CLINICAL VIGNETTE

PTEN Gene Mutation in a Young Woman with Multiple Cancers

Stephen C. Ross, MD

Introduction

The PTEN gene, referred to as the Phosphatase and Tensin Homolog Gene, is involved in regulating cell growth and division. It helps the body suppress tumor genes that can lead to uncontrolled cell growth and cancer. Mutations in the PTEN gene can lead to the loss of the tumor suppressing capabilities allowing cancer cells to grow and divide. This case illustrates how a mutation of the PTEN in a young woman lead to multiple cancers and the effort to find the gene mutation. The patient had a specific PTEN Mutation PHTS also known as Cowden disease.[1]

Case

The patient is now 39-yeard-old. At age 26, she developed papillary thyroid cancer and underwent total thyroidectomy and adjuvant radiation. No genetic testing was done at that time. At age 31, she was found to have a right parotid mucoepidermoid carcinoma and underwent parotidectomy and adjuvant radiation treatment without recurrence. Last year she was diagnosed with breast cancer and underwent bilateral skin sparing mastectomies. She also obtained genetic testing which indicated a mutation in the PTEN gene, consistent with Cowden syndrome. With high risk of developing uterine cancer, she underwent a total hysterectomy and bilateral salpingo-oophorectomy. She also had a colonoscopy done which was normal. Other family members were negative for PTEN gene mutations. This patient is also borderline macrocephaly and ASD (autism spectrum disorder).

Discussion

This patient has PTEN hamartoma syndrome (PHTS), also known as Cowden Syndrome. PHTS also includes Bannayan-Riley-Ruvalcaba syndrome (BRRS) and PTEN-related autism spectrum disorder. PHTS is a multisystemic disorder primarily characterized by hamartomas that can develop throughout the body, which may be associated with cancers. The disorder was originally described in 1963 by Lloyd and Davis. It is uncommon affecting 1 in 200,000 people. Cowden disease is thought to be caused by a germline variant of the PTEN gene on chromosome 10. It is inherited in an autosomal dominant fashion. Actual prevalence may be higher due to many undiagnosed cases.[2] Diagnosis have increased with increased genetic testing. The cancers most often associated with PHTS genetic abnormality are breast, thyroid and uterine cancer. Our patient also developed parotid cancer that would be related to hamartomas. The condition has high penetrance with 90% of affected patients displaying clinical findings by the third decade. There appears to be a female dominance in Cowden syndrome, and most patients reported in the literature are caucasion.[3]

The lifetime risks for different cancers with the pathogenic PTEN variants are reported as:

- Breast cancer: 67-85%
- Thyroid cancer: 34-38%. There can be other thyroid pathologies including multinodular goiters, adenomatous nodules, follicular adenomas and Hashimoto's thyroiditis.
- Uterine cancer: 28% Patients with the PTEN variant gene need to be followed closely for abnormal uterine bleeding with annual uterine ultrasounds. Endometrial biopsies are recommended with hysterectomy after childbearing. Oophorectomy is not indicated.
- Renal Cancer: 35% and renal ultrasound should be done starting at age 40 and every 1-2 years.
- Colon Cancer: Colon polyps are present in most adults with PHTS and include hamartomas, hyperplastic polyps, ganglioneuromas and adenomas. The risk of colon cancer is 9% and patients with PHTS should start screening colonoscopies at age 35 and every 5 years.
- Melanoma: There is a 6% risk of melanoma with PHTS and yearly skin exams are recommended.[4]

Physical characteristics of Cowden Syndrome also include macrocephaly, trichilemmomas, acral keratosis, hamartomas and oral papillomatosis. Brain abnormalities are commonly found in patients with Cowden syndrome. Neuroimaging has identified Lhermitte-Duclos disease, meningiomas, arteriovenous anomaly and cavernous malformations. Neurodevelopmental abnormalities associated with Cowden Syndrome consist of macrocephaly, autism spectrum disorder and developmental delays.[5]

The PTEN/PHTS gene mutation has autosomal dominant inheritance and genetic testing is recommended for first degree relatives.

Conclusion

This 39- year- old woman had multiple malignancies starting at the age of 31. She eventually underwent genetic testing and was found to have a variant of the PTEN Gene Mutation PHTS or

Cowden Disease. She successfully underwent all recommended screenings and surgeries.

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