Radiology Case Reports 16 (2021) 1424–1427

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journal homepage: www.elsevier.com/locate/radcr

Case report

Hypovascular pancreatic neuroendocrine tumor with hepatic metastases: A case report and literature review ☆,☆☆,★

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ARTICLE INFO

Article history:
Received 28 February 2021
Revised 12 March 2021
Accepted 13 March 2021

Keywords:
Carcinoid tumor
Hypoenhancing pancreatic neuroendocrine tumors
Hypovascular pancreatic carcinoid tumor
Hepatic neuroendocrine tumors

ABSTRACT

Hypovascular pancreatic neuroendocrine tumors are uncommon pancreatic tumors and commonly misdiagnosed as pancreatic ductal adenocarcinoma or chronic mass-forming pancreatitis. The liver is the organ most commonly affected by neuroendocrine tumor metastases but hepatic neuroendocrine tumor metastases are quite difficult to discriminate from other hepatic metastases and primary hepatic tumors. We describe a case of a 47-year-old man with incidentally detected multiple hepatic lesions on ultrasound. On further imaging technique including computed tomography and magnetic resonance imaging, the patient had an abnormal hypoenhancing lesion at the pancreatic tail and multiple hyperenhancing hepatic metastases that were diagnosed as hypovascular pancreatic well-differentiated neuroendocrine tumor Grade 2 with multiple hypervascular hepatic metastases after liver biopsy and surgery. Neuroendocrine tumor is a rare etiology among hypoenhancing pancreatic tumors, and must be considered to discriminate from pancreatic adenocarcinomas in cases there are multiple hyperenhancing hepatic metastases on the arterial phase without typical washout on the portal venous phase.

☆ Funding: Self-financed.
☆☆ Competing Interests: The authors do not report any conflicts of interest.
★ Author contributions: Ngo-Van D and Nguyen MD contributed to this article as co-first authors. All authors have read the manuscript and agree to the contents.
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https://doi.org/10.1016/j.radcr.2021.03.024

Introduction

Neuroendocrine tumors (NETs) derive most commonly from midgut organs, such as the small bowel, less commonly from hindgut organs, including the colon and rectum, and rarely from embryonic foregut organs, such as the bronchus, stomach, pancreas, and thyroid. Carcinoid tumors of the pancreas are rare NETs that originate from pancreatic enterochromaffin cells. The pancreatic body and tail are common locations of pancreatic NETs [1,2]. Pancreatic NETs typically appear as hypervascular enhancements compared to the adjacent pancreatic parenchyma [3]. Pancreatic NETs can be divided into three grades, low-grade (G1), intermediate-grade (G2), and high-grade (G3), based on the Ki-67 index and mitotic activity [4]. In recent studies, Grade 2 and 3 pancreatic NET were found to demonstrate hypovascular enhancement on both computed tomography (CT) and magnetic resonance imaging (MRI), which is similar to the imaging characteristics of pancreatic adenocarcinoma and chronic pancreatitis [4].

Metastases from NETs account for approximately 10% of all hepatic metastases, and the liver is the most common site for NET metastases. The most common origin of NETs that metastasize to the liver is the gastrointestinal tract, followed by the pancreas [5]. Metastases from NETs typically appear as multiple hypervascular lesions on CT or MRI imaging. Current research suggests substantial controversy exists regarding how hepatic metastases from NETs should be treated. Primary tumor resection plays a pivotal role in the treatment strategy, and systemic therapies and the roles of interventional radiology methods, such as radiofrequency (RF) ablation or embolization, continue to be evaluated and remain controversial [6].

In this article, we describe a case of atypical hypovascular pancreatic NET with multiple hepatic metastases and review the literature regarding the characteristic imaging features associated with hypovascular pancreatic NETs.

Case report

A 47-year-old man with an insignificant medical history was admitted to the hospital due to symptoms of anal fistula. Incidentally, on abdomen ultrasonography, multiple heteroechoic hepatic lesions with irregular contours and hypervascularization at the lesion periphery were observed and evaluated, with the largest lesion located in segment VI (Fig. 1).

On CT imaging, multiple hypodense hepatic lesions with heterogeneously strong enhancement were identified on the arterial phase. On the portal venous phase, some hepatic lesions, including lesions in segment VI, presented as slightly hypoattenuating, and smaller hepatic lesions presented as isoattenuating compared with the remaining hepatic parenchyma. In addition, a poorly enhancing region was observed at the pancreatic tail compared with the remaining pancreatic parenchyma, with ill-defined margins and an irregular contour. No enlarged lymph nodes were observed (Fig. 2). On MRI, multiple hepatic lesions were restricted on diffusion-weighted imaging (DWI) and presented

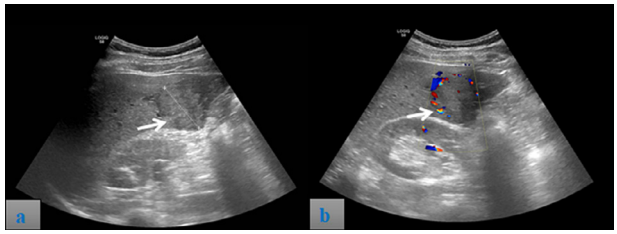

Fig. 1 – Hepatic lesion in segment VI on ultrasound. (A) Heteroechoic hepatic lesion with irregular contour (arrow) (B). The lesion periphery was hypervascular on Doppler ultrasound (arrow).

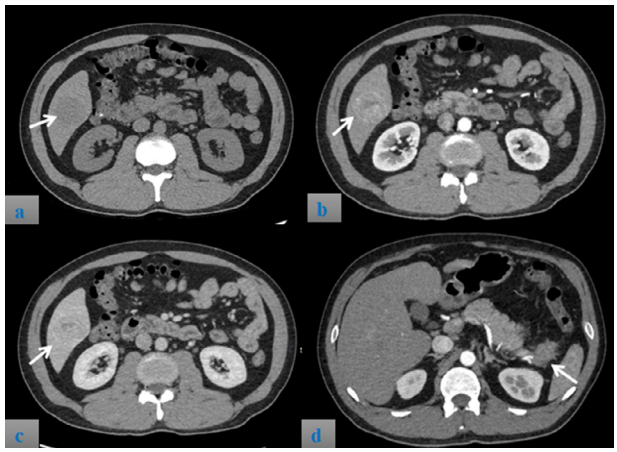

Fig. 2 – Computed tomography (CT) imaging with contrast materials: (A) Non-contrast enhancement: hypodense hepatic lesion in segment VI (arrow). (B) Arterial phase: heterogeneously strong enhancement (arrow). (C) Portal venous phase: slightly hypoattenuating compared with the adjacent parenchyma (arrow). Other hepatic lesions were no washout presented as isoattenuating compared with the adjacent parenchyma (not shown); (D) Arterial phase: compared with the remaining pancreatic parenchyma, a poorly enhancing region was observed at the pancreatic tail (arrow) with ill-defined margins and irregular contours (arrow).

heterogeneously strong enhancement on the arterial phase. On the venous phase, some hepatic lesions showed washout at the periphery, whereas other, smaller lesions demonstrated no washout. The lesion observed at the pancreatic tail was restricted on DWI (with similar signal intensity to the other hepatic lesions) and poorly enhancing compared with the remaining pancreatic parenchyma. No evidence of pancreatic duct dilation or pancreatic atrophy was detected (Fig. 3).

A hepatic biopsy was performed, targeting the segment VI lesion, and the histopathological results confirmed a well-differentiated NET, composed of rounded or ovoid cells with large nuclei and eosinophilic cytoplasm arranged in nests and sheets or around vessels (Fig. 4). Based on the imaging and histopathological results, the patient was diagnosed as pancreatic NET Grade 2 with hepatic metastases. After 1 month,

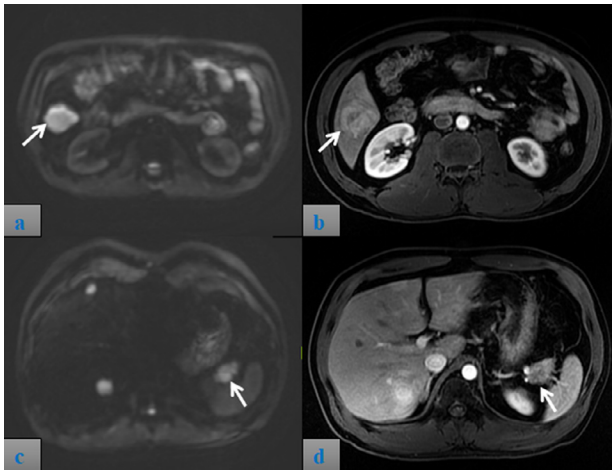

Fig. 3 – Magnetic resonance imaging (MRI). (A) Diffusion-weighted imaging (DWI) sequence: hyperintensity of the hepatic lesion signal at segment VI (arrow). (B) Arterial phase: heterogeneously strong enhancing (arrow). (C) DWI sequence: signal hyperintensity of the pancreatic tail lesion (arrow), which is similar to the presentation of hepatic lesions. (D) Arterial phase: poorly enhancing pancreatic tail lesion compared with the remaining pancreatic parenchyma (arrow).

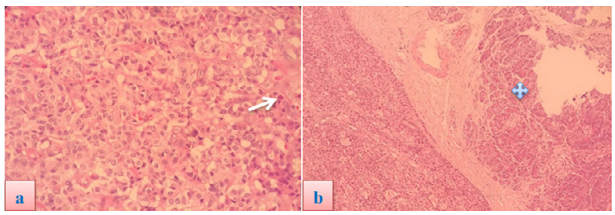

Fig. 4 – Photomicrographs of a histological section from the excised pancreatic tumor (A) showing round or ovoid cells, with large nuclei and eosinophilic cytoplasm (arrow) (H&E, × 200); (B) cells arranged in nests and sheets or around vessels, consistent with a well-differentiated neuroendocrine tumor (cross) (H&E, × 100).

the patient underwent abdominal surgery, during which distal pancreatectomy and splenectomy were performed, and the segment VI lesion was removed. During the operation, four hepatic lesions in segments IVa, VII, and VIII were treated with ultrasound-guided radiofrequency ablation.

Discussion

Pancreatic NETs account for 1% to 2% of all pancreatic neoplasms, occur most commonly in individuals aged 40 to 60 years, and can be divided into nonfunctioning and functioning tumors. Histopathologically, pancreatic NETs can be divided into three groups: well-differentiated endocrine tumors (G1), well-differentiated endocrine carcinomas (G2), and poorly differentiated endocrine carcinomas (G3) [3]. Pancreatic NETs are typically hyperenhancing on the arterial and portal venous phases due to the existence of rich capillary networks; however, up to 41.5% of pancreatic NETs can show atypical hypovascular enhancement [7]. Pancreatic NETS can present with homogeneous, ringlike, or heterogeneous enhancement, with ringlike and heterogeneous enhancement typically observed in large lesions with cystic degeneration or necrosis [1,3,8]. Calcification in these tumors is unusual [2]. Although previous studies have shown that high-grade pancreatic NETs are more likely to be hypoenhancing than lower grade pancreatic NETs, the correlation between tumoral grade and enhancement remains controversial [9,10]. According to Guo *et al.* [11], compared with G1 pancreatic NETs, G2 and G3 pancreatic NETs were more commonly associated with ill-defined margins, local invasions, or metastases and presented with hypoenhancement on the arterial phase and restricted diffusion on MRI imaging. Compared with pancreatic ductal adenocarcinoma, pancreatic NETs usually present with well-defined margins, less severe pancreatic duct dilatation, and a lower degree of distal parenchymal atrophy. According to Jeon *et al.* [10], when applying the features of a well-circumscribed margin and hyper- or isoenhancement on the portal venous phase, 64% sensitivity and 99% specificity were achieved for the discrimination of non-hypervascular pancreatic NETs from pancreatic ductal adenocarcinoma. Compared with chronic mass-forming pancreatitis, pancreatic NETs more commonly present with well-defined contours and are less frequently associated with calcifications and any history of pancreatitis [12]. In our case, the patient with G2 pancreatic NET showed ill-defined contours, and the pancreatic NET was hypoenhancing on the arterial and the portal venous phases, without calcification or ductal dilation, which was difficult to distinguish from pancreatic ductal adenocarcinoma.

NETs commonly metastasize, and the liver is the most common location for metastasis. Typically, the imaging findings of hepatic NET metastases include multiple solid lesions that are hypervascular. The cystic degeneration of a metastatic hepatic NET can be observed due to necrosis [13,14]. In hepatic NET metastases, calcification is uncommon, and hepatic tumors with a fluid-fluid level are highly suggestive of NET metastases [5]. According to Gulpinar *et al.* [14], arterial phase imaging is especially crucial in patients with NET metastases from the pancreas because 100% of patients with NETs metastases were hyperattenuating on the arterial phase, whereas 80.2% of patients were isoattenuating on the portal venous phase. According to Abdallah *et al.* [5], the enhancement pattern can suggest the site of the primary NET: a hypervascular tumor without washout on the portal venous phase suggests that the pancreas is the primary tumor site, whereas a hypervascular lesion with washout on the portal venous phase indicates a gastrointestinal origin. In our case, multiple hepatic lesions were heterogeneously hyperenhancing on the arterial phase, demonstrating both slight washout and no washout on the portal venous phase.

The treatment strategy for pancreatic NETs with hepatic metastases should be multidisciplinary and be personalized, according to the features of general health indicators, comorbidities, tumoral staging, and prognostic factors. Therapeutic methods available of pancreatic NETs include surgical treatment, loco-regional therapies, and pharmacological

treatments. Liver-directed therapies, including radiofrequency ablation (RFA), cryoablation, alkalization, transarterial embolization (TAE), and transarterial chemoembolization (TACE), can be considered for unresectable hepatic metastases [15]. Pancreatic NETs have a better prognosis, with enhanced long-term survival compared with common forms of pancreatic adenocarcinomas [1].

Conclusion

NETs are rare etiologies for hypoenhancing pancreatic tumors. Pancreatic NETs can be discriminated from pancreatic adenocarcinomas when multiple heterogeneously hyperenhancing hepatic metastases are identified, although they tend to be hypoenhancing relative to the adjacent pancreatic parenchyma.

Ethical Statement

Appropriate written informed consent was obtained for the publication of this case report and accompanying images.

Patient Consent

Informed consent for patient information to be published in this article was obtained.

REFERENCES

[1] Rashid SNA, Hamid SA, Saini SM, Gan GC. Primary carcinoid tumor of the pancreas with atypical presentation. Hong Kong J Radiol 2012;15:105–9.

[2] Prasad S, Patankar T, Joshi A, Deshmukh H. Pancreatic carcinoid: an unusual tumor in an uncommon location. J Postgrad Med 1998;44(4):97.

[3] Lewis RB, Lattin GE, Paal E. Pancreatic endocrine tumors: radiologic-clinicopathologic correlation. RadioGraphics 2010;30(6):1445–64. doi:10.1148/rg.306105523.

[4] Ren S, Chen X, Wang Z, Zhao R, Wang J, Cui W, et al. Differentiation of hypovascular pancreatic neuroendocrine tumors from pancreatic ductal adenocarcinoma using contrast-enhanced computed tomography. PLoS ONE 2019;14(2). doi:10.1371/journal.pone.0211566.

[5] Houat A de P, Atzingen AC von, Velloni FG, Oliveira RAS de, Torres UDS, D'lppolito G. Hepatic neuroendocrine neoplasm: imaging patterns. Radiol Bras 2020;53(3):195–200. doi:10.1590/0100-3984.2019.0038.

[6] Madoff DC, Gupta S, Ahrar K, Murthy R, Yao JC. Update on the management of neuroendocrine hepatic metastases. J Vasc Interv Radiol 2006;17(8):1235–50. doi:10.1097/01.RVI.0000232177.57950.71.

[7] Li J, Lu J, Liang P, Li A, Hu Y, Shen Y, et al. Differentiation of atypical pancreatic neuroendocrine tumors from pancreatic ductal adenocarcinomas: Using whole-tumor CT texture analysis as quantitative biomarkers. Cancer Med 2018;7(10):4924–31. doi:10.1002/cam4.1746.

[8] Baxi AJ, Chintapalli K, Katkar A, Restrepo CS, Betancourt SL, Sunnapwar A. Multimodality imaging findings in carcinoid tumors: a Head-to-Toe spectrum. RadioGraphics 2017;37(2):516–36. doi:10.1148/rg.2017160113.

[9] Karmazanovsky G, Belousova E, Schima W, Glotov A, Kalinin D, Kriger A. Nonhypervascular pancreatic neuroendocrine tumors: Spectrum of MDCT imaging findings and differentiation from pancreatic ductal adenocarcinoma. Eur J Radiol 2019;110:66–73. doi:10.1016/j.ejrad.2018.04.006.

[10] Jeon SK, Lee JM, Joo I, Lee ES, Park HJ, Jang JY, et al. Nonhypervascular pancreatic neuroendocrine tumors: differential diagnosis from pancreatic ductal adenocarcinomas at MR Imaging-retrospective cross-sectional Study. Radiology 2017;284(1):77–87. doi:10.1148/radiol.2016160586.

[11] Guo Cg, Ren S, Chen X, Wang Qd, Xiao Wb, Zhang Jf, et al. Pancreatic neuroendocrine tumor: prediction of the tumor grade using magnetic resonance imaging findings and texture analysis with 3-T magnetic resonance. Cancer Manag Res 2019;11:1933–44. doi:10.2147/CMAR.S195376.

[12] Ren S, Qian L, Daniels MJ, Duan S, Chen R, Wang Z. Evaluation of contrast-enhanced computed tomography for the differential diagnosis of hypovascular pancreatic neuroendocrine tumors from chronic mass-forming pancreatitis. Eur J Radiol 2020:133. doi:10.1016/j.ejrad.2020.109360.

[13] Ichiki M, Nishida N, Furukawa A, Kanasaki S, Ohta S, Miki Y. Imaging findings of primary hepatic carcinoid tumor with an emphasis on MR imaging: case study. SpringerPlus 2014;3:607. doi:10.1186/2193-1801-3-607.

[14] Gulpinar B, Peker E, Kul M, Elhan AH, Haliloglu N. Liver metastases of neuroendocrine tumors: is it possible to diagnose different histologic subtypes depending on multiphasic CT features? Abdom Radiol 2019;44(6):2147–55. doi:10.1007/s00261-019-01963-y.

[15] Nigri G, Petrucciani N, Debs T, Mangogna LM, Crovetto A, Moschetta G, et al. Treatment options for PNET liver metastases: a systematic review. World J Surg Oncol 2018;16(1):142. doi:10.1186/s12957-018-1446-y.