THYROID CANCER EPIDEMIOLOGY AND PREVENTION

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Introduction

The thyroid gland is made up of two lateral lobes which extend from the sides of the thyroid cartilage to the sixth tracheal ring. These are joined together by the isthmus which overlies the second to fourth tracheal rings.

The thyroid gland is the largest organ specialized in endocrine function in the human body.

Cells of Origin:

Thyroid gland contains two embryologically and functionally different cell types:

- The neuroendocrine Calcitonin producing C – cell and
- Endodermally derived follicular cell that produces T4 and Thyroglobulin

Thyroid cancers are derived from these two embryonic cell lines.

Classification of Thyroid Cancer:

1. Papillary Carcinoma

• 80% of thyroid cancer
• Peak age: 3rd, 4th decades
• More in women (3 folds)
• More in white

2. Follicular Carcinoma

• 10% of thyroid cancer
• Peak age: 4th and 5th decades
• More frequent in women
• Uncommon in black

3. Medullary Thyroid Carcinoma (MTC)

• 5 – 7% of thyroid cancer
• Sporadic type 80%
• Familial type 20%, point of mutation in the RET proto – oncogene. In kindred with MTC can identify affected persons can be identified before clinical or chemical changes can be detected (1,2)

4. Anaplastic Thyroid Carcinoma

• Arises from less differentiated thyroid cell
• Caused by external radiation (3)
• Occurs with greater frequency in areas of low iodine diet and endemic goiter area (4)
• More in elderly, 76% more in women (ratio 2:1)
• 1/3 of specimen have areas of well differentiated, rare in children
• Treatment ranges from debulking and post operatively radiation to systemic chemotherapy
• Median survival is 6 months

5. Thyroid Lymphoma
• It occurs with greater frequency than anaplastic carcinoma
• Incidence has increased in recent years
• Hashimoto's disease increased patient's risk of thyroid lymphoma about 70 fold (5)
• Mean: age from 60 to 65
• Female to Male: 8:1 (6)
• Prognosis depends on stage if confined to thyroid; 5 year survival rate is 85% if extending into surroundings neck structure (35%) and for disseminated disease rate (5%) (7)
• Treatment is radiotherapy alone and surgery and radiotherapy together are highly effective

. Secondary Thyroid Tumor
• Microscopic metastasis to thyroid gland found in autopsy specimens from patients with malignant melanoma, lung and breast carcinoma
• Usually undetectable clinically
• Does not alter the thyroid function

Epidemiology
Thyroid cancer is a relatively uncommon clinical problem. In USA, account for less than 1.5 of all cancer cases. This appears to be steadily increasing in incidence. In the 1970's, 8000 new cases / year. In 2002, there were 20, 700 cases /year but the death rate remained the same with fewer than 1300 case / year.

Thyroid cancer constitutes 92% of endocrine cancers (8). The incidence of thyroid cancer is high in males with thyroid nodules and among patients younger than 30 years old or older than 60 years of age (9)

The prevalence of occult thyroid carcinoma in autopsy specimen is about 10%. (10,11)

In Saudi Arabia (12): There were 415 cases of thyroid cancer accounting for 6% of all newly diagnosed cases in year 2004. This cancer ranked second among female population and 14th among male population. It affected 87 (21%) males and 328 (79%) females with a male to female ratio of 100:266.

Risk Factors

1. Benign Thyroid Disease
Because thyroid cancer occurs more often in solitary nodules than in multinodular goiters (MNG) the two are often managed differently; however, this may lead to a serious diagnostic error. Up to 50% of thyroid glands, with palpable solitary nodules have multiple lesions by ultrasound or at surgery. (13,14)

A dominant hypofunctional nodule in MNG or a diffuse goiter with large palpable cervical lymph nodes should be evaluated for carcinoma. Hashimato's thyroiditis can transform to lymphoma in 20 – 30% of the cases.

2. Radiation Exposure
This is an important risk factor for thyroid carcinoma and other head and neck neoplasms (15,16,17). Medical workers exposed to radiation have a significantly high prevalence of thyroid cancer than controls (18).

The risk of developing carcinoma is greatest after radiation exposure in childhood.
Likewise, persons exposed to radiation from atomic weapons and nuclear fallout accidents have a highly incidence of thyroid cancer.
The latest period for developing abnormality after radiation exposure is commonly between 10 – 20 years of age, but it can happen during childhood.

3. Diet
Epidemiologic studies relating diet, iodine consumption and iodine deficiency to thyroid cancer have not clearly demonstrated a universal link.
4. Genetic Factors
The evidence is growing that genetic factors may play a role in a small percentage of papillary and follicular thyroid carcinomas. Good example of that the well known association between Gardner's Syndrome (familial polyposis) and Cawden's disease (familial goiter and skin hematomas). (19,20)

5. Hereditary Medullary Thyroid Carcinoma
• A manifestation of multiple endocrine neoplasia:
- MEN 2A: Medullary thyroid cancer, pheochromocytoma, parathyroid neoplasia
- MEN 2B: Medullary thyroid cancer, Marfanoid features
- Familial medullary thyroid carcinoma with no other endocrine diseases.

Presenting Signs and Symptoms
Patients with thyroid cancer may have one or more of the following signs and symptoms:
1. Firm hard, painless lump in the front of the neck
2. Swelling in the neck (goiter)
3. Swallowing difficulty (pressure)
4. Hoarseness or change in voice (pressure or invasion of recurrent laryngeal nerve)
5. Coughing with hemoptysis (invasion of trachea)
6. Breathing difficulty (pressure)
7. Unexplained bone fractures (follicular)
8. Severe flushing or diarrhea (medullary)

Screening
Genetic testing can identify members of an affected kindred at birth. (21) It is indicated if a patient with familial MTC has a mutation in the RET proto – oncogene and is then indicated in all first – degree relatives. Those with a positive test, including children, should undergo thyroidectomy. Serum calcitonine measurement should be done during follow up visits. Patients with MEN 2A and MEN 2B should have urinary catechalamines and metanephrines and serum calcium level during follow up.
Although the molecular abnormalities in papillary and follicular thyroid carcinoma are undoubtedly important, no direct clinical application at this time, but it might in the future.

Prognosis and Outcome

For Well Differentiated Thyroid Cancer
Patient under 45 years old have better prognosis, women do better than men. There is linear relationship between tumor size and prognosis, also histological type and extent or local invasion of tumor are significant prognostic factors.

For Medullary Thyroid Cancer
Early therapy has improved survival with MTC in patients with MEN 2A, and has decreased the frequency of distant metastasis. The prognosis of patients with the MEN 2B is substantially worse than patients with MEN 2A but it is also improved by early diagnosis and therapy. Outcome is most favorable in patients with familial MTC without associated endocrine tumors.

Anaplastic Tumors
Dismal prognosis with a median survival of 6 – 12 months.

Prevention

Primary: Eliminate the Risk Factors
Due to the fact that not all the risk factors for thyroid malignancy are known, it is difficult to

conduct complete primary prevention.

Factors like exposure to radiation can be controlled by minimizing x – ray exposure to children and thyroid gland by using shields.

There is a scientific and political responsibility to control nuclear plants and avoid accidents, and early public notification if occurred.

Secondary: Early Detection and Treatment
In case of familial thyroid carcinoma:

- To conduct genetic screening
- And regular check up by physical exam and ultrasound testing. If any lesion is noted in thyroid gland, obtain biopsy.

Treatment includes:
• Surgical resection
• Clearance of lymph nodes, if any
    - + Radioactive Iodine
    - + External beam radiation
• Also thyroids hormone supplements post operatively

Tertiary: Prevent Recurrence and Decrease Mortality
For Well Differentiated Thyroid Carcinoma: Testing for metastasis using thyroid scan and also monitoring the serum thyroglobulin level.

For Medullary Thyroid Carcinoma: The monitoring of serum calcitonin gives very good indicator of treatment, efficacy and outcome.

In advanced thyroid cancer, palliative measures including pain control, protect airway (Tracheostomy), maintains enteral feeding (Gastrostomy).

Recommendations of Prevention and Early Detection of Thyroid Cancer

Primary Preventions:
• Avoid exposure to radiation neither accidental nor excessive medical exposure.
• Although it is not clear risk factor, but it is advisable to avoid low iodine in diet

Early Detection:
• No clinical and cost effective method with proven benefit for screening the population for thyroid cancer in general.

For Medullary Thyroid Cancer

Early Detection in Special Population:
• Calcitonin level in patient with MEN Syndrome for medullary carcinoma

• Close observation for certain benign condition e.g. Hashimoto's disease, Gardner's Syndrome and Cawden's Disease since there is association with thyroid cancer.

The serum calcitonin and serum thyroglobulin can be used as a marker for early detection of recurrence of some of the thyroid cancers.

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