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Mini Review

Thyroid Cancer: Subtypes and Management

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Abstract

The thyroid gland is an important endocrine gland in the body. It produces the hormones T3, T4 and calcitonin. Thyroid cancer is one of the common cancers and women have three times higher incidence than men. There are four different subtypes of thyroid cancers and the prognosis depends on these subtypes. Thyroid cancers are managed by surgery, radiation therapy, chemotherapy and targeted radionuclide therapy.

Keywords: Anaplastic Thyroid Cancer; Follicular Thyroid Cancer; Medullary Thyroid Cancer; Papillary Thyroid Cancer; Targeted Radionuclide Therapy

Abbreviations

ATC: Anaplastic Thyroid Cancer; DTC: Differentiated Thyroid Cancer; FTC: Follicular Thyroid Cancer; MTC: Medullary Thyroid Cancer; NIS: Sodium Iodide Symporter; Tg: Thyroglobulin; T4: Thyroxine; T3: Triodothyronine; TRH: Thyrotropin Releasing Hormone; TSH: Thyroid Stimulating Hormone.

Introduction

Thyroid cancer is one of the common cancers and accounts for about 3-4% of all the cancers reported. Women are three times more prone to thyroid cancer than men. It is the sixth most common cancer in women [1]. The disease starts in the thyroid gland and unless treated can spread to any part of the body. Five year survival rate for thyroid cancer is 98%. The survival is based on many factors including the sub type of cancer and the clinical stage of the disease at the time of diagnosis.

Thyroid gland

Thyroid gland is an endocrine gland having two lobes like a butterfly and spread in the neck below the Adams apple. The average weight of the thyroid gland in adult is approximately about 25 grams. Thyroid gland is responsible for the production of three hormones, triiodothyroine (T_3), thyroxine (T_4) and calcitonin [2]. T_3 and T_4 are the hormones regulating body metabolism. Calcitonin is involved in regulating calcium and phosphate metabolism and has opposite effect as that of the parathyroid hormone (PTH). Hormones T_3 and T_4 are secreted by the follicular cells whereas calcitonin is secreted by the parafollicular cells or the C cells of the thyroid gland.

The thyroid gland accumulates iodine from food through a well defined mechanism involving the sodium iodide symporter (NIS) protein [3]. About one third of the iodine ingested is accumulated in the thyroid gland. The thyroid gland also synthesizes a macro molecule called thyroglobulin (Tg) which is stored in the lumen of the follicular cells. The iodide ions trapped by the thyroid gland is used for iodinating the tyrosine which is part of Tg [4]. Tg acts as a large reserve of iodine in body. The thyroid hormones are synthesized and released as and when needed by the body. The hormone synthesis takes place by the coupling of iodotyrosines. One monoiodotyrosine and one diiodotyrosine combine to form T_3 and two diiodotyrosine combine to form T_4.

The production and release of the thyroid hormones are controlled by a feedback mechanism involving the endocrine glands, hypothalamus, pituitary and thyroid. The hypothalamus gland releases thyrotropin releasing hormone (TRH) which stimulates the pituitary to release thyroid stimulating hormone (TSH). The production and release of these hormones happens through a reverse feedback mechanism [5]. When there is a lower availability of thyroid hormones in blood higher amounts of TRH and TSH will be released. When there is an increase in the concentration of the thyroid hormones in blood, the release of both TRH and TSH gets reduced. Figure 1 illustrates the feedback mechanism.

Figure 1: Negative feedback mechanism involving hypothalamus, pituitary and thyroid gland to regulate the production and circulation of the thyroid hormones in blood.

The parathyroid gland having four small lobes each having the size of a grain of rice and weighing about 30 mg is also in the neck physically close to the thyroid gland. The functions of parathyroid gland are independent of that of thyroid. It produces parathyroid hormone (PTH) responsible for calcium and phosphate metabolism, but has opposite effect as that of calcitonin. Though rare, parathyroid cells can also become cancerous. Parathyroid cancer is not categorized along with thyroid cancer.

Diagnosis of thyroid Cancer

As in all other cancers, the diagnosis of thyroid cancer involves physical examination, laboratory tests and imaging tests [6].

Physical examination

Physical examination of the thyroid, neck and nearby lymph nodes is the first test for the diagnosis of thyroid cancer. Any enlargement in these regions needs further investigations.

Enlargement of thyroid or formation of nodules within the gland is not always cancer. Enlargement of thyroid gland is called goiter. A goiter can also be active making more thyroid hormones than needed. This is called 'toxic goiter' which is also not a case of cancer. This condition leads to hyperthyroidism in patients. When there is deficiency of iodine in the diet, thyroid gland will increase in size to make higher amounts of hormones. This is not cancer and is a situation called hypothyroidism.

There are situations when thyroid gland is enlarged with the formation of a benign tumor. Only 13-15% of goiter is known to be cancerous. Further tests will be needed to understand more about these nodules. Inflammation of the thyroid gland is also possible which is called thyroiditis, a non-cancerous thyroid disorder.

Imaging studies

An ultrasound imaging is preferred for the diagnosis of thyroid cancer. The size of the gland and presence of nodules can be ascertained from this examination. Involvement to nearby areas also can be detected in ultrasound examination. A CT examination is also done at times to get better information about the tumor.

Biopsy

Tissue samples from the enlarged nodules are collected for biopsy analysis. The images obtained from ultrasound examination are used as guidance for collecting the samples from tumor area. A fine needle is inserted to the thyroid gland and the tissue samples are collected from the suspected tumor area. This procedure is called fine needle aspiration cytology (FNAC).

Radioactive iodine uptake (RAIU)

A small dose of radioactive iodine ($Na^{131}I$) of approximately about a 2.5 mCi (37 MBq) is given to the patient. The medicine can be administered as a capsule or as a solution to drink. A whole body nuclear scan under a gamma camera is performed after 48 hours.

The radioactivity taken up at different parts of the thyroid gland as well as other parts of the body is indicative of the diseases. Though more useful to assess the thyroid status whether hypo or hyper active, RAIU is also done in thyroid cancer patients. RAIU is important to assess thyroid cancer metastasis especially post surgery and also to determine the dose of iodine needed.

Tumor markers

Thyroglobulin (Tg), thyroglobulin antibody (TgAb) and calcinotin are the tumor markers measured in blood when a patient is suspected of thyroid cancer. The elevation in the levels of these markers will indicate the presence of thyroid cancer and also the type of thyroid cancer.

Different types of thyroid Cancers

Thyroid cancer seen in all patients is not the same. There are four different types of thyroid cancers documented and the treatment and survival rate of each cancer is different.

Papillary thyroid cancer (PTC)

This is the most common form of thyroid cancer accounting for about 80% of the overall incidence. The cancer originates in the follicular cells of the thyroid gland. These cells are responsible for making the hormones. Solid tumors or nodules develop on the thy-

roid gland. The lymph nodes may be affected. Tg levels will be elevated and can be used as a test for diagnosis as well as follow up of thyroid cancer. The cancer cells will uptake radioactive iodine.

Treatment of PTC

Standard practice is to surgically remove the thyroid gland as well as nearby affected lymph nodes. Once the thyroid gland is removed the patients need to be given thyroid hormone supplementation for life time. Ablation of the remnant cancer cells with radioiodine ($Na^{131}I$) is a standard guideline for the treatment of PTC. This is done in a nuclear medicine department.

Thyroxin will be withdrawn for couple of weeks to enhance the levels of TSH to >30 mIU/ml. Administration of recombinant TSH is followed for patients having difficulty for hormone withdrawal. The radioactivity administered depends on the extent of cancer and physicians follow different protocols. One of the standard protocols is as follows. 100 mCi (3.7 GBq) of ^{131}I is given if remnant cancer is seen only in the thyroid. If soft tissue metastasis is seen the dose is increased to 150 mCi (5.55 GBq) and the dose is further increased to 200 mCi (7.4 GBq) if bone metastasis is also seen.

Radioiodine will accumulate cancer cells anywhere in the body to effectively treat all the metastasis. In order to avoid radiation dose to relatives and public coming in contact, the patient will be kept in isolation for two to three days.

Serum Tg and Tg-Ab levels are measured at intervals to monitor recurrence of the disease. Further treatment with radioactive iodine will be needed if hormonal levels are elevated. A complete cure of papillary thyroid cancer is feasible.

Follicular thyroid cancer (FTC)

About 15% of the thyroid cancers are follicular thyroid cancer. It is more aggressive than papillary thyroid cancer. Metastasis in other organs is more common with follicular thyroid cancer than with papillary thyroid cancer. Lung, bone, brain, liver, and skin are potential sites for metastasis. Serum Tg levels will be elevated during cancer and in recurrence after treatment.

Papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC) are also called differentiated thyroid cancer (DTC).

Treatment

Surgical removal of the thyroid gland and other involved tissues is the treatment for follicular thyroid cancer. Radioiodine therapy is also effective in FTC patients. External beam therapy is done if radioiodine response is poor.

Medullary thyroid cancer (MTC)

This is a rare type of cancer affecting ~3% of the total thyroid cancer patients. The cancer originates in the 'C' cells which are responsible for the production of calcitonin. The cancer is generally detected when there is a lump developed in the neck. Serum calcitonin levels will be elevated and can be used for diagnosis as well as follow up of thyroid MTC. Prognosis is poor compared to papillary and follicular thyroid cancer.

Treatment

The treatment of MTC is surgery, external beam therapy and chemotherapy. Radioiodine therapy is not useful for MTC. Targeted therapy using metaiodobenzylguanidine (^{131}I-MIBG) is practiced for MTC. About 1 mCi (37 MBq) of ^{131}I-MIBG is injected to the patients and whole body scan done starting at 24 hours upto 72 hours to detect cancer. If sufficient uptake is found, a therapy dose of about 100 mCi (3.7 GBq) will be administered. MIBG accumulates in medullary thyroid cancer both in primary and metastatic sites. The patients are kept in isolation ward for couple of days.

Anaplastic thyroid cancer (ATC)

ATC is one of the most aggressive forms of thyroid cancers affecting less than 1% of all the thyroid cancer patients. This generally occurs in elderly patients with more chance for men than women. The cancer grows very fast and spread to the other parts of the neck. Metastasis to other organs is also very common.

Treatment

Treating ATC is more difficult and most patient die within an year after detection of the cancer. Surgery, chemotherapy and radiation therapy are used for the management of ATC. Radioactive iodine therapy is not useful for treating ATC.

Conclusion

Thyroid cancer is one of the common cancers. It affects women more than men. Enlarged thyroid gland could be an indication of thyroid cancer but majority of the enlargements are not malignant. There are four different types of thyroid cancers abridged as PTC, FTC, MTC and ATC. PTC and FTC are together called differentiated thyroid cancer (DTC). The survival rates of the different types of cancers vary. Surgery followed by radioiodine therapy is the guideline for treating DTC. Differentiated thyroid cancers can be completely cured while most ATC patients die within a year of diagnosis. Targeted radionuclide therapy plays an important role in the management of thyroid cancer especially DTC and MTC.

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Conflict of Interest

Nil.

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