

Screening for Hereditary Cancer Syndromes

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Case scenarios are written to express typical situations that family physicians may encounter; authors remain anonymous. Send scenarios to afpjournal@aaafp.org. Materials are edited to retain confidentiality.

This series is coordinated by Caroline Wellbery, MD, Associate Deputy Editor.

A collection of Curbside Consultation published in *AFP* is available at <http://www.aaafp.org/afp/curbside>.

Case Scenario

My patient's wife died of pancreatic adenocarcinoma at 35 years of age. After her death, her doctor told my patient that their child might be at increased risk of developing pancreatic cancer. My patient asked if pancreatic screening and genetic testing were available for his eight-year-old daughter. He was referred to a genetic counselor specializing in cancer, who took a three-generation family history. It showed a strong family history of melanoma, suspicious for a hereditary cancer syndrome called familial atypical multiple mole melanoma (FAMMM) syndrome.

The genetic counselor recommended that my patient's brother-in-law or father-in-law (who had previously had melanoma), rather than his daughter, visit a geneticist to determine if he meets diagnostic criteria for FAMMM syndrome.

Several weeks later, the father-in-law and brother-in-law were found to meet the diagnostic criteria for FAMMM syndrome, but tested negative for a *CDKN2A* mutation.¹ What recommendations should I make based on these results?

Commentary

Family physicians play a key role in identifying patients in need of increased cancer surveillance because of a personal or family history of cancer. How does one know if a patient warrants genetic testing for hereditary cancer predisposition? The first step is to take a family history. Consideration of increased screening recommendations, genetic counseling, or risk-reducing strategies may be warranted if there is a personal or family history of (1) cancer occurring at an unusually young age, (2) multiple primary tumors, (3) rare cancers such as male breast cancer, (4) several family members having the same or related forms

of cancer, (5) criteria for genetic testing for a hereditary cancer syndrome, and (6) lack of environmental risk factors in a cancer with environmental triggers.² The ultimate goal is to determine whether a patient has a cancer risk that necessitates changes in lifestyle and medical management.

Genetic testing is not always informative, but the family history can provide the information needed to decide if a patient needs increased screening. The American College of Medical Genetics and Genomics and the American Academy of Pediatrics recommend performing presymptomatic genetic testing in minors at risk of childhood-onset conditions and deferring genetic testing for adult-onset conditions, unless an intervention initiated in childhood may reduce morbidity or mortality.^{3,4}

When an adult patient has an unexplained personal or family history of cancer, the best outcome is to identify a cancer-causing mutation. When a mutation is found, testing asymptomatic family members can identify "true positives" who are in need of increased screening and prevention strategies from "true negatives" who do not need increased screening. There are many reasons a patient's genetic test results can be negative, including a mutation in an as-yet-undiscovered gene, a mutation that current technology cannot detect, or a true sporadic cancer. However, when a mutation is not found, it is important to take a second look at the family history to determine whether the patient or family members meet increased screening guidelines based on family history alone.

FAMMM syndrome is an autosomal dominant disorder with increased risks of developing melanoma and pancreatic cancer. Patients who have FAMMM syndrome and a *CDKN2A* mutation have a 60% to 90% ►

Table 1. Resources on Inherited Diseases and Genetic Counseling

Resource	Description
Cancer.Net (http://www.cancer.net/navigating-cancer-care/cancer-basics/genetics)	A collection of patient-oriented information on cancer care from the American Society of Clinical Oncology and the Conquer Cancer Foundation
GeneReviews (http://www.ncbi.nlm.nih.gov/books/NBK11116/)	Covers the diagnosis, management, and counseling of heritable diseases in a series of peer-reviewed chapters
InformedDNA (http://informeddna.com/)	For physicians in rural areas; offers individualized genetic counseling by telephone
National Society of Genetic Counselors (http://www.nsgc.org/)	Includes tools for finding local genetic counselors and recommendations for including them in practice

chance of developing melanoma by 80 years of age and a 17% chance of developing pancreatic cancer by 75 years of age.^{5,6} The cancer risks for patients who have FAMMM syndrome without a *CDKN2A* mutation are variable.⁷ Because the family in this case scenario met the clinical diagnostic criteria for FAMMM syndrome, all family members, first-degree relatives, and some second-degree relatives should follow FAMMM syndrome screening guidelines and should consider enrolling in a clinical research screening program.⁸

FAMMM syndrome screening guidelines begin at 10 years of age with a baseline total body skin examination. There is no established screening guideline for individuals at increased risk of developing pancreatic cancer. However, International Cancer of the Pancreas Screening Consortium recommends consideration of pancreatic screening in *CDKN2A* carriers with one first-degree relative diagnosed with pancreatic cancer by endoscopic ultrasonography or by magnetic resonance imaging/magnetic resonance cholangiopancreatography. Consensus was not reached on the age to initiate screening.⁹ Currently, the effectiveness of screening for pancreatic cancer has not been established. It is recommended that screening be performed as part of a research protocol and/or at a center with demonstrated expertise in pancreatic diseases and a comprehensive genetic counseling program.⁹

Identifying a patient who is at increased risk of developing cancer or who has a hereditary cancer syndrome helps physicians make changes to a patient's medical management that address these risks.¹⁰ Diagnosis of a hereditary cancer syndrome affects not only the patient but also the patient's family members. Policy statements, as well as other research, stipulate that physicians have a duty to inform patients about a family's cancer risk.¹¹⁻¹³

This case demonstrates that partnering with a genetic counselor can save time and improve care by identifying patients or family members who would benefit from genetic screening.¹⁴ *Table 1* lists resources on genetic counseling and inherited diseases.

The authors thank Louise Amlie-Wolf, MS, CGC, and Daniel Morales for their assistance with the manuscript.

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