



## Birt-Hogg-Dube Syndrome: Difficulties in Diagnosis and Management in Developing Countries

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### Abstract:

Birt-Hogg-Dube syndrome (BHD) is a rare autosomal dominant inherited cancer syndrome characterized by benign tumors of the hair follicle (fibrofolliculoma), pulmonary cysts, spontaneous pneumothorax and increased risk for renal carcinoma. In developing countries like India where affordability and facility for FLCN BHD gene study are not available, presence of skin lesions, pulmonary cyst and renal hybrid tumor comprising of both oncocytoma and chromophobe renal cell carcinoma can contribute for diagnosis.

**Key words:** Birt-Hogg-Dube syndrome, Cysts, Genes, Hair Follicle, Kidney Neoplasms.

### Introduction

Birt-Hogg-Dube syndrome (BHD) is rare inherited syndrome characterised by multiple fibrofolliculomas, pulmonary cysts, pneumothorax and renal tumors. Fibrofolliculomas and lung cysts are most common manifestation. Renal tumors with variable histologies develop in about 30% of BHD affected individual, most frequently chromophobe renal carcinoma and hybrid onocytic tumors. Metastasis is uncommon but may develop. A genetic linkage analysis identified BHD gene, FLCN on short arm of chromosome 17 [1,2].

### Case Report

A 28 year old, premenopausal, nulliparous, female consulted for gradually progressive, dull abdominal pain and hematuria since 1 month. In

general, the examination was within normal limits except few papulous skin lesions (fibrofolliculoma) on face, and back [Fig.1]. No organomegaly was noticed on abdominal examination. The patient's haematological and biochemical workup was within normal limits. Urine routine and microscopic examination was within normal limits. CT abdomen and pelvis revealed left kidney measuring 11.7x4.8 cm with well-defined hypodense lesion measuring 5x5x4.7 cm seen arising from lower moiety of left kidney [Fig.2]. This lesion showed early enhancement on arterial phase and wash out on delayed phase. Bilateral renal veins and inferior vena cava showed normal contrast opacification and no evidence of thrombosis within. Right kidney was within normal limits. There were multiple enlarged non-necrotic lymph

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## Discussion

Birt-Hogg-Dube syndrome (BHD) is uncommon and associated with mutations in the FLCN gene, which encodes folliculin, which is preferentially expressed in the skin, kidney, and lung. The syndrome was characterized by the presence of fibrofolliculomas and/or trichodiscomas (skin), pulmonary cysts, spontaneous pneumothorax (lung), and renal tumors (kidney) [4]. The European Birt-Hogg-Dube Consortium has proposed a series of major and minor criteria for establishing the diagnosis. At least five fibrofolliculomas or trichodiscomas, at least 1 confirmed histologically, of adult onset and pathogenic germline mutation in FLCN are major criteria. The minor criteria are multiple lung cysts: basally located with or without spontaneous pneumothorax; renal cancer: early onset (<50 years), multifocal or bilateral renal cancer, or renal cancer of characteristic histologic forms (oncocytic-chromophobe hybrid histology) and first-degree relative with Birt-Hogg-Dube syndrome (BHD). Patients should fulfil one major or two minor criterion for diagnosis of Birt-Hogg-Dube syndrome (BHD) [3]. Pneumothorax and chest pain are clinically important signs and symptoms and warrant a thorough medical examination [4], and it is important to keep in mind that the onset of repeated pneumothorax generally starts at an earlier age than RCC in patients with BHD [5].

Staging and management of renal cancer is no different to renal cancer in patients without the syndrome. Once diagnosed, treatment is usually surgical, leaving as much renal parenchyma as possible with nephron sparing techniques instead of radical nephrectomy [6]. In the event of metastases, rapamycin analogs may be considered, given the implication of the FLCN gene in regulating the mTOR pathway, although more studies are needed to demonstrate benefit [1]. In our case, the patient was presented with renal symptoms and underwent for left radical nephrectomy with retroperitoneal lymph-nodes dissection. As the disease was limited

no further adjuvant therapy was advised. She was referred to dermatologist for evaluation. In view of small pulmonary cysts of lung, she was evaluated by respiratory medicine consultant.

## Conclusion

In developing countries like India, affordability and facility for FLCN BHD gene study are not available. The European Birt-Hogg-Dube Consortium proposed major and minor criteria for establishing the diagnosis seems reasonable.

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