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Medical Guidelines

Thyrotoxicosis- Diagnostic Approach

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Thyrotoxicosis is a clinical condition caused by excessive thyroid hormone action in tissues, manifested by various physiological, clinical, and biochemical findings. The condition known as Hyperthyroidism is a type of thyrotoxicosis caused by when thyroid glands abnormally have high rates of thyroid hormone synthesis and secretion, leading to its various clinical manifestations. There are numerous etiologies, symptoms, and potential treatment options for thyrotoxicosis. A precise diagnosis of thyrotoxicosis and its specific etiology is necessary for effective patient care and a better prognosis.

In general, the following pathophysiology may lead to thyrotoxicosis:

1. Trophic factors excessively stimulate the thyroid gland
2. Autonomous release of excess thyroid hormone leading to constitutive activation of thyroid hormone synthesis and secretion
3. Autoimmune, infectious, chemical, or mechanical insult leading to already stored Thyroid hormones being released excessively into circulation.
4. An extra thyroidal source of thyroid hormone, which may be either endogenous or exogenous

Hyperthyroidism is generally considered overt or subclinical, depending on the biochemical severity of the Hyperthyroidism, although the disease represents a continuum of overactive thyroid function. Overt Hyperthyroidism is defined as a sub-normal (usually undetectable) serum thyrotropin (TSH) with elevated serum levels of triiodothyronine (T3) and free thyroxine estimates (free T4). Subclinical Hyperthyroidism is a low or undetectable serum TSH with values within the normal T3 and free T4 reference range. Excessive and subclinical disease may lead to characteristic signs and symptoms, although subclinical Hyperthyroidism is usually milder.

Thyroid hormone affects almost every human tissue and organ system. Some of the most profound effects of increased thyroid hormone levels occur within the cardiovascular system. Partially treated or untreated thyrotoxicosis is associated with many clinical features.

The evaluation further includes taking a detailed medical history. Symptoms include weight loss, increased appetite, palpitations, anxiety, tremors, heat intolerance, increased sweating, changes in bowel movements, or

Classification of etiology of thyrotoxicosis		
Associated with Hyperthyroidism		
01	Excessive thyroid stimulation	Graves' disease (GD), Hashimoto s thyrotoxicosis, pituitary thyrotoph adenoma, pituitary thyroid hormone resistance syndrome Trophoblastic tumours producing hCG
02	Thyroid nodule with autonomous function	Thyroid solitary nodule, Toxic multinodular goitre, Thyroid cancer
Not associated with Hyperthyroidism		
03	Thyroid inflammation	Silent and postpartum thyroiditis Sub-acute thyroiditis
04	Exogenous thyroid hormones	Overtreatment with thyroid hormones Thyrotoxicosis facticia
05	Ectopic thyroid tissue	Metastatic thyroid carcinoma Struma ovarii

menstrual irregularities. History also includes a family history of thyroid disorders and past medical conditions or treatments.

A thorough physical examination is needed to check for signs of Hyperthyroidism, measurement of Pulse rate, atrial fibrillation, blood pressure, body temperature, respiratory rate, and body weight. Thyroid size, symmetry, tenderness, and nodularity should also be assessed along with cardiac, pulmonary, and neuromuscular function, and the presence or absence of eye signs, peripheral edema, or warm moist skin, hair loss, fine hand tremors, pretibial myxedema should also be checked in a thyrotoxic patient.

Biochemical testing for thyroid Hormones:

Thyroid-stimulating hormone (TSH) should be used as an initial screening test since it has the highest sensitivity and specificity of any blood test used to evaluate suspected thyrotoxicosis. And is easily available here. However, when thyrotoxicosis is highly suspected, serum TSH, free T4, and total T3 are evaluated at the initial evaluation, which increases diagnostic accuracy. If the pituitary-thyroid axis remains intact, there is an inverse log-linear relationship between free T4 and TSH, which causes substantial variations in serum TSH concentrations when free T4 levels are minimal. For determining thyroid hormone excess, serum TSH values are far more sensitive than direct thyroid hormone assays. Serum-free T4, T3, or both increases in overt Hyperthyroidism and TSH levels are below normal.

Only serum T3 may be increased in moderate Hyperthyroidism, while serum TSH will be low or undetectable. Serum T4 and free T4 may both be normal. These laboratory results, known as T3-toxicosis, might be the first signs of Hyperthyroidism seen in Graves' disease or an autonomous thyroid nodule. Protein binding impacts total T3 readings much like it does with T4. Assays for determining free T3 are less reliable and have less widespread validation than those for estimating free T4. Therefore, total T3 measurement is generally preferred in clinical practice over free T3.

Without a TSH-producing pituitary adenoma, thyroid hormone resistance, or spurious assay results due to interfering antibodies, a normal serum TSH level precludes the diagnosis of thyrotoxicosis.

A few items interfere with the thyroid hormone assays, which should be kept in mind while interpreting, like ingestion of biotin, binding protein disorders, heterophil antibodies, and the effect of many drugs, amiodarone, etc.

Establishing the cause of thyrotoxicosis

The etiology of thyrotoxicosis should always be determined. If the diagnosis is not evident based on the patients clinical presentation and initial biochemical evaluation, further diagnostic testing is indicated and can include, depending on available resources and expertise.

(1) Determination of the radioactive iodine uptake (RAIU)

(2) Measurement of TSH receptor antibody (TRAb)

(3) Measurement of thyroidal blood flow on ultrasonography.

A 123I or 99mTc pertechnetate scan should be obtained when the clinical presentation suggests a Thyroid adenoma (TA) or Thyroid multinodular goitre.

Radioactive iodine uptake scan (RAIU)

The concentration of given RAI in thyroid tissue after a predetermined amount of time, often 24 hours, is measured by RAIU. Pertechnetate, concentrated by the thyroid but not organified, is used in technetium uptake measurements. The percentage of administered technetium taken up by the thyroid after a set amount of time, typically 20 minutes, is measured by a technetium (TcO4) uptake.

These Uptake measurements are indicated when the diagnosis is in query, and it distinguishes various etiologies of thyrotoxicosis having elevated or normal uptake over the thyroid gland from those with near-absent uptake.

Thyroid scans can have different patterns. The pattern of RAIU in GD is diffuse if no coexistent nodules or fibrosis are present. The uptake pattern in a patient with a single TA generally shows focal uptake in the adenoma while surrounding and contralateral thyroid tissue suppressed uptake. The image in TMNG demonstrates multiple areas of focal increased and suppressed uptake. In

Thyrotoxicosis associated with a normal or elevated RAI uptake over the neck
Graves Disease
Thyroid adenoma or TMNG
Trophoblastic disease
Resistance to thyroid hormone (T3 receptor b mutation, THRBb)
TSH-producing pituitary adenomas
Thyrotoxicosis associated with a near-absent RAI uptake over the neck.
Acute thyroiditis
Subacute (granulomatous, de Quervain's) thyroiditis Palpation thyroiditis
Painless (silent) thyroiditis
Amiodarone-induced thyroiditis
Factitious ingestion of thyroid hormone
Iatrogenic thyrotoxicosis
Struma ovarii
Extensive metastases from follicular thyroid cancer

extensive autonomy, the image may be difficult to distinguish from that of GD. GD and nontoxic nodular goitre may coincide, resulting in positive TRAb levels and a nodular pattern on ultrasound or heterogeneous uptake images. The RAIU will be near zero in patients with painless, postpartum, or sub-acute thyroiditis; factitious ingestion of thyroid hormone; or recent excess iodine intake.RAIU scans are contraindicated in pregnant and breastfeeding mothers.

TRAb (TSH receptor antibody)

TRAb is cost-effective and has 70% to 100% sensitivity. If positive, TRAb confirms the diagnosis of the most frequent cause of thyrotoxicosis, Graves' disease. However, if negative, it cannot differentiate between alternative etiologies and can be negative in cases of extremely mild GD. The therapy chosen may have an impact on diagnostic testing.

Ultrasonography Neck

It is done mostly when thyroid uptake scans are contraindicated. It is mostly used for thyroid size, to differentiate cystic lesions from solid ones and to see radiological features of malignancy like micro calcification etc. Ultrasonography with colour flow Doppler can distinguish thyroid gland hyperactivity from destructive thyroiditis.

FNAC fine needle aspiration cytology (FNAC)

FNAC of thyroid tissue followed by histological diagnosis helps for the most accurate diagnosis of thyroid nodules. It has 85%percent diagnostic accuracy.

Computed tomography (CT scan) and Positron emission tomography (PET) scan

CT is used mostly for retrosternal and retro tracheal extension evaluation, and PET scans are usually for thyroid cancer follow-ups.

Additional tests Like ESR, CRP and Thyroglobulin for Thyroiditis and CBC, Serum Calcium and Alkaline phosphate may be required.

It is important to remember that the evaluation of Hyperthyroidism can be complex, and the specific tests ordered may vary depending on the thyrotoxic patient's symptoms, medical history, and physical examination findings. If you suspect thyrotoxicosis, a methodological approach for diagnosis and evaluation is recommended.

References

1. RossDouglas S, BurchHenry B, CooperDavid S, Carol G, Luiza M, RivkeesScott A, Ann S, StanMarius N, WalterMartin A. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. Thyroid. 2016;26(10):1343–421.
2. Wass J, Owen K. Oxford Handbook of Endocrinology and Diabetes. OUP Oxford. 2014