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An unexpected diagnosis of *MUTYH*-associated polyposis: A case study

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I. Introduction

In many ways, direct-to-consumer (DTC) testing has expanded patient access while creating a bridge between the general population and specialty genetic testing.[1] Despite this benefit, the lack of in-depth risk assessment and counseling may give individuals with negative results a false sense of reassurance. Similarly, a positive result interpreted without consideration of the broader family history may overlook additional risk factors and recommendations. This case study illustrates the value of DTC testing for hereditary cancer while demonstrating the importance of a follow-up genetic counseling consult.

II. Clinical Sequence of Events

The patient was a reportedly healthy 34-year-old Caucasian female who underwent DTC testing in 2019

Motivation for testing
- Curiosity and low out-of-pocket cost and avoidance of insurance prior authorization
- A known family history of cancer was not a factor, as she was not concerned about an increased risk for cancer

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DTC testing identifies biallelic/homozygous pathogenic *MUTYH* variants, confirmatory genetic testing recommended

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Patient consulted referring provider (RP)
- No referral made to Genetic Counselor or other cancer genetics specialist
- RP orders hereditary colorectal panel testing (22 genes) from CAP/CLIA certified laboratory
- Testing confirms biallelic pathogenic *MUTYH* variants (c.1187G>A)
- Testing reveals *BRCA2* variant of uncertain significance (c.3900_3902delGAC)

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RP refers patient for post-test genetic counseling at center not affiliated with the DTC laboratory

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Patient seen for post-test cancer genetic counseling and session includes:
- Review of *MUTYH*-associated polyposis (MAP)
- Discussion of management guidelines and recommendations for MAP
- Pedigree analysis and cancer risk assessment: Revealed family history of breast cancer
- Patient met the National Comprehensive Cancer Network (NCCN) testing criteria for hereditary breast and ovarian cancer susceptibility genes
- Discussion of follow-up genetic testing options based on family history of breast cancer
- Patient decision making: Patient elected expanded hereditary breast cancer panel

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RP orders expanded hereditary breast cancer panel and reveals no additional genetic findings

III. Case Study

This case study focuses on the post-test cancer genetic counseling session.

As outlined above, the consult included a review of the diagnosis of *MUTYH*-associated polyposis (MAP) and the importance of early and frequent surveillance as outlined in the National Comprehensive Cancer Network Guideline, Genetic/Familial High-Risk Assessment: Colorectal.[2]

Pedigree analysis revealed a paternal grandfather with breast cancer. This history was discussed in the context of the genes tested and the lab results including the association of male breast cancer (MBC) and *MUTYH* pathogenic variants as a potential explanation for the family history. A previous study concluded that *MUTYH* homozygous and heterozygous pathogenic variants may have a role in male breast cancer risk although larger scale collaborative studies are needed to better understand the link between *MUTYH* variants and MBC risk.[3]

Based on the pedigree analysis, the patient met the NCCN testing criteria for high-penetrance breast and/or ovarian cancer susceptibility genes. Follow-up testing was offered to rule out a pathogenic variant in another breast cancer susceptibility gene and the patient elected to proceed with an expanded breast cancer panel. Testing was negative.

IV. Discussion

Direct-to-consumer (DTC) genetic testing has gained popularity over the years.[4] People are drawn to low out-of-pocket cost and the simplicity of ordering genetic testing without a healthcare provider serving as an intermediary. DTC genetic testing is not designed to replace testing for those with a positive family history and DTC companies all recommended confirmatory testing and appropriate follow-up for those with positive results. For those who are unaware of an increased hereditary cancer risk, positive or negative results may provide a false sense of reassurance.

In this case, although DTC testing paved the way for the diagnosis of MAP, posttest genetic counseling provided the patient with an understanding of her cancer risks based on both the test results and allowed for an in depth assessment of her family history.

V. Conclusions

This case demonstrates the advantages of DTC testing in identifying patients at risk for hereditary cancer syndromes, the benefits of genetic counseling evaluations in interpreting DTC results in the context of the family history.

VI. References

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