PTEN gene

Associated Syndrome Name: *PTEN* hamartoma tumor syndrome (PHTS)

PTEN Summary Cancer Risk Table

CANCER	GENETIC CANCER RISK
Breast	High Risk
Colorectal	High Risk
Endocrine	High Risk
Endometrial	High Risk
Other	High Risk
Renal	High Risk
Skin	High Risk

PTEN gene Overview

PTEN hamartoma tumor syndrome (PHTS) [1, 2, 3, 4, 5]

- Individuals with *PTEN* mutations have *PTEN* hamartoma tumor syndrome (PHTS).
- Women with PHTS have a risk for breast cancer that is significantly increased over the 12.5% lifetime risk for women in the general population of the United States. Individuals with PHTS also have a significantly increased risk for colorectal, endometrial, thyroid, renal and melanoma cancers. These cancers are often diagnosed at relatively young ages.
- A recent study has demonstrated that patients have a high risk for developing a second primary PHTS-associated cancer following their first diagnosis, and the risk may be particularly high for a second primary breast cancer.
- There is some evidence for an increased risk for neuroendocrine tumors in individuals with PHTS. The data are not conclusive at this time and there are currently no medical management recommendations that address this possible risk.
- Patients with PHTS often have a wide variety of other, non-malignant features of the condition, some of which may require medical attention. Examples are macrocephaly, colorectal polyps of various types, Lhermitte-Duclos disease (a hamartomatous brain tumor), and distinctive skin findings such as trichilemmomas, acral keratoses and papillomatous papules. Developmental delay and/or autism spectrum disorders may also be present.
- A subset of patients with PHTS may have a diagnosis of other syndromes, such as Cowden syndrome (CS), Bannayan-Riley-Ruvalcaba syndrome (BRRS), *PTEN*-related Proteus syndrome or Proteus-like syndrome, based on other clinical features. Some of these conditions have features that may require intervention in infancy or childhood.
- Although there are high risks for cancer in patients with PHTS, these risks can be reduced with appropriate medical management. Guidelines from the National Comprehensive Cancer Network (NCCN) are listed below. Management of patients with PHTS poses challenges due to the complexity of the condition and it is recommended that patients with *PTEN* mutations and a diagnosis of PHTS be managed by a multidisciplinary team with expertise in medical genetics and the care of patients with hereditary cancer syndromes.

PTEN gene Cancer Risk Table

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Overall Cancer Risk (male and female)	To age 70 [6, 7, 8]	70%-98%	19.8%
Female Breast	To age 70 [4, 6, 7, 8]	60%-88%	7.6%
Endometrial	To age 70 [4, 6, 7, 8]	6%-50%	1.9%
Thyroid	To age 70 [4, 6, 7, 8]	17%-40%	0.9%
Renal	To age 70 [4, 6, 7, 8]	3%-31%	0.9%
Colorectal	To age 70 [4, 6, 7, 8]	5%-15%	1.8%

CANCER TYPE	AGE RANGE	CANCER RISK	RISK FOR GENERAL POPULATION
Melanoma	To age 70[4, 6, 8]	6%-12%	1.0%
Other - Non-malignant features of PHTS	All ages[3, 4, 5]	PHTS is associated with non-malignant clinical features, some of which may require medical intervention as early as infancy (see Overview)	NA

PTEN 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)
Overall Cancer Risk	Comprehensive physical examination, with particular attention to thyroid cancer. General education about the signs and symptoms of cancer.[4]	18 years or 5 years before the youngest age of a PHTS-related cancer in family	Annually
Female Breast	Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness.[4]	Individualized	NA
	Clinical breast examination[4]	25 years, or 5 to 10 years younger than the earliest diagnosis in the family, whichever comes first.	Every 6 to 12 months
	Mammogram and breast MRI with and without contrast[4]	30 years, or 10 years younger than the earliest diagnosis in the family, whichever comes first	Annually
	Consider risk-reducing mastectomy.[4]	Individualized	NA
Endometrial	Patient education about the importance of quickly seeking attention for endometrial cancer symptoms, such as abnormal bleeding or menstrual cycle irregularities[4]	Individualized	NA
	Consider transvaginal ultrasound.[4]	After menopause	Individualized
	Consider screening with endometrial biopsies.[4]	Age 35	Every 1 to 2 years
	Consider hysterectomy.[4]	After completion of childbearing	NA
Thyroid	Thyroid ultrasound[4, 9]	12 years	Every 1 to 3 years
	Physical examination, including neck palpation[9]	12 years	Annually
Renal	Consider renal ultrasound.[4]	40 years	Every 1 to 2 years
Colorectal	Colonoscopy[4, 10]	35 years, or 5 to 10 years younger than the earliest diagnosis in the family if a family member was diagnosed under age 40	Every 5 years

CANCER TYPE	PROCEDURE	AGE TO BEGIN	FREQUENCY (UNLESS OTHERWISE INDICATED BY FINDINGS)
Melanoma	Dermatology exam[4]	Individualized	Annually
Other - Non-malignant features of PHTS	Comprehensive physical examination. Dermatologic management may be indicated for some patients. Consider psychomotor assessment in children and brain MRI if there are symptoms.[4]	18 years or earlier if symptoms are present	Annually

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 PTEN 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.

Since *PTEN* mutations carry a risk for complications in children and some screenings are recommended to begin at young ages, mutation testing should be considered as soon as a diagnosis of any PHTS-condition is suspected. If genetic testing is not performed, thyroid screening should be considered for children at risk for inheriting a *PTEN* mutation beginning in childhood.[4]

Parents who are concerned about the possibility of passing on a *PTEN* mutation to a future child may want to discuss options for prenatal testing and assisted reproduction techniques, such as pre-implantation genetic diagnosis (PGD).[4]

References

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