Ethical Obligations and Counseling Challenges in Cancer Genetics

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Abstract
Cancer genetics is creating new practice opportunities in medical genetics, oncology, and primary care. The ethical and counseling challenges of this new area of practice are not unique but sometimes take new form in the context of genetic risk. This article uses cases to explore the issues associated with shared family risk, including competing concerns of family members, duty to warn relatives of genetic risk, and testing of children and other relatives. The ethical obligations of clinicians start with the need to maintain competence in the face of rapidly evolving science. Clinicians should be able to identify patients within their practice who are candidates for genetic testing. When genetic susceptibility to cancer is identified, patients should be offered counseling and follow-up, with referral as appropriate, to ensure delivery of care consistent with current standards. When patients experience barriers to needed health care, clinicians should advocate for their needs. Clinicians must ensure the autonomy and informed decision-making of all members of cancer-prone families. Clinicians must also provide emotional support and accurate information about cancer risks and cancer risk reduction measures, including uncertainties. Teamwork among different specialties is important in addressing these challenges. (JNCCN 2006;4:185–191)

Cancer genetics is changing the practice of medical genetics, oncology, and primary care. The potential to predict future cancer risk has also captured public attention. In a recent newspaper commentary, a woman who tested positive for a BRCA mutation noted that “with tests like these, modern science acts as a crystal ball— warning us of dark events that may come.” The ethical obligations and counseling challenges posed by cancer genetics reflect the imperfect ability to predict or prevent illness.

Although the drama inherent in cancer genetics has received much attention, particularly the psychologic impact of knowing about future risks of cancer, the challenges clinicians face are not unique to cancer genetics. These challenges involve balancing truth-telling and emotional support, advocating for patient needs, and, perhaps most importantly, maintaining the necessary competence to assist patients in making decisions in the face of rapidly evolving science. Yet these challenges sometimes take new form in the context of genetic risk for cancer. This article explores these issues through composite cases based on clinical experience.

Addressing Family Distress
One of the hallmarks of genetic medicine is shared risk among family members, as illustrated in case 1.

Case 1: A 20-year-old college student comes to discuss genetic testing at the insistence of her father. Her mother died at age 44 from widely metastatic breast cancer. In the last few weeks of her mother’s life, BRCA testing identified a deleterious mutation in the BRCA1 gene. The student reports that her father now wants her to have testing to determine whether she should have her breasts removed.

Identifying genetic risk often creates complex emotional reactions—and sometimes conflicting interests—among family members. In case 1, the patient’s father appears to be the motivating force behind her seeking care, and parental coercion is a possibility. However, because the patient has a 50% risk of having the deleterious BRCA1 mutation, her father’s concern is
well-founded. How does the clinician act in the patient’s best interests\textsuperscript{2,3} in this clinical setting?

Although the needs of the family as a whole must be considered, each member of a cancer-prone family needs separate attention and advocacy. In this case, the patient’s concerns are the first priority. The patient’s decision to have BRCA testing is not urgent, because no preventive measures are recommended before age 25. Therefore, the patient has time to mourn her mother and reflect on the implications of testing before making a decision. In addition, prophylactic mastectomy is not the only option available. Education and supportive counseling are likely to be her immediate needs.

The father’s concerns are also important. Although he does not share the genetic risk for cancer, he shares its burdens. The tension between father and daughter will likely be mitigated if he also understands the lack of urgency. A joint counseling session or separate meeting with the father may be appropriate.

Even with such efforts, the patient’s decisions may ultimately conflict with her father’s wishes. She might, for example, decide against prophylactic mastectomy and defer testing indefinitely. Her father then might need help with dealing with a mix of feelings, including grief, protectiveness, and frustration. The clinician must respect the autonomy of each family member while attending to their often differing needs. Assistance from a psychologist with expertise in cancer genetics may be appropriate.\textsuperscript{4}

**Giving Bad News**

Part of the clinician’s job is to be truthful to patients, even when the news is threatening. In case 1, the clinician has the difficult task of also informing the patient about her substantial risk for ovarian cancer. Current estimates suggest that women with a BRCA1 mutation have a cumulative risk of 45\% for developing ovarian cancer by age 70.\textsuperscript{1} This information may be unexpected because families whose immediate experience has been with breast cancer are often unaware that breast and ovarian cancer share a genetic risk.

Risk for developing ovarian cancer poses serious challenges for women at the beginning of adulthood. Because the benefit of ovarian cancer screening has not been proven, the recommended prevention for women at high risk is oophorectomy. This surgery is ideally performed premenopausally, when it is estimated to reduce breast cancer risk by 50\% or more and ovarian cancer risk by 85\% to 95\%.\textsuperscript{6,7} However, the trend in today’s society is toward later childbirths. Therefore, a 20-year-old woman may be a decade or more away from even considering childbirth. The risk for developing ovarian cancer threatens not only her health but also her life plan. She may benefit from support beyond what a caring clinician can provide; referral to a support group or a psychotherapist familiar with these issues may be warranted.\textsuperscript{4}

**Physician Competency**

Case 1 also illustrates that competence is a clinician’s first obligation in medical ethics.\textsuperscript{7} In this case, the clinician requires knowledge of risk reduction for women at high risk for breast and ovarian cancer. The patient’s father is correct to assume that prophylactic mastectomy is the most effective way to protect his daughter from breast cancer, but other options are also available. Few women at high risk for breast cancer choose prophylactic mastectomy,\textsuperscript{8,9} and increasing evidence suggests that breast screening with magnetic resonance imaging in addition to mammography provides much higher sensitivity than mammography alone.\textsuperscript{10} Physicians are obligated to provide authoritative information about screening, chemoprevention, and prophylactic surgery, and limits in the current knowledge regarding efficacy and mortality benefits.\textsuperscript{11}

Case 2 further illustrates the importance of clinician competency.

**Case 2:** A 35-year-old woman is diagnosed with invasive breast cancer. Both her mother and maternal aunt died of breast cancer at age 40 and 32, respectively (Figure 1). The only other known family history of cancer is a first cousin who died of osteosarcoma at age 12. No information is available concerning the health of the patient’s grandparents. The woman’s BRCA test results are negative for a mutation.

What is the implication of a negative test result for this patient who has a worrisome personal and family history of cancer? When a family history suggests inherited cancer risk, a genetic risk is likely even when test results are negative. Current BRCA testing fails to detect an estimated 15\% of mutations.\textsuperscript{12} In this case, however, the wrong genetic test was ordered. The
A combination of childhood osteosarcoma and early breast cancer is consistent with the Li-Fraumeni syndrome, a rare genetic condition associated with osteosarcoma, soft tissue sarcoma, brain tumors, and breast and other cancers. Causative \( p53 \) mutations are identified in 70% of families with Li-Fraumeni syndrome.

As this case illustrates, the clinician must either have the expertise to address the patient's problem or refer the patient to a clinician who does. In cancer genetics, this expertise includes knowledge of rare cancer syndromes and the genetic research that defines new syndromes over time. For example, mutations in the \( CDH1 \) gene (e-cadherin) have been identified as a cause of gastric cancer. In at least one family, the cancer predisposition was identified through a family history of breast cancer.

Expectations are different for different medical specialties. Thus, primary care providers must provide competent triage. Detailed collection of family history on all patients is not feasible in primary care practice, but the primary care provider should be able to identify features of family history and clinical presentations that merit further evaluation. Some online resources can assist clinicians, notably the Gene-Tests Web site, which contains authoritative reviews of many genetic conditions, and the National Cancer Institute’s PDQ system, which includes information about cancer genetics for clinicians. Primary care providers are also expected to provide continuity care for patients with inherited cancer syndromes and will often play a key role in assuring patient support and completion of recommended cancer screening.

The American Society of Clinical Oncology (ASCO) has defined more detailed expectations for cancer genetics knowledge among oncologists, and ASCO also provides educational resources to assist members. Standardized guidelines, such as those of the National Comprehensive Cancer Network, provide another needed resource. In addition, a partnership with medical genetics is important for both primary care providers and oncologists; genetics professionals can help other clinicians identify patients who would benefit from genetic counseling and can provide the intensive pre- and posttest counseling required with most genetic tests for cancer susceptibility.

**Obligation to Family Members**

If the patient in case 2 has an identifiable \( p53 \) mutation, this finding has important implications for her biologic relatives. Several other family members are potentially at risk (Figure 1). The patient’s 2 siblings have a 50% risk of inheriting the mutation; if so, they face personal cancer risks and their children are at risk for inheriting the cancer-predisposing mutation. The patient’s uncle might also have inherited the mutation, despite his lack of history of cancer, and his 3 children are potentially at risk.

If the patient’s mother was alive, experts would recommend testing her to confirm that she also had a \( p53 \) mutation. Because she is not, many experts would recommend testing the patient’s father; a negative test result supports maternal inheritance and confirms that no further testing is required on the father’s side of the family. This case illustrates the importance of further exploration of family history after genetic testing confirms a diagnosis.

**Duty to Warn Relatives of Shared Risk**

Shared family risk is at the heart of questions about the duty to warn: Do patients or their doctors have a duty to inform family members of a potential cancer risk and the option to undergo genetic testing? In its 2003 policy statement on genetic susceptibility testing, ASCO affirmed the providers’ duty to inform individuals undergoing cancer genetics testing about the importance of communicating test results to family members, but also stated that “… the cancer care provider’s obligations (if any) to at-risk relatives are best fulfilled by
communication of familial risk to the person undergoing testing...”

However, limited case law raises the possibility that providers’ duty to inform of genetic cancer risk may extend beyond the patient to relatives. The 2 most notable cases involving genetics are Pate v Threlkel and Safer v Pack. In the case of Pate v Threlkel, the adult child of a patient with medullary thyroid carcinoma brought a malpractice action against the parent’s physician on the grounds that the physician had a duty to warn the patient of the hereditary nature of the condition so that her adult children could be tested. The court supported a duty to warn, but stated that such an obligation would be fulfilled if the patient were informed by the physician about the genetic implications of the condition, consistent with the ASCO statement.

In the case of Safer v Pack, a plaintiff with familial adenomatous polyposis sued the estate of her deceased father’s physician, claiming the physician had a duty to warn not only her father but also immediate family members. A request for a summary judgment dismissing the case was denied, and the judge explicitly stated it may be necessary to “…resolve a conflict between the physician’s broader duty to warn and his fidelity to the expressed preference of the patient that nothing be said to family members about the details of the disease.” Attorney and bioethicist Karen Rothenberg cites these cases as a cause of major concern for physicians, concluding that they “highlight our need for better understanding of family relationships, [and families’] privacy and confidentiality concerns…”

In 1998, the American Society of Human Genetics recommended that disclosing information about genetic risk to family members without patient consent would be permissible only if 1) attempts to encourage disclosure by the patient had failed; 2) the condition was serious and treatable or preventable; or 3) the harms of nondisclosure were greater than the harms of disclosure. This approach is consistent with the well-known Tarasoff v Regents of the University of California case, in which a psychiatrist was sued by the parents of a young woman who was murdered by the psychiatrist’s client. In this case, the court found that the psychiatrist should have warned of his client’s homicidal intent. The court articulated circumstances that justify such a breach of patient confidentiality: the risk posed must be foreseeable and imminent, concern an identifiable individual, and be possible to avert if action is taken. Whether inherited risks for cancer ever meet this standard remains unresolved.

Even if the ASCO position defines the standard of care, the issue of how best to assist patients in informing family members is not established. What educational materials or counseling will provide appropriate assistance to patients as they prepare for discussions with family members? How should clinicians document the assistance they provide? Patients may find it difficult to talk with family members about an inherited risk for cancer. A reasonable expectation might be that clinicians will provide written materials explaining the genetic risk and testing options, which patients can then share with family members. However, the Safer case raises the possibility that more stringent expectations may be defined over time, particularly for high-risk cancer syndromes that can be prevented effectively.

**Risks to Children**

As one component of shared risk, parents may face difficult questions about testing children and informing them about their risk, as illustrated in case 3.

**Case 3:** Shortly after the birth of his second child, a 28-year-old man is diagnosed with familial adenomatous polyposis (FAP) after undergoing a workup for rectal bleeding. His father had emigrated from Italy at the age of 20 and died in a motor vehicle accident at age 32. His paternal grandmother reportedly died of abdominal cancer. No additional family history is known. The patient undergoes a subtotal colectomy. Examination of the resected colon identifies an invasive colon cancer. Further workup reveals a possible abdominal metastasis.

This patient is dealing simultaneously with many different stresses. He has a newly diagnosed cancer that was unexpected considering his age and limited family history. The workup suggests metastatic disease that may be life-threatening. In addition, he must absorb this information while caring for 2 young children who may have inherited the cancer-predisposing condition.

The patient and his wife face a difficult decision about whether to seek genetic testing for their children. Up to 90% of patients with FAP have an identifiable mutation in the APC gene. If a mutation is detectable in the patient, his children can also be tested. Usually,
testing would be offered at approximately 8 years of age, because this is the earliest age at which screening begins for FAP. This approach follows guidelines of the American Society of Human Genetics/American College of Medical Genetics and the American Academy of Pediatrics, which recommend genetic testing in childhood only when results will influence clinical management.29,30

The patient and his wife may choose to test their children sooner to alleviate anxiety about the risk status. If either child (or both) has inherited FAP, they will face difficult decisions regarding when and how to share this information, when to begin screening, and how to discuss possible prophylactic surgery. These discussions may be even more difficult if one child is affected and the other is not.4 Although some studies suggest that children accept information about their own risk without a significant increase in depression or anxiety, more research is needed.4 Long-term psychologic support may be needed, and some studies suggest that a child’s reaction to risk may depend on the experience with cancer in the family,4 including, in this case, the potential early death of a parent. In addition, the patient may feel profound guilt at having passed on the cancer predisposition.

Survivor guilt can also be an issue in families with inherited cancer, as illustrated in case 4.

Case 4: The patient diagnosed with FAP (case 3) has 2 sisters who seek genetic testing for the APC mutation identified in their brother. One sister tests negative, but the other sister tests positive, indicating she has FAP. A subtotal colectomy is recommended; however, she is uninsured and does not have sufficient funds to pay for the operation. The unaffected sister seeks follow-up to confirm her negative test result. During the discussion she confesses that she has remorse about escaping what seems to her to be a family curse. She explains that she ought to have been the one with the positive test because, unlike her sister, she has good health insurance.

Survivor guilt has been cited as an explanation for the dysphoric feelings some family members experience after a negative test result.4,13 In this case, the sister’s guilt feelings are compounded by her concerns for her sister’s health coverage.

Addressing Access

The burdens of a cancer predisposition are far greater if the recommended health care cannot be guaranteed. In addition to identifying appropriate counseling options, the clinician needs to offer any available help to patients who are uninsured or underinsured. Some hospitals and medical practices offer assistance or delayed payment plans to patients who are financially disadvantaged. A benefits counselor may be able to assist patients in identifying coverage options. Although clinicians do not usually deal directly with patients’ insurance status, ethical practice includes a commitment to the just distribution of health care resources.32 This is a difficult obligation to discharge in the U.S. health care system because most access issues are beyond the individual clinician’s control. Clinicians should be aware of the assistance available in their area and willing to spend time helping patients determine what care is truly essential and to advocate for their patients within the health care system.

Dealing with Uncertainty

Cancer genetics, as a rapidly evolving field of clinical science, also poses challenges related to uncertainty.

Case 5: A 50-year-old man is concerned about his family history of pancreatic cancer. Both his father and his aunt have died of the disease, and a first cousin was recently diagnosed with it (Figure 2). He heard a radio show about discoveries in cancer genetics and seeks genetic testing to determine whether he will get pancreatic cancer.

Figure 2 Family history of the patient described in case 5. The arrow indicates the patient. Diagonal lines indicate deceased family members. Abbreviation: CA, cancer.
The patient’s family history suggests an autosomal dominant predisposition to pancreatic cancer (Figure 2). Cancer is present in 3 sequential generations; occurs in both men and women; and has affected 2 of 3 siblings at risk in the second generation. These observations are consistent with case reports of familial pancreatic cancer. Pancreatic cancer has also been observed in other cancer syndromes, including breast-ovarian, von Hippel Lindau disease, dysplastic nevus melanoma, hereditary nonpolyposis colorectal cancer, multiple endocrine neoplasia type 1, and hereditary pancreatitis, and has been associated with BRCA2 and CDKN2A mutations in some families. Thus, the patient is justified in his concerns. He appears to be at 50% risk to have inherited a predisposition to this cancer. However, a genetic test is unlikely to be helpful in the absence of family history suggesting one of the associated cancer syndromes. In addition, no proven measures for early cancer detection exist. Researchers have suggested endoscopic and radiologic screening strategies, but systematic data to evaluate the benefits and harms are not yet available.

The clinician’s primary obligation in this setting is to be forthright about the uncertainties. Patients from cancer-prone families hope for definitive information about their risk and specific strategies for reducing it. When a risk is identified, they (and their doctors) have an understandable motivation to act. However, for this patient, there is no guarantee that screening will be beneficial. Ultimately, the most important support the clinician can provide is to present the uncertainties and help the patient weigh the advantages and disadvantages of using unproven screening strategies. Consultation with researchers may also be appropriate to determine whether screening trials or other research studies are available for which the patient may be eligible.

Conclusion

The ethical obligations of clinicians can be summarized according to the major principles of medical ethics (Table 1). To provide benefit and avoid harm, clinicians must have appropriate knowledge. They must be able to recognize candidates for whom genetic testing is appropriate and either implement testing and follow-up or refer patients to specialists who can provide these services. In an era of rapidly evolving knowledge, primary care providers, oncologists, genetics specialists, and other professionals need to work collaboratively to ensure that patients receive the current standard of care.

Clinicians also have important obligations under the principle of autonomy. Patients often have choices of risk-reducing strategies, such as prophylactic mastectomy versus breast screening. Providers must ensure that patients have adequate knowledge to make decisions compatible with their preferences. This principle requires truth-telling. In cancer genetics, the obligation to be truthful includes difficult discussions about risk and uncertainties in the risk-reducing measures available. As in other areas of medical practice, bad news must be provided honestly but supportively.

| Table 1 Ethical Obligations of Clinicians Related to Cancer Genetics |
|------------------------|------------------------|------------------------|
| Principle          | Obligation                           | Major Implications                        |
| Beneficence/Avoidance of harm | Provide care in keeping with current standards | • Appropriate use of family history and clinical indicators to identify candidates for testing |
|                      |                                      | • Provision of recommended counseling, testing, and care, directly or through referral |
| Autonomy                        | • Ensure patient has knowledge for informed decision-making | • Adequate counseling by a knowledgeable clinician before and after testing; |
|                      | • Provide truthful information about risk and uncertainties in risk assessment and care | • Ongoing support |
|                      | • Respect patient choices            | • Consistent care recommendations         |
| Justice                           | Assist patients to access care for which they are eligible | • Where appropriate, advocacy to ensure that patients receive needed care |
Finally, clinicians must be attentive to justice concerns. This obligation is incorporated in the requirement for competent practice: clinicians should provide consistent care that ensures that all eligible patients have the opportunity for testing and appropriate follow-up care. This obligation also includes advocacy for patients who experience barriers in accessing health care.

References

23. Fite v Threlkel, 661 So.2d 278 (Fla. 1995).
27. Tarasoff v Regents of the University of California, 551, P.2d 334 (Cal. 1976).