CHAPTER 6

MAGNETIC RESONANCE IMAGING FINDINGS OF SUBTYPES OF RENAL CELL CARCINOMA

Mehmet SERINDERE[1]

INTRODUCTION

90% of kidney tumors and the most common epithelial cancer in adults are renal cell carcinoma (RCC) (1). The median age at diagnosis is 64 years and is more common in males. Various genetic conditions have been associated with the development of RCC, the most common of which is von Hippel-Lindau disease. Environmental risk factors are smoking and obesity. Although the classic triad of RCC is defined as flank pain, hematuria and flank mass, it is seen only in 5-10% of cases (2,3).

The World Health Organization classification divides RCC into different histological groups (4); the percentage of clear cell RCC (ccRCC), papillary RCC (pRCC) and chromophobe RCC (chrRCC) are 70% to 75%, 10% to 21%, and 5% of all RCC cases, respectively (4,5).

Due to the heterogeneity of imaging features and overlapping imaging characteristics, the lack of reliable imaging criteria for the recognition of malignant and benign masses remains a challenge. Various imaging parameters have been stated to differentiate renal lesions. The two main benign lesions that may be difficult to distinguish from RCC are angiomyolipomas, particularly the lipid-poor subtype, which are the most frequent benign solid renal neoplasms in general, and oncocytomas, which account for 3-7% of all renal tumors (6,7).

Magnetic Resonance Imaging (MRI) currently serves a problem-solving role in the diagnosis of suspected RCC and in pre-operative planning, particularly for distinguishing soft tissue enhancement within kidney lesions. In addition, unique imaging features of papillary RCC have been reported, including hypointense T2 signal on MRI, marked hypoenhancement in all phases of dynamic contrast MRI, and loss of signal on opposite-phase imaging (8,9) (Figure 1). T1-weighted hypointense RCCs have less aggressive pathological characteristics and favorable clinical behavior compared to T1-weighted isointense or T1-weighted hyperintense RCCs (10).

[1] MD., Hatay Education and Research Hospital, Department of Radiology, drserindere@hotmail.com

In this article, the diagnostic value of MRI was reviewed in the diagnosis of the subtypes of RCC. The MRI findings of the RCC subtypes are summarized in Table 1.

Table 1. Summarized MRI findings of the RCC subtypes

Subtypes of RCC	Incidence Rate	MRI findings	Enhancement pattern	ADC
ccRCC	70-75%	T1- hypointense or isointense T2-hyperintense or isointense	Strong	Significantly higher ADC But in some studies, no significant difference
pRCC	10-21%	low T2 signal intensity	progressive	lower ADC than ccRCC
chrRCC	5%	moderate to low T2 signal intensity	moderate	lower ADC than ccRCC

ADC= apparent diffusion coefficient, MRI= Magnetic Resonance Imaging, RCC= Renal cell carcinoma, ccRCC= clear cell renal cell carcinoma, pRCC= papillary renal cell carcinoma, chrRCC= chromoprobe renal cell carcinoma

THE MRI FINDINGS OF RENAL CELL CARCINOMA SUBTYPES

Clear Cell Renal Cell Carcinoma

The most frequent subtype, ccRCC, is heterogeneously hypervascular, similarly enhanced as the renal cortex, and contains regions of necrosis and bleeding when larger (11). ccRCCs tend to invade vessels (45% of tumors), frequently the renal vein and inferior vena cava, hereby, tumor thrombosis develops. Therefore, it is important to evaluate vascular involvement and spread (12,13).

On MRI, the ccRCC is characteristically hyperintense or isointense on T2-weighted images, hypointense or isointense on T1-weighted images (14,15). Generally, ccRCC shows a strong enhancement with a peak in the corticomedullary phase after contrast agent administration (16). Central necrosis, a common finding in ccRCCs, appears as a homogeneous hypointense area in the center of the mass on T1-weighted images, moderate to high signal intensity on T2-weighted images, and lack of contrast enhancement after contrast agent administration. Higher tumor grade is associated with larger size, intralesional necrosis, retroperitoneal vascular collaterals, renal vein thrombosis, and disruption of the tumor capsule (17). ccRCC may have T1-weighted hyperintensity due to intralesional hemorrhage, in which case it may be difficult to distinguish it from benign,

proteinaceous or hemorrhagic cysts (18). In such cases, assessment of contrast enhancement based on image subtraction may be helpful (19).

Previous studies of dynamic contrast-enhanced perfusion MRI have shown that ccRCC has a greater enhancement in the corticomedullary phase than the renal cortex with clearing during the nephrographic phase, however, pRCC is less enhanced than the renal cortex in both post-contrast phases (15).

Diffusion-weighted imaging (DWI) may be beneficial to diagnose renal masses, particulary in patients for whom gadolinium contrast cannot be used. Restricted diffusion and low apparent diffusion coefficient (ADC) values may be encountered in both malignant and benign solid masses, such as RCC, oncocytoma, angiomyolipoma, and abscess. Benign cystic lesions do not restrict diffusion and show higher ADC values. It has been reported that ccRCCs have significantly higher mean ADC values than non-ccRCCs (20-22). But, some studies reported no significant difference in ADC values between ccRCC and non-cc RCC (23).

Papillary Renal Cell Carcinoma

pRCC often looks like a homogeneous mass and may be bilateral and multifocal more frequently than ccRCC; When it is >3 cm, it may be heterogeneous in terms of the existence of hemorrhage, calcification or necrosis (24,25). It rarely contains macroscopic fat (24). Two different types of pRCC: "Type 1" includes a monolayer of small cells with sparse cytoplasm and low grade nuclei and is generally resulted in a better prognosis; "Type 2" has high nuclear grade cells with abundant eosinophilic cytoplasm and is resulted in an even worse prognosis than ccRCC (24,26).

pRCCs generally have low T2 signal intensity and hypovascularity with progressive enhancement after contrast administration (27-29). The imaging feature of pRCC differs from ccRCC, as hypervascular ccRCCs typically appear with higher signal intensity on T2-weighted images, and show decreased signal intensity on opposite-phase images than in-phase images due to its fat content. Moreover, although low signal intensity on T2-weighted images were observed in lipid-poor angiomyolipomas that tend to show avid enhancement after contrast agent administration, while pRCCs are hypovascular and show progressive enhancement (15). The reasons why it is difficult to distinguish a renal cyst from pRCC include: the presence of hypovascularity in pRCC, the potential pseudo-enhancement of renal cysts, and the eventual hyperdensity of complicated cysts on non-contrast computed tomography (CT); therefore, the use of a small peripheral area of interest is recommended to assess the presence of enhancement. (30).

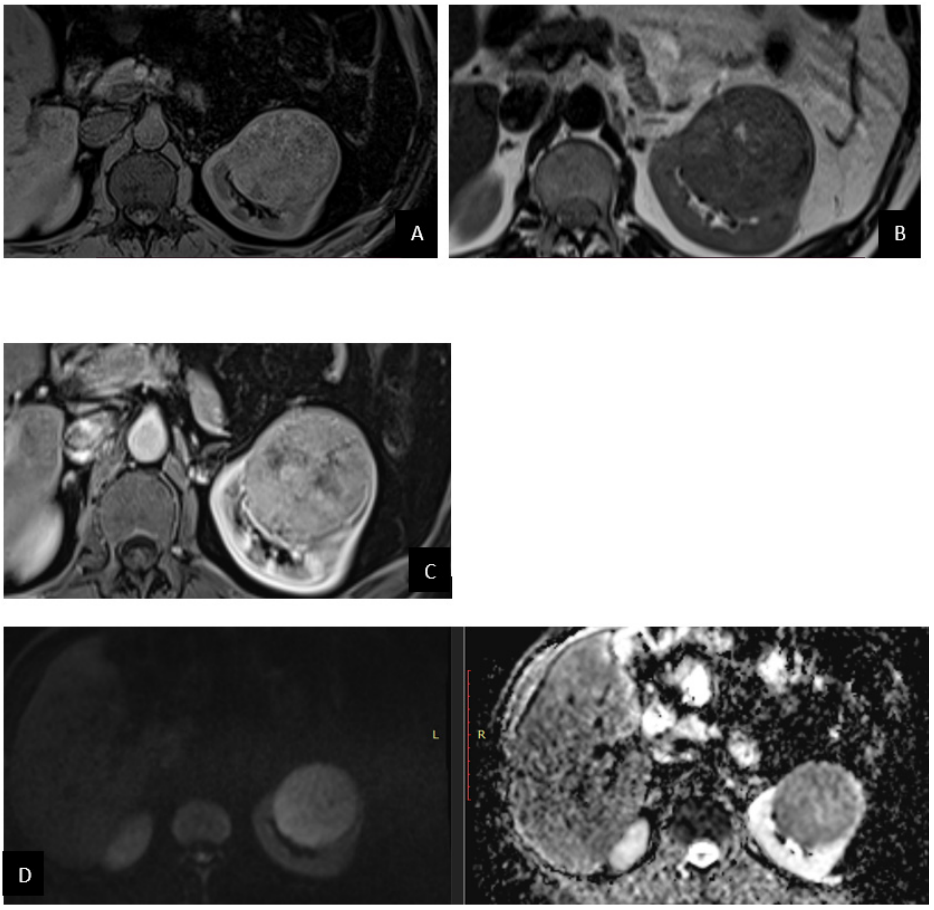

Figure 1. MRI findings of RCC lesion in upper pole of left kidney. A: In pre-contrast three dimensional fat suppressed T1-weighted gradient echo image, the lesion showed isointensity compare to paraspinal muscle, B: Turbo spin echo T2-weighted image showed the lesion that was isointense compare to paraspinal muscle with cyctic change central of lesion. C: Post-contrast three dimensinal fat suppressed T1-weighted gradient echo image showed the lesion with heterogeneous enhancement. D: The lesion showed restricted diffusion in DWI and ADC map.

It has been reported that pRCCs show lower ADCs than ccRCCs, but overlap exists and other MRI imaging findings should be evaluated when distinguishing them (22,31).

Chromophobe RCC

chrRCCs are usually large, well-circumscribed homogeneous lesions (12). With a 5-year survival rate of approximately 78-93%, these tumors usually have a better

prognosis than ccRCCs (32,33). However, there is malignant potential in chrRCC cases and the liver is the frequent region of metastasis (10). Approximately 86% are stage T1 or T2 at presentation, and less than 5% of cases have renal vein invasion. Lymph node and distant metastases have rarely been defined. Macroscopically, chrRCCs are solid, well-circumscribed tumors and have tan-brown color and a slightly lobulated surface (12). Histopathologically, these tumors were assumed to originate from intercalated cells of the renal cortex and consist of varying amounts of cells with clear or eosinophilic cytoplasm arranged in a sheet-like structure along the vascular septa (17). chrRCCs tend to be well-circumscribed and homogeneous and do not have a distinctive feature on MRI. The signal intensity of chrRCCs varies significantly on T2-weighted images; but, they tend to show moderate to low signal intensity on T2-weighted images (34). Cystic change and central necrosis are rare features even in larger tumors (17). Responsible for an inhomogeneous pattern, one-third of chrRCC cases have a central scar or necrosis and this situation is associated with worse prognosis (35).

The gadolinium contrasting pattern of these lesions appears "moderate". This pattern is less than ccRCCs and more than pRCCs (36).

Oncocytoma and chrRCC have overlapping imaging findings, consistent with their similar pathological features (37). Therefore, these two lesions have no CT or MRI features that allow these two lesions to be clearly distinguished from each other (38). Calcifications may occur in 38% of cases, but perinephric invasion and vascular involvement are uncommon (39).

It has been reported that chrRCCs have lower ADCs than ccRCCs (22,40). Wang et al. (22) and Choi et al. (41) reported that pRCCs have lower ADCs than chrRCCs, however, Yu et al. (42) reported the opposite finding. Due to conflicting results, DWI probably has limitations to distinguish several subtypes, similar to the situation in liver lesions, where it has limitations to distinguish between several solid benign and malignant liver masses (43).

CONCLUSION

There are major differential diagnoses such as angiomyolipoma, urothelial carcinoma, oncocytoma, and lymphoma while diagnosing renal masses with MRI. If imaging features are not adequate to make a diagnosis, biopsy should be applied. In this way, the pre-ablation diagnosis may also be confirmed and described the histological grade of the tumor and aided in prognostic evaluation by biopsy (36).

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