CASE REPORT

Oncocytoma of the adrenal gland in Birt-Hogg-Dube syndrome

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SUMMARY

A 32-year-old man was referred to our surgical unit with a left adrenal lesion. He was previously diagnosed with Birt-Hogg-Dube syndrome after presenting with a left pneumothorax and an incidental finding of a right apical lung mass. This syndrome is characterised commonly by benign skin hamartomas, recurrent pneumothoraces and an increased risk of renal tumours. He was unable to tolerate a biopsy of his lung lesion, however, this lung lesion was thought to be benign. Given the size of his adrenal lesion and radiological appearances, we performed a laparoscopic left adrenalectomy. Pathology confirmed that based on morphological appearances and immunohistochemical staining, this may represent an oncocytic tumour of the adrenal gland. This is only the third published case of an oncocytic tumour of the adrenal gland in a patient with Birt-Hogg-Dube syndrome.

BACKGROUND

Birt-Hogg-Dube (BHD) syndrome is an autosomal dominant condition resulting from germline mutations in the folliculin (FLCN) gene, a tumour suppressor gene, located on chromosome 17p11.2. The syndrome is characterised most commonly by benign skin hamartomas (fibrofolliculomas, trichodiscomas and angiofibromas), pulmonary cysts and recurrent pneumothoraces and most seriously by an increased risk of renal tumours. This case is important because it alerts the clinician to the possibilities of any organ being affected in patients with genetic syndromes and ensures that the differential diagnoses are broad in these patients. There are only two published cases in the literature and this report adds further to the body of evidence regarding BHD syndrome.

CASE PRESENTATION

A 32-year-old man, previously fit and well, presented to his local hospital with left-sided pleuritic chest pain following exercise. He had an X-ray which showed a left pneumothorax and a right-sided apical mass. A chest drain was inserted and he had a CT scan which confirmed a 7 cm right-sided apical mass with benign appearances and showed a 3.7 cm heterogeneous mass in the left adrenal gland with calcification within (figure 1). He had no medical or surgical history. He took anabolic steroids on a regular basis. He was a smoker and drank alcohol occasionally. His father died from renal cancer at age 40.

INVESTIGATIONS

Following his CT scan, an MRI scan was performed which showed a 3.3 cm heterogeneous left adrenal lesion with benign appearances. On MRI, the lesion demonstrated enhancement on the portal venous phase and did not contain macroscopic fat. There was calcification in the rim of the lesion suggestive of benign appearances. Functional tests of adrenocortical hormone excess were all negative (24-hour urinary cortisol excess/overnight dexamethasone suppression tests, plasma rennin/aldosterone, urinary/plasma metanephrines and steroid hormone profiles).

He was discussed at the respiratory multidisciplinary team (MDT) meeting and biopsy of this lung lesion was recommended and he was also referred to endocrinology for his adrenal lesion. During his biopsy, he reported extreme pain during the procedure and it was abandoned. It was felt that given the pain he experienced at the time of the procedure and appearance of the lesion on imaging that the lesion may be a neurofibroma and given the family history of renal cancer, he was referred to the clinical geneticist to confirm or dispute a diagnosis of neurofibromatosis (NF). He had no clinical stigmata of NF such as café au lait or axillary freckling or neurofibromas. Genetic testing was negative for NF and Von Hippel-Lindau syndrome but confirmed the presence of BHD syndrome. He was heterozygous for the pathogenic sequence variant of c.1285 dupC and testing was made available for other at risk family members. Four generation pedigree testing is currently awaited.

He was also referred to the endocrine unit at a tertiary referral centre and his images discussed at the adrenal MDT. His adrenal lesion was thought to most likely represent a pheochromocytoma. Although plasma and urine metanephrines were negative, the imaging characteristics of a heterogeneous mass with a Hounsfield unit of 30–40 with calcifications within were suggestive of a pheochromocytoma and resection of his adrenal lesion was recommended.

DIFFERENTIAL DIAGNOSIS

The list of differential diagnoses included a non-secreting pheochromocytoma, lipid poor adrenal adenoma, metastatic disease from a lung or renal primary and adrenocortical cancer. Although rare, this can also represent Carney triad (association with pulmonary chondroma, paraganglioma, gastrointestinal tumour and rarely an adrenal

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Figure 1 Cross-sectional CT demonstrating left adrenal mass with right apical lung mass.

adenoma). The imaging characteristics were more in keeping with an indeterminate lesion and given his genetic predisposition, the possibility of a malignant lesion was considered.

TREATMENT

This patient underwent a laparoscopic left adrenalectomy. He did not require perioperative cover with steroids. Intraoperatively, the lesion appeared well circumscribed and was non-adherent to adjacent structures. There was minimal handling of the gland until the adrenal vein was divided. He remained normotensive during the operation and was discharged the following day.

OUTCOME AND FOLLOW-UP

He recovered well from the operation. His histological diagnosis was confirmed after extensive consultation with pathologists throughout the UK.

Histological findings were suspicious for an oncocytoma of the adrenal gland with the specimen containing nests of cells with abundant clear to granular eosinophilic cytoplasm. Markers for paired box gene 8, renal cell cancer, CD117 and CD10 were all negative and therefore not in keeping with typical renal cell cancers. Staining was also negative for pheochromocytoma. Ki 67 was also low at 1%–2%. There were no major or minor criteria based on the modified Weiss criteria.

Immunohistochemistry for succinate dehydrogenase B was also positive indicating that an SDH mutation was also unlikely. Additionally, none of the criteria for the Biscaglia scoring system were satisfied and therefore the tumour was classified as a benign oncocytoma of the adrenal gland.

Given the increased likelihood of renal cell cancer in patients with BHD syndrome, he will require yearly surveillance scans for an indeterminate period of time. At present, the patient does not want a biopsy or removal of his lung lesion although he may alter his decision in the future.

DISCUSSION

BHD syndrome was first described in 1977 and is an autosomal dominant syndrome caused by germline mutations in the FLCN gene located on chromosome 17. It is thought this predisposes to a loss of function of the FLCN protein which leads to the development of fibrofolliculomas which affects 90% of patients by their 30s, pulmonary manifestations such as pulmonary cysts

and more severely by renal cell cancers which occur in 12%–34% of patients with BHD.¹

Renal tumours in this syndrome are typically oncocytomas, chromophobe or mixed chromophobe and oncocytic.² Oncocytomas of the adrenal gland in patients with BHD have rarely been reported in the literature. To date, there are four published reports of adrenal lesions in BHD syndrome^{3–6}; however, only two of these report a diagnosis of oncocytomas of the adrenal gland.^{3,6} Oncocytic tumours are rare and often have unpredictable behaviour, but are mostly benign.⁷

Our patient presented atypically with a pneumothorax and given his radiological findings and family history of early-onset renal cancer, a high index of suspicion for a genetic syndrome was warranted. It was essential to determine the functional status of his adrenal lesion before operating as this could potentially have catastrophic effects particularly if it was catecholamine producing. Unfortunately, our patient did not want his lung lesions investigated despite the importance of this being emphasised. We are hopeful that he reconsiders this decision as this will provide concrete evidence linking all three pathologies together (lung mass, adrenocortical tumour and BHD syndrome).

Confirmation of the histological diagnosis required extensive collaboration among pathologists throughout the UK, given the rarity of the syndrome and difficulty in differentiating from other histological subtypes, however, numerous immunohistochemistry tests and markers confirmed the diagnosis. The European BHD consortium recommends annual screening with MRI for patients with a genetic mutation.⁸ As such our patient will require annual surveillance and given the fact that he is a smoker, this also increases his risk and appropriate smoking cessation strategies need to be employed. Additionally, screening of his family members is also important to identify potential carriers of the gene and allow appropriate counselling and discussion of risks.

Adrenocortical tumours have been described in patients with genetic syndromes such as Li-Fraumeni syndrome, MEN 1, Beckwith-Wiedemann syndrome, Carney complex and Lynch syndrome.^{9,10} Although rare, BHD should now be considered alongside these syndromes as a predisposing risk factor for adrenocortical tumours.

Learning points

- ▶ There should be a high index of suspicion for adrenal lesions in patients with genetic syndromes as it helps identify unusual pathology which may be potentially malignant.
- ▶ Incidentally detected adrenal lesions should be assessed to determine if they are hormone producing or malignant as these often require resection.
- ▶ Birt-Hogg-Dube syndrome should be considered as a genetic syndrome predisposing to adrenocortical tumours.

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