

Managing Families With a Hereditary Cancer Syndrome

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Oncology is one of the first specialties 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