Chapter 13
Introduction

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It has been a privilege to edit the section on Thyroid Diseases, and we are honored to have excellent authors discussing three important thyroid cancers (see chaps. 14, 15 and 16). Thyroid cancer incidence has been increasing at a very rapid rate, probably due to increased detection of thyroid nodules by radiologic techniques, as well as a change in the underlying molecular mechanisms which cause or propagate this disease [1]. Therefore, it have become important to recognize the staging system for thyroid cancer and to decide which patients require more intensive therapy and monitoring [1].

Papillary thyroid cancer (PTC) is the most common form of thyroid cancer and, in general, is treated with thyroidectomy (total or lobectomy) and sometimes with radioactive iodine [1]. Despite the fact that papillary thyroid cancer is usually very treatable and that most patients do well, the prognosis in older patients may be more guarded. Further, men seem to have a worse prognosis than woman, although the reasons for this are presently unclear. In their chapter Motazedi and Burman (see chap. 14) review various aspects of PTC. Risk factors, such as age, gender, and thyroid pathology, are discussed as well as hereditary disorders, such as Cowden's syndrome, which increase the likelihood of developing thyroid cancer, are reviewed. Appropriate management following thyroidectomy may include radioactive iodine scan and therapy and during monitoring includes physical exam, serum TSH and thyroglobulin levels, and neck ultrasound. In selected patients with aggressive disease, further radiologic studies including CT, PET, and bone scans and radioactive iodine scans/therapy may be indicated. Motazedi and Burman (see chap. 14) also note the use of FDA-approved oral chemotherapy to treat selected patients with oncogene targeted oral chemotherapy. Some patients may only require a thyroid lobectomy, whereas other may need a total thyroidectomy and additional treatment as noted.

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Radioactive iodine therapy has been used to treat PTC for about 80 years, but its use recently has been more limited to patients with more aggressive disease who are also radioactive iodine sensitive [1].

Patel and Bernet (see chap. 16) review the important clinical aspects of medullary thyroid cancer (MTC). Although less common than PTC, MTC can be aggressive, especially when detected later in its course [2]. Most cases of MTC occur sporadically, but a significant number are familial, related to a germline RET mutation. Familial disorders that are associated with MTC include multiple endocrine neoplasia type 2 (MEN2A and MEN2B) and familial MTC (see chap. 16).

It is important that all patients with MTC be assessed for the presence of a germline RET mutation. The finding of a specific relevant germline RET mutation in the initial patient mandates that all first-degree relatives be screened as well. The penetrance of a RET germline mutation is about 100%, and, therefore, a prophylactic thyroidectomy is usually recommended. The specific timing of the surgery depends on the clinical circumstance as well as the specific codon mutation identified [2].

All patients with a RET mutation should also be screened for a pheochromocytoma and hyperparathyroidism, especially prior to a thyroidectomy (or any surgery).

MTC patients are monitored by following serum TSH as well as serum calcitonin and CEA. Calcitonin doubling time is a reasonable assessment of progression of disease. Radiologic studies such as neck ultrasound, CT chest, MRI abdomen and adrenal glands, and bone scan are indicated in patients with residual evidence of disease after thyroidectomy. Oral chemotherapy is available for patients with aggressive or progressive disease. Several TKIs have been approved by the FDA, and specific targeted agents may also be available. It appears that early detection of MTC especially through RET testing of patients with familial MTC with early thyroidectomy decreases the risk of progression or return of disease.

Munir and Veytsman (see chap. 15) review salient aspects of anaplastic thyroid cancer (ATC). ATC is one of the most lethal tumors known, and it has a very poor prognosis [3]. It may occur de novo but also may occur in the setting of a previously known PTC. It is characterized by a rapidly growing neck mass and local symptoms such as sudden onset of hoarseness, neck discomfort, dysphagia, and/or dyspnea. Distant metastases may be noted at the time of diagnosis.

Treatment modalities may include thyroid/neck surgery or debunking, external beam radiation therapy, and/or chemotherapy [3]. Each case is evaluated individually with respect to which treatments may possibly be beneficial taking into account the potential adverse effects. The thyroid pathology typically shows spindle cells, giant cells, and/or squamoid cells with poorly differentiated thyroid cells. ATC typically does not stain (or stains poorly) for thyroglobulin, TTF1, or PAX8. However, ATC may stain for oncogenes, most notably bRAF. ATC that does not stain for bRAF may be a candidate for more standard chemotherapy, such as doxorubicin and paclitaxel. However, newer developments promulgated from M.D. Anderson Cancer Center indicate that early determination of bRAF status is critical [4]. If a bRAF mutation is present, treatment is instituted with combination of dabrafenib and trametinib as specific targeted agents. Monitoring includes clinical and

radiologic assessment. The rapid assessment and treatment of a bRAF mutation appears to be an important development in the treatment of patients with ATC.

In summary, there have been new, important developments in the management of PTC, MTC, and ATC mainly focusing on improved diagnostic and treatment modalities. The utility of performing either germline or somatic genetic analysis (depending on the tumor type) and the implementation of specific targeted chemotherapy appear to be an advance in thyroid cancer management.

References

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