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A Study of Primary Hepatic Neuroendocrine Tumors Comparing CT and MRI Features With Pathology

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ABSTRACT

***Objectives**: Primary hepatic neuroendocrine tumors (PHNET) are extremely rare and difficult to distinguish from primary and metastatic liver cancers since PHNETs blood supply comes from the liver artery. This study aims to investigate CT and MR imaging findings of primary hepatic neuroendocrine tumor (PHNET) and correlation with the 2010 WHO pathological classification.*

***Methods**: We examined CT and MRI scans from 29 patients who were diagnosed with PHNET and correlated the data with the 2010 WHO classification of neuroendocrine tumors.*

***Results**: As tumor grades increase, the capsule begins to lose integrity and tumor apparent diffusion coefficient (ADC) values decrease(grade 1: 1.39 ± 0.20× 10−3 mm2/s versus grade 2: 1.26 ± 0.23× 10−3 mm2/s versus grade 3: 1.14 ± 0.17× 10−3 mm2/s).*

***Conclusions**: CT and MRI can reflect tumor grade and pathological features of PHNETs, which are helpful in accurately diagnosing PHNETs.*

KEYWORDS : Neuroendocrine tumor

Introduction

Neuroendocrine carcinoma (NEC) is rare and originates in the gastrointestinal tract, neuroendocrine cells, and pancreas. Although it resembles adenocarcinoma, well-differentiated NEC behaves biologically in a more benign fashion [1]. However, one report has shown that undifferentiated NECs could possess invasive and metastatic characteristics [2]. Primary hepatic neuroendocrine tumors (PHNET) are rarer than NEC, grow slower, and have the ability to become malignant. Only a minority of patients have carcinoid syndrome. On CT and MRI scans, PHNETs resemble hepatocellular-carcinoma (HCC), but patients with PHNETs have a better prognosis. Despite tumor recurrence, patients with carcinoid syndrome have a satisfactory 5-year survival rate of 74–78 % and a 5-year recurrence rate of 18 % after a hepatectomy [2–5]. Since CT and MRI scans are sensitive in finding primary liver lesions and metastases, these techniques could help clinicians identify suitable therapeutic approaches and further improve the survival rate of patients.

However, there is some controversy surrounding whether CT and MRI scans can predict tumor grade and malignancy. One research group reported that the CT features of hepatic neuroendocrine tumors vary and do not correlate with their pathologic diagnoses [6]. Another report found that well-differentiated primary neuroendocrine tumors resemble echinococcus cysts on CT and MRI scans [7].

In this study, we retrospectively investigated 29 patients diagnosed with PHNET by surgery or puncture and summarized the characteristics of CT and MRI scans as a way to improve the accurate of diagnosis of PHNET. Additionally, we correlated our findings with the 2010 WHO classification of gastrointestinal neuroendocrine tumors

Materials and Methods

Between January 2002 and December 2011, 29 patients (13 males, 16 females; median age: 47.2 years of age) with PHNETs were studied. All patients underwent CT and MRI scanning and provided written informed consent. The Hospital institutional review board approved this study.

Results: Using pathology and the 2010 WHO classification of PHNET, eight cases were defined as G1, 10 cases were defined G2, and 11 cases were defined G3. Based on CT imaging (Table 1) and MRI data (Table 2), all G1 liver lesions were singular with only one lesion located in left lobe and remaining lesions the in right lobe. All lesions showed enhanced capsules in the delayed phase of post-enhancement CT while one lesion appeared plateau-like type. Seven out of eight patients with G1 PHNETs underwent a MRI examination in addition to a CT scan (Table 2**).** For the ten patients with G2 PHNETs, CT scans revealed both single and multiple lesions with necrosis (Table 1). The dynamic-contrast enhancement curves illustrated type III. Hemorrhage was seen in one tumor (Fig. (Fig.3)3) with no evidence of lymph node metastases.

Discussion

In this work, we found that careful imaging with CT and MRI scans could accurately reflect the histological features of primary hepatic neuroendocrine tumors (PHNETs) and increase the likelihood of a correct diagnosis. A tumor that originates from neuroendocrine cells is a neuroendocrine tumor (NET). There are two types of NETs: neural neuroendocrine tumors and epithelial neuroendocrine tumors. Primary hepatic neuroendocrine tumors (PHNETs) develop in the intrahepatic bile duct epithelium and have an extremely low incidence of 0.17 % [8].

Hepatic NECs have a better prognosis than hepatocellular carcinoma [9], but characteristic local invasion, metastases, and serious complications of carcinoid syndrome contribute to the poor outcome of patients with hepatocellular carcinoma [10–12].

Zhu Z et al. [13] reported that PHNETs appear as a single tumor. Our MRI and CT scans revealed that G1 PHNETs usually have single lesions in the right lobe whereas G3 PHNETs commonly have multiple diffuse lesions or one large tumor accompanied by several satellite lesions. PHNETs are difficult to distinguish from liver cancer [14].

ADC values showed that the PHNET had restricted diffusion compared with the surrounding normal liver, which confirmed that the PHNET was malignant. As PHNET lesions grew in size, the number of intrahepatic lesions increased from single to multiple, focal hemorrhage, necrosis, and portal venous thrombosis became prevalent [15]. Su M et al., [16] analyzed six cases of PHNET with multiple lesions. These tumors appeared as nodular or ring-like enhancements that suggest that

PHNET is not of a multifocal origin, which is common to liver cancer.

Individuals who have a history of taking oral contraceptives have a higher incidence of hepatic adenomas [17]. According to Burke C et al., [18] liver-specific contrast agents could be used to distinguish FNH from PHNETs. Liver metastases have a rich blood supply as well, but the characteristic bull's eye pattern on MRI and CT scans distinguish liver metastases from PHNETs.

One limitation of our study is the small sample size, which results from the low incidence of this rare tumor. Therefore, future studies must include more cases, which will allow for the inclusion of statistical data.

Conclusion

In conclusion, the appearances of CT and MRI reflect the biologically benign fashion of G1 and G2 PHNETs and the malignant growth of G3 PHNETs.

Tables:

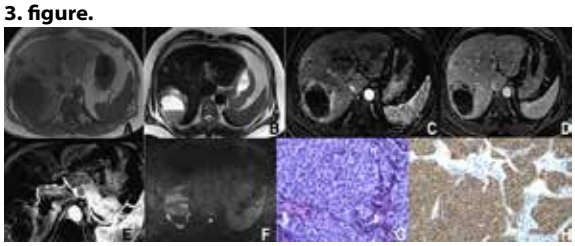
1. CT appearance of PHNET

Pathological grade	Case	Lesion		location		Unenhanced CT				Contrast enhanced series (attenuation)						Type of dynamic enhanced curves	
		Single	Multiple	Right	left	Hypo	Hyper	homogeneity		Arterial phase		Portal phase		Delayed phase		Type II	Type III
								Yes	No	Markedly hyper	Moderately hyper	Hyper	iso	Hyper	Iso		
G1	8	8	0	7	1	7	1	6	2	7	1	8	0	8	0	1	7
G2	10	7	3	6	1	10	0	4	6	8	2	8	2	9	1	1	9
G3	11	4	7	2	2	10	1	0	11	9	2	11	0	9	2	1	11

2. MR appearances of PHNET

Pathological grade	Case	Lesion		location T1W1		Unenhanced MRI			Post-enhanced MRI				ADC value
						T2W2							
		Single	Multiple	Right	left	Hypointense	Mildly Hyperintensity	Markedly hyperintensity Yes No Markedly	Enhancement		Type of dynamic enhanced curves		
									Mild	Type II	Type III		
G1	7	7	0	6	1	7	5	1	6	1	1	6	1.39±0.20
G2	8	6	2	5	1	8	7	1	8	0	0	8	1.26±0.23
G3	9	4	5	2	2	9	3	6	9	0	0	9	1.14±0.17

3. figure.



MRI and histology of grade 3 PHNET. Transverse T1-weighted (**a**), transverse T2-weighted (**b**), contrast-enhanced dynamic T1-weighted at the arterial phase (**c**) and delayed phase (**d**). Figure **e** and **f** illustrate liver arterial reconstruction, and transverse diffusion-weighted imaging(b = 800 s/mm^2, respectively). This grade 3 tumor (8.4 cm in size) was located in the right lobe with a cystic change in the liver wall. Multiple satellite nodules show marked peripheral enhancement in the arterial phase and slight hyper-intensity relative to the surrounding liver parenchyma in the delayed phase. Diffusion-weighted imaging (Figure **f**) shows high peripheral signal intensity, which reflects the diffuse restriction of water. Figure **e** confirms that the tumor blood supply comes from the liver artery. HE staining of liver tumor cells with atypia, varying sizes, multiple mitosis rates, and irregular nucleoli (**g**). Staining for the neuroendocrine marker, synaptophysin (Syn) was positive (**h**). Magnifications: G and H = 100X

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