



From the Desk of Editor

Dear readers!

Thyroid cancer is a disease in which malignant cells arise from the tissues of the thyroid gland. Thyroid Cancers account for about 14,000 new cases in india. Thyroid malignancies are divided into papillary carcinomas (80%), follicular carcinomas (10%), medullary thyroid carcinomas (5-10%), anaplastic carcinomas (1-2%) , primary thyroid lymphomas (rare) and primary thyroid sarcomas (Rare) .

Thyroid carcinoma most commonly manifests as a painless, palpable and solitary thyroid nodule. Factors that may increase the risk of thyroid cancer include female sex, age, exposure to high levels of radiation and certain inherited genetic syndromes etc. Most thyroid cancers may be cured, especially those have not metastasized to distant parts of the body. The primary management for most patients with thyroid cancer is surgical removal of the entire thyroid gland. The patients with cancer likely to recur may be helped by giving Radioactive iodine (RAI) after surgery. Targeted drugs, such as kinase inhibitors, anti-angiogenesis drugs and other targeted drugs may work in some cases when standard chemotherapy drugs do not work and they also have less severe side effects.

With regards

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Thyroid Cancer

Thyroid Cancer Risk Factors:

The following are associated with higher likelihood of developing thyroid cancer:

- Female gender
- History of goiter or thyroid nodules
- Family history of thyroid cancer
- Low dietary iodine
- Medical radiation or ionizing radiation exposure during childhood
- Age over 45: important determinant of thyroid cancer stage and associated with poor outcomes

Symptoms Associated with Thyroid Cancer:

Thyroid cancer may not cause early symptoms and is sometimes found during a routine physical exam. Some possible symptoms are as follows:

- A lump in the neck
- Trouble breathing
- Trouble swallowing
- Hoarseness
- Trouble swallowing
- Hoarseness
- Swollen lymph nodes
- Persistent pain in the throat or neck

Diagnosis:

Most thyroid nodules are detected during routine physical examinations or a doctor evaluation for a different purpose. There is a wide differential diagnosis for thyroid nodules, which are present in a spectrum of diseases.

Possible steps in evaluating a nodule may include the following:

- Physical examination, including a laryngeal exam
- Neck ultrasound.
- Fine needle aspiration (FNA) biopsy, often under ultrasound guidance: It is the most accurate and effective way to determine if a nodule is benign or malignant without surgery.

Well-differentiated thyroid cancer is generally managed by near total thyroidectomy. Post-thyroidectomy residual (remnant) thyroid tissue needs to be ablated with radioactive 131-iodine to facilitate followup. It has also been shown that ablation of remnant tissues reduces the frequency of recurrence

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and may reduce mortality. High levels of thyroid stimulating hormone (TSH) is essential for effective ablation of remnant tissue as it stimulates iodine uptake by thyroid cells. Traditionally this high level has been achieved by withholding thyroxine therapy for 4-6 weeks after thyroidectomy, causing endogenous TSH to rise. However, since the patient becomes hypothyroid there can be a severe negative impact on the patient's quality of life. A highly purified, recombinant form of the naturally occurring human protein TSH, rhTSH, has been developed and used as an alternative to withholding thyroxine as pre-treatment for radioiodine ablation. After thyroidectomy and I^{131} ablation of residual thyroid tissue, follow-up for patients with well differentiated thyroid cancer has traditionally consisted of periodic radioiodine whole body scanning (WBS) and serum thyroglobulin (Tg) testing.

Surgical Management of well Differentiated Thyroid Cancer

The term Differentiated Thyroid Cancer (DTC) is used for the tumors arising from the cells lining the thyroid follicles which includes papillary (PTC), follicular (FTC) and Hurthle cell Carcinoma (HCC). While surgical resection has remained the gold standard for their treatment, controversies still exist regarding the extent of surgery because of indolent nature of majority of these tumors. There has also been many changes in the surgical approach to thyroidectomy as a result of instrument innovations, such as harmonic scalpel, Liga Sure, intraoperative nerve monitoring, application of minimally invasive surgery such as use of video assisted thyroidectomy and advent of robotic surgery.

Surgical Management

The extent of surgical resection recommended for treatment of DTC includes thyroid lobectomy/hemithyroidectomy, near total or total thyroidectomy with or without prophylactic central node dissection. The study of various prognostic factors has enabled proper risk stratification. These include age at diagnosis, tumor size, grade of tumor, extra thyroidal extension, completeness of resection, lymph node involvement, multi centricity and presence of distant metastasis. Thyroid lobectomy/ hemi-thyroidectomy should be reserved for very small tumors < 1 cm, confined to one lobe with a favourable Histology. Therapeutic lymph node dissection is recommended as and when there is clinical and/ or cytological evidence of lymph node metastasis.

Medullary Thyroid Cancer (MTC)

- MTC are rare neuroendocrine tumors arising from parafollicular / C (calcitonin) cells around

- 20-25% present as part of hereditary spectrum, the remaining 75-80% presenting in sporadic fashion.
- The hereditary tumors are transmitted as a part of MEN2 syndrome either alone (FMTC) or as a part of combination spectrum of MEN2A/ 2B2. R E T (Rearranged during Transfection) is a protooncogene located on locus 10q 11.2 and it's the gain in function mutations associated with this gene, transmitted in an autosomal dominant fashion, which give rise to various phenotypes of hereditary MTC related to MEN2 syndrome.
- After cytological diagnosis of MTC, both serum calcitonin and CEA measurements, along with genetic RET mutation testing, are recommended.
- The presence of pheochromocytoma and hyperparathyroidism should be excluded in cases of hereditary MTC.

Biochemical Evaluation of MTC

- Measurement of calcitonin carries both diagnostic as well as prognostic values and helps defining timing of surgical intervention.

Surgical Treatment

- Surgical treatment is the only definitive treatment for MTC since the tumor cells do not concentrate radioactive iodine.
- Therefore no role of postop RAI therapy for pure MTC.

Therapeutic RAI (I^{131}) Treatment:

Recommended for tumors found on examination, by imaging, or by increased Tg levels if unresectable. Tumor should concentrate I^{131} , and palpable neck disease should be resected before RAI treatment. For patients with RAI-responsive residual tumors (suspected or proven):

- RAI treatment is recommended (100-200 mCi); upper limit 600 mCi
- Should be followed by post-treatment whole-body I^{131} imaging

Systemic Chemotherapy of Thyroid Cancers

- Cytotoxic chemotherapeutic combinations (most commonly based on doxorubicin) have a short lasting and low response rate.
- Currently only two orally administered TKIs, Vandetanib and cabozantinib have the potential to provide significant and durable response.
- Other TKIs, though not FDA approved but with therapeutic potential against MTC, are sunitinib, pazopanib.

Treatment of Iodine Refractory Thyroid Cancer

- Some patients may still progress after RAI



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- They are labelled as Radi-iodine Refractory Differentiated Thyroid Cancer (RR-DTC).

Management of RR-DTC:

- Levothyroxine treatment: serum TSH <0.1 mU/L
- Local treatments when needed: surgery, external radiation, radiofrequency, or cryoablation
- Stable disease: follow-up
- Targeted therapy as first line
- DTC is highly treatable and frequently curable with surgery, post operative radioactive iodine (RAI) treatment in some cases, and thyroid-stimulating hormone (TSH) suppression.
- Systemic therapies represent an important treatment option for differentiated thyroid tumors that are nonresectable, not responsive to RAI, and not amenable to EBRT.
- Sorafenib is the first targeted systemic agent to demonstrate benefit in RAI-refractory thyroid cancer.
- Lenvatinib has also demonstrate promising activity for patients with RAI-refractory DTC.
- Systemic therapy should be used in patients with advanced symptomatic disease, relatively large tumor burden, and demonstrable disease Progression.

Targeted systemic agents may have significant side

effects. To avoid premature or unnecessary withdrawal treatment, thus depriving patients of the potential for life-prolonging benefits, side effects should be proactively and aggressively managed.

Need for newer therapies:

Until recently, the treatment options were limited for patients with metastatic disease that did not respond to the above treatments and for those with medullary and anaplastic thyroid cancer. Despite optimal therapy, up to 25% of patients will have recurrent disease, with 7% distant recurrence, and importantly over 30% of this distant metastasis will be RAI-non-avid.

Lenvatinib: It is a once-daily oral capsule used for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC). The most common side effects with lenvatinib are hypertension, diarrhoea, decreased appetite and weight, tiredness, nausea, proteinuria, stomatitis, vomiting, dysphonia, headache and palmar-plantar erythrodysesthesia.

Conclusion

The advent of targeted systemic therapies represents a major advance for patients with RAI refractory DTC, a disease for which there were previously few treatment options.

Activities of SoMex

1. SoMex organized CME on "Immuno Oncology treatment in various Malignancies" on 26th April 2019 (Dr. Vinit Talwar, Medical Director, Rajiv Gandhi Cancer Institute New Delhi and Dr. Purvish M. Parikh, Mumbai were chief speakers)
2. SoMex will organize "3rd Neuro Critical Care Update 2019" at Jaipur on 29th & 30th June 2019 (Organizing Secretary Dr. Sunit Shah). For more details visit <http://www.neuroupdatejaipur.in>
3. SoMex will organize "3rd Precision Oncology and Annual International Breast Cancer conference 2019" at Jaipur from 11-13 October, 2019 (Organizing Secretary Dr. Sandeep Jasuja). For more details visit <http://www.precisiononcologyindia.com>

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