Case report

Renal Manifestation of Birt–Hogg–Dubé Syndrome Depicted by 18F-fludeoxyglucose Positron Emission Tomography/Computed Tomography in a Patient with Hurtle Cell Thyroid Malignancy

Emmanouil Panagiotidis, Nagabhushan Seshadri, Sobhan Vinjamuri

Department of Nuclear Medicine, Royal Liverpool University Hospital, Liverpool, Merseyside, UK

Abstract

Birt–Hogg–Dubé (BHD) syndrome is an autosomal dominant genetic disorder characterized by small papular skin lesions (fibrofolliculomas) causing susceptibility to kidney cancer, renal and pulmonary cysts, spontaneous pneumothoraces, and several noncutaneous tumors. We report a case of a 67-year-old woman, with a previous history of right hemithyroidectomy for adenomatous lesion. She presented with a swelling in the right thyroid bed that on subsequent biopsy revealed features of metastatic carcinoma. 18F-fludeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) performed for the detection of primary malignancy showed increased high-grade metabolic activity in the right supraclavicular soft tissue mass extending into the superior mediastinum. Moreover, on low-dose CT, there have been bilateral renal interpolar cortical lesions with mild metabolic activity. Given the fact that the right neck mass was highly unlikely to represent renal metastases in the absence of widespread metastatic disease, surgical excision of the right neck mass was performed. The histology of the mass was in keeping with hurtle cell thyroid carcinoma. In regard to renal lesions, bilateral partial nephrectomy was performed, which was consistent with chromophobe renal cell carcinoma, raising the suspicion of BHD that was confirmed by the subsequent genetic evaluation. It is well established that 18F-FDG PET/CT study is not an optimal modality for evaluation of renal lesions. However, careful assessment of the CT features in conjunction with the associated metabolic activity of the 18F-FDG PET component increases the diagnostic accuracy of PET/CT.

Keywords: 18F-fluorodeoxyglucose positron emission tomography/computed tomography, Birt–Hogg–Dubé syndrome, chromophobe renal cell carcinoma, hurtle cell thyroid cancer

Introduction

Birt–Hogg–Dubé syndrome (also known as BHD) is a hereditary condition named after three Canadian doctors who first described it in 1977 – Arthur R. Birt, Georgina R. Hogg, and William J. Dubé. It is a cancer susceptibility syndrome caused by dominantly inherited mutations in the folliculin (FLCN) gene. The affected individuals are at risk of renal cell carcinoma (RCC) and spontaneous pneumothorax associated with lung cysts and white skin papules called fibrofolliculomas.[1] RCC affects 34% of mutation carriers, and most tumors are of chromophobe, oncocytoma, hybrid, or clear cell histology.[2-4] In addition, nearly 38% and 84% of BHD cases have a history of pneumothorax and fibrofolliculomas, respectively. Pulmonary cysts occur

Address for correspondence:
Dr. Emmanouil Panagiotidis,
Royal Liverpool University Hospital, Prescot Street, Liverpool, Merseyside, UK.
E-mail: mpanagiotidis@gmail.com

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in the majority of adults with BHD syndrome, leading to spontaneous pneumothorax in at least a quarter of the affected individuals.[2,5,6] Thyroid nodules have been associated with the BHD phenotype, present in 65% of individuals and 90% of families with the syndrome.[7] However, a connection between BHD and thyroid cancer has not been substantiated.[8]

Case Report

A 67-year-old woman with a history of right hemithyroidectomy for adenomatous lesion presented with swelling in the right thyroid bed. Ultrasound-guided biopsy of the right supraclavicular mass revealed features of metastatic carcinoma. 18F-fludeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) [Figure 1] which was performed to look for primary malignancy revealed a complex 2.2 cm left interpolar posterior cortical lesion containing few internal calcifications with moderate-grade 18F-FDG activity (maximum standardized uptake value [SUV_{max}] 4.7) (thin arrow) [Figure 2]. Also, there is a 2.4 cm solid lesion in the right renal interpolar cortex posteriorly with low-grade activity (SUV_{max}: 2.2), invading into the deeper cortex and medulla (thick arrow) [Figure 2]. Moreover, there was a photopaenic fluid density of 2.5 cm left renal lesion anteriorly due to benign cyst. On the neck, there was an 18F-FDG avid 2.4 cm × 2 cm soft tissue lesion in the right supraclavicular region with peripheral metabolic activity (SUV_{max}: 6.7) predominantly and central photopaenia indicating central necrotic component. There was an evidence of surgical clips on the low-dose CT in keeping with previous right thyroid lobectomy [Figure 3]. Low-dose CT of the lung shows pulmonary cysts.

Discussion

BHD is a hereditary condition named after three Canadian doctors who first described it in 1977. The clinical characteristics include cutaneous manifestations (fibrofolliculomas, trichodiscomas/angiofibromas, perifollicular fibromas, and acrochordons), pulmonary cysts/history of pneumothorax, and various

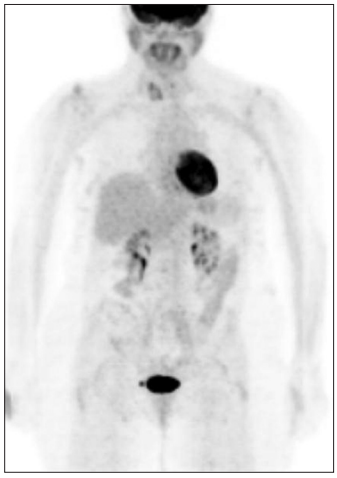

Figure 1: Maximum intensity projection positron emission tomography/computed tomography

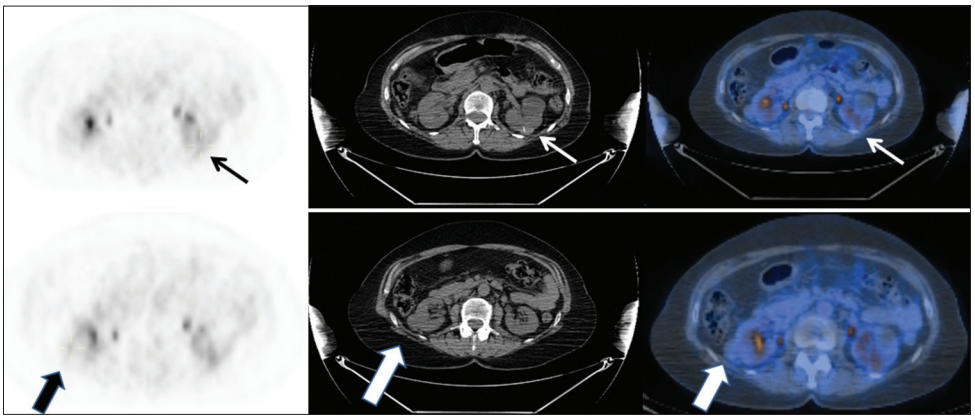

Figure 2: Transaxial positron emission tomography, low-dose computed tomography, and fused images of 18F-fludeoxyglucose positron emission tomography/computed tomography scan at the level of kidney

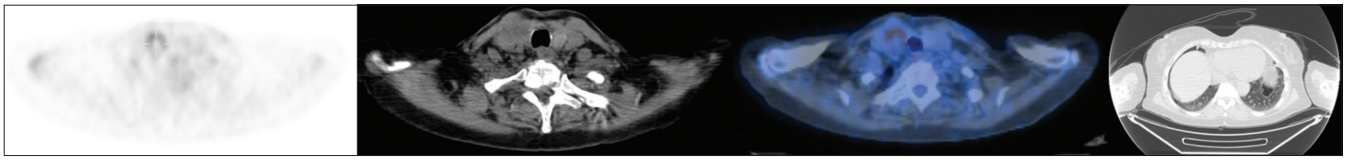

Figure 3: Transaxial positron emission tomography, low-dose computed tomography, and fused images of 18F-fludeoxyglucose positron

types of renal tumors.[1] Disease severity can vary significantly even within the same family. Skin lesions typically appear during the third and fourth decades of life and typically increase in size and number with age. Lung cysts are mostly bilateral and multifocal; most individuals are asymptomatic but at high risk for spontaneous pneumothorax.[5] There is a 7-fold increased risk for renal tumors that are typically bilateral and multifocal and usually slow growing; median age of tumor diagnosis is 48 years.[4] The most common renal tumors are a hybrid of oncocytoma and chromophobe histologic cell types (the so-called oncocytic hybrid tumor) and chromophobe histologic cell types. Some families have renal tumor and/or autosomal dominant spontaneous pneumothorax without cutaneous manifestations.[5] BHD syndrome is inherited in an autosomal dominant manner. Offspring of an individual with BHD syndrome have a 50% chance of inheriting the pathogenic variant.

Although thyroid nodules have been associated with the BHD phenotype, present in 65% of individuals and 90% of families with the syndrome, no connection between BHD and thyroid cancer has been substantiated.[7,8] In this case report, we present a patient with no cutaneous manifestation but with bilateral renal tumors and thyroid cancer. Recently, there was a case report of two patients with RCC and dermatological features that were detected with FLCN gene.[9] The two BHD patients were diagnosed with papillary thyroid carcinoma, which was treated with total thyroidectomy and prophylactic bilateral central lymph node dissection. However, in our case, the thyroid pathology was different, consistent with hurtle cell thyroid carcinoma. 18F-FDG PET/CT is not an optimal evaluation tool for renal/urinary tract pathology. However, careful assessment of the CT features in conjunction with the associated metabolic activity of the 18F-FDG PET component increases the diagnostic accuracy of PET/CT.

Conclusion

In our case, 18F-FDG PET/CT study depicted bilateral renal lesions with low/moderate metabolic activity and pulmonary cysts suggestive of BHD syndrome in a patient with right supraclavicular lesion. Although 18F-FDG PET/CT is not an optimal evaluation tool for renal/urinary tract pathology, thorough assessment of both PET and low-dose CT components for detection of renal neoplastic lesions is advised.

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Nil.

Conflicts of interest
There are no conflicts of interest.

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