FLCN gene

Associated Syndrome Name: Birt-Hogg-Dubé syndrome (BHDS)

FLCN Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Other	High Risk
Renal	High Risk
Skin	Elevated Risk

FLCN gene Overview

Birt-Hogg-Dubé syndrome (BHDS) [1, 2, 3, 4, 5, 6, 7]

- Individuals with mutations in the *FLCN* gene have a condition called Birt-Hogg-Dube syndrome (BHDS).
- Patients with BHDS have a high risk of developing both benign (non-cancerous) and malignant (cancerous) renal tumors. Tumors are often multifocal and affect both kidneys. These tumors are usually present at relatively young ages. The risk for renal cancer in individuals with BHDS is estimated to be 7-fold higher than the risk in the general population. The risk for any type of malignant or benign renal tumor is estimated to be between 25% and 35%.
- Patients with BHDS are at increased risk for skin melanoma.
- Most patients with BHDS will also develop benign tumors of the hair follicle (fibrofolliculomas). These may be present in large numbers and often recur after removal. These are mostly a cosmetic problem.
- Patients with BHDS are very likely to have lung cysts, which can lead to spontaneous pneumothorax (lung collapse).
- Studies have looked at the possibility that patients with BHDS have an increased risk for a wide range of other benign tumors and cancers, including colorectal polyps and cancer, salivary gland tumors, and thyroid nodules and cysts. However, the data are not conclusive at this time and there are currently no medical management guidelines related to these possible risks.
- It is appropriate to offer genetic counseling to individuals with BHDS who are of reproductive age to discuss reproductive risks and options. There are additional considerations before and during pregnancy for women with BHDS.
- Although there are high risks for tumors and other medical issues in patients with BHDS, it may be possible to reduce these risks with appropriate medical management. Guidelines from the National Comprehensive Cancer Network (NCCN) and the European BHDS Consortium are provided below. Since this is a complex condition, and there is still uncertainty about all of the associated risks, patients with *FLCN* mutations should be managed by a multidisciplinary team with expertise in medical genetics and experience in the surveillance and treatment of patients with hereditary renal cancer conditions.

FLCN gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Renal	To age 80[3, 4, 8, 9]	10%-37%	1.5%
Melanoma	To age 80[5, 9]	Elevated risk for skin melanoma	1.6%
Other - Non-malignant features of BHDS	All ages[1, 2, 3, 4, 6, 7]	BHDS is associated with a high risk for lung cysts and life-threatening spontaneous pneumothorax (lung collapse), as well as benign skin tumors.	NA

FLCN Cancer Risk Management Table

The overview of medical management options provided is a summary of professional society guidelines. The most recent version of each guideline should be consulted for more detailed and up-to-date information before developing a treatment plan for a particular patient.

This overview is provided for informational purposes only and does not constitute a recommendation. While the medical society guidelines summarized herein provide important and useful information, medical management decisions for any particular patient should be made in consultation between that patient and his or her healthcare provider and may differ from society guidelines based on

a complete understanding of the patient's personal medical history, surgeries and other treatments.

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Renal	Abdominal MRI (preferred) or CT, with and without contrast[7, 10]	Age 20, or earlier if there is a family history of renal tumor before age 30 years	Every 1 to 3 years
Melanoma	Currently there are no specific medical management recommendations for melanoma risk in mutation carriers. However, the increased risk for melanoma warrants consideration of risk-reduction strategies, including frequent self-examination of the skin, consideration of clinical skin examinations, and minimizing exposure to the sun and other sources of UV radiation.[11, 12]	Individualized	NA
Other - Non-malignant features of BHDS	Evaluation for lung cysts and attention to the risk for pneumothorax, as well as dermatological consultation[7]	At diagnosis	Individualized

Information for Family Members

The following information for Family Members will appear as part of the MMT for a patient found to have a mutation in the FLCN gene.

This patient's relatives are at risk for carrying the same mutation(s) and associated cancer risks as this patient. Cancer risks for females and males who have this/these mutation(s) are provided below.

Family members should talk to a healthcare provider about genetic testing. Close relatives such as parents, children, brothers and sisters have the highest chance of having the same mutation(s) as this patient. Other more distant relatives such as cousins, aunts, uncles, and grandparents also have a chance of carrying the same mutation(s). Testing of at-risk relatives can identify those family members with the same mutation(s) who may benefit from surveillance and early intervention.

It is appropriate to offer genetic counseling to individuals with BHDS who are of reproductive age to discuss reproductive risks and options. There are additional considerations before and during pregnancy for women with BHDS.

References

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