Pancreatic Metastases from Renal Cell Carcinoma Presenting as Intestinal Obstruction

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Introduction

Renal cell carcinoma (RCC) is well known to radiologists and surgeons for its notorious propensity for venous spread by tumour thrombus as well as for its expansile osteolytic skeletal metastases. However, it is a lesser known fact that RCC is an unpredictable tumour which can manifest with very late metastases at unexpected sites, even after successful resection of early stage lesions [1]. We report a rare case of RCC metastatic to the pancreas 16 years post-nephrectomy, who presented clinically with features of subacute gastrointestinal obstruction.

Case Report

A 65 years old male presented to the gastroenterology outpatient department of our hospital in April 2008 with progressively increasing symptoms of dyspepsia, post-prandial fullness of abdomen and weight loss (12 kg) of two months duration. He had no associated respiratory, neurological, musculoskeletal or urologic symptoms. He gave past history of having undergone radical nephrectomy in 1992 for RCC (Robsons Stage IIIa) involving his right kidney. No adjuvant chemotherapy was administered postoperatively in view of favourable histopathology of the tumour, being well differentiated RCC. He was placed on regular yearly oncosurgery followup and had been disease free up to his last visit in Nov 2007. On clinical examination, there was no pallor or lymph node enlargement. On abdominal examination, a well healed surgical scar of right nephrectomy was seen and non tender hepatomegaly was palpable two cm below the right subcostal margin. 'Succussion splash' test was clinically positive suggesting gastric outlet obstruction. He was therefore referred for detailed imaging and laboratory investigations, including ultrasonography (USG) of the abdomen, barium meal study and an upper gastrointestinal endoscopy (UGIE).

The USG showed presence of a solitary, heteroechoic, rounded lesion of five cm diameter located in segment VII of the liver; visualization of the retroperitoneum in the preliminary USG was hindered by the overlying stomach distended with gas and food residue. Barium meal study also showed a distended stomach with markedly delayed gastric emptying even after 24 hours which was inferred as gastric outlet obstruction. In addition to findings of dilated stomach with food residue, UGIE revealed a site of obstruction distal to second part of the duodenum (D2), which had normal mucosa. Hemogram, liver function tests and renal function tests were within normal limits. Tumour markers levels, namely alpha fetoprotein (AFP), carcino-embryonic antigen (CEA) and CA-19.9, were not elevated. Urinary hydroxy indole acetic acid (HIAA) estimation for carcinoid tumour was also within normal range.

In view of the preliminary inconclusive investigations, the patient was subjected to a contrast enhanced computerized tomography (CECT) study of the abdomen in May 2008. A triple-phase study protocol was used with parameters of 5mm/0.75mm/12mm (display field of view (FOV)/ detector width/ table increment per rotation) and rotation time of 0.42 seconds on our 16-slice multi-detector CT scanner (Model: Somatom Sensation 16, Siemens, Germany). Bowel opacification was achieved by oral administration of 3% iodinated contrast medium. This was followed by intravenous 100 ml of non-ionic contrast medium (300 mg% iodine content) injected at the rate of 3.5 ml/ seconds using bolus tracking technique for contrast optimization. The CECT abdomen study revealed two nodular enhancing lesions in the pancreas, one each in the regions of the uncinate process and the tail, each measuring approximately two cm in diameter. The uncinate process lesion was noted to be infiltrating the junction of second and third parts of the duodenum causing incomplete luminal obstruction locally with proximal dilatation of D1 and D2 segments and the stomach. No tumour recurrence was identified at the

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Fig. 1 : (a) Axial CECT abdomen image showing enhancing lesion in the tail of pancreas (arrow) posterior to the stomach which is distended with oral contrast medium. (b) Axial CECT abdomen image showing enhancing nodular lesion in the uncinate process of pancreas (white arrows); the right renal fossa is occupied by bowel loops with no local tumour recurrence.

nephrectomy site (Fig. 1).

The segment VII liver lesion was also well defined and exhibited arterial phase enhancement and ‘wash-out’ in the venous phase images, enhancement characteristics being similar to the pancreatic lesions (Fig. 2). No tumour recurrence in the right renal fossa, ascitis, abdominal lymph node enlargement or osteolytic bone lesions were detected. The left kidney was normal in morphology and enhancement characteristics. Based on the clinical history and imaging findings, a diagnosis of pancreatic and hepatic metastases from RCC was made, with differential diagnosis on imaging of metastatic carcinoid tumour.

Patient was subsequently taken up for exploratory laparotomy and gastrojejunostomy to relieve his symptomatic small bowel obstruction. All imaging findings were confirmed per-operatively and the uncinate process lesion seen to be unresectable due to infiltration of the duodenum and transverse mesocolon. Besides a retrocolic isoperistaltic gastrojejunostomy, the tail of pancreas lesion was excised by a distal pancreatectomy. Histopathological analysis confirmed the imaging diagnosis of metastases of RCC in the pancreas, with clusters of ‘clear’ cells exhibiting nuclear pleomorphism and prominent nucleoli, separated from the pancreatic parenchyma by a fibrous capsule (Fig. 3). In view of his disseminated and inoperable metastases, the patient was placed on palliative chemotherapy with Tab Sunitinib orally and is presently under oncology followup as an out-patient.

Discussion

Pancreatic metastases are a rarity and are seen in only 3-12% of patients with disseminated malignancy at autopsy, majority being metastases from primary sites such as lung, breast, kidney and colo-rectal malignancies [2]. Metastases form only 2% of all malignant pancreatic neoplasms and RCC metastasizing to the pancreas is also a rare phenomenon, seen in less than 3% of all metastatic RCC [3]. However, when these rarities converge, it forms a unique association in that RCC is the most common primary tumour in 30% of all patients with pancreatic metastases [2,3]. Akatsu et al [4] even

Fig. 2 : Coronal reformatted arterial phase image of the CECT abdomen showing hypervascular enhancing lesions in the liver (straight white arrow), uncinate process (notched white arrow) and tail of pancreas (straight black arrow).

Fig. 3 : (a) Histopathological examination (HPE) (200x) : Section shows normal pancreas (short arrow) separated by fibrous stroma (curved arrow) from the tumour (long arrow). (b) HPE (400x): Section shows tumour cells arranged in nests separated by delicate fibro vascular stroma. The tumour cells show clear cytoplasm and pleomorphic nuclei.

recommend that irrespective of the clinical interval since nephrectomy, metastases from RCC should be considered if any patient with a pancreatic tumour gives past history of surgery for RCC.

Pancreatic metastases from RCC exhibit certain common features. These patients are usually detected many years after nephrectomy. Kassabian et al [1] had reported mean interval of 12 years with a range of 4-15 years, in their single institution series, but most of the recent studies have reported a mean interval ranging from 6-8 years [3-5]. On CT imaging, all workers have reported the lesions as well defined tumours with characteristic hypervascularity manifesting as contrast enhancement seen in over 75% patients [1,2,4]. It has been reported in the literature that patients with pancreatic metastases were variably symptomatic, with symptoms ranging from abdominal/back pain, weight loss, gastrointestinal bleeding/obstruction or early satiety. Our patient presented clinically 16 years after his radical nephrectomy, with significant weight loss and symptoms suggestive of gastric outlet obstruction and exhibited enhancing nodular hypervascular tumours in the uncinate process and tail of the pancreas.

Patients with pancreatic metastases from RCC are considered as favourable candidates for surgical

resection, even in the presence of multifocal disease or other metastatic sites [6]. Surgical procedures varied according to the site and extent of the growth and included distal pancreatectomy, pancreatoduodenectomy or tumour enucleation. Postoperative disease-free survival has been reported to be more than three years, especially if metastatic disease is restricted to the pancreas, and current trend favours aggressive surgical intervention to perform pancreatic metastasectomy [4,6]. In our patient, the uncinate process mass had infiltrated locally into the duodenum and transverse mesocolon, and hence was not offered surgical removal, whereas the pancreatic tail metastasis was excised completely.

Currently, chemotherapy regimens for metastatic RCC are limited in options and tumour response. Newer chemotherapeutic agents namely interferon alfa and sunitinib malate have been tried in these patients. Sunitinib malate, an orally administered multi-targeted tyrosine kinase inhibitor used to treat gastrointestinal stromal tumours (GIST), is currently under review for its role in metastatic RCC and early reports suggest favourable response. Sunitinib treatment regime, with dosage of 50 mg once daily for four weeks followed by two weeks without treatment, has shown progression free survival period of up to 11 months, as well as lesser treatment related fatigue vis-a-vis interferon alfa [7].

In conclusion, we have reported this case to highlight multiple rare but specific facets which merit attention during the postoperative followup of patients with RCC. Presentation after a long disease-free interval of 16 years post-nephrectomy with symptoms relating to bowel obstruction and metastatic involvement of the pancreas, which is otherwise an uncommon site for metastatic disease, were seen in our patient. Each of these facets

is a rarity in itself, but in the background of known RCC, becomes a distinctive combination. The review of current literature on the subject also defines the surgical and chemotherapeutic options in vogue at present for management of metastatic RCC to the pancreas. This case report underlines the unpredictability of metastases from RCC, both in time-frame as well as the location and the awareness needed to facilitate its early diagnosis, keeping in view the limited management options.

Conflicts of Interest

None identified

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Answers to MCQs

1. (d)	2. (c)	3. (d)	4. (c)	5. (c)
6. (c)	7. (c)	8. (d)	9. (a)	10. (a)
11. (d)	12. (a)	13. (b)	14. (d)	15. (a)