ORIGINAL REPORT

MDCT patterns of presentation of pancreatic metastases from renal cell carcinoma

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Abstract
Objective: To determine the frequency of pancreatic metastasis from renal cell carcinoma in patients studied with MDCT during 2007 and to describe the patterns of presentation on MDCT.
Material and methods: We retrospectively studied 133 patients with renal cell carcinoma who underwent MDCT between January and December 2007. Forty-nine patients presented with disseminated disease. We analyzed the frequency, location, and patterns of presentation of pancreatic metastases.
Results: Pancreatic involvement was identified in six patients. Four patients had isolated pancreatic nodules and two presented multiple nodules. A total of nine pancreatic lesions ranging between 8 mm and 40 mm were detected. All nodules had increased uptake of contrast material in the arterial phase except for one in a patient with multiple nodules, due to necrosis. Two cases were associated with pancreatic duct dilation. Histology was obtained in only one patient.
Conclusion: Pancreatic involvement of renal cell carcinoma was detected in 4.5% of patients, ranking fifth in frequency in patients with disseminated disease. The arterial phase is necessary to detect pancreatic involvement of renal cell carcinoma. The pattern of presentation is nearly constant, helping differentiate pancreatic metastasis from primary pancreatic adenocarcinoma.

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Introduction

Renal cell carcinoma (RCC) is the seventh most common neoplasm in men and the twelfth most common in women, accounting for approximately 2.6% of all neoplasms.1 It is slightly more common in men than in women, with a male-to-female ratio of 1.6:1, and commonly presents in the sixth and seventh decades. The histopathologic subtype classification of RCC (conventional, papillary, chromophobe, collecting duct, and unclassified RCC) is of interest because of its association with survival.2,1

Computed tomography (CT) has been widely used in the evaluation of RCC because it provides information about the tumor itself, its relationship to the adjacent tissues, and distant spread.4 In addition, CT is paramount in the monitoring of patients after treatment to rule out local recurrences and/or distant metastasis,5 given the prognostic implications associated to these findings.

Metastases are detected in 25–30% of patients at diagnosis,6 and locally advanced disease is seen in approximately 20% of cases.7 Up to 50% of patients develop metastatic or recurrent disease in early stages after nephrectomy for RCC.7 Recurrence occurs within the first three years after surgery in 85% of patients, but cases of recurrence after more than 20 years have also been reported.7 In 1–4% of patients, metastases are solitary. This is particularly important because resection of the solitary lesion greatly improves survival.8–10 RCC typically metastasizes to lung, bone, liver, adrenal gland, contralateral kidney, and brain. Metastases to other sites, including the pancreas, are uncommon.

Metastatic lesions in the pancreas are rare, accounting for approximately 3–10% of all malignancies found in series of autopsies. Only 2–3% of all malignant lesions in the pancreas are secondary, with lung, colon, breast cancer and melanoma being the most common primary tumors.6,9

We studied the multidetector CT (MDCT) studies of 133 patients with a history of RCC performed during 2007 in our center. We analyzed the occurrence and frequency of pancreatic metastases, as well as their location and patterns of presentation, by assessing the number, size, morphology and dynamic behavior of the lesions.

Material and methods

Patients

Ethics committee approval was waived because the studies were analyzed retrospectively.

We reviewed the chest-abdominal MDCT studies of 166 patients with a history of RCC performed between January and December 2007 in the Section of Thoracic and Oncologic Radiology of our hospital. A total of 39 MDCT studies for initial staging and 94 follow-up MDCT studies were included. Distant metastases were identified in 49 patients on MDCT. Studies were reviewed by the same radiologist. An average of nine follow-up studies was reviewed from each patient (range 4–11 studies). Images and reports were both reviewed.

Imaging technique

MDCT studies were performed with two multislice Philips Brilliance CT 64- and 16-channel scanners (Eindhoven, Netherlands). Two helical scans were performed after intravenous contrast administration in all patients, except in three patients with a history of iodinated contrast allergy.
The first scanning, performed in arterial phase from the lung apex to the renal fossa, started 30 s after contrast administration. The second scanning, performed in portal phase from the dome of the diaphragm to the pubic symphysis, started 60 s after contrast administration.

Imaging parameters were rotation time of 0.5 s, FOV of 300–350 mm, depending on the patient size, and a pitch of 1.17–1.18.

A volume of 100 cc of non-ionic iiodinated contrast agent was administered, with a flow rate of 2 ml/s.

A Work Station Philips Brilliance (Eindhoven, Netherlands) was used for image post-processing, using different windows (lung, mediastinum, abdomen, liver and bone), multiplanar reconstructions and maximum intensity projections.

Diagnostic criteria

Lesions with compatible histology, de novo pancreatic nodules or lesions that increased in size during follow-up in patients with metastatic disease in other regions were classified as pancreatic metastases.

Results

Pancreatic lesions were identified in seven patients. One patient with a large kidney tumor that extended locally into the pancreas was excluded; consequently, six patients met the inclusion criteria for pancreatic metastasis (4.5% of patients with RCC). The pancreas was the fifth most common site of spread (Table 1). Metastases showed no predilection for any particular part of the pancreas.

Five of the six patients were men. Mean age was 71.3 years (range 63–79 years). Mean time between initial diagnosis and detection of pancreatic metastases was 30.3 months (range 12–49 months), and they all were metachronous.

Metastases appeared as nodules within the pancreatic gland on MDCT. Nodules were solitary in four patients. One was 18 mm in size and was located in the pancreatic body; two were found in the pancreatic tail and were 13 mm and 40 mm, respectively; the fourth nodule was a 15 mm lesion in the uncinate process (Figs. 1 and 4). These solitary nodules were seen as hyperattenuating masses in the arterial phase— which reflects hypervascularity—, and as iso- or hypoattenuating lesions in the portal phase. One of these patients had no metastatic disease in other sites, and the pancreatic mass was surgically resected. The results of the histopathologic examination confirmed metastasis from a RCC. In the remaining three patients, the solitary nodules were encountered in a clinical setting of metastatic disease to the bone, muscle, liver, lung and adrenal gland.

Nodules were multiple in two of the six patients, with the following distribution: two solid nodules, hyperattenuating in the arterial phase, were identified in one of the patients. One of the nodules was 10 mm in size and was located in the pancreatic head, and the other was 8 mm in size and located in the uncinate process. The DCT study of this patient also showed a hypoattenuating ill-defined lesion, 12 mm in size, located in the pancreatic head, probably due to necrosis. Follow-up examinations showed that the nodules had enlarged. In the other patient with multiple nodules, two solid nodules were identified. One was located in the pancreatic head, which was 15 mm in size and hyperattenuating in both the arterial and portal phase, and the

| Table 1 Location and frequency (expressed as number of cases and percentage) of metastases in patients with renal cell carcinoma. |
|---|---|
| Location of metastases | No. of cases (%) |
| Lung | 37 (28.8) |
| Liver | 16 (12.12) |
| Bone | 13 (9.8) |
| Adrenal glands | 12 (9.09) |
| Pancreas | 6 (4.5) |
| Muscle | 4 (3) |
| Subcutaneous cellular tissue | 2 (1.5) |
| Brain | 2 (1.5) |
| Pleura | 1 (0.75) |
| Thyroid | 1 (0.75) |

Figure 1 66-year-old patient with metastatic disease to lung, liver, bone and muscle. Follow-up MDCT shows a hypervascular nodule in arterial phase (a), in the pancreatic body, with mild dilation of the duct of Wirsung. In a later phase, the nodule becomes isoattenuating (b) relative to the pancreatic parenchyma (arrows).
second nodule, found in the tail, was 14 mm in size, and was hyperattenuating with an hypoenhancing central component in the arterial and portal phase (Figs. 2 and 3).

Both cases showed dilation of the duct of Wirsung distal to the pancreatic nodule (Table 2).

Discussion

The appearance of pancreatic metastases on MDCT is typical and practically constant. Metastases should be differentiated from primary pancreatic adenocarcinoma, which shows different radiologic features.

According to the literature, the RCC metastasizes, in decreasing order of frequency, to the lung, bone, liver, contralateral kidney or/and adrenal gland, and to the central nervous system. Atypical metastases from RCC have also been reported, corresponding to uncommon sites or unusual radiologic presentations.11 We must be familiar with these unusual locations because some patients may benefit from local resection. In addition, these lesions should not be mistaken with primary tumors.

Pancreatic metastases from RCC are relatively rare. The study by Hirota et al.13 included the 66 cases of pancreatic metastases from RCC reported in the world literature up to 1996. They occurred in 0.25–3% of all patients with metastatic RCC.12–14 In our study, the frequency of pancreatic metastases from RCC was 4.5%, slightly higher than the frequency reported in studies published to date. This is probably due to the improved technical equipment, the advent of multidetector CT, and the increasingly widespread use of imaging modalities. Nonetheless, our results were not significantly higher.

Metastatic disease to the pancreas may be synchronous or, like in our patients, metachronous. Metachronous metastases occur years after nephrectomy for RCC and we should know how to differentiate them from primary pancreatic tumor, especially in patients with solitary metastases, because the therapeutic approach and prognosis differ considerably.15,16 Surgical resection has proven to improve survival of patients with pancreatic metastases from RCC, particularly those with solitary lesions or lesions located in one single region of the pancreas. Imaging studies are essential for detection of metastases in these patients, as they are usually asymptomatic.
Since ultrasonographic findings of primary and secondary tumors are unspecific in most patients, CT has become the modality of choice for the detection and differentiation of these tumors.

In our study, pancreatic metastases from RCC appeared as intrapancreatic masses or nodules, solitary or multiple, with maximum diameters ranging from 8 to 40 mm. In most cases (all except one lesion), lesions demonstrated intense early enhancement, which reflects hypervascularity of the tumor, and were seen as hyperattenuating masses relative to the surrounding parenchyma (Fig. 1). In the portal phase, lesions became iso- or hypodense relative to normal pancreatic tissue (Figs. 2–4), making their detection difficult. Morphologic and dynamic features of the lesions exhibit a practically constant pattern. This is in agreement with the cases reported in the literature6,7 and helps differentiate metastases from primary pancreatic adenocarcinoma. Adenocarcinoma is typically hypovascular and appears as a lesion with low attenuation coefficient in both arterial and late phases. For this reason, an early arterial phase prior to the portal phase is highly recommended to improve the detection and characterization of pancreatic lesions. However, this typical presentation of pancreatic metastases from RCC is not pathognomonic, and it is therefore essential to make a differential diagnosis with other hypervascular lesions such as pancreatic islet cell tumor and metastases from breast carcinoma, where clinical and analytical data as well as a previous history of neoplasm play a crucial role.17,18

The lesion that was hypoattenuating in both the arterial and portal phase should be considered separately, and the hypoattenuation was probably due to necrosis phenomena.

In conclusion, although RCC is a relatively common neoplasm, metastases to the pancreas are very rare (4.5% of patients in our series, fifth most common location). The characteristic presentation of pancreatic metastases as nodules, solitary or multiple, which appear as hypervascular masses in the arterial phase, and iso-hypointense in late phases, in patients with a history of RCC, helps differentiate them from primary pancreatic adenocarcinoma, with important prognostic implications.

**Table 2** Distribution of the cases according to age (years), time elapsed from initial diagnosis (months), multiplicity of metastases, size (mm), dynamic behavior in the arterial phase (hypervascularity), and dilation of the pancreatic duct.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Time from diagnosis</th>
<th>Type of metastasis</th>
<th>Size of metastases</th>
<th>Hypervascular arterial phase</th>
<th>Dilation of pancreatic duct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>63</td>
<td>35</td>
<td>Multiple</td>
<td>12, 10, 8</td>
<td>Yes/No</td>
<td>No</td>
</tr>
<tr>
<td>Men</td>
<td>65</td>
<td>31</td>
<td>Solitary</td>
<td>11</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Men</td>
<td>79</td>
<td>12</td>
<td>Solitary</td>
<td>9</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Men</td>
<td>66</td>
<td>28</td>
<td>Solitary</td>
<td>13</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Men</td>
<td>76</td>
<td>34</td>
<td>Solitary</td>
<td>12</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Women</td>
<td>79</td>
<td>42</td>
<td>Multiple</td>
<td>15, 14</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Figure 4** 76-year-old patient with a history of RCC and metastatic disease to liver, bone and adrenal glands. (A) Follow-up MDCT in arterial phase shows a hypervascular solitary nodule in the pancreatic tail (arrow). (B) The nodule becomes isoattenuating in the venous phase. The lesion was histologically confirmed.

**Authorship**

1. Responsible for the integrity of the study: EIC
2. Conception of the study: EIC, JAS
3. Design of the study: EIC, JAS
4. Acquisition of data: EIC
5. Analysis and interpretation of data: EIC, JAS
6. Statistical analysis: N/A
7. Bibliographic search: GGR
8. Writing of the manuscript: EIC, GGR
9. Critical review with intellectually relevant contributions: JAS
10. Approval of the final version: JAS, GGR, EIC.

**Conflicts of interest**

The authors declare not having any conflicts of interest.
MDCT recommendations

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