Medullary thyroid cancer (MTC) consists of a rare, undifferentiated tumor and often is described as having a chronic and indolent disease process. Approximately 5%–10% of all thyroid malignancies are MTC, and about 25% of patients diagnosed with the disease have a genetic form that was inherited through a mutation of the RET proto-oncogene. The mutation is expressed by an autosomal dominant allele and, if inherited, has almost a 100% chance of developing into a malignancy. Detection of the germline mutation identifies individuals at risk and enables prophylactic treatment for the prevention of MTC. As a result, patients and family members commonly undergo genetic testing during the diagnostic phase and experience certain psychosocial stressors. The purpose of this article is to provide an overview of MTC and its symptoms, treatment, prognosis, and genetics. The psychosocial effects of genetic testing on the quality of life of patients with MTC also will be described. By learning more about the pathophysiology and psychosocial stressors, nurses can facilitate proper counseling and increase the likelihood of positive outcomes for their patients.

At a Glance

✦ Medullary thyroid cancer (MTC) is a cancer of the parafollicular cells of the thyroid gland. Although 75% of MTC cases are sporadic and develop without genetic involvement, 25% are genetically inherited.

✦ A child born to a parent with familial MTC has a 50% chance of inheriting the germline mutation of the RET proto-oncogene, which, if inherited, has almost a 100% chance of developing into the malignancy.

✦ Addressing issues related to genetic testing can enable healthcare providers to assist patients in adjusting to psychosocial stressors.

Cancer Society (2006) estimated that 30,180 people will be diagnosed with thyroid cancer in 2006. Six percent of all women and 1.5% of all men will develop a single palpable thyroid nodule.
at some point in their life. About 10%–15% of the palpable nodules will be malignant (Van Nostrand et al., 2004). Although a thyroid neoplasm statistically may appear to be primarily a benign disease, it has the potential, as with any carcinoma, to be aggressive and spread throughout the lymph system and to distant locations. Because thyroid carcinoma grows slowly, patients require close monitoring and surveillance to ensure cure and avoid recurrence.

Four different types of thyroid carcinoma exist: papillary, follicular, anaplastic, and medullary (Samaan et al., 1993). Each is caused by an abnormality of a specific cell type. The thyroid has two cell types: follicular and parafollicular. Follicular cells are the predominant cells and produce thyroid hormone, which is important for the control of body functions, including metabolic rate, growth, and mental function. Malignant tumors in follicular cells include papillary, follicular, and anaplastic thyroid carcinoma. Conversely, MTC is a malignant tumor of the parafollicular cells (Samaan et al.). Parafollicular cells (also known as C cells) produce calcitonin, which is important for controlling calcium balance. Because calcitonin acts independently from thyroid hormone, it serves as a serum marker for the presence of MTC (Samaan et al.).

Medullary Thyroid Cancer

MTC often spreads beyond the thyroid gland to involve the lymph nodes located along the ventral and lateral neck and the mediastinum (Samaan et al., 1993). Most MTC tumors are painless, firm nodules usually discovered during a routine physical examination (Van Nostrand et al., 2004). However, sometimes a thyroid nodule may be discovered incidentally through imaging studies. The first step in the diagnostic evaluation usually consists of obtaining a fine needle aspiration. If the pathology appears suspicious for MTC, the patient is tested for germline mutations before proceeding with surgery. Patients who present with a thyroid nodule often already have some local spread of the cancer to lymph nodes in the neck and sometimes even have metastasis to other locations (Van Nostrand et al.).

Genetics

Genetic testing, specifically RET sequencing, is used in early detection of MTC. Detection of the germline mutation identifies individuals at risk and enables prophylactic treatment for prevention of metastasis. Approximately 98% of all mutations responsible for the inherited forms of MTC are known (Alsanea & Clark, 2001). A child born to a parent with familial MTC has a 50% chance of inheriting the germline mutation of the RET protooncogene which, if inherited, has almost a 100% chance of developing into the malignancy (Hilden, Watterson, & Garr, 1996; Van Nostrand et al., 2004). A thyroidectomy is the only prophylactic measure to prevent MTC and is recommended at ages as young as five or six years (Niccoli-Sire et al., 2003). A thyroidectomy offers nearly 100% “cure” and long-term survival (Van Nostrand et al.). If the thyroid gland is not removed, MTC will develop almost 100% of the time (Hilden et al.; Van Nostrand et al.).

Symptoms

Patients diagnosed with MTC may suffer from thyroid dysregulation symptoms, such as hair loss, an inability to concentrate, sleep disturbances, fatigue, undesired weight changes, palpitations, heat or cold intolerance, constipation, depression, or anxiety. A major complaint from patients with MTC is diarrhea. Approximately 30% of patients have watery diarrhea (as many as 10–20 bowel movements a day), which tends to be more severe in patients with advanced disease and usually reflects a poor prognosis (Samaan et al., 1993). The cause is unknown.

Patients with MTC also may suffer from benign or malignant tumors, including parathyroid adenoma, pheochromocytoma, mucosal neuroma, or intestinal ganglioneuromatosis. The tumors are symptoms of multiple endocrine neoplasia (MEN), which is a syndrome of endocrine tumors that often accompanies inherited MTC. As a result, patients are diagnosed with MEN-2A or MEN-2B, depending on the symptoms present (Samaan et al., 1993). MTC with MEN involvement is more aggressive, and patients have a poorer prognosis than those with sporadic or familial MTC (Van Nostrand et al., 2004). Most frequently, a pheochromocytoma will be present, creating persistent or intermittent hypertension, headaches, palpitations, tachycardia, and excessive sweating without exertion (Samaan et al.). Fortunately, most patients with familial disease are asymptomatic and are discovered through genetic or biochemical screening in predisposed families (Van Nostrand et al.).

Treatment

The management of thyroid cancer overlaps multiple medical specialties, requiring consultation and active intervention by endocrinology, oncology, and surgery teams. The treatment of choice for MTC is a total thyroidectomy because the tumor may be multifocal in the thyroid gland. Patients who undergo a thyroidectomy require lifelong thyroid-stimulating hormone to regulate the metabolic system. When properly medicated, patients with MTC will have thyroid-stimulating hormone in the normal range (Van Nostrand et al., 2004).
If the tumor has spread beyond the thyroid, a central neck dissection may be necessary. Unfortunately, as many as 30% of patients with MTC develop some sort of recurrent malignancy after surgery. In some cases, multiple surgeries are required to remove the recurrent growth of cancer in the neck region (Moley, DeBenedetti, Dilley, Tisell, & Wells, 1998; Samaan et al., 1993; Van Nostrand et al., 2004). The indolent nature of MTC leaves healthcare providers and patients frustrated because the tumors cannot be guaranteed to be completely eradicated after surgery. Radioactive iodine is not an appropriate treatment modality for patients with MTC, and, at this time, evidence is inconclusive regarding the efficacy of chemotherapy and/or radiation therapy.

Prognosis

MTC is a slow-growing carcinoma that is incurable, thus creating a chronic status once it develops. Patients with MTC have an overall five-year survival rate of 80%–90% and a 10-year survival rate of 60%–75% (Van Nostrand et al., 2004). MTC is not gender specific. Sporadic MTC more often is associated with patients 50–60 years of age, whereas patients diagnosed with familial MTC usually are younger (National Cancer Institute [NCI], 2006b). For the best possible outcome, patients require close monitoring and surveillance.

Effects of Genetic Testing

Health-related QOL may be defined as the extent to which an individual's expected physical, emotional, and social well-being is affected by a medical condition or its treatment and represents a subjective appraisal of the impact of illness or its treatment (Cella, 1995). In their study of differences between QOL in patients with and without cancer, Baker, Haffer, and Denniston (2003) demonstrated that patients with cancer have significantly reduced QOL when compared to patients without cancer. However, studies pertaining specifically to QOL in patients with thyroid cancer are scarce. Schultz, Stava, and Vasilopoulou-Sellin (2003) found that thyroid cancer survivors reported that their overall health was affected more frequently than survivors of other cancer types. In addition, Crevenna et al. (2003) reported that QOL in patients with thyroid cancer was negatively affected by recurrence or metastatic disease and its associated morbidity. The QOL of patients with MTC is affected by thyroid dysregulation symptoms, by multiple surgeries for recurrent malignancy that may induce high levels of emotional or physical stress, by chronicity because patients live years with no resolution of disease, and by the consequences related to ascertaining genetic risk.

The psychosocial consequences for patients obtaining genetic knowledge have not been studied widely among those with cancer (Freyer et al., 1999). The results are inconsistent in the few reports published, and the sample populations involved included only individuals who wanted to be tested and informed (i.e., a self-selected population). One study of 77 patients with MTC reported high levels of frustration and latent dissatisfaction related either to the management of genetic information given by clinicians and its psychosocial consequences or simply to the knowledge of the genetic risk for cancer (Freyer et al., 1999).

Frustration and dissatisfaction were significantly more likely in carriers of the germline mutation as compared to noncarriers, but the existence of a cause-effect relationship is unknown. In a French study of 82 individuals at risk for MTC and 200 women at risk for familial breast or ovarian cancer syndrome, researchers reported negative effects on QOL related to genetic testing as a result of the knowledge of the genetic risk of cancer and its consequences in terms of morbidity and follow-up (Freyer et al., 2001).

NCI (2006a) identified several psychosocial stressors that may affect the QOL of patients undergoing genetic testing. See Figure 1 for a brief list of the potential stressors.

A study conducted at New Mexico State University using the Sickness Impact Profile and a survey tool asking about the impact of genetic testing reported that patients with MTC (N = 53) had no significant difference in overall QOL when comparing participants who underwent genetic testing with those who did not (Keatts, 2005). However, a qualitative analysis of responses from the patients, reflecting on their experiences related to genetic testing, indicated that they did suffer from similar psychosocial stressors paralleling those recognized by NCI (2006a). For example, participants reported significant anxiety for themselves and loved ones. One participant reported that the stress from genetic testing was “over the top.” NCI (2006a) reported that anxiety related to genetic testing may be a result of an altered sense of self and/or life course.

Participants in the Keatts (2005) study inferred psychosocial stresses that were related to genetic testing that resulted in changes to family dynamics. Family members without the mutated gene may be rejected by affected family members because of the loss of a common risk status, resulting in stigmatization by self or others (NCI, 2006a). One patient stated, “Of two sons, one was positive, [resulting in his] thyroid removed at age 8; very stressful time” (Keatts). Another patient listed family members who received positive results after undergoing genetic testing to be “myself and one brother [out of three], two of my three children, six of 13 of my first cousins on father’s side [not all of their children yet tested].”

Many participants reported relief in having no genetic mutation: “relief my three young children did not inherit,” “relief to

- An altered sense of self and life course
- Survivor guilt or guilt related to the possible transmission of genetic risk to children
- Social discrimination
- Potential neglect of routine surveillance resulting from misunderstanding of a negative result
- Adverse emotional reactions when family members feel coerced to undergo genetic testing
- Strain in communication within and beyond the family, resulting in a disruption of family dynamics
- Fear of financial difficulties related to increased screening or prophylactic treatment, insurance, or employment

Figure 1. Psychosocial Stressors That May Affect the Quality of Life of Patients Undergoing Genetic Testing

Note: Based on information from National Cancer Institute, 2006a.
know it is not familial,” “it’s provided some sense of security for my children and siblings” (Keatts, 2005). For some, the value of genetic testing for an individual may be the relief of a negative test in the face of an affected family member. However, others receiving negative results experience stress as they attempt to readjust their risk status assumptions. For example, “I was tested in 2000 and I am still not 100% sure it is not familial,” and “It gives us some peace of mind that the rest of the family will not have MTC; however, there is always a small doubt lingering” (Keatts).

Misconceptions about genetic disease have the potential to stir blame and guilt in families (NCI, 2006b). Survivor guilt, guilt about the possible transmission of genetic risk to children, and the potential neglect of routine surveillance because a negative result was misunderstood also were illustrated in the Keatts (2005) study. Many participants found to be positive for a RET proto-oncogene mutation reported feeling negligible for potentially transmitting the gene to their offspring. One participant who did not have an RET proto-oncogene mutation reported that “most are okay with it since I came up sporadic. Father still refuses . . . says he doesn’t want to know if he ‘gave’ it to me,” and another said that “it was a great relief to know I won’t pass it on to my children and that it isn’t genetic.”

For some families, the costs of increased screening or prophylactic treatment, insurance, employment, or social discrimination as a result of genetic testing became a new concern. Five participants in the Keatts (2005) study were from the same family, and one reported that 13 out of 14 family members tested positive; totally turned our lives upside down for more than two years. Eleven of us have had our thyroids removed in three years; two more still to go.

Because a family history, usually in the form of a pedigree, is used to assess genetic risk by establishing patterns consistent with modes of inheritance as well as disease history, misidentified paternity is another psychosocial stressor related to genetic testing identified by NCI (2006a). One unintended benefit for an adopted participant was to develop a relationship with her biologic family.

I am adopted and have never wanted to contact my biological parents or siblings; however, the thought that this disease might be familial started a process to contact them. Fortunately, I found that my MTC was sporadic (Keatts, 2005).

Nursing Implications

The dissemination of genetic information has the potential to cause psychological consequences that directly impact the QOL of patients and families. Oncology nurses have a significant role in facilitating proper counseling for patients who undergo genetic testing. Common psychosocial stressors related to genetic testing that nurses need to be aware of, as outlined by NCI, include patients’ feelings of an altered sense of self, guilt or other emotional strain, fear of discrimination or financial difficulties, misinterpretation of results, and strain in communication (NCI, 2006a). By understanding and being able to identify stressors, nurses are able to assist patients in weighing the risks and benefits of genetic testing and to ensure that informed decisions are made.

Nurses may assist in helping patients identify the positive aspects of genetic testing. A positive genetic test result provides an excellent opportunity to receive counseling on ways to reduce risk. Some of the options for people with positive test results include starting screening at a younger age, getting screened more often, or deciding to undergo certain screening tests not recommended for people at average risk. Patients also may benefit from certain medications, lifestyle changes, or even preventive surgery. Nurses are able to assist patients and families in adjusting to the results and making decisions about appropriate prevention or treatment.

Conclusions

Understanding the social, emotional, and behavioral consequences of changes in health status will assist healthcare providers in learning how patients perceive multifaceted problems and identifying areas for specific interventions. This concept is central to the increasing interest among healthcare professionals and patients in the balance between QOL and length of life (Johnson, King, & Murray, 1983). QOL encompasses a holistic approach to cancer management, which is congruent with traditional nursing philosophy. Nursing is, and has been, a leader in addressing QOL issues; therefore, nurses must be knowledgeable about how malignancies, including indolent forms, affect an individual’s psychosocial and functional status. As genetic testing evolves, future QOL studies will be needed to demonstrate individual consequences of genetic testing, effectiveness of information delivery, and psychotherapeutic interventions. Research will ensure the quality of care for patients undergoing presymptomatic genetic testing in the field of oncology.

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