

Managing Families With a Hereditary Cancer Syndrome

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Oncology is one of the first subspecialties to experience the full impact of the genomics revolution; oncology nurses regularly use genomic science in prevention, screening, diagnostics, prognostics, selection of treatment, and monitoring of treatment effectiveness in cancer care (Mahon, 2009). Genetic tests are now routinely ordered to determine risk for developing and appropriate management of hereditary breast and ovarian cancer, hereditary nonpolyposis colorectal cancer, and many other hereditary cancer syndromes—often without formal genetic assessment by a credentialed professional. Two cases will be reviewed that demonstrate the complexities of providing and coordinating care for at-risk relatives with a genetic predisposition to developing cancer.

Case Study 1

The first case illustrates the potential positive aspects that can occur when a family with suspected hereditary predisposition is managed by a credentialed genetics professional.

A 39-year-old woman was diagnosed with colorectal cancer after an episode of rectal bleeding. The colorectal surgeon appropriately referred her for genetic counseling based on her young age of onset. A pedigree was constructed. The proband's (i.e., patient's) mother died from pancreatic cancer and one great paternal aunt was diagnosed with endometrial cancer. Pretest counseling was completed and the proband was motivated to undergo testing not only for herself, but to better understand the risks to her two young children and siblings. Testing for mutations associated with nonpolyposis colon cancer, *MLH1*, *MSH2*, and *MSH6*, were offered based largely on her young age at diagnosis and were found to be negative. Shortly after the results came back, testing for *PMS2* (defects in this gene are associated with DNA mismatch) became available and the patient was recontacted about the possibility of adding

the test. The patient chose to add the test and was found to have an unusual *PMS2* mutation not previously reported and subsequently had a prophylactic total hysterectomy to reduce her risk of endometrial (estimated risk, 60%) and ovarian cancer (estimated risk, 15%). She is on a schedule for a yearly upper endoscopy and colonoscopy (estimated risk of first colon cancer, 85%; second colon cancer, 50%).

The proband immediately contacted her siblings, who presented for genetic testing within two weeks. One sister tested positive. At that point, it was clear that it was not a de novo mutation but it was unclear if transmission was maternal or paternal and if other relatives were at risk. Because the proband's mother was deceased, her father was tested for the known mutation and found to be negative, so it was concluded that the mother was the obligate carrier. Her mother had one brother, who was deceased, with five offspring. Testing was offered to these first cousins. Three presented for testing within a week of testing the proband's father. Two siblings lived in other cities and counselors were identified to coordinate their care. Two of the siblings from the proband's uncle tested positive; therefore, the uncle also was an obligate carrier. Follow-up was arranged for the adult children of those who tested positive.

Case Study 2

The second case illustrates the negative outcomes that can occur when risk is not communicated to all family members.

A 20-year-old woman presented with vertebral fracture from metastatic breast cancer. Her mother reported one aunt with later-onset breast cancer; the father was estranged from his family and did not report any cancer. The proband was offered testing based on her extremely young age of onset and was found to have a mutation in *BRCA2*. Her 23-year-old sister also was found to have the

mutation; she was subsequently found to have metastatic breast cancer at the time of her prophylactic mastectomy, two months after her sister (the proband) was diagnosed. The proband's brother also had a mutation; the mutation was not de novo. Next, the mother was offered testing for the specific mutation and she tested negative. The father was offered testing and found to be the carrier. At the time of testing, he was clearly informed that if he tested positive, he had an ethical obligation to contact his siblings, even if they were estranged, and inform them of the possible increased risk. He tested positive and subsequently contacted his 56-year-old sister. After discussion, he learned that she had already had genetic testing and was known to have the same mutation. It had been done through her oncologist five years earlier.

The proband was devastated because, had she known she had the increased risk, she would have considered prophylactic measures; she subsequently died a year later. The oncologist had correctly ordered the testing and recommended prophylactic surgery (bilateral mastectomy and oophorectomy) for the 56-year-old paternal aunt of the proband. Of great concern, however, was that none of the other siblings of this aunt seemed aware of their risk or had undergone testing. The genetics professional provided counseling and testing for the other four siblings, and three tested positive. They have since undergone appropriate prophylactic measures and testing is now being coordinated for their offspring as they become old enough to consider testing.

Commentary on the Cases

Case 1 clearly illustrates the importance and complexity of genetic testing. First, genetic testing is continually evolving. A family who has previously tested negative for common mutations should be offered testing as new mutations are identified; this is a regular component of the practice of genetics

professionals (Rubinstein, 2008). More importantly, the case illustrates the importance of carefully constructing a pedigree and informing members of potential risk. In a study of 860 primary care providers, most respondents (83%) reported that they routinely assess hereditary cancer risk; however, only 33% reported that they take a full, three-generation pedigree for risk assessment (Vig et al., 2009). Without a full pedigree, identifying what other relatives might be at risk is impossible, particularly if a mutation is detected.

The family in Case 1 was a close, cooperative family who communicated well, as evidenced by the quick follow-up. The pedigree also illustrates how important it is to identify all family members at risk. The genetics professional took the extra step to determine if the risk was from the maternal or paternal side and worked with the proband to systematically inform at-risk relatives. The surgeon who referred the proband for formal genetic counseling and testing made a huge difference in the outcome for the proband, so her risk could be identified and she could engage in preventative behaviors (total hysterectomy) and aggressive screening (colonoscopy and upper endoscopy) to detect problems early. That ultimately should decrease costs associated with later-stage detection of cancer and improve her quality of life. The careful follow-up and identification of other at-risk members also will help those family members who are mutation-positive to engage in aggressive screening and prophylaxis to truly prevent a cancer.

For those who tested negative for the known family *PMS2* mutation, a sense of relief was gained, as well as cost savings, because they do not need aggressive screening or prophylactic surgery; they can follow screening recommendations for those of average risk.

Case 2 is an unfortunate case that clearly demonstrates the devastating effect when testing is done for one individual without adequate information, support, and follow-up to ensure that other family members receive adequate information about risk and how to access genetic services. In this case, the oncologist treated the individual correctly but did not address the importance of care for other members at risk. The approach of the genetics professional is to treat the family (Wiseman, Dancyger, & Michie, 2010). Had the proband been informed, the outcome may have been different for her and her sister.

Clinical Considerations in Genetic Testing

Guidelines on who should provide genetic cancer risk assessment services to high-risk individuals have been published by many groups (American Congress of Obstetricians and Gynecologists, 2009; Jenkins, 2009; Lancaster et al., 2007; Trepanier et al., 2004; Weinstein, 2009). Qualifications of professionals who provide cancer genetics counseling services are shown in Figure 1.

Most of the guidelines issued by professional groups recommend follow-up care for other at-risk family members, although the exact extent of follow-up care and who should provide it is not always clearly specified (Liao, 2009). Genetic medicine is different because the uses and abuses of genetic information may extend beyond the patient to the family (Offit & Thom, 2007). When a person chooses to undergo genetic testing, the results have implications for the person being tested as well as for other family members. For that reason, genetics professionals consider the family, not just the individual.

When genetic testing moves away from a credentialed genetics professional, the ordering provider often interprets the test for an individual. If the provider is an oncologist or other subspecialist, they may not see other family members who do not have a cancer diagnosis—it often is unclear who should care for the rest of the family. Family members at risk may not know how to access genetics care or be able to afford such care.

The legal extent to which the healthcare provider who orders genetic testing is responsible for the care of other family members is not completely clear either. Consequently, genetics professionals will inform the patient, work with the patient to identify other family members at risk, and send a follow-up letter that informs the patient about the risk and how family members can access genetic care. All of those activities are time consuming. A few cases have occurred where a family member has not been informed of risk, resulting in an emerging case law referring to a putative “duty to warn” of inherited cancer risk. That duty implies a possible ethical obligation for the healthcare provider to inform at-risk relatives. Most genetics professionals inform the patient (or proband) who was tested of the potential risks and how they must be communicated to relatives. In many cases, a relative or relatives will seek care with the same genetics professional. If a relative needs

- **Geneticists** are physicians with board certification in genetics from the American Board of Medical Genetics who have completed a fellowship in genetics and passed a board examination. Certification is offered in clinical genetics, clinical biochemical genetics, clinical cytogenetics, and clinical molecular genetics.
- **Licensed genetics counselors** are healthcare professionals with specialized graduate degrees and experience in the areas of medical genetics and counseling. The American Board of Genetic Counseling certifies genetic counselors.
- **Genetic nurses** have specialized education and training in genetics with the goal of caring for patients' genetic and genomic health. They are credentialed by the Genetic Nursing Certification Commission (GNCC) after evaluation of a portfolio. GNCC provides recognition for clinical nursing practice in health care with a genetics component. Nurses who are prepared with a master's in nursing may qualify for the advanced practice nurse in genetics credential, and those prepared with a baccalaureate in nursing may qualify for the genetics clinical nurse credential.

Figure 1. Qualified Genetics Professionals

the services of a genetics professional in another geographic locality, genetics professionals can locate colleagues in that geographic location to coordinate care.

To maximize communication with other at-risk relatives, patients undergoing genetic testing should receive detailed pretest genetic counseling education to empower the patient to communicate with their at-risk relatives their intent to pursue testing and their willingness to share information. In addition, post-test counseling should reiterate the implications of a positive result for at-risk relatives and conclude with a written summary that patients can share with their family. That strategy is common and routinely applied in genetic counseling sessions (Chan-Smutko, Patel, Shannon, & Ryan, 2008; Wham et al., 2010). Assistance and support may be needed to optimize the communication of the genetic information within at-risk families (Hayat Roshanai, Lampic, Rosenquist, & Nordin, 2010). Most counselees who have formal pre- and post-test genetic counseling will share the information they have received at the genetic counseling session with their at-risk relatives. In a study of 238 individuals who had undergone genetic counseling, 73% had informed all of the

Clinical Highlights: Managing Hereditary Risk for Developing Cancer

Scope of the Issue

As many as 5%–10% of all cancers have a hereditary component. Those cancers include hereditary breast and ovarian cancer, hereditary nonpolyposis colorectal cancer, familial adenomatous polyposis, hereditary melanoma, von Hippel-Landau syndrome, multiple endocrine neoplasia syndrome, and many other less common hereditary syndromes (Lindor et al., 2008). Genetic testing for these syndromes is commercially available and may be ordered by credentialed genetics professionals, primary care providers, and other subspecialists.

Identification of At-Risk Individuals and Family

Identification of hereditary risk involves taking a detailed family history, including age of cancer onset, current age, and age at death, as well as documentation of other health problems associated with hereditary cancer risk (e.g., polyps, dysplastic nevi) (Lynch, Lynch, & Attard, 2009). Optimally, a minimum three-generation pedigree is constructed. One of the challenges in accurate pedigree construction is obtaining a comprehensive family history because the clinical significance of the information obtained is highly dependent on the accuracy and reliability of the information reported by the patient (Roth et al., 2009). For that reason, genetics professionals often verify the accuracy of the information using pathology and other records. The pedigree is critical to calculating the risk of developing cancer, calculating the risk of having a mutation, and identifying other family members at risk who might benefit from genetic consultation (DeMarco et al., 2007). Risk assessment is the core element of genetic counseling and is a skill that credentialed genetics healthcare professionals are trained to perform and then communicate to patients and families (Wham et al., 2010).

Once risk is calculated, options for genetic testing usually are discussed, including who might be the ideal candidate to test; typically, this would be an individual already diagnosed with suspected hereditary cancer. The discussion should include information about

the implications of and management strategies for a positive result, negative result, or a result that demonstrates a variant of unknown significance. Such a discussion also should include a dialogue of how the results will be shared with other family members (Hayat Roshanai, Lampic, Rosenquist, & Nordin, 2010). Credentialed genetics professionals typically inform people who are undergoing testing, particularly during pretest counseling, that genetic testing has implications for both the person being tested and other family members. The responsibility to inform other family members of potential risk ultimately will fall to the person who is undergoing testing, with support from the genetics professional. In addition, one of the primary goals of genetic counseling is to provide basic psychological and emotional support, particularly when a hereditary cancer syndrome is identified (Wham et al., 2010).

Providing adequate information about risks is time consuming. A typical initial genetics consultation will take one to three hours; disclosure of results also takes time, as does sending a follow-up letter identifying not only the risks to the person tested but also other family members who might benefit from additional evaluation (DeMarco et al., 2007; Stol, Menko, Westerman, & Janssens, 2010; Wham et al., 2010).

Implications for Nursing

Families can be encouraged to be proactive in understanding their family history by using a Web-based tool to document their family history (<https://familyhistory.hhs.gov/fhh-web/home.action>) (Woodward, 2009). Nurses can encourage families to use this tool because it provides an excellent place for families to document their family history and share information with each other.

When nurses encounter families with multiple generations of cancer, cancer diagnosed at an earlier age than expected, or families with clusters of cancers, they should refer these families to a genetics professional. For families that have undergone genetic testing, oncology nurses can help ensure that recommendations for screening and prevention are implemented and support patients and families as they cope with and adjust to a diagnosis of hereditary cancer.

Advocating for competent and comprehensive genetics care is an important and ongoing challenge for nurses (Mahon, 2009). Nurses need to be aware that genetics is rapidly changing the face of cancer prevention and early detection. They must consider the complexities of genetic risk assessment and appropriately refer patients and families for care.

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relatives they perceived to be at-risk. Barriers to not informing relatives included loss of contact or lack of closeness (Chivers Seymour, Addington-Hall, Lucassen, & Foster, 2010).

Implications for Nursing

When genetic testing is not carried out by a genetics professional, a great concern arises that other family members may not be informed of the risk of potentially deadly diseases that may be prevented with aggressive screening and surgical prophylaxis. Inherent in the responsibility of ordering a genetic test is the awareness that at-risk family members need to be contacted. Identification of at-risk family members is based on a three generation pedigree followed up with coordinated care for the family.

Patients expect oncology nurses to play a role in risk identification and, in many cases, to provide and support a genetics referral. In addition, patients will need ongoing support after receiving genetic test results. When oncology nurses identify patients with possible genetic risk, they must reinforce the fact that other family members may have increased risk as well and assist the patient and family in obtaining comprehensive genetic care (Miller et al., 2010).

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