

Metastasis to the Pancreas: Characterization by Morphology and Contrast Enhancement Features on CT and MRI

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Key Words

Metastasis · Pancreas · Renal cell carcinoma · Magnetic resonance imaging · Computed tomography

Abstract

Aims: To investigate the characteristics of metastasis to the pancreas using computed tomography (CT) and magnetic resonance imaging (MRI). **Methods:** Twenty-two patients with metastases to the pancreas were examined preoperatively by MRI (7/22) and/or multidetector CT (15/22). Pre- and post-contrast images were acquired and morphology, size, and contrast enhancement of the tumor analyzed. Subsequently, all patients underwent surgery, and the histopathologic findings were compared with the imaging results. **Results:** In 22 patients, a total of 29 metastases were found on CT and MRI. These metastases originated from renal cell carcinomas (RCC; 22/29), colorectal carcinoma (3/29), and other malignancies (4/29). The metastases differed not in size or location, but in their contrast enhancement characteristics. RCC metastases had either intense homogeneous enhancement (in small lesions) or rim enhancement (in large lesions). Outer regions of colorectal metastases showed no difference from normal pancreatic tissue, whereas the inner area showed hypo-enhancement due to central necrosis. **Conclusion:** Imaging features of metastases from RCC point to their primary origin. While they can be distinguished from primary adenocarcinoma of the pancreas, differentiation

from endocrine carcinoma might be difficult. Differentiation of colorectal carcinoma remains to be investigated on larger numbers of cases.

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Introduction

The vast majority of pancreatic malignancies are primary tumors. Metastasis to the pancreas is rare and accounts for less than 5% of all pancreatic malignancies [1–3]. A variety of tumors, such as renal cell carcinoma (RCC), colorectal carcinoma, and lung cancer, are known to metastasize into the pancreas [4]. In case of inoperability, different chemotherapeutic approaches are required. However, solitary pancreatic metastases are difficult to differentiate and may be misdiagnosed as primary cancer of the pancreas. Therefore, if the patient has a history of extrapancreatic malignancies and a tumor is detected within the pancreas, metastasis must be considered.

Fine-needle biopsy can be performed to assess the histological type of the tumor [5]. Alternatively, noninvasive imaging may be a promising tool for differentiating a pancreatic metastasis from a primary adenocarcinoma and for classifying the histological type of the metastasis itself on the basis of morphologic criteria and contrast-enhancement characteristics [6].

Table 1. Numbers of patients, metastases and contrast enhancement characteristics

Histologic type	Patients	Metastases	Contrast enhancement compared to normal pancreas	Enhancement characteristics	Size (\pm standard deviation), cm ²
Renal cell carcinoma	15/22	22/29	Hyperenhancement (21/22)	Homogeneous (12/22) Rim enhancement (10/12)	5.1 \pm 4.5 25.4 \pm 23.8
Colorectal adenocarcinoma	3/22	3/29	Isoenhancement (3/3)	Rim enhancement with central necrosis (3/3)	51.7 \pm 49.3
Liposarcoma	1/22	1/29	Hypoenhancement	No enhancement, no necrosis	14.6
Breast cancer	1/22	1/29	Isoenhancement	Rim enhancement with central necrosis (1/1)	128.6
Merkel cell carcinoma	1/22	1/29	Isoenhancement	Rim enhancement with central necrosis plus calcification	94.6
Carcinoma of unknown primary	1/22	1/29	Isoenhancement	Homogenous enhancement without necrosis (1/1)	12.9

In this study we describe the imaging characteristics of 29 metastases found in 22 patients to determine their origin and to distinguish them from primary cancer of the pancreas.

Patients and Methods

From October 2002 until December 2006, 488 patients with pancreatic malignancies underwent partial or total pancreatectomy. Of these patients, 36 had a metastatic disease and 22 underwent preoperative imaging at our institute, either by computed tomography (CT; 15/22) or magnetic resonance imaging (MRI; 7/22). After imaging, all patients underwent surgery with histologic analysis of the origin of the metastasis.

Computed Tomography

CT scans were obtained with a multi-slice CT scanner (Somatom Plus 4 Volume Zoom, Siemens Medical Solutions, Erlangen, Germany) using a hydro protocol with water- and drug-induced distension of the stomach and duodenum (1–1.5 liters tap water and *N*-butylscopolaminiumbromide from Boehringer-Ingelheim, Germany, respectively) [5]. Initially, unenhanced scans were obtained (2.5 mm collimation, 10 mm slice thickness, 15 pitch, 120 kV, 100 mAs). Bolus tracking at the level of the celiac trunk was subsequently performed using 130 ml of contrast medium (Ultravist 370, iopromide; Schering, Germany), injected at a rate of 5 ml/s in the antecubital vein. Ten seconds after reaching the trigger point (60 HU), arterial phase imaging was performed. A second breath-hold acquisition (venous phase) was obtained 120 s after initiation of the injection of contrast material. Both scans were acquired with the following settings: 2.5 mm collimation, 15 mm pitch, 120 kV, 130 mAs, reconstructed slice thickness 3 mm.

Magnetic Resonance Imaging

Examinations were performed using a 1.5 Tesla MR scanner (Symphony, Siemens Medical Solutions, Erlangen, Germany). Different sequences were used. According to the study protocol, here we only describe the T2-weighted and the pre- and post-contrast T1-weighted images that were acquired in all study patients. (1) T2-weighted TSE-sequence: TR 5,226 ms, TE 128 ms, voxel

size 1.7 \times 1.4 \times 5 mm; (2) T1-weighted Flash-2-D: TR 179 ms, TE 4.1 ms, flip $<70^\circ$, voxel size 2 \times 1.4 \times 4 mm or 1.9 \times 1.5 \times 6 mm, and (3) dual-phase T1-weighted Flash-3-D after administration of contrast material (Magnevist, Bayer-Schering Pharma, Berlin, Germany) in the arterial and venous phase: TR 5 ms, TE 2 ms, FoV 300–450 mm, matrix 254 \times 168, voxel size 1.8 \times 2.3 \times 2.5 mm.

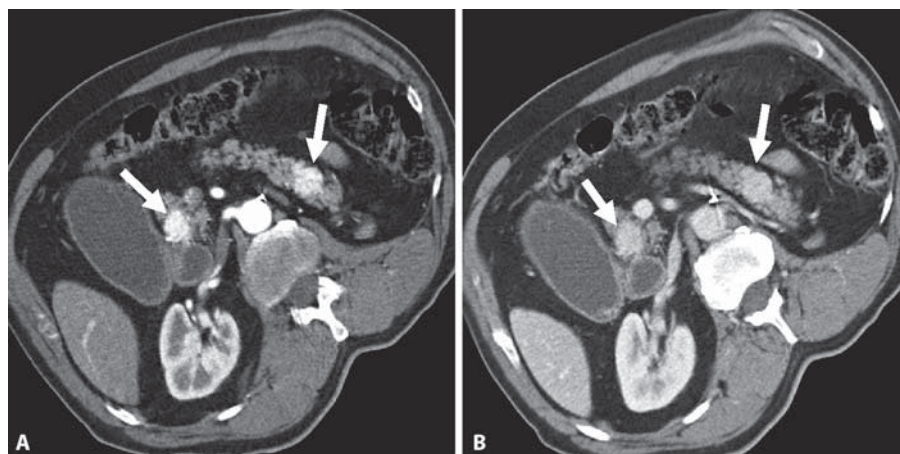
Image Analysis

CT and MRI findings were retrospectively evaluated in consensus by two radiologists with 12 and 3 years of experience in radiology, respectively. The cases were presented to the radiologists who were blinded to the histological diagnosis. Images were analyzed to determine the number and location of the metastases. Assuming that the tumor is spheroid, the volume was estimated as $(x \times y \times z \times \pi)/6$ [7]. The contrast enhancement of the tumor tissue was analyzed, compared with the enhancement of normal pancreatic tissue, and accordingly classified as (I) hypo-enhancement, (II) iso-enhancement, and (III) hyperenhancement. The enhancement characteristic was further classified into (a) homogeneous enhancement of the entire tumor, (b) inhomogeneous enhancement of the entire tumor, and (c) rim enhancement without enhancement of the central part of the tumor. Finally, results were compared to the histopathologic analysis.

Results

In 22 patients, 29 metastases to the pancreas were found on imaging. Image analysis was performed on the metastases detected. Lesions that were only detectable on histological examination could not be included in the retrospective analysis of the images. The origin of the metastases was RCC in 15 patients (total of 22 tumors; 13 patients with a single metastasis, 1 patient with 4 tumors, and 1 patient with 5 tumors), colorectal carcinoma in 3 patients (1 tumor per patient), and liposarcoma, Merkel cell carcinoma, breast carcinoma, and carcinoma of unknown primary (CUP) in 1 patient each (table 1). The median interval between the primary carcinoma and the oc-

Fig. 1. Arterial (A) and venous (B) phase CT images of two metastases from renal cell carcinoma within the head and tail of the pancreas (arrows). Both lesions have strong and homogeneous enhancement after contrast administration as compared with normal pancreatic tissue. The best differentiation of the lesions is possible on the arterial phase images, but strong enhancement of the metastases is also visible in the venous phase images.



currence of pancreatic metastasis was 130 (range 12–264) and 24 (range 18–30) months for RCC and colorectal carcinoma, respectively. The remaining intervals are 48 months for liposarcoma, 108 months for breast cancer, 11 months for CUP, and an unknown interval for Merkel cell carcinoma. Due to the prolonged time interval, most patients with RCC were not included in the regular follow-up and in most cases the diagnosis was incidental (e.g. abdominal sonography while presenting with inguinal hernia). In contrast, all patients with colorectal carcinoma underwent regular follow-up and had symptoms (e.g. abdominal pain).

Tumors showed no predilection for any particular part of the pancreas and did not differ significantly in size (RCC $17.1 \pm 20.6 \text{ cm}^2$, colorectal carcinoma $51.7 \pm 49.3 \text{ cm}^2$, $p = 0.34$), although RCC metastases showed a tendency to be smaller. However, this lack of significance might be related to the small sample of metastases from colorectal carcinoma.

On MRI, RCC lesions were hypointense compared with normal pancreatic tissue on pre-contrast T1-weighted images and hyperintense on T2-weighted images. In non-contrast enhanced CT scans, RCC metastases had the same density as normal pancreatic tissue. Following contrast agent administration, on both CT and MRI most RCC metastases (21/22) showed intense enhancement on arterial and venous phase images compared with normal pancreatic tissue. Tumors smaller than 1.5–2 cm in diameter enhanced homogeneously (fig. 1), while in larger lesions rim enhancement was present (fig. 2). However, one RCC lesion (1/22) with a diameter of 1.5 cm showed only intermediate enhancement without the typical hyperenhancement.



Fig. 2. The typical rim enhancement of a larger renal cell carcinoma metastasis is visible on the post-contrast arterial phase image. However, the inner area of the tumor shows no enhancement due to devascularization caused by central tumor necrosis.

Colorectal carcinomas (3/3) had the same characteristics as RCC on both pre-contrast MRI and CT images. After administration of contrast medium, the outer rim (2–4 mm) enhanced identically to the pancreatic tissue whereas the inner parts of the tumor did not enhance due to central necrosis (fig. 3).

The liposarcoma (only CT examination) enhanced less than normal pancreatic tissue, while breast carcinoma, Merkel cell carcinoma and the CUP metastases had identical enhancement to normal pancreatic tissue (only CT examinations).

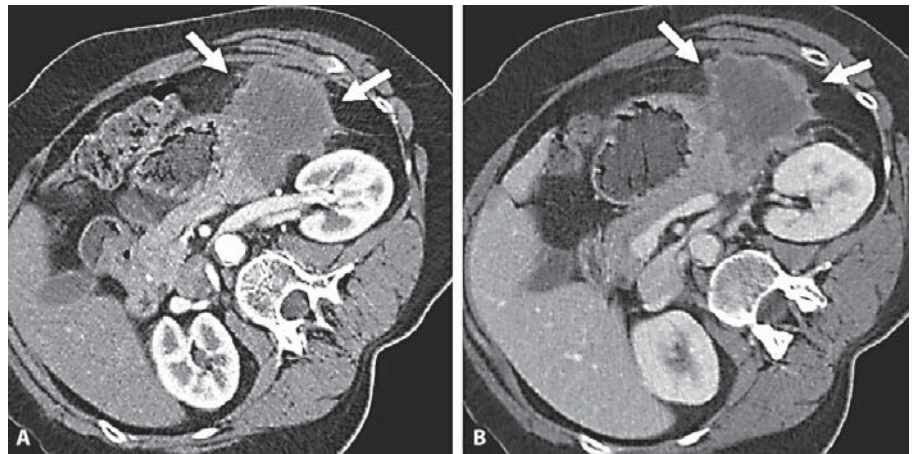


Fig. 3. Arterial (A) and venous (B) phase CT images of a colorectal metastasis. The outer rim of the colorectal metastasis has the same enhancement as normal pancreatic tissue, while the inner area has no enhancement at all, due to a large central necrosis.

Discussion

The pancreas is a rare site of metastasis from other malignancies, accounting for less than 5% of pancreatic tumors [1]. Due to the rarity of pancreatic metastasis, many of these cases might be misdiagnosed as primary pancreatic neoplasms. However, if the patient has a history of malignant disease – which for RCC may even be more than 25 years after the initial diagnosis – metastasis must be considered [2]. In our study, 7.3% of patients who underwent oncologic pancreatotomy had metastatic disease. Most primary tumors were RCC, which were also prominent among the primary tumors responsible for pancreatic metastases in four previous radiologic studies [6, 9–11]. These metastases are most prevalent in the pancreas according to surgical resection series [4].

The practical importance of distinguishing RCC metastasis from primary ductal adenocarcinoma of the pancreas lies in differences in prognosis and management [8]. It has been shown that surgical resection for solitary pancreatic metastasis from RCC is the most effective treatment option, leading to a 5-year survival rate of up to 75% in recent reports [2]. If the tumor is inoperable, fine-needle biopsy can be performed to assess the histological type of the tumor and allow an individualized chemotherapeutic approach. As a future method, immunohistochemical and nucleic acid-based assays have shown promising results in the detection of disseminated tumor cells in the peripheral blood [12, 13]. While under investigation, this method has yet to be translated into clinical routine.

Alternatively, noninvasive imaging also seems suited to differentiate RCC metastasis from primary adenocarcinoma of the pancreas. The strong enhancement exhib-

ited by tumor tissue in many of our cases reflects a degree of vascular perfusion that is not typical of primary pancreatic adenocarcinoma. Metastases from RCC were often seen as hyperattenuating masses, either with homogeneous enhancement or with a highlighted rim and nonenhancing internal components, depending on their size. This behavior, which reflects hypervascularization of vital tumor tissue and diminished or absent perfusion of necrotic components, is also typical for primary RCC [14]. In contrast, intense enhancement is very uncommon in pancreatic ductal adenocarcinomas due to their desmoplastic composition. They typically appear as a uniformly nonenhancing mass on CT examinations [15, 16]. Therefore, these two entities may be reliably distinguished.

The differentiation of nonhyperfunctioning endocrine carcinoma from metastatic RCC can be more problematic as they share morphologic and contrast enhancement features. Both types of malignancies are typically hypervascularized, but are subject to central necrosis and cystic degeneration when they have reached a certain size [17]. In addition, both malignancies may be solitary or multiple. Therefore, if the patient has a history of RCC and a hypervascularized tumor is detected within the pancreas, metastasis must be considered.

Large metastases from colorectal carcinoma also have a hypo- or even devascularized center without contrast enhancement. However, unlike RCC, the outer rim is not hypervascularized and, therefore, shows merely isoattenuation after administration of contrast medium. Additionally, the central parts often have a liquid character. Primary adenocarcinoma, though also not hyperenhancing, regularly shows homogeneous enhancement with almost the same characteristics as normal pancreatic tissue

[15, 16]. This points to the conclusion that large metastasis from colorectal carcinoma with central necrosis might be differentiated from primary adenocarcinoma. However, our small number of cases does not permit any clear statement about differentiating the two tumor types, especially since our collective does not include small colorectal metastases. Those tumors would most probably consist of vital tumor tissue, which would provide the same isoattenuation as the vital rim of the larger metastases presented in our study. Therefore, the isoattenuating tumor might be misinterpreted as a primary adenocarcinoma [18]. The same is true for liposarcoma, CUP, breast cancer, and Merkel cell carcinoma. Here, the solitary metastases found in our study do not permit conclu-

sions to be drawn regarding the general behavior of this tumor type.

In summary, the behavior of RCC metastases to the pancreas has been elucidated. Their characteristic imaging features point to the conclusion that they can be differentiated from primary adenocarcinoma of the pancreas, however distinguishing it from nonhyperfunctioning endocrine carcinoma might be problematic, as both types share morphologic and contrast enhancement characteristics. It may also be possible to distinguish large metastases from colorectal carcinoma from primary malignancies of the pancreas; however, this still has to be investigated with a larger number of cases, especially since our study did not include small metastases from colorectal carcinoma.

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