Coordination of Genetic Care: More Important and Complicated Than it Seems

Suzanne M. Mahon, DNSc, RN, AOCN, AGN-BC

ABSTRACT

Families with hereditary risk for developing malignancy benefit from organized, coordinated care by a genetics professional. This report presents a case illustrating the potential errors that can occur when genetic care is fragmented and not coordinated, including ordering too much or not enough genetic testing, failing to communicate with the family who is at potential genetic risk, failing to communicate what the results of testing mean, and failing to recommend appropriate care, which may lead to psychosocial distress and late-detected cancers. This case highlights the complexities of genetic care and why management by a genetics professional results in more fiscally responsible care, appropriate genetic testing, and comprehensive care for all family members at risk.

J Natl Compr Canc Netw 2019;17(11):1272–1276
doi: 10.6004/jnccn.2019.7343

Providing comprehensive coordinated care for families with hereditary susceptibility to developing malignancy can ultimately reduce the morbidity and mortality associated with malignancy in a cost-effective manner. The ramifications and importance of this aspect of genetic care are often underestimated.¹ This report presents a case that demonstrates the financial, psychosocial, and public health implications of coordinated care and professional genetic evaluation in families with hereditary risk for developing cancer.

Case Report

A 71-year-old man was diagnosed with breast cancer in 2018 and referred by his medical oncologist for genetic evaluation. At age 69 years, he had been diagnosed with prostate cancer (Gleason score 7) and treated with radiotherapy (RT). While undergoing treatment, he had mentioned to his physician that he found a small lump in his breast and had been told it was an ingrown hair.

At his genetics consultation in 2018, a pedigree was constructed and reviewed with the family (Figure 1). Among the proband's (III-6) 3 daughters, one (IV-7) had been diagnosed with early-onset breast cancer at age 39 years and had undergone genetic testing in 2010, which revealed a known pathogenic mutation: *BRCA2* c.7558C>T (p.Arg2520*).

Approximately 8 months after this familial *BRCA2* mutation was identified in his daughter with breast cancer, another daughter (IV-6) sought testing through her primary care provider. She was tested in the same laboratory as her sister and had full sequencing for *BRCA1/2* including 5-site rearrangement testing, which was negative.

When the proband presented for genetic testing in 2018, the third daughter (IV-5) accompanied him to the appointment and also requested testing. They received counseling about the strengths, risks, and limitations of testing and, given the family history and the known mutation, were offered single-site *BRCA2* testing for the known mutation. Their samples were submitted for testing to the laboratory, where a positive control was used. Two days later, the laboratory called to say that the daughter had previously undergone testing for 25 genes, including *BRCA2*, in 2016, the results of which were

Figure 1. Truncated pedigree. Roman numerals refer to generation; arabic numerals refer to members within a generation. The arrow represents the proband, who is the first person to seek genetic counseling in a family. Men are represented by squares and women by circles. Abbreviation: d, age at death.

negative, and therefore her testing was canceled. As expected, the proband tested positive on the single-site test for the known *BRCA2* mutation.

The proband's sister (III-3), who had early-onset breast cancer 20 years earlier, presented for testing and follow-up counseling; her single-site test, as expected, was also positive. Heeding the information about informing other family members, she called them, distributed cards at a family reunion on how to access services, and brought other relatives to appointments, including her sons, who were 40 and 44 years of age. When her sons (IV-1 and IV-2) underwent genetic testing, their paternal history was reviewed and found to be significant for a father (III-1) with colon cancer diagnosed at age 45 years and who died at age 46 years. A panel of 46 genes was offered to each of the sons to better clarify whether they inherited risk from their father and mother. Unfortunately, both sons tested positive for the known *BRCA2* mutation, and one son was found to have a second pathogenic mutation: *MUTYH* c.1187G>A (p.Gly396Asp). It was not clear whether this mutation came from his paternal or maternal side, so their mother (III-3) underwent testing for the *MUTYH* mutation and was found to carry it. The sons' care was managed based on the *BRCA2* mutation, and because of their paternal family history and genetic testing results, earlier and more frequent colon cancer screenings were considered.

Five family members who had only been tested for the *BRCA2* mutation were informed by the proband's sister that their testing may be incomplete. They returned for additional *MUTYH* testing, and 2 tested positive for the mutation. At the time of writing, 24 family members had undergone testing for both mutations. An estimated 18 additional relatives had yet to undergo testing for both known familial mutations; if their results are positive, testing will be extended to their offspring.

Lessons Learned

Importance of an Accurate Pedigree

This large family demonstrates how an accurate pedigree directs care and is continually revised (11 times in 15 months) to reflect updated cancer history and testing results. The pedigree has been invaluable for identifying which family members might benefit from testing. The proband's sister was given a copy of the pedigree that was highlighted to identify which family members should be offered testing, and she used it to systematically inform family members at a family reunion.

There are known barriers to accurate pedigree construction. A consistently identified limitation is the lack of pedigree-drawing software in electronic medical records.² Research suggests that only a minority of nongenetics professionals consistently draw a pedigree or adequately document family history.³ Potential implications of incomplete family history include inaccurate or incomplete risk assessment, which may result in inappropriate testing or failure to identify at-risk relatives who may also need testing.⁴ If family members with mutations are not identified, this can result in missed opportunities for cancer prevention.² Genetics professionals coordinate this care; when a mutation is detected, genetics professionals facilitate testing or identify a genetics professional in another region if family members live elsewhere.

Fiscal Responsibility

The familial pathogenic *BRCA2* mutation was detected in the proband's family in 2010, after one of his daughters was diagnosed with breast cancer. Another daughter (IV-6) had more extensive testing than needed with the comprehensive *BRCA1/2* sequencing, and his other daughter (IV-5) had far more testing than needed with

a 25 multigene panel when single-site testing would have been appropriate. Neither had genetic counseling. The daughter who underwent the extensive testing in 2016 never even received her results. She had told her gynecologist that her sister had a mutation and so the 25 multigene panel was ordered, but she seemed unaware that it had been performed and that her results were negative, even though she had seen that provider twice since the results had become available. The findings were never discussed.

Testing for both of these daughters represents a costly and excessive practice. Costs range from approximately \$250 for single-site testing to \$2,760 for full *BRCA1/2* testing to $\geq$ \$4,100 for a multigene panel.^{5,6} Ordering multigene or panel testing when single-site testing is adequate is fiscally irresponsible. Furthermore, to order testing and never share the results is negligent; it is pointless to order testing if it is not used to guide care.⁷ Studies suggest that nongenetics professionals are more likely to order the more expensive comprehensive testing in patient scenarios when less expensive testing would be appropriate, with inappropriate testing occurring approximately 22% to 26% of the time.^{8,9} In one study, involvement of a genetics healthcare provider halved the likelihood that comprehensive *BRCA* testing was ordered among 266 patients for whom single-site testing may have been sufficient ($P=.02$).¹⁰ Inappropriate testing severely limits the ability to obtain insurance coverage for proper testing at a future time, resulting in unnecessary barriers for patients and time-consuming preauthorizations.¹¹

Preventing cancer and detecting it early saves financial resources and results in less morbidity and mortality. The daughter who underwent testing in 2016 and never received the results could have been spared worry about her risk. Sparing family members who have population risk from excessive worry and unnecessary screening saves financial resources.

Evolving Recommendations for Care

For the daughter who had *BRCA2*-mutated breast cancer (IV-7), it is not clear what her medical oncologist communicated regarding recommendations for ongoing care and further cancer prevention and detection. At diagnosis, she underwent appropriate risk-reducing surgeries, including bilateral mastectomy and bilateral salpingo-oophorectomy. However, knowledge about *BRCA2* and other pathogenic mutations is continually evolving, and recommendations now include more intensive prostate screening for men, consideration of melanoma screening, and, in some cases, pancreatic screening.¹² This daughter was unaware of these updated recommendations. Genetics professionals will consistently remind patients to check back on an annual basis

to ensure recommendations for care are still current; they will also serve as a resource to the provider managing follow-up care of a patient with a pathogenic mutation.¹³

Missed Opportunities for Cancer Prevention and Early Detection

It is also not clear what the medical oncologist communicated to the daughter about risks to other relatives or whether a pedigree was constructed. There was no history of malignancy on the daughter's maternal side (IV-7), and her father (III-6) was not offered testing in 2010 when the daughter's *BRCA2* mutation was first detected. The father had an extensive maternal family history of prostate and breast cancer, which is clearly associated with an increased risk for developing cancer.¹² This was a very large family with many relatives potentially at risk for developing cancer. The father was later diagnosed with prostate cancer and had even questioned a change in his breast at that time, but no one questioned the family history of malignancy until 2 years later after he was diagnosed with breast cancer. His breast cancer was large when it was finally evaluated, nearly a year after he first mentioned it. Men with a known *BRCA2* mutation should receive education on the importance of male breast awareness and prompt evaluation of any change found during the breast examination.¹² Had the father been offered single-site *BRCA2* testing for the known familial mutation in 2010, he might have been aware of his increased risk for prostate and male breast cancers and undergone more intensive screening, potentially resulting in earlier cancer detection. Consequently, he underwent extensive chemotherapy for his breast cancer, which was costly and associated with significant morbidity.¹⁰ The ultimate impact and goal of genetic testing is to identify all individuals at high risk for cancer before they are affected to maximize the opportunity for prevention and early detection.¹⁴ The opportunity was missed in this family.

Coordinating care for this large family is time-consuming, but is systematically identifying which family members have increased risk for 2 different mutations. These members can potentially benefit from risk-reducing surgeries or more frequent and aggressive screening for cancer. Those who test negative can follow population guidelines for the early detection and prevention of cancer. Cascade testing should occur when one member of a family has been diagnosed with a pathogenic mutation.⁶ For the family discussed in this report, genetic counseling and testing should have been offered to all of the daughter's first-degree relatives aged ≥ 25 years, including parents, siblings, and offspring, because each had a 50% chance of also inheriting the pathogenic mutation. Testing is very informative and less expensive at this stage, because it is known which

pathogenic gene is responsible; in most cases, single-site testing for the known mutation is sufficient.

When individuals are informed that they have a genetic risk for cancer, it is stressful, which can impede their understanding of recommendations for care.¹⁵ A semistructured interview study of 22 relatives and 10 persons with a known *BRCA* mutation found that relatives who learned information about genetic risk from a family member recalled significantly less accurate information than those informed directly by genetics health professionals ($P=.001$).⁷ In this study, only 53% of the information about general genetics and hereditary cancer recalled by patients was accurate, which may be due to the high volume of information. Multiple sources of information, including direct contact with genetics health professionals, may improve its accuracy. Similar results were found in a study of 473 participants, of which >90% were white, female, and *BRCA* mutation carriers. Of the 276 patients (58%) with genetics healthcare provider involvement, 97% recalled a pretest discussion compared with 59% of those without genetics healthcare provider involvement ($P<.001$).¹⁰ Repeated visits and a follow-up letter summarizing results and recommendations for care are often required for an individual to fully understand the meaning of genetic results.¹⁶ Genetics professionals routinely send patients a letter with a summary of the recommendations, which provides a range of benefits, including greater patient understanding, greater patient involvement, reduced anxiety, increased satisfaction, and more accurate risk perception.¹⁰ Furthermore, a letter provides a document that patients can share with relatives to reinforce the importance of genetic counseling and genetic testing. Group counseling can also be an effective strategy for working with families with hereditary risk, enabling all family members to obtain information about genetic risk and allowing them to ask questions within the context of their specific family history and genetic risk while also reinforcing concepts about genetics, the testing process, and recommendations among family members.¹⁷

Pretest counseling always includes a discussion about the responsibility of the proband to inform other family members if a pathogenic change is detected, but the genetics professional will identify who should be offered testing. An effective means to identify these family members is to highlight them on the pedigree and provide the family with copies and instructions on how to contact the genetics professional to access care. In this family, all but a few relatives live in the region and have been able to access counseling and testing with the same genetics professional. For those living in other regions, the genetics professional identified a counselor in their area and provided the family with test results and the most up-to-date pedigree to facilitate appropriate testing.

Genetics professionals also know to always access both sides of the family to accurately assess risk prior to offering testing. This family illustrates the complexities of this process. Unfortunately, the risk to the sons of the sister with early-onset breast cancer is not completely understood. Their care is being managed based on the results of the mother's testing and consideration of the paternal history of early-onset colon cancer.

Looking Forward

ASCO has identified that there are very few oncologists whose primary focus is cancer-risk assessment and genetic counseling; these individuals usually have additional postfellowship training.¹⁸ Another identified barrier to oncologists focusing on this area is poor reimbursement. The availability of a highly trained physician who focuses on genetic risk can lead to more support for a robust genetic program.¹⁹

Genetic counseling is time-consuming but has clear benefits. Time constraints in busy primary care and oncology practices make it difficult to provide comprehensive coordinated genetic care to an entire family. Even if the provider correctly orders testing for their patient, they will not likely be providing care to the rest of the family, potentially missing an opportunity for cancer prevention and early detection. Incomplete risk assessment and pedigree construction by nongenetics professionals has been associated with inadequate consent, wrong tests being ordered, negative emotional outcomes, wasted financial health resources, and late-stage cancer diagnosis.²⁰ Although an oncologist may be able to properly manage an individual patient, and the effort may be well intentioned, the present case illustrates the complexities and potential errors that can occur when care is not coordinated for a family. More than 50 hours of clinical care have been expended during the care of this family. NCCN recommends that individuals with suspected hereditary risk for developing cancer be referred to a genetics professional for further evaluation and, ultimately, coordination of care.¹² With meticulous and systematic pedigree construction and assessment, followed by targeted testing, the risk associated with 2 specific mutations is being clarified for this family, affording those at elevated risk a true opportunity for cancer prevention and early detection. When used correctly and with coordination of care for the entire family, genetic testing can be a powerful tool in oncology.

Submitted June 23, 2019; accepted for publication August 5, 2019.

Disclosures: The author has not received any financial consideration from any person or organization to support the preparation, analysis, results, or discussion of this article.

Correspondence: Suzanne M. Mahon, DNSc, RN, AOCN, AGN-BC, Division of Hematology/Oncology, Saint Louis University, 3rd Floor West Pavilion, 3655 Vista Avenue, St. Louis, MO 63110. Email: suzanne.mahon@health.slu.edu

References

1. Benseid TA, Veach PM, Niendorf KB. What's the harm? Genetic counselor perceptions of adverse effects of genetics service provision by non-genetics professionals. *J Genet Couns* 2014;23:48–63.
2. Baldwin LM, Trivers KF, Andrilla CH, et al. Accuracy of ovarian and colon cancer risk assessments by U.S. physicians. *J Gen Intern Med* 2014;29:741–749.
3. Wood ME, Kadlubek P, Pham TH, et al. Quality of cancer family history and referral for genetic counseling and testing among oncology practices: a pilot test of quality measures as part of the American Society of Clinical Oncology Quality Oncology Practice Initiative. *J Clin Oncol* 2014;32:824–829.
4. Mahon SM. The three-generation pedigree: a critical tool in cancer genetics care. *Oncol Nurs Forum* 2016;43:655–660.
5. Foote JR, Lopez-Acevedo M, Buchanan AH, et al. Cost comparison of genetic testing strategies in women with epithelial ovarian cancer. *J Oncol Pract* 2017;13:e120–e129.
6. Hampel H. Genetic counseling and cascade genetic testing in Lynch syndrome. *Fam Cancer* 2016;15:423–427.
7. Jacobs C, Dancyger C, Smith JA, Michie S. Accuracy of recall of information about a cancer-predisposing BRCA1/2 gene mutation among patients and relatives. *Eur J Hum Genet* 2015;23:147–151.
8. Miller CE, Krautscheid P, Baldwin EE, et al. Genetic counselor review of genetic test orders in a reference laboratory reduces unnecessary testing. *Am J Med Genet A* 2014;164A:1094–1101.
9. Haidle JL, Sternen DL, Dickerson JA, et al. Genetic counselors save costs across the genetic testing spectrum. *Am J Manag Care* 2017;23:SP428–430.
10. Cragun D, Camperlengo L, Robinson E, et al. Differences in BRCA counseling and testing practices based on ordering provider type. *Genet Med* 2015;17:51–57.
11. Ramos E, Haidle JL. Genetic testing: multiple problems to solve. *J Clin Oncol* 2018;36:518–519.
12. Daly M, Pilarski R, Berry MP, et al. NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast and Ovarian. Version 3.2019. Accessed June 23, 2019. To view the most recent version, visit NCCN.org.
13. King E, Mahon SM. Genetic testing: challenges and changes in testing for hereditary cancer syndromes. *Clin J Oncol Nurs* 2017;21:589–598.
14. Childers CP, Childers KK, Maggard-Gibbons M, Macinko J. National estimates of genetic testing in women with a history of breast or ovarian cancer. *J Clin Oncol* 2017;35:3800–3806.
15. Delikurt T, Williamson GR, Anastasiadou V, Skirton H. A systematic review of factors that act as barriers to patient referral to genetic services. *Eur J Hum Genet* 2015;23:739–745.
16. Burton-Chase AM, Hovick SR, Peterson SK, et al. Changes in screening behaviors and attitudes toward screening from pre-test genetic counseling to post-disclosure in Lynch syndrome families. *Clin Genet* 2013;83:215–220.
17. Buchanan AH, Rahm AK, Williams JL. Alternate service delivery models in cancer genetic counseling: a mini-review. *Front Oncol* 2016;6:120.
18. Fabian CJ, Meyskens FL Jr, Bajorin DF, et al. Barriers to a career focus in cancer prevention: a report and initial recommendations from the American Society of Clinical Oncology Cancer Prevention Workforce Pipeline Work Group. *J Clin Oncol* 2016;34:186–193.
19. Stoll K, Kubendran S, Cohen SA. The past, present and future of service delivery in genetic counseling: keeping up in the era of precision medicine. *Am J Med Genet C Semin Med Genet* 2018;178:24–37.
20. Vadaparampil ST, Scherr CL, Cragun D, et al. Pre-test genetic counseling services for hereditary breast and ovarian cancer delivered by non-genetics professionals in the state of Florida. *Clin Genet* 2015;87:473–477.