Status of Ocular Surface in Thyrotoxicosis

Thesis

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وأنزل الله عليك
الكتاب والحكمة
وعلَّمَكَ مَا لَمْ تَكُن
تَعْلَمُ وكَانَ فَضْلُ
اللَّهِ عَلَيْكَ عَظِيماً
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Eman Mahmoud Ahmed

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List of Abbreviations

µm	micrometer
2ry thyrotoxicosis	Secondary thyrotoxicosis
CALT	Conjunctival Associated Lymphoid Tissues
CIC	Conjunctival Impression Cytology
DES	Dry Eye Syndrome
Fig.	Figure
GD	Graves' disease
IC	Impression Cytology
LG	Lacrimal Gland
MALT	Mucosal Associated Lymphoid Tissue
mg	Milligram
mm	Millimeter
MMC	Mitomycin C
mU / L	milli Unit / Litter
OGD	Ophthalmic Graves' Disease
OSDI	Oculars Surface Disease Index
OSSN	Oculars Surface Squamous Neoplasia
PAS	Periodic Acid Schiff
P-Value	Probability
r	Pearson's Correlation Coefficient
RT - PRC	Reverse Transcriptase - Polymerase Chain Reaction
SD	Standard deviation
Sec	Second
SLK	Superior Limbic Keratoconjunctivitis
T3	Triiodothyronine
T4	Thyroxin
TFBUT	Tear Film Break Up Time
TR – Abs	Thyroid Receptors - Antibodies
TSH	Thyroid Stimulating Hormones
X2	Chi – square

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Thyrotoxicosis

Thyrotoxicosis, the disease which results from the biochemical and physiologic effects of excess thyroid hormone regardless of cause, is one of the more common endocrine disorders. By definition, hyperthyroidism is a term restricted to situations in which the thyroid gland is responsible for overproducing thyroid hormone. Arbitrarily the causes of thyrotoxicosis can be differentiated into those associated with a high uptake on radioactive iodine or technetium scanning (most commonly Graves' disease (GD)) and those with a low uptake (Table 1) ***(Elston and Conaglen, 2005).***

Thyrotoxicosis can be associated with hyperthyroidism or can also occur in the absence of increased thyroid hormone secretion. The most common cause of thyrotoxicosis is GD, in which autoantibodies bind to and stimulate the thyrotropin (also called thyroid stimulating hormone TSH receptors found on the surface of thyroid follicular cells, which results in excess production of T3 and T4. The next most common cause is autonomous overproduction of thyroid hormones by one (solitary toxic adenoma) or more (toxic multinodular goiter) nodules within the thyroid. The frequency of these causes varies with iodine intake ***(Laurberg et al., 2001).***

Two main hormones are synthesised and released by the thyroid: thyroxin T4 and triiodothyronine T3. T4 is a prohormone and is present in higher concentrations than T3, whereas T3 is biologically active through interaction with specific nuclear receptors that are present in nearly all tissues.T3 regulates energy production and metabolic rate and has profound effects on cardiac, hepatic, and neuromuscular function, as well as on fetal and postnatal growth and development ***(Franklyn and Boelaert, 2012).***

Prevalence and incidence:

The prevalence and incidence of thyroid disorders is influenced primarily by sex and age. Thyroid disorders are more common in women than men, and in older adults compared with younger age groups ***(DeRuiter, 2002).***

AETIOLOGY/ RISK FACTORS:

In general, thyrotoxicosis can occur by different factors. The thyroid is inappropriately stimulated by trophic factors or there is constitutive activation of thyroid hormone synthesis and secretion leading to autonomous release of excess thyroid hormone. The thyroid stores of preformed hormone are passively released in excessive amounts owing to autoimmune, infectious, chemical, or mechanical insult, or there is exposure to extra-thyroidal sources of thyroid hormone, which may be either endogenous (struma ovarii,

metastatic differentiated thyroid cancer) or exogenous (factitious thyrotoxicosis) ***(Bahn et al., 2011).***

Smoking is a risk factor, with an increased risk of both GD and toxic nodular goiter. In areas with high iodine intake, GD is the major cause, whereas, in areas of low iodine intake, the major cause is nodular goiter. A correlation between diabetes mellitus and thyroid dysfunction has been described. In a Scottish population with diabetes, the overall prevalence of thyroid disease was found to be 13%, highest in women with type 1 diabetes (31%). As a result of screening, new thyroid disease was diagnosed in 7% of people with diabetes (hyperthyroidism in 1%) ***(Nygaard, 2010).***

Table (1): Causes of thyrotoxicosis.

Thyrotoxicosis with high radioiodine Uptake	**Thyrotoxicosis with low radioiodine Uptake**
Autoimmune – Graves' disease Autonomous thyroid tissue – Toxic multinodular goiter – Solitary toxic adenoma TSH-mediated – TSHoma (rare) HCG-mediated – Hyperemesis gravidarum – Hydatidiform mole/ choriocarcinoma (rare) – Testicular tumors (rare)	Thyroiditis – Subacute – Postpartum – Drug-induced e.g. interferon, amiodarone – Radiation Autonomous thyroid tissue with iodine load e.g. amiodarone/x-ray contrast Excessive exogenous thyroid hormone intake Ectopic thyrotoxicosis – Struma ovarii (ectopic thyroid tissue) (rare) – Metastatic follicular cancer with with functioning metastases (rare)

(Elston and Conaglen, 2005)

Clinical features of thyrotoxicosis:

Presenting symptoms resulting from excess metabolic activity include tiredness, heat intolerance, unexplained weight loss, excess sweating, palpitations, tremor and irritability.

Older patients with 'apathetic thyrotoxicosis may present predominantly with weight loss, anorexia, muscle weakness, depression and lethargy.

Occasional patients may present with sudden onset profound muscle weakness (which may progress to a flaccid tetraparesis), associated with severe hypokalemia, which resolves completely on restoration of the serum potassium ***(Elston and Conaglen, 2005).***

Ocular involvement might be present in GD; other diverse complications include anemia (which has a reported prevalence in thyrotoxicosis of 22%) ***(Gianoukakis et al, 2009).***

Investigations:

All patients with known or suspected hyperthyroidism should undergo a comprehensive history and physical examination, including measurement of pulse rate, blood pressure, respiratory rate, and body weight. In addition, thyroid size; presence or absence of thyroid tenderness, symmetry, and nodularity; pulmonary, cardiac, and neuromuscular function; and

presence or absence of peripheral edema, eye signs, or pretibial myxedema should be assessed ***(Ventrella and Klein, 1994).***

Biochemical evaluation

Serum TSH measurement has the highest sensitivity and specificity of any single blood test used in the evaluation of suspected hyperthyroidism and should be used as an initial screening test ***(de los santos et al., 1989).***

However, when hyperthyroidism is strongly suspected, diagnostic accuracy improves when both a serum TSH and free T4 are assessed at the time of the initial evaluation. The relationship between free T4 and TSH (when the pituitary-thyroid axis is intact) is an inverse log-linear relationship; therefore, small changes in free T4 result in large changes in serum TSH concentrations. Serum TSH levels are considerably more sensitive than direct thyroid hormone measurements for assessing thyroid hormone excess ***(Spencer et al., 1990).***

In overt hyperthyroidism, usually both serum free T4 and T3 estimates are elevated, and serum TSH is undetectable; however, in milder hyperthyroidism, serum T4 and free T4 estimates can be normal, only serum T3 may be elevated, and serum TSH will be <0.01 mU/L (or undetectable) ***(Bahn et al., 2011).***