Oncogenetic testing for persons with Birt-Hogg-Dubé syndrome

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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
  - 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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Source: KCE Report 243

How to cite this document:

Robays J, Stordeur S, Hulstaert F, Baurain J-F, Brochez L, Caplanusi T, Claes K, Legius E, Rottey S, Schrijvers D, t'Kint de Roodenbeke D, Ullman U, Van Maerken T, Poppe B. Oncogenetic testing, diagnosis and follow-up in Birt-Hogg-Dubé syndrome, familial atypical multiple mole melanoma syndrome and neurofibromatosis 1 and 2. – Summary Good Clinical Practice (GCP) Brussels: Belgian Health Care Knowledge Centre (KCE). 2015. KCE Reports 243C.

Publication date: April 2015
Legal depot: D/2015/10.273/33.

This document is available on the website of the Belgian Health Care Knowledge Centre.