Updates in management of cancer thyroid

An essay

Submitted for partial fulfillment of master degree in general surgery

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Aknoweldgment

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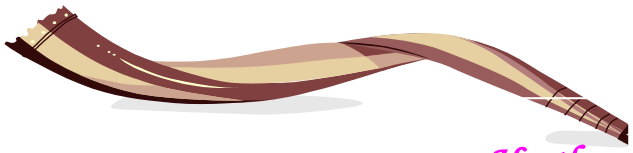

Haytham Abd el-Aziz

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List of abbreviations

AJCC	American Joint Comitte of Cancer
ATC	Anaplastic Thyroid Carcinoma
FTC	Follicular Thyroid Carcinmoma
PTC	Papillary Thyroid Carcinoma
MTC	Medullary Thyroid Carcinoma
FMTC	Famillial Medullary Thyroid Carcinoma
DTC	Diffrentiated Thyroid Carcinoma
CEA	Carcinoemberyonic Antigen
RET	Rearrangment after Transformation
FNAB	Fine Needle Aspiration Biopsy
RND	Radical lymph Node Dissection
MRND	Modified Radical lymph Node Dissection
MEN	Multiple Endocrine Neoplastic syndrome
TNM	Tumor – Node – Metastases
SAN	Spinal Accessory Nerve
IJV	Internal Juglar Vein
SCM	SternoCleidoMastoid
IPI	International Prognostic Index
IPC	Incidental Papillary Carcinoma

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Protocol

Of an Essay

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Introduction

Cancer of the thyroid is the most common endocrine malignancy. Some 5-10% of patients with thyroid cancer will die of their disease. Thyroid neoplasms arising from follicular cells (adenoma, carcinoma, and follicular/papillary carcinoma) show a broad range of overlapping clinical and cytological features. A clear distinction between benign and malignant disease based solely on cytological examination of a needle biopsy specimen may be difficult. For this reason, a surgical procedure to remove all or a large portion of the thyroid gland may be necessary to obtain sufficient tissue for a definitive diagnosis of follicular thyroid cancer. Pathological examination showing capsular or vascular invasion may be required for this determination**.(Asari R,2009)**

The thyroid is particularly sensitive to the effects of ionizing radiation. Exposure to ionizing radiation results in a 30% risk for thyroid cancer.A history of exposure of the head and neck to x-ray beams, especially during childhood, has been recognized as an important contributing factor to the development of thyroid cancer**.(Schlumberger M,2006)**

Thyroid cancers are found more often in patients with a history of low-dose or high-dose external irradiation to the cervical or thyroid area. The most common thyroid tumor to develop after exposure to radiation is papillary thyroid cancer. Patients whose thyroid cancer has developed following radiation to the head and neck area may present with more extensive disease. Overall, about 5% of patients with thyroid cancer have metastases beyond the cervical or mediastinal area on initial presentation, 2-3% of patients with papillary thyroid cancer and 11% of patients with follicular thyroid cancer**.(Johnson TL,2002)**

Seven percent of the individuals exposed to the atomic bomb blasts in Japan developed thyroid cancers. However, exposure to fallout from the Chernobyl nuclear accident was asssociated with increases in papillary rather than follicular thyroid carcinoma. Exposure to diagnostic x-rays does not increase the risk of developing thyroid cancer. **(McCabe CJ,2008)**

Thyroid cancers are divided into papillary carcinomas, follicular carcinomas, medullary thyroid carcinomas (MTCs), anaplastic carcinomas, primary thyroid lymphomas, and primary thyroid sarcomas. Papillary carcinoma represents 80% of all thyroid neoplasms. Follicular carcinoma is the second most common thyroid cancer, accounting for approximately 10% of cases. MTCs represent 5-10% of neoplasms. Anaplastic carcinomas account for 1-2%. Primary lymphomas and sarcomas are rare**.(McCabe CJ,2008)**

Follicular thyroid carcinoma (FTC) is a well-differentiated tumor. In fact, FTC resembles the normal microscopic pattern of the thyroid. FTC originates in follicular cells and is the second most common cancer of the thyroid, after papillary carcinoma. Follicular and papillary thyroid cancers are considered to be differentiated thyroid cancers; together they make up 95% of thyroid cancer cases. **(Koperek O,2009)**

Papillary/follicular carcinoma must be considered a variant of papillary thyroid carcinoma (mixed form), and Hurthle cell carcinoma should be considered a variant of FTC**(Scheuba C,2009)**

Hürthle cell carcinoma of the thyroid gland is an unusual and relatively rare type of differentiated thyroid cancer. Hürthle cell cancer accounts for only about 3-10% of all differentiated theyroid cancers; therefore, few institutions have extensive experience with Hürthle cell neoplasms. According to the World Health Organization (WHO), these neoplasms are considered a variant of follicular carcinoma of the thyroid and are referred to as follicular carcinoma, oxyphilic type**.(Williams MD,2011)**

Primary lymphomas of the thyroid gland represent approximately 2-5% of all thyroid malignancies. Most thyroid lymphomas are non-Hodgkin B-cell tumors. The next most common histological type is low-grade malignant lymphoma of mucosa-associated lymphoid tissue (MALT). Hodgkin lymphoma, Burkitt cell lymphoma, and T-cell lymphoma have also been reported.**(Klee GG,2008**)

Despite its well-differentiated characteristics, follicular carcinoma may be overtly or minimally invasive. In fact, FTC tumors may spread easily to other organs. Life expectancy of affected patients is related to their age; the prognosis is better for younger patients than for patients who are older than 45 years. Patients with FTC are more likely to develop lung and bone metastases than those patients with papillary thyroid cancer. The bone metastases in FTC are osteolytic. Older patients have an increased risk of developing bone and lung metastases**.(Kaserer K ,2009)**

Activating point mutations in the Ras oncogene are well known in patients with follicular adenoma and carcinoma, especially in poorly differentiated (55%) and anaplastic carcinoma (52%).**(Hoffmann M,2009)**

About 10-15% of all thyroid cancers are follicular in united states but internationally Thyroid cancers are quite rare, accounting for only .5% of all cancers in adults and 3%inchildren.The highest incidence of thyroid carcinomas in the world is among female Chinese residents of Hawaii. In Hawaii, incidence of FTC ranges from 10-30 new cases a year per million inhabitants. During the last few years, the frequency of FTC has appeared to increase; ,however, this increase is related to improvement in diagnostic techniques and a successful campaign of information about this carcinoma. Of all thyroid cancers, 17-20% are follicular. According to world epidemiologic data, follicular carcinoma is the second most common thyroid neoplasm; in some geographic areas, however, FTC is the most common thyroid tumor. Relative incidence of follicular carcinoma is higher in areas of endemic goiter.**(Lloyd RV,2002)**

FTC occurs more frequently in whites than in blacks Incidence is higher in women than men by a factor of 2-3 or more. The ratio varies by patient age. **(Karga H,2001)**

Thyroid carcinoma is common in all age groups, with an age range of 15-84 years (mean age, 49 years). In older adults, FTC tends to occur more frequently than papillary carcinoma. **(Lemoine NR,2005)**

Many cases of FTC are subclinical.The most common presentation of thyroid cancer is an asymptomatic thyroid mass, or a nodule, that can be felt in the neck**.(Lee JK,2000)**

Record a thorough medical history to identify any risk factors or symptoms. For any patient with a lump in the thyroid that has appeared recently, focus on obtaining history regarding every prior exposure to ionizing radiation, as well as the cumulative lifetime exposure. Consider family history of thyroid cancer. **(Kaserer K,2009).**

Some patients have persistent cough, difficulty breathing, or difficulty swallowing.Pain seldom is an early warning sign of thyroid cancer.Other symptoms (eg, pain, stridor, vocal cord paralysis, haemoptysis, rapid enlargement) are rare. These symptoms can be caused by less serious problems**. (Am J Pathol,1987)**

At diagnosis, 10-15% of patients have distant metastases to bone and lung and initially are evaluated for pulmonary or osteoarticular symptoms (eg, pathologic fracture, spontaneous fracture **.(Renehan AG,2008)**

The principal sign of thyroid carcinoma is a firm and nontender nodule in the thyroid area. This mass is painless. Some patients have a tight or full feeling in the neck, hoarseness, or signs of tracheal or esophageal compression.Palpable thyroid nodules are usually solitary, with a hard consistency, an average size of less than 5 cm, and ill-defined borders. This nodule is fixed in respect to surrounding tissues and moves with the trachea at swallowing**.(Zeiger MA,2010)**

Although follicular cancer is frequently present in goitrous thyroids, the relationship between prolonged elevation of thyroid-stimulating hormone (TSH) and follicular carcinoma is not known. Several reports have shown arelationship between iodine deficiency and the incidence of thyroid carcinoma. **(Mitsutake N,2005)**

Thyroid cancer is autonomous and does not require TSH for growth, whereas benign thyroid lesions do. Therefore, when exogenous thyroid hormone feeds back to the pituitary to decrease the production of TSH, thyroid nodules that continue to enlarge are likely to be malignant. However, consider that 15-20% of malignant nodules are suppressible**.(Umbricht C,2010**)

Ultrasonography is the first imaging study that must be performed in any patient with suspected thyroid malignancy.Ultrasonography is noninvasive and inexpensive, and it represents the most sensitive procedure for identifying thyroid lesions and determining the diameter of a nodule (2-3 mm). Ultrasonography is also useful to localize lesions when a nodule is difficult to palpate or is located deeply Ultrasonography can determine whether a lesion is solid or cystic and can detect the presence of calcifications. The rate of accuracy of ultrasonography in categorizing nodules as solid, cystic, or mixed is near 90%. Ultrasonography may direct a fine-needle aspiration biopsy (FNAB).Disadvantages of thyroid ultrasonography are that the test cannot distinguish benign nodules from malignant nodules, and it cannot be used to identifytrue cystic lesions**.(Segev Dl,2003)**

Thyroid scanning is helpful and specific in localizing the tumor preoperatively and residual thyroid tissue immediately postoperatively. It also is used to follow-up for tumor recurrence or metastasis. Thyroid scanning could be useful in diagnosing thyroid tumors in patients with benign lesions (by FNAB) or solid lesions (by ultrasonography).**(Bogdanova T,2004)**

Chest radiography, CT scanning, and MRI usually are not used in the initial workup of a thyroid nodule, except in patients with clear metastatic disease at presentation. **(Abrosimov A ,2004)**

Fine-needle aspiration biopsy (FNAB) is considered the best first-line diagnostic procedure for a thyroid nodule; it is a safe and minimally invasive test. It is the required procedure for the diagnostic evaluation of the classic solitary thyroid nodule**.(Williams ED,2011)**

The initial treatment for cancer of the thyroid is surgical. The exact nature of the surgical procedure to be performed depends for the most part on the extent of the local disease. A consensus approach might be to perform a total thyroidectomy if the primary tumor is larger than 1 cm in diameter or if there is extrathyroidal involvement or distant metastases. Clinically evident lymphadenopathy should be removed with a neck dissection. If the primary tumor is less than 1 cm in diameter, a unilateral lobectomy might be considered. About 4-6 weeks after surgical thyroid removal, patients must have radioiodine to detect and destroy any metastasis and any residual tissue in the thyroid Aradioiodine uptake is noted , **(Scheubac,2009).**

Some studies show lower recurrence rates and increased survival rates in patients who have undergone total thyroidectomy. This surgical procedure also facilitates earlier detection and treatment of recurrent or metastatic carcinoma. This surgical option is mandatory in patients with FTC ascertained by postoperative histologic studies (ie, if a very well-differentiated tumor is discovered) after a one-side lobectomy, with or without isthmectomy**,(Vickery AL Jr,2000)**

The most useful drugs for postsurgical treatment of FTC are L-thyroxine (L-T4) and radioiodine. Antineoplastic drugs such as cisplatin and doxorubicin may be useful for palliation in patients with metastases in patients with FTC, systematic psychotherapeutic intervention may be very helpful**,(Gaz RD,2004)**

Perform postoperative scinti scan of the neck after 4-6 weeks without thyroid hormone replacement. At this time, a scan of the neck demonstrates whether thyroid tissue is still present. If thyroid tissue is present, a dose of radioactive iodine is administered to destroy residual tissue. The patient is then placed on lifelong thyroid replacement with L-T4. Repeat the scinti scan 6-12 months after ablation and, thereafter, every 2 years. Prior to the

scan, L-T4 must be withdrawn for approximately 4-6 weeks to maximize thyrotropin stimulation of any remaining thyroid tissue**.(Mayall ES,2007).**

FTC prognosis is related to age, sex, and staging. In general, if cancer is not extending beyond the capsule of the gland, life expectancy is affected minimally. Prognosis is better in female patients and in patients younger than 40 years. Survival rate is at least 95% with appropriate treatments**.(Wright PA,2005)**

Mean survival rate after 10 years is 60%. Metastases are still rare and are due to angioinvasion and hematogenous spread. Lymphatic involvement is even rarer, occurring in fewer than 10% of cases. In some patients, metastases are found at diagnosis**.(Thor A,2003)**

Autopsy reviews show a high incidence of microscopic foci of thyroid carcinoma worldwide. Unlike medullary thyroid carcinoma, FTC is not part of a multiple endocrine neoplasia (MEN) syndrome. **(Bos JL,2003)**

As a result of the increasing knowledge of the biological basis for thyroid cancer development, therapeutic agents that target these biological abnormalities have been identified. Multiple clinical trials have been carried out in the past decades such as tyrosine kinase inhibitors.**(Hay ID,2002)**

Chinese investigators treated 11 patients with dedifferentiated thyroid cancer using 1 mg/kg/day of all-trans retinoic acid followed by radioactive iodine also Lithium has been reported to increase tumor dosages of RAI in DTC , Statins have been shown to be potent inhibitors of the 3-hydroxy-3-methyl-glutaryl-CoA reductase. In vitro studies show an effect of statins on growth and invasion of tumor cell also Gene therapy can be particularly attractive for the treatment of thyroid cancer because of the possibility of selecting targeting of therapeutic genes to tumor cells by application of tissue-specific promoters, such as the thyroglobulin and calcitonin promoter**.(Schlumberger M,2006)**

In addition, immunotherapy with dendritic cells has been successfully evaluated in a transgenic mouse model for MTC and this approach has occasionally been tested in humans.**(Kebebew E,2009).**