VOLUME 4 | ISSUE 3

HJR

Abdominal Imaging ORIGINAL ARTICLE

Pancreatic metastases from renal neoplasms and neuroendocrine pancreatic tumours: is a differential diagnosis possible with CT?

Maria Chiara Ambrosetti, Giulia Angela Zamboni, Alessandro Fighera, Giancarlo Mansueto

Istituto di Radiologia, Policlinico GB Rossi, Azienda Ospedaliera Universitaria Integrata di Verona, Italy

SUBMISSION: 15/5/2019 | ACCEPTANCE: 20/8/2019

ABSTRACT

Purpose: Both pancreatic metastases from renal cell carcinoma (pRCC) and pancreatic endocrine tumours (pNET) appear typically as hypervascular, well-defined lesions, and a differential diagnosis may be extremely difficult. Our purpose was to assess the value of CT and CT texture analysis in the differential diagnosis when considering only one lesion per patient, therefore excluding the added value of multiplicity.

Material and Methods: In this retrospective study, we compared the MDCTs performed on 31 patients with pRCC to 31 patients with pNET matched by size, performed at our institution in the last 6 years. We analysed margins, size, location, qualitative assessment of enhancement intensity and homogeneity in the arterial and venous phases, vascular invasion and dilatation of main pancreatic duct (MPD). Texture analysis was performed on a subgroup of 22 Patients with pNET and 22 Patients with pRCC.

Results: No significant difference was observed in lesion distribution. Twenty-nine pRCCs and 27 pNETs appeared hyperdense to the normal pancreatic parenchyma in the arterial phase (p=n.s.). Twenty-three pRCCs and 17 pNETs appeared hyperdense to the normal pancreatic parenchyma in the venous phase, again with no statistically significant difference (all p=n.s.). No significant difference was found on homogeneity both in arterial and venous phase. Regarding texture analysis, only skewness calculated in the arterial phase was significantly different between the two groups of patients.

Conclusions: Both pRCC and pNET are hypervascular lesions with sharp margins, usually not associated with MPD dilatation or vessel infiltration. We did not find significant imaging features or quantitative parameters to support the differential diagnosis. The best diagnostic clue for pRCC is a history of renal cell carcinoma.

CORRESPONDING AUTHOR, GUARANTOR

Maria Chiara Ambrosetti,
Istituto di Radiologia, Policlinico GB Rossi, Azienda Ospedaliera Universitaria Integrata di Verona, P. le LA Scuro 10, 37134 Verona, Italy,
Email: mchiara.ambrosetti@gmail.com

KEY WORDS
Pancreatic renal cell metastases; Pancreatic neuroendocrine tumours; MDCT

Introduction

Pancreatic metastases are rare and represent 2-5% of all pancreatic tumours. The most common primary tumours that give metastases to the pancreas are renal cell carcinoma (RCC), lung cancer, breast cancer, colorectal cancer, and melanoma [1-3]. The most common metastases are those from RCC, for which the pancreas seems to be an elective site for metastatic spread [4, 5]. Metastases from RCC (pRCC) can present after long disease-free intervals, and the mean intervals reported in the literature are longer than 10 years [6]. On the other hand, neuroendocrine tumours of the pancreas (pNET) have a reported prevalence at autopsy of 0.8 to 10% [7]. Due to the increased use and high resolution of diagnostic imaging, their incidental detection has increased over the decades.

Both pRCC and pNET appear typically as hypervascular, well-defined lesions, and a differential diagnosis may be extremely difficult [6, 7]. Moreover, the long disease-free interval in patients with a history of RCC can pose significant problems in differential diagnosis when a single hypervascular lesion is identified in the pancreas. Given the disparity in prognosis and management of patients affected by the two different entities, the possibility of a reliable differential diagnosis at imaging would be important, especially at multidetector computed tomography (MDCT) since patients with RCC are most commonly examined by means of contrast-enhanced MDCT.

Kang et al. have recently described that relative percentage washout and lesion multiplicity could be useful to this purpose, whereas other imaging features are not useful for a diagnosis [8]. Van der Pol also described qualitative and quantitative CT features of pRCC and pNET considering all the pancreatic lesions concluding that pNETs are larger, more frequently solitary, contain calcifications, cause main pancreatic duct (MPD) dilation and are subjectively and quantitatively more heterogeneous tumours [9]. To our best knowledge, all the papers published in the literature analysed all pancreatic lesions in each patient. We wanted to assess the value of CT in the differential diagnosis when considering only one lesion per patient, therefore excluding the added value of multiplicity and focusing on the peculiar CT features of the lesion itself for the differential diagnosis between a single pRCC and a pNET.

The primary objective of our study was therefore to compare the MDCT features of pancreatic metastases from RCC with those of pNET, considering only one lesion per patient. The secondary objective was to assess if texture analysis could provide additional information useful for a differential diagnosis.

Material and Methods

The radiological, surgical and oncological databases were reviewed to identify patients with pRCC or pNET seen at the University Hospital GB Rossi in Verona between January 2008 and April 2019. Exclusion criteria were: patients who did not undergo CT, patients who had only non-contrast or single phase study and patients with low quality imaging due to severe respiratory motion.

We identified 31 patients with pathology-proven pRCC with multiphasic MDCT images available in our archives, and selected 31 patients with pNET, matched by size by selecting the closest diameter from the tumours included in a database of 135 pathology-proven pNET. Six patients with pRCC and 27 patients with pNET underwent surgery whereas in 25 patients with pRCC and 4 patients with pNET, histopathology was obtained by biopsy. When patients had more than one lesion, only the largest one was analysed.

Scans had been performed on different generations of CTs, most commonly on 64-row CT scanners, with multiphasic acquisitions that included a late arterial phase and a venous phase acquisition after administration of non-ionic iodinated contrast agents, and often included a non-contrast scan. Images were evaluated on a PACS workstation in consensus by two radiologists with 10 and 15 years of experience in abdominal imaging, respectively (MCA, GAZ).

For each lesion the two readers analysed the following features: site (head, body or tail of the pancreas), diameter, margins (sharp or irregular), vascularisation in the post-contrast phases, homogeneity, presence of vascular infiltration and caliber of the MPD upstream to the neoplasm. Both in the arterial and in the venous phase each le-

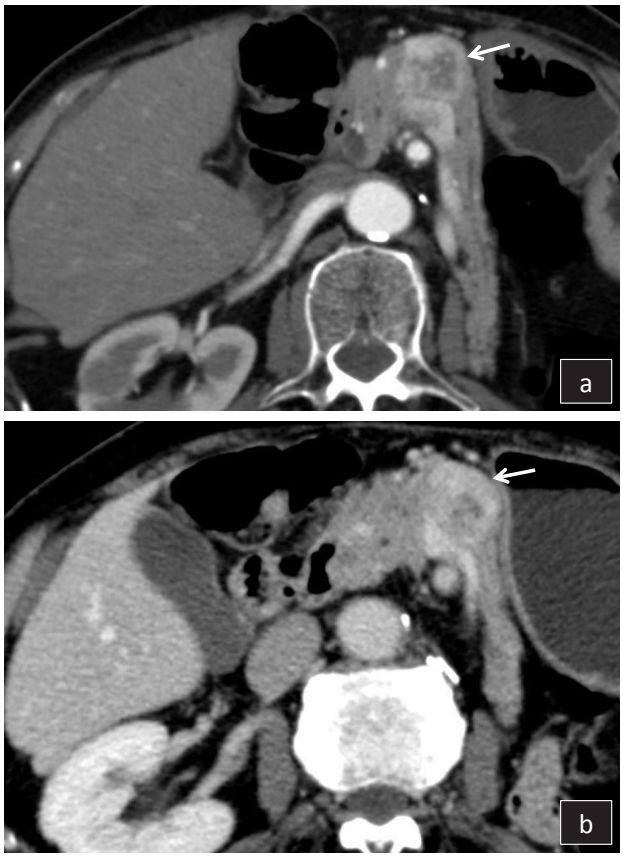

Fig. 1. *Arterial phase (a) and venous phase (b) axial MDCT images of pNET. A single inhomogeneous and hypervascular lesion (arrows) both in the arterial (a) and venous (b) phase is well recognisable in the body of the pancreas.*

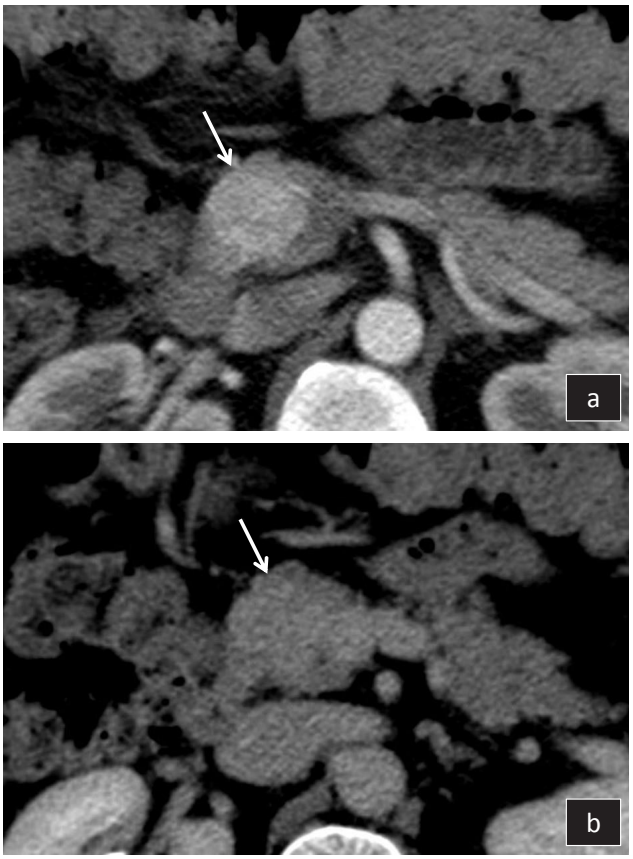

Fig. 2. *Arterial phase (a) and venous phase (b) axial MDCT images of pRCC. A homogeneous and hypervascular in the arterial (a) and isovascular in the venous (b) phase lesion (arrows) is recognisable in the head of the pancreas.*

sion was subjectively evaluated as hypervascular, isovascular or hypovascular compared to the normal pancreatic parenchyma and the enhancement pattern was considered homogeneous or inhomogeneous. In order to correct possible variations in contrast injection and scan protocols, we performed a semiquantitative analysis, by comparing subjectively the density of the lesions to that of the normal pancreas.

One author performed the analysis on the texture values using LIFEx software (http://www.lifexsoft.org/) on a subgroup of pRCC and pNET for which DICOM data were available for the arterial phase scan and, when available, for the non-contrast scan. Analysis was performed drawing a 2D ROI on the axial slice with the largest tumour area, including the entire lesion. Both image series were loaded and layered in the program at the same time, using the arterial phase as a reference in order to achieve best image registration possible and compensate for respiratory movements of the pancreas. First order parameters of the derived histograms (skewness, kurtosis, energy and entropy) were considered. Statistical analysis was performed using GraphPad Prism version 6.01 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com. Unpaired T-test and Fisher's test were used. A p-value <0.05 was considered as significant.

Results

The 31 patients with pRCC included 16 females and 15 males, with a mean age of 67.9 years (range 50-80 years). The 31 patients with pNET included 18 females and 13 males, with a mean age of 53 years (range 18-70). The difference in age between the two groups was statistically significant ($p< 0.0001$).

As a confirmation of the size matching of the lesions, no difference was observed in the diameter of the lesions in the two groups (25.94 ± 2.8 mm for pRCC vs 27.52 ± 3.1 mm

Table 1. First-order texture statistics

	Unenhanced			*Arterial phase*		
	pRCC	pNET	p	pRCC	pNET	p
energy	0.01688 ± 0.001505	0.0160 ± 0.001124	0.64	0.02348 ± 0.006050	0.0205 ± 0.005154	0.71
entropy log10	1.818 ± 0.02849	1.862 ± 0.02984	0.31	1.842 ± 0.06569	1.891 ± 0.06691	0.60
mean intensity	34.95 ± 2.968	34.18 ± 3.299	0.87	156.3 ± 8.874	134.5 ± 7.950	0.08
standard deviation	19.89 ± 1.050	23.10 ± 2.167	0.23	32.95 ± 2.230	31.18 ± 2.127	0.57
skewness	-0.1219 ± 0.03220	-0.1555 ± 0.06637	0.68	-0.3796 ± 0.07195	-0.1320 ± 0.07372	0.02
kurtosis	3.109 ± 0.1045	3.218 ± 0.1507	0.58	3.292 ± 0.1485	3.127 ± 0.1301	0.42

for pNET; p=0.7121). Size range was 7-84 mm for pNET and 6-65 mm for pRCC.

Although this does not reflect the entire distribution of the lesions, since we chose to analyse only the largest pRCC lesion in patients with multiple lesions, the distribution of the analysed lesions in the two groups was not significantly different: 18 pRCC were in the pancreatic head, 5 in the body and 8 in the tail, while 18 pNETs were in the head, 6 in the body and 7 in the tail.

None of the pRCC and only one pNET showed calcifications (p=1). All the lesions in both groups had well-defined margins (p=1).

There was no significant difference in MPD diameter upstream to the lesion (mean diameter 2.2 ± 0.5 mm for pRCC vs 2.7 ± 0.6 mm for pNET; p=0.4831). Dilatation of MPD was found only in three patients with pNET located at the head of the pancreas and with mean diameter of the lesion of 50 mm and in one patient with pRCC of 31 mm located at the body of the pancreas.

Twenty-nine pRCCs and 27 pNETs appeared hyperdense to the normal pancreatic parenchyma in the arterial phase (p=0.5853). Twenty-three pRCCs and 17 pNETs appeared hyperdense to the normal pancreatic parenchyma in the venous phase, again with no statistically significant difference (p=0.1702). Sixteen pRCC appeared homogeneous, compared to 22 pNET (p=0.1919). **(Figs. 1, 2)**.

Texture analysis was performed on a subset of 22 patients with pancreatic NET (13 female and 9 male with a mean age of 52.6 years) and on 22 patients with RCC pancreatic metastases (10 female and 12 male with a mean age of 66.2 years). Texture analysis showed a significant difference in skewness calculated in the arterial phase (p=0.02; **Table 1**). No significant difference was observed for any of the other analysed parameters.

Discussion

The detection of a hypervascular pancreatic lesion in a patient with a history of RCC can pose problems of differential diagnosis between metastatic lesions and endocrine tumours, because pRCC can present with metastases after many years, and both lesions appear most commonly hyperdense in the arterial phase [8]. Kang et al. have suggested calculating the relative percentage washout of these lesions, with an optimal cut-off value of relative percentage wash-out (RPW) for the discrimination of pRCC from pNET of 19%, which provides an accuracy of 83.8% [8]. It has also been reported that the density measured in the solid homogeneous portions of pRCC is higher than the density measured in pNET [8]. However, it might be difficult to apply this when analysing a lesion in a single patient, and the attenuation values might be influenced by contrast and scan parameters. Van der Pol et al. described pNET as being larger tumours, more frequently solitary, with calcifications, responsible of upstream MPD dilation and subjectively and quantitatively more heterogeneous tumours as compared to pRCC. Actually the authors didn't focus only on the imaging features of the pancreatic lesion itself [9].

In our series, we focused only on the largest lesion in the pancreas, and we first assessed if qualitative and semi-quantitative analyses might provide some assistance in this differential diagnosis. In agreement with the previous literature reports, we did not observe any significant difference

between the two groups in lesion location, margins, homogeneity, density compared to the normal pancreatic parenchyma in the arterial and venous phases and presence of calcifications or MPD dilatation.

We subsequently performed texture analysis, to assess if this might aid in the differential diagnosis. Among all the parameters that we analysed, only skewness calculated in the arterial phase showed a significant difference between pRCC and pNET.

Interestingly, no difference was observed in the attenuation of the two groups of lesions in the arterial phase scan derived from the texture analysis, differently from what reported by Kang. However, since not all our studies had been performed with the same scan protocol, we cannot make inferences from this and we had chosen not to perform a quantitave analysis of enhancement.

Some limitations must be noted in our study. First of all, it is a retrospective study that includes examinations acquired over a relatively long period. Therefore acquisition protocols were not constant over time, nor were contrast administration protocols. This, however, could not be avoided when studying a lesion that is not common, such as the pRCC. In order to correct possible variations in contrast injection and scan protocols, we performed a semiquantitative analysis, by comparing subjectively the density of the lesions to that of the normal pancreas. As a second limitation, only patients with multiphasic MDCT examination performed in our institution or present in our imaging archives were included in this study (participation and image-based selection bias).

Notwithstanding these limitations, we can conclude that in our series we did not identify any qualitative or semi-quantitative CT feature helpful for a differential diagnosis of a single hypervascular lesion between pRCC and pNET. Texture analysis does not appear to provide additional information useful for a differential diagnosis. **R**

Conflict of interest

The authors declared no conflicts of interest.

References

1. Ng CS, Loyer EM, Iyer RB, et al. Metastases to the pancreas from renal cell carcinoma: Findings on three-phase contrast-enhanced helical CT. *AJR Am J Roentgenol* 1999; 172(6): 1555-1559.
2. Sellner F, Tykalsky N, De Santis M, et al. Solitary and multiple isolated metastases of clear cell renal carcinoma to the pancreas: An indication for pancreatic surgery. *Ann Surg Oncol* 2006; 13(1): 75-85.
3. Tsitouridis I, Diamantopoulou A, Michaelides M, et al. Pancreatic metastases: CT and MRI findings. *Diagn Interv Radiol* 2010; 16(1): 45-51.
4. Ballarin R, Spaggiari M, Cautero N, et al. Pancreatic metastases from renal cell carcinoma: The state of the art. *World J Gastroenterol* 2011; 17(43): 4747-4756.
5. Kassabian A, Stein J, Jabbour N, et al. Renal cell carcinoma metastatic to the pancreas: A single-institution series and review of the literature. *Urology* 2000; 56(2): 211-215.
6. Cheng SKH, Chuah KL. Metastatic renal cell carcinoma to the pancreas: A review. *Arch Pathol Lab Med* 2016; 140(6): 598-602.
7. Lewis RB, Lattin GE, Paal E. Pancreatic Endocrine Tumours: Radiologic-Clinicopathologic Correlation. *RadioGraphics* 2010; 30(6): 1445-1464.
8. Kang TW, Kim SH, Lee J, et al. Differentiation between pancreatic metastases from renal cell carcinoma and hypervascular neuroendocrine tumour: Use of relative percentage washout value and its clinical implication. *Eur J Radiol* 2015; 84(11): 2089-2096.
9. van der Pol CB, Lee S, Tsai S, et al. Differentiation of pancreatic neuroendocrine tumours from pancreas renal cell carcinoma metastases on CT using qualitative and quantitative features. *Abdom Radiol* 2019; 44(3): 992-999.

READY - MADE CITATION

Ambrosetti MC, Zamboni GA, Fighera A, Mansueto G. Pancreatic metastases from renal neoplasms and neuroendocrine pancreatic tumours: is a differential diagnosis possible with CT? *Hell J Radiol* 2019; 4(3): 17-21.