Oncogenetic testing for persons with Birt-Hogg-Dubé syndrome

Birt-Hogg-Dubé syndrome (BHD) is an autosomal dominant condition. Skin fibrofolliculomas, pulmonary cysts, spontaneous pneumothorax, and renal cancer can occur. The BHD prevalence is estimated to be 1/200 000. To date, approximately 500 families have been reported worldwide.[1, 2 3]

Clinical Recommendations

- Referral to a specialist genetics clinic for counselling and testing should be considered based on personal and family history, whether the individual is affected or not.
- If possible, genetic testing for a family should usually start with the testing of an affected individual (mutation searching/screening) to try to identify a mutation in the relevant gene.

Patients should be considered as a case of Birt-Hogg-Dubé syndrome if they fulfil **one major or two minor criteria for diagnosis**:

Major criteria

- At least five fibrofolliculomas or trichodiscomas, at least one histologically confirmed, of adult onset
- Pathogenic FLCN germline mutation

Minor criteria

- Multiple lung cysts: bilateral basally located lung cysts with no other apparent cause, with or without spontaneous primary pneumothorax
- Renal cancer in adults: early onset (<50 years) or multifocal or bilateral renal cancer, or renal cancer of mixed chromophobe and oncocytic histology.
- A first-degree relative with BHD

The following patients should be **referred for genetic testing and counselling:**

- Patients fulfilling the criteria for Birt-Hogg-Dubé syndrome mentioned above
- Patients with multifocal or bilateral renal cancer
- Patients with renal cancer of mixed chromophobe and oncocytic histology

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- Patients with renal cancer onset below 40 years of age with oncocytic histology
- Patients with unexplained cystic lung disease, and with lung cysts that are bilateral and basally located
- Patients who have familial cystic lung disease, familial pneumothorax or familial renal cancer
- Patients with any combination of spontaneous pneumothorax and kidney cancer or with a family member presenting with this combination
- Patients with a first-degree relative with BHD.

- Early detection of at-risk individuals affects medical management. However, in the absence of an increased risk of developing childhood malignancy, it is **recommended to delay predictive genetic testing** in at-risk individuals **until** they reach **age 18 years** and are able to make informed decisions regarding genetic testing.

For patients with **confirmed BHD syndrome**:

- Consider a yearly MRI of the kidney starting at age 20 to 25 years; if the MRI is not conclusive a CT scan may be required. Ultrasound is appropriate for the follow-up of lesions but is less sensitive than MRI and CT for screening purposes
- Consider a low-dose high-resolution thoracic CT scan before surgery that requires general anaesthesia
- Discourage smoking and scuba diving.

References

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2. Khoo SK, Giraud S, Kahnoski K, Chen J, Motorna O, Nickolov R, et al. Clinical and genetic studies of Birt-Hogg-Dube syndrome. J Med Genet. 2002;39(12):906-12.
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