

An Unusual Case of Birt-Hogg-Dube Syndrome With Renal Involvement

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INTRODUCTION

Recent investigations of the underlying pathophysiology of renal cell carcinoma (RCC) has resulted in the identification of involved molecular pathways, including the inactivation of the von Hippel-Lindau gene in most sporadic cases of RCC.⁽¹⁾ They are characterized by one specific histological type. In contrast, kidney tumors in patients with Birt-Hogg-Dube syndrome (BHD) consist of a variety of histological types.⁽²⁾ We report a patient with multiple renal cell tumors in one kidney with a history of spontaneous pneumothorax, but without skin lesions which are typical signs of BHD syndrome.

CASE REPORT

A 67-year-old woman was admitted to our institution with a left-sided kidney tumor highly suspicious for RCC. The patient mentioned an open right-sided thoracotomy in her medical history due to a spontaneous pneumothorax. Recurrent left-sided flank pain was mentioned, as well. Typical skin lesions were not detected. The family history was unremarkable, with the notable exception of recurrent spontaneous pneumothoraxes

in the patient's son. Computed tomography scan showed a high-density tumor formation (4.9 cm in diameter, dorsal) along with a deformed kidney caused by multiple mixed hyperdense and hypodense cystic structures (Figure 1). Since the patient was allergic to contrast medium, magnetic resonance imaging was performed and revealed 2 more suspicious 3.2-cm and 1.7-cm lesions. The contralateral kidney was hypoplastic with multiple small cysts. Bone scan did not reveal bone metastases.

Radical nephrectomy was performed because of multiple kidney tumors and suspicion of infiltration of the renal pelvis during the operation. Pathologic examination of the kidney revealed numerous cystic and solid tumors measuring 5 mm to 4.5 cm in diameter. Histologically, they were of various subtypes of renal cell tumors including clear cell carcinomas, papillary adenomas and carcinomas, chromophobe carcinomas, and oncocytomas, sometimes composed as hybrid tumors. In addition, many clear cell preneoplastic tubules were noted (Figure 2). Birt-Hogg-Dube syndrome was diagnosed on the basis of these remarkable pathologic findings and the patient's history;

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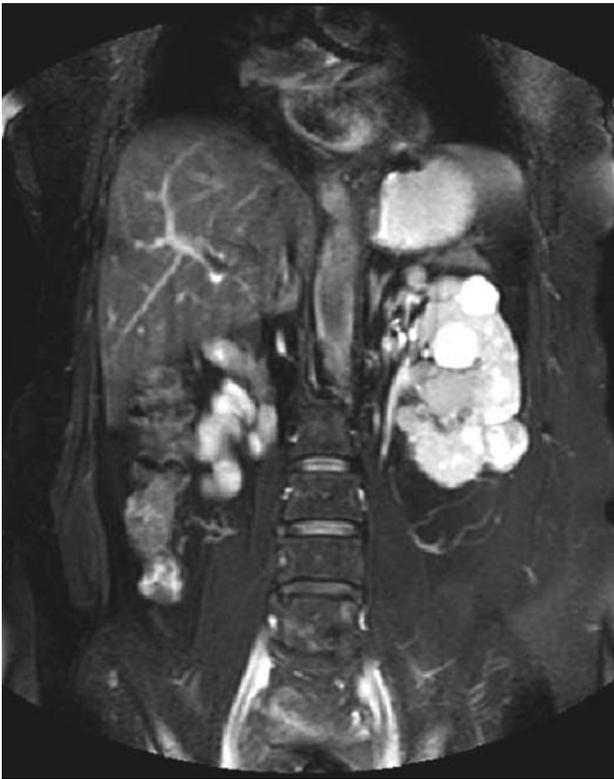


Figure 1. Magnetic resonance imaging showed multiple kidney tumors with different signal activities on the left side and a hypoplastic right kidney with multiple small cysts.

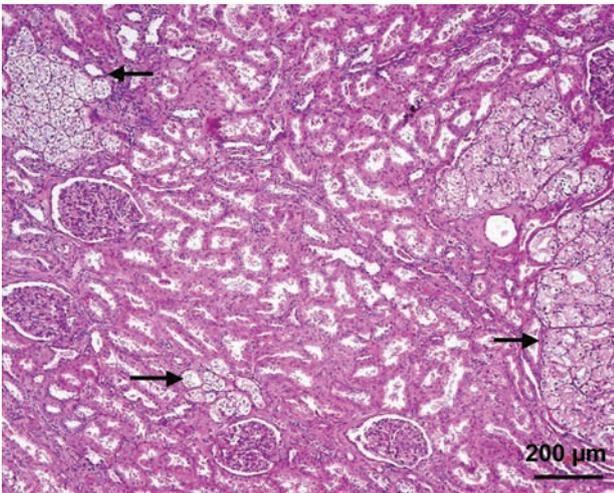


Figure 2. Typical histological aspect of renal cell carcinoma in Birt-Hogg-Dube syndrome. A very early clear cell carcinoma (upper left arrow), a chromophobe carcinoma (right arrow), and a clear cell preneoplastic tubular lesion (lower left arrow) was noted (hematoxylin-eosin).

the patient's son also mentioned spontaneous pneumothoraxes in his history. The family was cared by the urologists to screen for urinary tract tumors. To date, no renal tumors in family were found.

DISCUSSION

The Birt-Hogg-Dube syndrome is a rare autosomal dominant condition usually characterized by a triad: skin tumors (fibrofolliculomas, trichodiscomas, and acrochordons), kidney neoplasms, and spontaneous pneumothoraxes. In some patients, skin lesions as a typical hallmark of this syndrome cannot be found.⁽³⁾ Since first described in 1977 by Birt and colleagues,⁽⁴⁾ the gene has been mapped on chromosome 17p11.2, expressing folliculin on protein level.⁽⁵⁻⁷⁾ Although the function of this protein is not fully understood, mutations on its gene are linked to RCC in animal models and in the families with BHD syndrome.^(3,8)

In our patient, clinical signs of the BHD syndrome were not completely developed. Typical skin lesions were not detected, making it even more difficult to include BHD syndrome in the differential diagnoses. In the literature, patients with missing typical skin lesions are described, as well.⁽³⁾ The diagnosis was made retrospectively, combining all the information on pathology, patient's history, and family history. This clearly shows the necessity of precise clinical information for the investigating pathologist.

CONCLUSION

In cases of kidney tumors associated with spontaneous pneumothorax and/or skin lesions, BHD syndrome should be considered as a differential diagnosis. Intense follow-up of the families with members who have BHD syndrome should include genetic screening, ultrasonography of the kidneys, and other radiographic methods.

CONFLICT OF INTEREST

None declared.

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