

Birt-Hogg-Dubé Syndrome: A Case Report Describing Sonographic Evaluation of Salivary Gland Oncocytomas

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ABSTRACT

Birt-Hogg-Dubé (BHD) syndrome is a rare hereditary disorder associated with autosomal dominant hereditary epithelial carcinomas, in which patients have an increased incidence of renal cell carcinomas, scattered hamartomas, pulmonary cysts, and spontaneous pneumothoraces. Other less common findings include lipomas, parathyroid adenomas, salivary gland tumors, and colonic polyps/tumors. Early diagnosis of BHD can help establish renal screening and reduce mortality by early detection and more effective treatment of renal cell carcinoma. This case report describes the sonographic features of salivary gland oncocytomas found in a patient with BHD.

Keywords: Birt-Hogg-Dubé, Color Doppler, Oncocytoma, Pneumothorax, Salivary gland, Ultrasound

INTRODUCTION

Birt-Hogg-Dubé (BHD) is a rare autosomal dominant hereditary syndrome first described in 1977 that arises due to a mutation in the folliculin (FLCN) gene, a tumor suppressor gene located on chromosome 17p11.2.^[1] The condition has been reported in more than 400 families.^[2] Most patients with an FLCN mutation have benign skin hamartomas of the head and neck most commonly associated with the hair follicle and known as

fibrofolliculomas. Additional findings include pulmonary cysts with an incidence of spontaneous pneumothoraces in 25% of patients.^[3] It is important to highlight that BHD is a hereditary renal cell carcinoma (RCC) syndrome and patients have a significantly increased risk of both benign and malignant renal lesions.^[2,4] Other less common findings of BHD include lipomas, parathyroid adenomas, salivary tumors, and colonic polyps/tumors. Early detection of BHD allows for focused treatment, leading to decreased morbidity and mortality. The most common salivary gland tumor reported in BHD is a salivary gland oncocytoma which can present as a palpable neck or facial mass. Ultrasound evaluation of the salivary glands is a fast, inexpensive modality which can accurately assess pathology without radiation exposure.^[3] The salivary glands on ultrasound are typically homogenous structures that are hyperechoic compared to adjacent muscles.^[5] Their evaluation can be challenging due to body habitus, complexity of the surrounding anatomic structures, and the extension of the parotid glands into the deep spaces

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of the neck. In this case, we will present the sonographic characteristics of salivary gland oncocytomas in a patient with BHD, differential considerations, and literature search.

included salivary gland oncocytoma versus pleomorphic adenoma. Given the multiplicity and the patient’s medical history, most likely etiology was felt to be salivary gland oncocytomas in a patient with known history of BHD.

CASE REPORT

A 51-year-old female with a history of the left-sided spontaneous pneumothoraces and bilateral kidney lesions [Figure 1] presented with enlarging palpable nodules in the right submandibular and left parotid regions. Gray scale, ultrasound, and color flow Doppler of the neck were performed which revealed a homogenous well-circumscribed hypoechoic lesion in the right submandibular gland measuring approximately 1.5 × 0.9 × 0.9 cm and an additional 1.5 × 1.3 × 1.1 cm lesion in the left parotid gland [Figure 2]. Both of these lesions demonstrated diffuse hypervascularity. The working differential diagnosis

DISCUSSION

There are multiple hereditary RCC syndromes including BHD, Von Hippel–Lindau (VHL), hereditary papillary RCC (HPRCC), hereditary leiomyomatosis and RCC (HLRCC), BAP1 mutant disease, and tuberous sclerosis complex that increase the risk of developing cancer, in particular, renal cell carcinoma.^[1,6,7] These syndromes are summarized in Table 1.

BHD is an autosomal dominant hereditary syndrome that arises due to a mutation in the FLCN tumor suppressor gene.

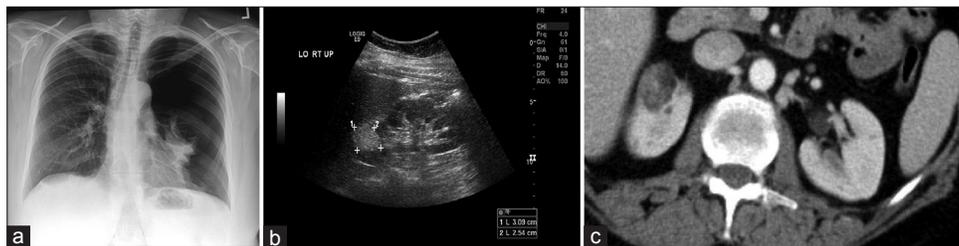


Figure 1: 51 year old female with Birt-Hogg-Dube Syndrome. (a) Chest radiograph demonstrates a large left pneumothorax. (b) Grayscale longitudinal plane image demonstrates a 3.1 × 2.5 cm well circumscribed hyperechoic lesion in the upper pole of the right kidney suggestive of Angiomyolipoma (AML). (c) Axial contrast enhanced image demonstrates corresponding hypoattenuating lesion containing macroscopic fat compatible with AML.

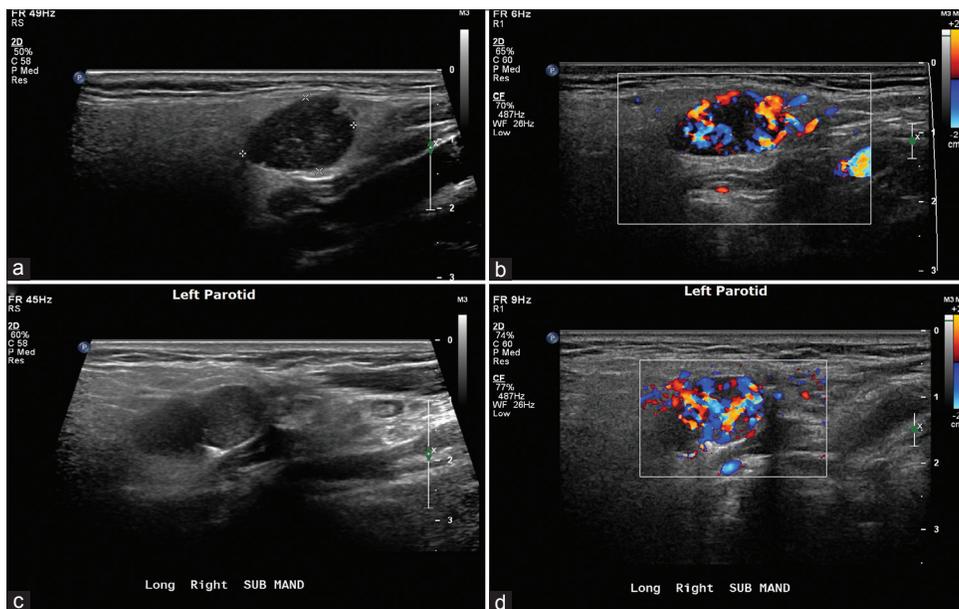


Figure 2: 51 year old female with Birt-Hogg-Dube Syndrome and Salivary Gland Oncocytomas. (a) Longitudinal Grayscale image demonstrated a 1.6 × 1.3 × 1.1 cm homogenous hypoechoic lesion in the left parotid gland. (b) Corresponding color Doppler image demonstrate diffuse hypervascularity. (c) Longitudinal Grayscale image of parotid gland demonstrates a 1.5 × 0.9 × 0.9 cm homogenous hypoechoic lesion in the right submandibular gland. (d) Corresponding real time color Doppler image demonstrate diffuse hypervascularity.

Table 1: Inherited syndromes with cancer predisposition and increased risk of renal cell carcinoma

Syndrome	Gene	Renal cancer type	Other cancers	Non-neoplastic findings
BAP1 mutant disease	BAP1	Clear cell	Melanoma Mesothelioma	Epithelioid atypical Spitz tumors
Von Hippel–Lindau disease	VHL	Clear cell	Hemangioblastoma Pheochromocytoma Neuroendocrine tumors	Renal and pancreatic cysts
Tuberous sclerosis complex	TSC1, TSC2	Angiomyolipoma	giant cell astrocytomas and angiomyolipomas	Angiofibromas on the face
Birt-Hogg-Dubé syndrome	FLCN	Oncocytic, chromophobe	–	Lung cysts, pneumothorax, fibrofolliculomas
Hereditary leiomyomatosis and renal cell cancer	FH	Papillary Type 2	–	Cutaneous/uterine leiomyomas
Hereditary papillary renal cell cancer	MET	Papillary Type 1	–	–

FLCN: Folliculin

Table 2: Key features of solitary salivary tumors

Salivary gland tumors	Border	Features	Ultrasound characteristics
Pleomorphic adenoma	Well defined	Benign. Most common solitary lesion. Slow growing, painless mass. Large tumors can cause facial nerve weakness.	Hypoechoic homogenous well-circumscribed mass. Often lobulated, poorly vascularized. May show posterior acoustic enhancement and can contain calcifications.
Oncocytoma	Well defined	Benign. Rare lesion presents in the 6 th decade. Most common lesion in patients with BHD.	Hypoechoic, homogenous, well circumscribed.
Warthin tumor	Well defined	Benign slow-growing tumor found almost exclusively in the parotid. More common in men. Bilateral in 15% of cases. Associated with smoking. Presents in the 5 th and 6 th decade.	Ovoid, with well-defined margins and multiple irregular, small, sponge-like anechoic areas. Tumors that are large tend to have a higher proportion of cystic content. Commonly found in the parotid tail.
Mucoepidermoid carcinoma	Variable	Most common malignant salivary gland lesion. Slow growing, presents as firm, painless mass. Typically presents between the ages of 30 and 50. Associated with CMV.	US imaging depends on aggressiveness of the tumor. May present as a heterogeneous hypoechoic lesion with ill-defined irregular borders. Less aggressive lesions typically present as heterogeneous hypoechoic well-circumscribed lesions. Can be partially or completely cystic.
Adenoid cystic carcinoma	Variable	Rare malignant salivary gland lesion. Has a propensity for local recurrence and late distal metastases. Can be infiltrative with perineural spread.	Appearances vary depending on aggressiveness. More aggressive lesions appear heterogeneous with ill-defined irregular borders.
Acinic cell carcinoma	Variable	Presents in the 5 th decade. More common in women. Can present as a painful nodule. Associated with radiation exposure and family history.	Variable appearance, typically round irregular lesion, can have cystic components.
Metastasis	Variable	Rare site of metastasis, typically metastasis to intraparotid lymph nodes. Cutaneous squamous cell carcinoma and metastatic melanoma are the most common entities.	Most commonly is an abnormal lymph node that presents as a hypoechoic heterogeneous mass, can have cystic degeneration.

BHD presents most commonly with epithelial hamartomas, pleural cysts, spontaneous pneumothoraces, and renal cell carcinoma.^[2,4] In BHD, the most common renal tumor is a hybrid chromophobe/oncocytic renal cancer.^[3] Chromophobe RCCs are derived from intercalated cells that reside in the renal collecting duct; patients with inactivating mutations in the FLCN gene are at risk of developing bilateral chromophobe RCCs with multiple foci.^[8] Early diagnosis of BHD is a key to ensure appropriate renal screening and early detection of RCC which significantly decreases mortality in these patients.

Sonographic evaluation of the salivary glands can be challenging due to their location; the parotid gland can be especially challenging due to its deep location often extending behind the acoustic shadow of the mandible. Our patient presented with enlarging palpable nodules in the right submandibular and left parotid regions. The multiple hypoechoic well-circumscribed lesions in our patient with a history of renal lesions and pneumothoraces are most compatible with salivary gland oncocytomas. Oncocytoma is the most common salivary gland solitary lesion in patients with BHD.^[1,2] Oncocytomas occur in multiple organs, for example, renal and thyroid oncocytomas, and are named for their characteristic cell type, the oncocyte.^[7,9] Oncocytes are epithelial cells with excess number of mitochondria that have a strong eosin stain.^[8,10] On ultrasound, oncocytomas are homogeneously hypoechoic, well-circumscribed, and differentiated tumors with increased vascularity. The differential diagnosis for solitary salivary gland lesions is summarized in Table 2 and includes pleomorphic adenoma, Warthin tumor, adenoid cystic carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma, and metastasis.^[6,8,11,12,13]

Differentiating these lesions can be challenging. Malignant lesions can have more infiltrative poorly differentiated margins; however, less aggressive tumors can be well circumscribed and are difficult to differentiate from more benign lesions. Unlike an oncocytoma which is homogenous in echotexture, these malignant lesions tend to be more heterogeneous and can be partially cystic.^[14,15] It is important to consider the clinical history when evaluating salivary gland lesions.

CONCLUSION

Sonographic evaluation of salivary gland lesions is a fast and inexpensive method. This case report illustrates the imaging features of salivary gland tumors and the importance of clinical history in diagnosis. Oncocytomas are the most common lesion of the salivary gland in patients with BH; early detection can result in appropriate treatment and decrease mortality.^[16,17]

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