Clinical Approach to Thyroid Cancer and Nodules

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The age - and gender - adjusted incidence of thyroid cancer has increased faster than that of any other malignancy in recent years. Although the increasing incidence probably partially reflects earlier detection of subclinical disease, database found an increase in the rates of differentiated thyroid cancer of all sizes, including tumors greater than 4 cm. Following the second most common cancer in women in Turkey is thyroid cancer. Thyroid follicular epithelial-derived cancers are divided into three categories: papillary, follicular and anaplastic cancer. Papillary and follicular cancers are considered differentiated cancers and patients with these tumors are often treated similarly despite the numerous biologic differences. Most anaplastic cancers appear to arise from differentiated cancers. Other malignant diseases of the thyroid include medullary thyroid cancer (MTC), primary thyroid lymphoma and metastases (breast, colon, renal cancer and melanoma). MTC accounts for about 4% of all thyroid cancer cases. MTC presents worldwide as part of an autosomal dominantly inherited disorder in about 20-25% of cases and as a sporadic tumor in the rest. *RET* gene mutation occurring in the germline that results in expression of abnormally overactive Ret protein in all tissues in which it is expressed causes these speciŞc inherited syndromes. It leads not only to hereditary medullary thyroid cancer but also to the other inherited forms of thyroid cancer. As with all cancers, early diagnosis and treatment is important. The prevalence of clinically unapparent thyroid nodules is estimated with ultrasonography (USG) at 20% to 76% in the general population. The prevalence of palpable thyroid nodules is 3% to 7%. Factors suggesting an increased risk of malignant potential is history of head and neck irradiation, family history of medullary thyroid carcinoma, multiple endocrine neoplastic type 2, or papillary thyroid carcinoma, age <14 or >70 years, male sex, growing nodule, firm or hard consistency, cervical adenopathy, fixed nodule, persistent dysphonia, dysphagia, or dyspnea. USG characteristics associated with malignancy are hypoechoic pattern and/or irregular margins, a more tall-than-wide shape, microcalcifications or chaotic intranodular vascular spots. Incidentalomas detected by positron emission tomography with fludeoxyglucose should undergo USG evaluation plus ultrasound-guided fine-needle biopsy (FNAB) because of the high risk of malignancy. Laboratory evaluation in patients with thyroid nodules always measure serum thyrotropin-stimulating hormone (TSH). If TSH level is increased, measure free thyroxine (fT4) and thyroperoxidase antibody. TSH-receptor antibody measurement should be performed in patients with TSH levels below the reference range. Calcitonin measurement is mandatory in patients with a family history or clinical suspicion of MTC or multiple endocrine neoplasia type 2. Thyroid scintigraphy should be performed in case of thyroid nodule or multinodular goiter and suppressed TSH. Clinical management of thyroid nodules should be guided by the combination of USG evaluation and FNAB. FNAB is currently the best triage test for the preoperative evaluation of thyroid nodules. Most (60-80%) of the results of FNAB are classified as benign; for the rest, 10-20% are follicular lesion/neoplasm, 3.5% to 10% malignant, 2.5% to 10% suspicious and 10% to 15% are nondiagnostic. If initial FNAB is nondiagnostic, it should be repeated with USG guidance. Repeated FNAB of follicular lesion is not recommended because it does not provide additional information. Molecular and histochemical markers are currently not recommended for routine use; their use may be considered in selected cases. The use of molecular markers (i.e. BRAF, RAS, RET/PTC, Pax8-PPARγ, galactine-3) may be considered in patients with indeterminate cytology. If a cytology result is diagnostically suspicious, surgery is recommended. If FNAB result is differentiated thyroid carcinoma, surgery is recommended. For anaplastic carcinoma, lymphoma and metastatic lesion, further diagnostic workup is recommended before surgery. Serum thyroglobulin should be measured in every 6-12 months during the follow-up of differentiated thyroid carcinoma. Carcinoembryonic antigen and calcitonin should be measured in postoperative 2-3 months in MTC. Screening of at-risk family members should be done by testing for germline mutations in the RET proto-oncogene. Surgery is the primary treatment of patients with differentiated thyroid cancer, followed by radioiodine and then fT4 therapy. The primary treatment for MTC is extensive and meticulous surgical resection. There is limited role of radiotherapy (RT). RT can be given alone or in combination with surgery or chemotherapy in symptomatic recurrent cancer.

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