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LETTER TO THE EDITOR

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Dear Editor,

We would like to comment on a case of Birt-Hogg-Dubé (BHD) syndrome reported in this issue by M. Schreuer et al, JBR-BTR, 2011, 94: 29-31. Individuals with this rare autosomal dominant inherited disorder – named after three dermatologists who described the syndrome in 1977 – are susceptible to develop 1) noncancerous tumors of the hair follicles, 2) renal tumors (predominantly chromophobe renal cell carcinoma) and 3) thin-walled cystic lung lesions. The diagnosis of BHD is based on these clinical findings and confirmed by molecular genetic testing. We would like to take the opportunity to emphasize the unique position of the radiologist to suggest this syndrome in patients imaged and diagnosed with both multiple solid renal tumors and cystic pulmonary lesions.

Hereditary renal cancer is a true challenge for radiologists and surgeons (1-3). A priori knowledge of the genetic predisposition allows screening the patient and his relatives to detect cancer at an early stage in order to treat synchronous and metachronous renal cancerous lesions with nephron-sparing surgical techniques, such as partial nephrectomy and radiofrequency ablation. The main hereditary syndromes known to have an increased risk to develop renal cell carcinoma (RCC) are listed in Table I. Patients with Von Hippel Lindau (VHL) disease and tuberous sclerosis (TS) have an increased risk of developing clear cell RCC's, lesions characterized by strong, peripheral enhancement of the viable tumor parts in the arterial imaging phase (on CT and MRI) and often central foci of degeneration and necrosis. In the majority of cases, the diagnosis of VHL or TS is based on symptomatic extrarenal manifestations. Two subtypes of hereditary papillary RCC syndromes are known, type I presenting with multiple bilateral tumors, and type II solitary tumors with a more aggressive behavior and an association of uterine leiomyomas and sarcomas.

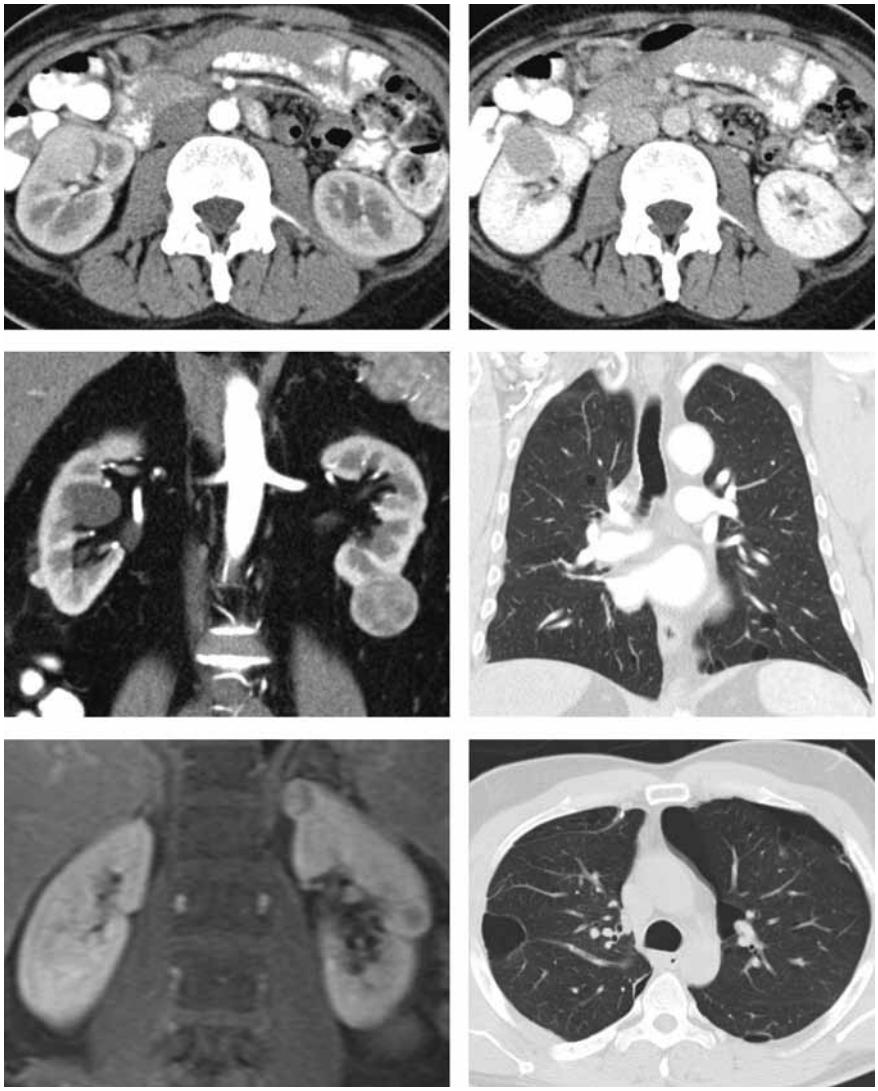

Fig. 1. — BHD syndrome in 3 patients diagnosed with multifocal chromophobe RCC's and cystic lung lesions. Top row: 39-year-old female showing bilateral, homogeneously, arterial middle-level enhancing (left image) and venous hypo-enhancing (right image) chromophobe renal cell cancers. Middle row: 77-year-old male, coronal CT showing bilateral hyper-enhancing RCC's (left image) and multiple lung cysts (right image). Bottom Row: 43-year-old male, coronal contrast enhanced MRI showing two left-sided RCC's (left image) and bilateral pulmonary cysts complicated by left-sided pneumothorax (right image).

The RCC's observed in both papillary subtypes are typically hypovascular malignancies on contrast enhanced cross-sectional imaging. Both the clear and papillary cell type RRC's originate from the cells of the proximal renal tubule. On the contrary, chromophobe renal carcinomas, as observed in BHD syndrome, originate from the intercalated cells of

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Table I. — Hereditary RCC syndromes.

	predominant RCC		cell of origin	other renal lesions	typical imaging clues
Von Hippel Lindau	clear cell	→	proximal renal tubule	cysts	hyper-enhancing renal mass(es) + renal cysts + extrarenal manifestations (haemangioblastoma, pancreatic cysts and neuroendocrine tumors)
Tuberous sclerosis	clear cell	→	proximal renal tubule	angiomyolipoma, cysts, papillary - chromphobe RCC, oncocytoma	hyper-enhancing renal mass(es) + renal cysts, angiomyolipoma + extrarenal manifestations (hamartoma, lymphangioleiomyomatosis)
Hereditary papillary RCC's	papillary	→	proximal renal tubule	none	hypo-enhancing renal mass(es)
Birt-Hogg-Dubé	chromophobe	→	intercalated cell of renal collecting duct	oncocytoma, clear cell and papillary RCC	middle-level enhancing renal mass(es) + thin-walled lung cysts (pneumothorax)

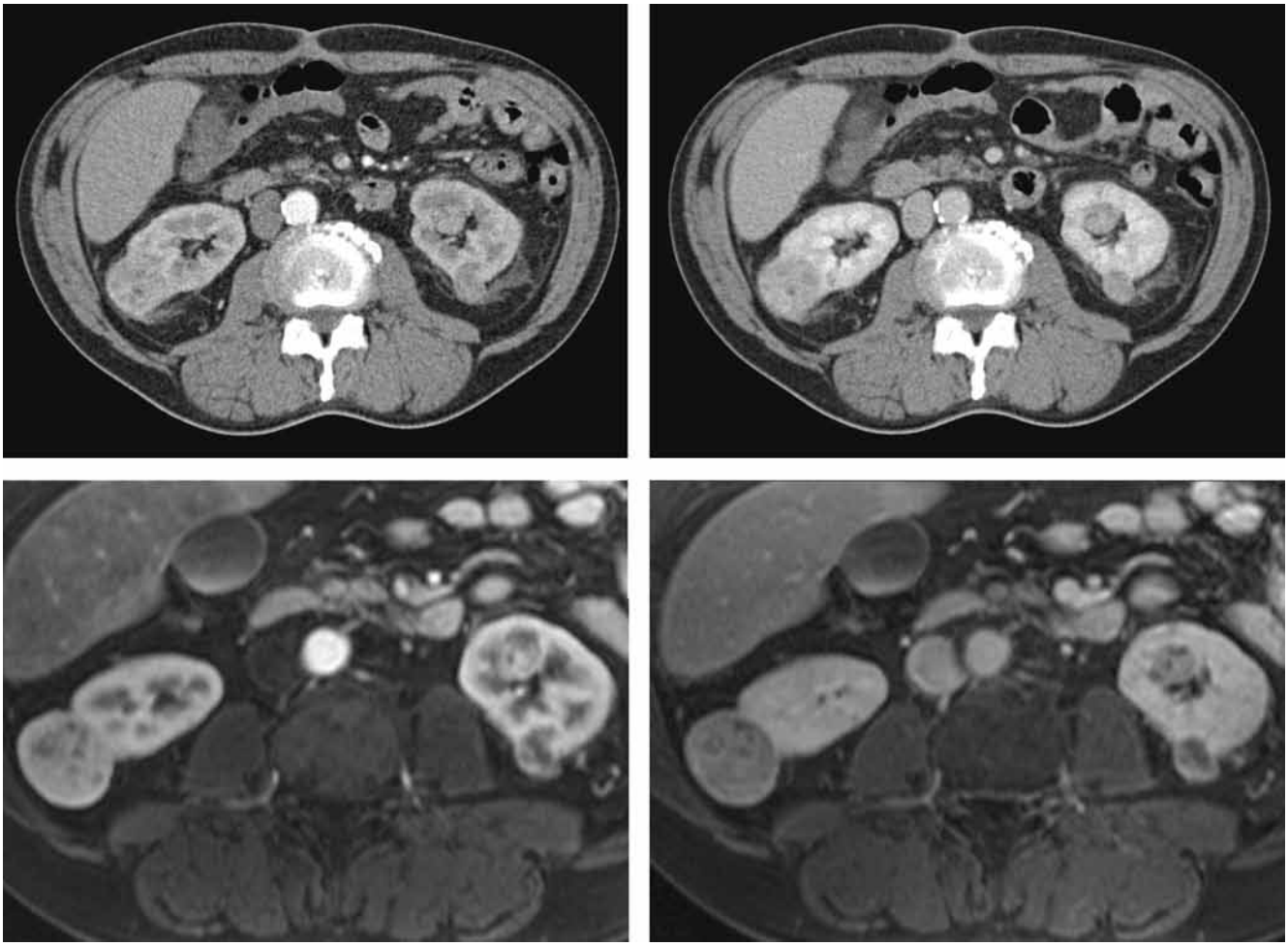

Fig. 2. — 65-year-old male presenting with renal dysfunction and bilateral renal tumors; top row: arterial and venous CT, bottom row: arterial and venous MRI. No extrarenal abnormal findings were present. Biopsy confirmed the diagnosis of renal oncocytosis.

Table II. — Incidence of pulmonary lesions in patients with Birt-Hogg-Dubé syndrome diagnosed with RCC.

	number of patients	pulmonary lesions (cysts, pneumothorax)	age at diagnosis RCC (youngest in case > 1)
Kluijt I. et al. *Clinical Genetics*, 2009	3	3/3	27
Westermann D.H. et al. *Urologe*, 2010	1	1/1	47
Bielefeld G. et al. *Rev Med Interne*, 2010	1	1/1	20
Warwick G. et al. *J Med Case Reports*, 2010	1	1/1	50
Imada K. et al. *Br J Dermatol*, 2009	1	0/1	68
Janitzky A. et al. *Urol J*, 2008	1	1/1	67
Souza C. et al. *AJR*, 2005	1	1/1	27
Stavrakoglou A. et al. *QJM*, 2010	1	1/1	56
Welsch M.J. et al. *Int J Dermatol*, 2005	1	1/1	52
Patients identified at our hospital	6	6/6	39

the renal collecting duct and often show a middle-level enhancement in the arterial phase and have lower attenuation than renal parenchyma in the venous phase, with a more homogeneous pattern in the latter phase compared to the clear cell type. A history of multiple chromophobe renal carcinomas is characteristic for BHD and should prompt radiologists to review available lung imaging. The incidence of thin-walled pulmonary cysts (resembling bullous emphysema) is very high in BHD patients presenting with renal cancer and a highly specific imaging key feature to suggest the diagnosis. Figure 1 shows the renal and pulmonary imaging findings in 3 patients with proven BHD. Table II lists a literature review on the co-existence of pulmonary lesions in BHD patients diagnosed with renal cancer and for whom pulmonary imaging findings were reported, together with the imaging findings of 6 patients with BHD identified at our hospital. Pulmonary lesions were present in 16 of the 17 cases (94%). It is important to add that there is another disease entity which predisposes to develop tumors originating from the intercalated cells of the renal collecting duct, referred to as renal oncocy(toma)-tosis (4-6). In this extremely rare hereditary syndrome, of which the causative gene is less known, patients typically present with renal dysfunction and multiple renal oncocytic tumors / oncocytomas on imaging. Since chromophobic and oncocytic tumors are believed to originate from the same precursor cell, differentiating BDH from renal oncocytosis syndrome can be difficult. The absence of extrarenal manifestations (≠ VHL and TS) and cystic lung lesions (≠ BHD) is an important imaging discriminator to suggest renal oncocytosis. Figure 2 shows cross-sectional images for a biopsy proven case of renal oncocytosis.

In summary, the combination of meta- or synchronous solid renal tumors and cystic pulmonary lesions should prompt the radiologist to suggest the diagnosis of an underlying BHD syndrome. Recognizing this disease entity is important for patient follow-up and family screening.

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