Birt-Hogg-Dubé Newsletter

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You are receiving this email because you have expressed an interest in BHD. We hope you will enjoy this and future editions. If you do not wish to receive this newsletter, please see the end of the newsletter for instructions.

BHDSyndrome.org updates

We are pleased to launch the new patient information pages. These have been updated to include new information, and rewritten to be less technical.

There are three brand new sections: frequently asked questions; a glossary of terms, which spells out the more difficult or unfamiliar terms phonetically; and a brief description of the science of BHD specifically written for patients.

We have designed a new Medical Education Kit. The kit contains three important papers written by BHD experts, describing the best treatment regimens, which patients can print out to give to their doctors to educate them about BHD.

BHD Patient Registry launched

The Cancer in our Genes International Patient Databank (CGIP) was launched on 20th March 2014. This is a patient registry for BHD, VHL, HLRCC and SDHB patients. The registry is an initiative of Ilene Sussman, Joyce Graff and the team at the VHL Alliance, and is part-funded by the Myrovlytis Trust. To read more about the registry, or to find out how to take part, please click here.

Getting to know you

This quarter, meet Geneva from the USA who was diagnosed with BHD in 2013, and Brian Iritani. Brian Iritani is Professor of Comparative Medicine at the University of Washington. His work focusses on the genetics underlying immune cell and cancer development. The interviews can be found here.

BHD Research Highlights

Noteworthy papers from the last quarter include:

Clinical:

Sauter and Butnor. Pathological findings in spontaneous pneumothorax specimens: does the incidence of unexpected clinically significant findings justify routine histological examination? Histopathology, 2014. [Epub ahead of print]

- Sauter and Butnor retrospectively reviewed the histopathological features lung resections taken from 72 patients with spontaneous primary pneumothorax over ten years. Six cases (8.3%) yielded clinically significant findings, including one case of Birt-Hogg-Dubé syndrome. The authors suggest that routine screening of lung resections taken during surgery for pneumothorax should be performed, due to the high rate of clinically significant findings.

Johannesma *et al*. The pathogenesis of pneumothorax in Birt-Hogg-Dubé syndrome: A hypothesis. Respirology, 2014. Nov;19(8):1248-50.

- Johannesma *et al*. report a natural history of Birt-Hogg-Dubé lung cysts based on the follow up of six patients. They conclude that BHD is unlikely to be a progressive degenerative disease. Additionally, they hypothesise that loss of *FLCN* in the epithelial cells lining cysts means they are less able to stretch under mechanical stresses. This causes cysts to burst, allowing air to build up in the pleural space and causing a pneumothorax. The authors suggest that pleurectomy combined with chemical pleurodesis may reduce the recurrence of pneumothoraces in BHD patients.

Johannesma *et al*. Birt-Hogg-Dube Syndrome Patients With And Without Pneumothorax: Findings On Chest CT. American Journal of Respiratory Critical Care Medicine, 2014. 189; A6416

- Johannesma *et al*. assessed the number, location, distribution, diameter, and shape of lung cysts in 18 BHD patients with a history of recurrent pneumothoraces, and 27 BHD patients with no history of pneumothorax. They found that pneumothorax was strongly correlated with the number of cysts, but not with any other characteristics analysed.

Sirintrapun *et al*. Oncocytoma-like renal tumor with transformation toward high-grade oncocytic carcinoma: a unique case with morphologic, immunohistochemical, and genomic characterization. Medicine (Baltimore), 2014. Oct;93(15):e81.

- Sirintrapun *et al*. describe a rare case of somatic *FLCN* mutation contributing to a sporadic case of metastatic renal cell carcinoma, and the first known case of a benign oncocytoma transforming to a high grade carcinoma.

Wagle *et al*. Response and acquired resistance to everolimus in anaplastic thyroid cancer. N Engl J Med, 2014. Oct 9;371(15):1426-33.

- Wagle *et al*. (2014) describe the case of a patient with anaplastic thyroid cancer, who had a sustained response to Everolimus for 18 months, at which point her tumour became resistant. Whole exome sequencing of germline, pretreatment, and resistant tumour DNA revealed that the pretreatment tumour had inactivating mutations in *TSC2*, *TP53* and *FLCN*, and the resistant tumour had developed a missense mutation in mTOR that prevents everolimus binding. The authors suggest that sequencing tumour DNA before and during treatment may suggest the most effective treatment regimen.

Benusiglio *et al*. Renal cell tumour characteristics in patients with the Birt-Hogg-Dubé cancer susceptibility syndrome: a retrospective, multicentre study. Orphanet Journal of Rare Diseases, 2014. Oct 2014, 9:163

- Benusiglio *et al*. report the renal cell tumour characteristics of a cohort of 33 BHD patients with renal tumours. The median age at the diagnosis of the first tumour was 46, 61% of patients had a solitary tumour at diagnosis, and 70% of tumours were of oncocytic or hybrid oncocytic/ choromophobe histology. Four patients had metastatic disease at diagnosis, but all survived with metastatic disease for more than 5 years, indicating that metastatic BHD renal tumours are less clinically aggressive than other forms of metastatic renal cancer.

To participate in an interview feature, submit information or suggest a topic for the next newsletter, please contact us at contact@BHDSyndrome.org.

BHD foundation