Concurrent germline PTEN and BRCA1 pathogenic variants in a patient with Cowden syndrome and treated breast cancer: a case report

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INTRODUCTION

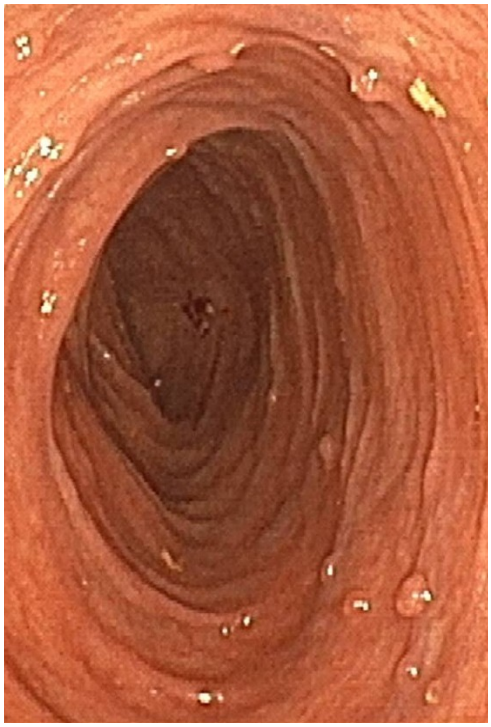
Pathogenic variants in BRCA1 are well-established to confer a markedly increased risk of breast and ovarian malignancies. Similarly, individuals harboring pathogenic alterations in PTEN exhibit a substantially elevated predisposition to various neoplasms. As both genes function as pivotal tumor suppressors, affected patients warrant meticulous genetic counseling and surveillance.

OBJECTIVE

The objective of this case report is to delineate the clinical course of a young female patient initially treated for breast cancer who, twelve years later, was found to harbor pathogenic variants in two critical tumor suppressor genes—BRCA1 and PTEN—and who also manifested with multiple colonic and gastric polyps.

CASE

A 37-year-old female patient presented for evaluation of recent colonoscopy and upper endoscopy findings, which revealed **more than ten hyperplastic polyps.** She reported a past medical history notable for a quadrantectomy of the left breast performed twelve years prior, with histopathological analysis demonstrating multiple foci of intraductal **carcinoma** excised with negative margins. On physical examination, she exhibited **numerous cutaneous lesions, including pedunculated papules on the neck, axillae**, and inframammary regions bilaterally, as well as acral keratoses on the dorsal aspects of the hands and feet. Her family history was significant for a mother who succumbed to gastric cancer and a maternal aunt who had been treated for breast cancer.



A recent PET scan showed no evidence of suspicious lesions. Germline genetic testing identified two heterozygous pathogenic variants: **BRCA1 c.5074+2T>C and PTEN c.697C>T (p.Arg233).**

DISCUSSION

This is the first documented case of Cowden syndrome with concurrent PTEN and BRCA1 pathogenic variants. BRCA1 mutations confer ~60% lifetime risk for breast/ovarian cancer. The PTEN variant results in premature stop codon, producing nonfunctional protein. PTEN pathogenic variants increase risk for breast, thyroid, endometrial, renal, colorectal cancers, and melanoma. This patient requires intensive counseling, surveillance, and consideration of prophylactic mastectomy and oophorectomy.

CONCLUSION

This case represents the first documented occurrence of Cowden syndrome with concurrent pathogenic variants in both PTEN and BRCA1. Given this unique molecular profile, the patient requires intensive surveillance and genetic counseling to ensure early detection and appropriate management of associated malignancies.