchful waiting.

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