Inherited Medullary Thyroid Cancer: Estranged Parent with MEN2

Posted 1-12-05

Key Points

Genetics

- Medullary thyroid cancer is a relatively rare form of thyroid cancer that can occur sporadically or as part of an inherited syndrome, multiple endocrine neoplasia type 2 (MEN2).
  - MEN2 accounts for about 25% of medullary thyroid cancer.
  - In MEN2, medullary thyroid cancer often occurs in early childhood.
- MEN2 is an autosomal dominant condition caused by specific mutations in the *RET* gene.
- The current standard of care for MEN2 includes genetic testing of all potentially affected family members, including infants. Asymptomatic family members who have inherited the causative mutation are offered prophylactic thryoidectomy.

Ethics

- When an inherited risk is identified, physicians should counsel patients about the benefits of identifying and informing family members who are potentially at risk, and may need to assist patients in their efforts to inform family members.

Learning Objectives

Participants will be able to:

- Understand autosomal dominant inheritance;
- Understand the use of *RET* testing in families with MEN2, as part of a strategy to prevent medullary thyroid cancer;
- Understand the justification for genetic testing of asymptomatic children to identify mutations that cause MEN2.

Family History Issues

All biological descendents of a person with MEN2 have a risk of inheriting MEN2. First-degree relatives (parents, brothers and sisters, and children) typically have a 50% chance of inheriting the causative mutation. However, MEN2 may occur as the result of a new (de novo) mutation; when a de novo mutation occurs, parents and siblings are unlikely to have the mutation.

Red Flags 

About 25% of medullary thyroid cancer is due to MEN2. Suspicion of this syndrome is highest when the cancer occurs in a person under age 50, is multifocal, or is seen in the presence of other medical complications of MEN2, such as hyperparathyroidism or pheochromocytoma.

Case 30. Difficulties in Family Testing for a Cancer Syndrome

A 35-year-old man is diagnosed with medullary carcinoma of the thyroid and undergoes a successful thyroidectomy. He has no family history of thyroid cancer, pheochromocytoma or other endocrine abnormalities. He is an only child; his father died at age 32 in an automobile accident, and his mother is in good health at age 67. Given the early age at which the patient's cancer occurred, his endocrinologist recommends testing for mutations in the *RET* gene. The tests are performed, and the patient is found to have a mutation associated with multiple endocrine neoplasia type 2 (MEN2). Annual screening for pheochromocytoma and hyperparathyroidism is initiated.

In addition, he is referred to medical genetics, where he is counseled about autosomal dominant inheritance and the risk to future children. He asks whether a child already born would be at risk, because he has a ten-year-old son, with whom he has not been in contact for many years. He is counseled that his child has a 50% chance of inheriting MEN2 and should be tested. The patient is initially reluctant to contact the mother of his child, and he refuses to give the genetic counselor permission to contact her.

Later, reflecting on counseling he has received, he decides to call the mother of his child to let her know of their son's risk and the recommendation that

the child be tested. She tells him she doesn't ever want to hear from him again and hangs up. He seeks further help from his primary care provider, a resident in a primary care training program. He notes that he and the mother of his child parted under bad circumstances. He has had little or no communication with his son or her since then, so he is not surprised that she is unwilling to talk with him now. He asks his primary care provider to contact her to explain the need for follow-up for his son. The resident wants to know how to proceed.

Clinical Care Issues

This patient is already receiving appropriate clinical care for his cancer and for potential complications of MEN2.

However, his child is also at risk. According to current practice standards, children of a person with MEN2 should be tested to determine whether they have inherited the *RET* mutation. If the child has inherited the *RET* mutation, a prophylactic thyroidectomy would be recommended. Medullary thyroid cancer associated with MEN2 can occur in early childhood, and thyroidectomy is usually performed before five years of age, so evaluation of the patient's son has urgency.

Risk Assessment

The patient's son has a 50% likelihood of having inherited MEN2.

Genetic Counseling and Testing

When genetic risk is identified, genetics professionals typically encourage family members to share information with relatives who may benefit from testing. In MEN2, risk to children is usually discussed as part of the initial counseling (as occurred in this case) and follow-up testing is arranged as part of care for the family as a whole. Here, because the parents of the child at risk are estranged, the father cannot participate in his son's care. However, he has given his primary care provider permission to contact his son's mother to assure appropriate care for their son. This permission is important, and should be documented in writing, because current privacy regulations require a patient's explicit permission before medical information is shared [Health Insurance Portability and Accountability Act of 1996 (HIPAA)]. In this circumstance, it is permissible for the clinician to contact the mother directly. If permission had not been given, however, the genetics

professional and the primary care provider would need to consider whether they had a duty to inform the mother of her son's risk despite the lack of permission. (See discussion below in Ethical/legal/social/cultural issues.)

Interventions

Recommended management for asymptomatic patients with MEN2 includes prophylactic thyroidectomy in early childhood, and screening for pheochromocytoma and hyperparathryroidism [*GeneReview*: MEN2; www.cancer.gov].

Ethical/Legal/Social/Cultural Issues

Duty to warn family members?

The physician's duty to disclose information to a family member depends on the clinical situation. The American Society of Human Genetics has published a position statement on this issue [ASHG Statement 1998]. This document suggests that disclosure to relatives at risk, despite a patient's refusal, is permissible under exceptional circumstances when:

- Attempts to encourage disclosure on the part of the patient have failed;
- Harm is highly likely, serious, imminent, and foreseeable;
- At-risk relatives are identifiable;
- Disease is preventable, or medically accepted standards for treatment or screening are available;
- The harm from failing to disclose outweighs the harm from disclosure.

Privacy regulations underscore the provider's obligation to maintain the confidentiality of medical information [Health Insurance Portability and Accountability Act of 1996 (HIPAA)]. However, if the information represents a significant, imminent and remediable threat to another's person's health, the provider may need to consider whether s/he has a duty to contact the person at risk (or in the case of a minor, as here, the minor's guardian or legal representative), in the absence of explicit permission. This is similar to cases of a patient making a serious threat to injure another identifiable person, in which the provider may be obligated to inform the person at risk. Most cases of genetic risk provide less clear-cut evidence of imminent risk. In this case, if the patient had not given permission to contact his son's mother, the clinicians involved in his care would have had to consider

whether they had such a duty, based on the potential benefit to the son of a prophylactic thyroidectomy if he had inherited the *RET* mutation from his father. Finding the correct balance between the obligation to disclose and the obligation to maintain patient confidentiality may be difficult, and it may be appropriate to seek legal counsel if this conflict arises.

Resources

- **American Cancer Society**
  1599 Clifton Road NE
  Atlanta, GA 30329
  Phone: 1-800-227-2345

- **CancerNetwork.com**

- **National Cancer Institute (NCI) Cancer Information**

- **National Cancer Institute**

- **Cancer.gov Thyroid Cancer Homepage**

- **National Library of Medicine Genetics Home Reference**
  Multiple endocrine neoplasia

- **GeneTests Online Medical Genetics Information Resource**

- ***GeneReviews*, GeneTests Online Medical Genetics Information Resource**

- **GeneTests Resources for MEN2**

References

American Society of Human Genetics and American College of Medical Genetics Report (1995) Points to consider: Ethical, legal, and psychosocial implications of genetic testing in children and adolescents

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