Ordering the Correct Genetic Test: Implications for Oncology and Primary Care Healthcare Professionals

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Genetic testing for hereditary cancer syndromes is becoming increasingly more common. Once a mutation is detected in a family, other family members can undergo single-site mutation testing to determine if they have inherited the increased risk for developing cancer, with the intent of providing tailored and appropriate cancer prevention and early detection measures. Ordering the correct single-site test is critical to providing appropriate recommendations for cancer prevention and early detection.

Case Study

An advanced practice credentialed genetic nurse (APNG) was contacted by J.M., a 26-year-old single mother, about obtaining genetic testing for a known family mutation in the MSH2 gene, which is one of the genes associated with the HNPCC syndrome also known as Lynch syndrome. Such a mutation is associated with an 80% lifetime risk for developing colorectal cancer and a 70% chance of developing endometrial cancer, as well as other cancers (Lindor, McMaster, Lindor, & Greene, 2008). J.M. was uninsured and travelled more than 140 miles for the services, all of which were to be covered by charitable funding for the uninsured. The patient was carefully instructed prior to the appointment to bring a copy of the test results from any known relative who had tested positive for the mutation. J.M. said that she understood this request and would do so.

The patient arrived at the appointment with a copy of test results from a first cousin who had tested negative for the known mutation. The APNG explained that she would be unable to order the test that day because the policy was to order a test off of a positive result. J.M. was upset and frustrated because she had driven a great distance and said that her other relatives had simply gone to their doctors and had saliva tests ordered without any requirements. A pedigree was constructed, which J.M. perceived as unnecessary because a known mutation in the family had already been established. She was instructed that the pedigree was necessary for identifying other family members that might benefit from testing.

Information from the pedigree helped determine that a paternal uncle had been the first to be tested and that J.M.’s father had died of colon cancer at age 57 years. Another living paternal aunt had tested negative, as did two female cousins (the daughters of the previously mentioned paternal uncle). The report that J.M. had brought was from one of the cousins.

The patient received pretest counseling on the implications of testing for this mutation and was informed that, assuming her father was an obligate carrier, she had a 50% chance of having the mutation. J.M. was instructed to return with a copy of the positive test result and the APNG explained that, although simply ordering the test and sending the specimen off of the negative test result J.M. brought to the appointment would be easier, the possibility that the wrong test would be ordered meant that it could not be done.

J.M. sent a copy of the positive test result a week later. The uncle with the positive test result had a mutation in the MSH2 1215 gene; however, the negative test result for J.M.’s cousin was determined to be for the MSH2 1216 gene. The wrong test had been ordered for the cousin at some point, probably as a result of a copying error or that the handwriting on the test request form was illegible. The tests for the other cousin and the aunt were then reviewed and it became apparent that both of the cousins had undergone testing for the wrong mutation. The aunt’s test had been correctly ordered. The mistake apparently occurred when one of the cousin’s tests was incorrectly ordered from the aunt’s report. The other cousin’s test was ordered by a different primary care physician, but it was ordered off of her sister’s
test. The APNG realized this error and arranged for the two cousins to be retested for the correct mutation. One came back negative and one, unfortunately, was positive. The cousin who tested positive was devastated as she thought she was negative and no additional screening or prophylactic surgery would be needed after she had originally received the negative results. The positive test came with recommendations for annual colonoscopy and upper endoscopy, aggressive gynecologic screening, and potentially a prophylactic hysterectomy in the next 10 years. The cousin’s colonoscopy was negative and she had not suffered any notable physical problems; however, psychological distress certainly occurred after the wrong test was ordered and adequate genetic counseling and support were not provided.

Regarding J.M., she did return for the test, had the correct mutation sequenced, and received a negative result. However, the cousin who tested positive required many hours of follow-up. Although J.M. would not have suffered harm from having the test ordered from the negative results she had originally brought in, this case demonstrates the potential risks of not ordering the correct test.

### Implications for Nurses

Many professional organizations advocate that, prior to genetic testing, appropriate patient education and counseling must be available and that credentialed genetic professionals are best suited to provide it (Berliner & Fay, 2007; Rubininstein, 2008). Such professionals include physicians with fellowship training in genetics, master’s-prepared genetic counselors, and APNGs (Brierley et al., 2010). Genetic testing in the United States has little regulation beyond laboratory safety and technique and, in theory, any healthcare provider who orders laboratory tests can order genetic testing. Having subspecialty credentialing is not required to provide pre- and post-test counseling (Hogarth, 2010; Twomey, 2011).

Healthcare professionals clearly face pressure from patients on a regular basis to order genetic tests, often because of media exposure as well as from genetic testing companies who emphasize that testing is a convenient service that patients have readily available to them.

### TABLE 1. Common Genetic Syndromes Seen in Clinical Oncology Practice

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene (Chromosome Location)</th>
<th>Common Features (Penetrance&lt;sup&gt;a&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast or ovarian cancer</td>
<td><em>BRCA1</em> (17q21) <em>BRCA2</em> (13q12.3)</td>
<td>Breast cancer (87%) Ovarian cancer (44%) Male breast cancer (8%) Pancreatic cancer (7%)</td>
</tr>
<tr>
<td>Cowden</td>
<td><em>PTEN</em> (10q23.3)</td>
<td>Breast cancer (30%–50%) Thyroid cancer (5%–10%) Endometrial cancer (5%–10%) Facial trichilemmomas Hamartomatous polyps of the stomach, small bowel, and colon (60%)</td>
</tr>
<tr>
<td>Familial adenomatous polyposis</td>
<td><em>APC</em> (5q21–q22)</td>
<td>Colon adenocarcinoma (in unscreened individuals; 7%–87% by age 45 years) Hepatoblastomas Medulloblastomas Gliomas Ependymomas</td>
</tr>
<tr>
<td>Hereditary diffuse gastric cancer</td>
<td><em>CDH1</em> (16q22.1)</td>
<td>Diffuse gastric cancer (67%–83%) Lobular breast carcinoma</td>
</tr>
<tr>
<td>Hereditary melanoma</td>
<td><em>CDKN2A</em> (1p36) <em>CDK4</em> (12q14)</td>
<td>Melanoma (30%–67%) Pancreatic cancer</td>
</tr>
<tr>
<td>Hereditary nonpolyposis colorectal cancer</td>
<td><em>MLH1</em> (3p21.3) <em>MSH2</em> (2p11–p22) <em>PMS1</em> (2q31–q33) <em>PMS2</em> (7p22) <em>MSH6</em> (2p16) <em>MSH3</em> (5q11–q12)</td>
<td>Colon cancer (82%) Endometrial cancer (70%) Ovarian cancer (12%) Stomach cancer Bladder cancer Sebaceous adenomas</td>
</tr>
<tr>
<td>Hereditary paraganglioma</td>
<td><em>SDHD</em> (11q23) <em>SDHC</em> (1q21) <em>SDHB</em> (1p36)</td>
<td>Paraganglioma (29%–73%) Renal cell cancer Astrocytomas Papillary thyroid carcinoma Parathyroid adenoma</td>
</tr>
<tr>
<td>Li-Fraumeni</td>
<td><em>TP53</em> (17p13.1)</td>
<td>Osteogenic, chondrosarcoma, and rhabdomyosarcoma Breast cancer Brain cancer (particularly glioblastomas)</td>
</tr>
<tr>
<td>Multiple endocrine neoplasia type 1 (MEN1)</td>
<td><em>MEN1</em> (11q13)</td>
<td>Pancreatic or duodenal neuroendocrine tumors (30%–80%) Gastrinomas (54%) Carcinoids Pituitary Adrenal</td>
</tr>
<tr>
<td>Multiple endocrine neoplasia type 2a, 2b, and familial medullary thyroid cancer</td>
<td><em>RET</em> (10q11.2)</td>
<td>Medullary thyroid cancer (nearly 100%) Pheochromocytoma</td>
</tr>
<tr>
<td>MYH-associated polyposis&lt;sup&gt;a&lt;/sup&gt;</td>
<td><em>MYH</em> (1p32.1–p34.3)</td>
<td>Colon cancer Duodenal cancer</td>
</tr>
<tr>
<td>Neurofibromatosis type 1 (NF1)</td>
<td><em>NF1</em> (17q11.2)</td>
<td>Neurofibrosarcomas Malignant schwannomas Neurofibromas</td>
</tr>
</tbody>
</table>

<sup>a</sup>Penetrance when known; exact penetrance is unclear for some features.
<sup>b</sup>Autosomal recessive

Note. Based on information from Lindor et al., 2008; Weitzel et al., 2011.
TABLE 1. Common Genetic Syndromes Seen in Clinical Oncology Practice (Continued)

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<tr>
<th>Syndrome</th>
<th>Gene (Chromosome Location)</th>
<th>Common Features (Penetrance&lt;sup&gt;a&lt;/sup&gt;)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurofibromatosis type 2 (NF2)</td>
<td>NF2 (22q12.2)</td>
<td>Gliomas, Ependymomas, Vestibular schwannomas, Meningiomas, Spinal cord schwannomas</td>
</tr>
<tr>
<td>von Hippel-Lindau</td>
<td>VHL (3p25–p26)</td>
<td>Malignant renal cell carcinoma (clear cell type), Pancreatic islet cell carcinomas, Carcinoid tumors, Pheochromocytomas, Endolymphatic sac tumors, Hemangioblastomas</td>
</tr>
</tbody>
</table>

<sup>a</sup>Penetration when known; exact penetration is unclear for some features.

<sup>b</sup>Autosomal recessive

Note. Based on information from Lindor et al., 2008; Weitzel et al., 2011.

in the primary care setting (Matloff & Brierley, 2010). Subsequent recommendations for the patient and family are directly related to correctly ordering the genetic test and interpreting the results. Three common errors that occur when nongenetics professionals are involved in genetic testing include (a) the wrong genetic test is ordered, (b) genetic test results are misinterpreted, and (c) inappropriate or inadequate genetic counseling results in psychosocial distress or other negative outcomes (Brierley et al., 2010).

**Unique Challenges**

Regardless of the clinical setting where testing is ordered, the use of genetic knowledge for clinical decision making presents unique challenges, sometimes without specific guidelines to address these challenges (Mahon, 2011). Confidential genetic test results belong to the patient, but have significant implications for other family members. Maintaining confidentiality can be difficult, particularly if the need for confidentiality is not respected by some family members or family members are unwilling to share information with other relatives (Williams, Skirton, & Masny, 2006). Ethical challenges for the healthcare provider also arise if patients withhold consent to share information that would be helpful to relatives. This was not a family situation where obtaining the correct positive result was difficult, but that can become a challenge for healthcare providers caring for families who are unwilling to share information about risk or test results amongst themselves. Genetics professionals focus on the implications of testing on the family as well as the individual and have experience dealing with such issues.

Unfamiliarity with a genetic syndrome also can compromise the genetic testing process. Other than family history, HNPCC has no known specific phenotype or clinical presentation and, therefore, clinicians may not easily recognize patients with this common form of hereditary colorectal cancer (Singh, Schiesser, Anand, Richardson, & El-Serag, 2010). In this case, how well the primary care provider understood the implications of HNPCC testing is unclear; the cousin who subsequently tested positive was unprepared for the implications of the test, including aggressive screening and potential prophylactic surgery, suggesting that she had inadequate pretest counseling when the testing was initially completed.

Many physicians and nurses have limited knowledge of genetics and may not be able to provide genetic counseling and testing (Matloff & Caplan, 2008). Those providers are challenged by a lack of knowledge and the rapid pace of genetic discovery (Carroll et al., 2011; Miller et al., 2010). An interview of 40 primary care providers by Wood, Stockdale, and Flynn (2008) identified time constraints as a major limitation in the implementation of genetic services. Lack of patient visit time to assemble the appropriate information was a prominent concern, as was the time required to keep current of emerging information. Genetic testing companies often offer on-site training to primary care providers, but a few hours of training by sales employees with an inherent conflict of interest in selling genetic tests is not ideal. Unfortunately, the liability risks to providers who take on the responsibility for genetic counseling and testing is likely quite high (Matloff & Caplan, 2008). Nurses and primary care providers are in a position to facilitate referrals for specialized genetic services for clients when indicated. This action requires recognizing when the patient has a potential genetic condition (see Table 1) and that the setting is not sufficient to address the genetic concerns of that patient (Hamilton, 2009).

Genetic information has unique aspects in comparison to other medical information because it carries potential value, but also danger, for individuals other than the person tested (Surbone, 2011). An ethical concept frequently discussed in relation to genetic testing is nonmaleficence, meaning do no harm (Offit & Thom, 2007). A false-negative test result (such as what occurred in this case) can result in potential and substantial harm because of an inaccurate risk assessment and subsequent application of inadequate prevention and early detection measures. Potential harms are inherent in genetic testing, such as health, psychological, and social risks, as well as financial costs and potential discrimination for life, disability, or long-term care insurance (Bunnik, Schermer, & Janssens, 2012). Healthcare providers who order these tests need to be aware of the risks and the potential for error and should only order such tests if they have the training to order the correct test and interpret the results appropriately.

Ordering a genetic test might appear simple, but it is much more complex than collecting a blood or saliva sample. The number of healthcare professionals with experience and training in genetics is limited, but the solution may not be to continue to offer services without subspecialty training and credentialing just because the patient requests it or it...
seems more convenient (Mahon, 2009). Patients and families could potentially suffer negative consequences from this strategy, as the case presented in this article demonstrates. Oncology nurses should be challenged to obtain additional training as well as credentialing in genetics to better serve at-risk patients and families as well as know when to refer a family to a genetics professional. Additional resources and information can be found in Figure 1.

**References**


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