



CLINICAL STUDY OF THYROID RELATED ORBITOPATHY WITH SPECIAL REFERENCE TO LID RETRACTION AND ITS MANAGEMENT (Z - MYOTOMY)

Ophthalmology

Dr. S. Nehru.*

M.S., D.Ophthal., Chief Civil Surgeon, Dept of ophthalmology, Govt Kallaikurichi Medical College Hospital, Kallaikurichi. *Corresponding Author

Dr. N. Cibee.

M.S.Ophthal., Dept of ophthalmology, Melmaruvathur Adhiparasakthi Institute Of Medical Sciences And Research Centre.

ABSTRACT

Introduction: Graves' orbitopathy has been known for close to 200 years. Graves' disease with its complex manifestations and unpredictable clinical course has three clinical entities 1. hyperthyroidism associated with diffuse hyperplasia of the thyroid gland 2. infiltrative ophthalmopathy 3. infiltrative dermopathy (localized pre-tibial myxoedema).

Aim Of The Study: To study in detail about various presentations of thyroid Related orbitopathy with special reference to lid retraction and its management (Z - MYOTOMY).

Materials And Methods: Thyroid orbitopathy was diagnosed in 30 patients who attended Regional Institute of Ophthalmology and Government Ophthalmic Hospital between May 2004 and August 2005 and they were subjected for detailed study.

Results: Thirty cases of TRO who attended our special clinic were subjected for detailed study. with females are more affected i.e., 70% and 63.6% showed bilateral involvement with 70% of them having axial proptosis. Symptoms of thyrotoxicosis were present in almost all cases. More than 55% of pt. had only mild proptosis and 93% of TRO has associated thyroid swelling also. 20 patients were put on antithyroid drugs while 6 on thyroxine. marginal Z myotomy was carried out in 5 patients.

Conclusion: Most of the patients with TRO are females belonging to 30 – 50 yrs of age. Though many of them had toxic thyroid symptoms and swelling, even enlargement of EOM on USG, 'B' scan orbit and CT scan the proptosis was mostly minimal. Those with proptosis required systemic steroids for arresting progression of ophthalmic disease. Simple procedure of marginal 'z' myotomy gives good acceptable cosmetic results especially in females.

KEYWORDS

Graves Orbitopathy, Proptosis, Thyrotoxicosis, 'Z' Myotomy

INTRODUCTION

Graves' orbitopathy has been known for close to 200 years. Since its first description Graves' disease with its complex manifestations and unpredictable clinical course has fascinated and frustrated internists, surgeons, ophthalmologists and immunologists alike Rootman refers to the orbital changes and ocular abnormalities as Graves' orbitopathy because it is an orbital rather than an ophthalmic process.

Mc Kenzie has given the most pragmatic current definition of Graves' disease.

A multisystem disorder of unknown etiology characterized by one or more of three clinical entities

1. hyperthyroidism associated with diffuse hyperplasia of the thyroid gland
2. infiltrative ophthalmopathy
3. infiltrative dermopathy (localized pre-tibial myxoedema).

The onset, course, severity and relationship to the systemic disease is variable. Grave's orbitopathy usually occurs in association with hyperthyroidism but some patients with typical features of Grave's orbitopathy may be hypothyroid or even euthyroid.

Hyperthyroidism – Also known as thyrotoxicosis, is a state in which there is an excess of circulating thyroid hormones, namely T3 or T4. It may be primary or secondary. Primary thyrotoxicosis is also known as Graves' disease. The gland is diffusely enlarged and there are signs of a hypermetabolic state. The eyes may or may not be involved. Secondary thyrotoxicosis occurs when a patient with a previously abnormal gland (eg. Nodular goiter) assumes a hyper functional state.

OPHTHALMIC FEATURES OF HYPERTHYROIDISM

Eye	Stare, gritty sensation, increased lacrimal secretion, diplopia, decreased colour and contrast vision, dry eyes, increased sensitivity to light, angry looking eyes, puffy lids.	Lid retraction, lid lag, chemosis, proptosis (exophthalmos), infiltrative ophthalmopathy, ocular muscle paresis, exposure keratopathy
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PATHOLOGY

The extra-ocular muscles are infiltrated by round cells i.e. lymphocytes, plasma cells and occasional mast cells. There is deposition of hydrophilic mucopolysaccharides, and the formation of collagen causes degenerative changes in the extra ocular muscles thus

reflecting target effects of the disease on the orbital myocyte and the endomysial fibroblast.

IMMUNOLOGY

The Hypothesis put forth for the pathogenesis in the past

- a. Warthin's concept of a thymico- lymphatic body, which is a consequence rather than a cause.
- b. Hyper function of the anterior pituitary, with release of excess thyroid stimulating hormone (thyrotropin) is disproved. Since in primary myxoedema also thyroid stimulating hormone increases, but there is no exophthalmos.
- c. Exophthalmos producing substances (EPS), distinct from thyrotropin

Humoral Evidence – Long Acting Thyroid Stimulator (LATS) an IgG immunoglobulin, only 50-60% of Graves' thyrotoxic patients had detectable levels of LATS

Thyroid – stimulating immunoglobulins (TSI) have now replaced LATS as the suspect humoral factor. These IgG immunoglobulins, undetected by the LATS assay, have been found in the sera of over 90% of Graves' thyrotoxic Patient.

Classification of Eye Changes of Grave's Disease – Werner's NOSPECS

Class	Grade	Suggestion for Grading
0	No physical signs or symptoms	
I	Only signs – limited to upper lid retraction, lid lag	
II	Soft Tissue involvement with symptoms and signs	
	0	- Absent
	A	- Minimal
	B	- Moderate
	C	- Marked
III	Proptosis	
	0	- Absent
	A	- 3-4 mm increase over upper normal
	B	- 5-7 mm increase over upper normal

	C	- 8 mm or more increase
IV	EOM Involvement	
	0	- Absent
	A	- Limitation of motion at extremes of gaze
	B	- Evident restriction of motion
	C	- Fixation of globe or globes
V	Corneal Involvement	
	0	- Absent
	A	- Stippling of cornea
	B	- Ulceration
	C	- Clouding, necrosis, perforation
VI	Sight Loss Caused by Optic Nerve Involvement	
	0	- Absent
	A	- Disc pallor or chocking or visual field defect; vision 20/20 – 20/60 (6/6 – 6/18)
	B	- Vision 20/80 – 20/200 (6/24 – 6/60)
	C	- Vision <20/200 (<6/60) (blindness – failure to perceive light)

Van Dyk proposed an expansion of Werner's class II soft tissue changes with the mnemonic **RE LIE F**.

R – Resistance to retro displacement of the eye.

E – Edema of the conjunctiva

L – Lacrimal gland enlargement

I – Injection of conjunctiva

E – Edema of lids

F – Fullness of lids

Course of the disease

Thyroid ophthalmopathy is typically a self-limited process that becomes quiescent within 3 to 5 years of its onset. Spontaneous remissions and exacerbations have been reported in thyroid ophthalmopathy in the pre-treatment era.

- Eyelid retraction may improve in upto 50% of the patients.
- Proptosis usually remains stable once it reaches its maximum.
- Ocular motility can also vary with time, and unless vision is threatened, patients should be followed up for periods of upto 6 months to ensure stability before therapeutic intervention.
- Visual loss – As many as 10% of patients with thyroid eye disease develop severe, vision threatening ophthalmopathy.

Patients with optic neuropathy may show spontaneous improvement. In one analysis of 32 untreated eyes, 19% had final visual acuity ranging from counting fingers to no light perception.

LABORATORY EVALUATION

1 TSH	suppressed
2 Total serum T3 and T4 levels and the Thyroid Hormone – Binding Ratio (THBR), which is measured as T3 resin uptake	all are increased.
3 ¹³¹I uptake – measured after 2 hours and after 24 hours	Increased uptake

IMAGING IN THYROID RELATED ORBITOPATHY

1. The Ultra-sonography can demonstrate subtle changes occurring in extra ocular muscle and orbital fat.

2. **Computed Tomography in Thyroid Related Orbitopathy:** About 90% of patients with thyroid orbitopathy will have bilateral computed tomography abnormalities, even if the clinical involvement is unilateral

Inferior rectus > Medical rectus > Superior rectus > lateral rectus.

Managing Graves' Orbitopathy

Unless there is an immediate threat to vision, surgical treatment should be postponed until the active phase of the disease subsides so as to avoid surgical over correction. Sight threatening corneal exposure or optic neuropathy may require immediate surgical intervention

regardless of the state of the disease.

Treatment Of Hyper Thyroidism

1. **Anti-thyroid drugs** 2. **Oral Radioactive Iodine Therapy** 3. **Surgical Thyroidectomy** – It is reserved for patients whose disease cannot be controlled with medical treatment or for those who will not tolerate or accept radioablation.

Medical Management of Orbitopathy

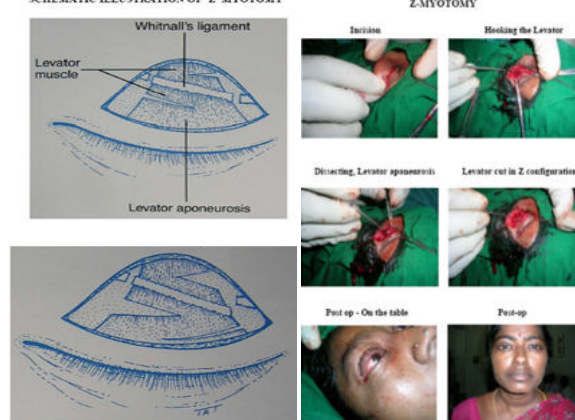
1. **Steroid Indications:** optic neuropathy, acute orbital inflammation
2. **Immunosuppressive Therapy**– agents like cyclosporine, cyclophosphamide, methotrexate and azathioprine are reserved for rare patients who fail or cannot undergo standard treatment with steroids or radiation or surgery. 3. **Orbital Irradiation** Radiation typically has no effect on chronic stable Grave's orbitopathy. Dose – 2000 cGy total dose in small fractions, over a period of 2 weeks to minimize the undesirable side effects.

Surgical Management – Multiple surgical procedures involving the orbit, muscles and eye lids are often required to correct the functional consequences of Grave's ophthalmopathy. An optimal result is likely if the disease has been quiescent for at least 6 months.

Sequence of surgery – orbital decompression, prior to strabismus surgery and finally eyelid surgery.

Surgeries are mainly to decrease the Exophthalmous or to decrease the starring look due to lid retraction. There are newer modalities for treating lid retraction like 'Z' Myotomy which gives a good cosmetic result especially in female patients.

SCHEMATIC ILLUSTRATION OF 'Z' MYOTOMY



MATERIALS AND METHODS

Thyroid orbitopathy was diagnosed in 30 patients who attended Regional Institute of Ophthalmology and Government Ophthalmic Hospital between May 2004 and August 2005 and they were subjected for detailed study.

Inclusion Criteria

1. Patients with proptosis of thyroid origin 2. Patients with lid retraction.

Exclusion Criteria

1. Patients with multiple endocrine abnormalities were not included in the study.
2. Patients with proptosis due to cystic lesions were not included.
3. Patients with suspicious malignant thyroid disease were not included.
4. Bilateral proptosis due to any other cause.

Patients Evaluation

All patients who were included in the study were worked up in the following manner

1. Detailed History

2. Complete ocular examination

3. Thyroid status evaluation which included

- Thyroid function tests from endocrinology Department
- Radiological investigations like X-ray orbit and CT scan
- USG neck for thyroid mass
- 'B' scan for EOM enlargement / to ruled out optic nerve compression.

- Radio iodine uptake study using I 131 (or) Tc 99m Perchnetate
- FNAC/ Biopsy of the thyroid gland.

RESULTS & ANALYSIS

Total numbers of 30 cases reported to our hospital with thyroid eye disease were studied. Their clinical profiles were analysed for the following parameters.

1	Age incidence	No of patients		
	16- 30	36.6%		
	31-40	46.6%		
	41-60	16.6%		
2	Sex incidence			
	Male	9		
	female	21		
3	Laterality of Proptosis			
	Bilateral	22		
	Unilateral	8		
4	Direction of Proptosis			
	Axial	21		
	Eccentric	1		
	No proptosis	8		
5	Complaints			
	Protrusion	18		
	Watering	15		
	Retrobulbar Discomfort	15		
6	Toxic Symtoms			
	Weight loss	12		
	Tremor	11		
	Sweating	8		
	Tachycardia	6		
7	Lid Signs	No. of cases with Bilateral presentation	Cases with unilateral presentation	
	Dalrymple sign	10	9	
	Vongrafe's sign	12	6	
	Kochers sign	8	8	
	Stellwag sign	6	6	
	Rosenbach sign	2	2	
8	Visual Acuity			
	6/6 – 6/18	26	26	
	6/18 – 6/60	2	1	
	Less than 6/60	2	3	
9	Exophthalmometry			
	Proptosis Grade	Numerical Value	No. of eyes	
	Normal	<20	18	
	Mild	21 – 23	34	
	Moderate	24 – 27	8	
	Severe	>27		
10	Nature of Thyroid swelling	No. of patients		
	Diffuse	18		
	Nodular	6		
	Multi-nodular	4		
	No swelling	2		
11	Thyroid function Tests	T3	T4	TSH
	Increased	22	22	6
	Decreased	6	6	22
	(N) Euthyroid	2	2	2
12	Radio Iodine Uptake Scan			
		Alpha	Beta	Gamma
	No. of cases	7	2	-
13	USG orbit – 'B' Scan			
	No. of cases	Muscle Thickening	No Muscle Thickening	
	30	12	18	
14	CT Scan – orbit			
	No. of cases	EOM Enlargeme nt	Normal Study	
	11	10	1	

15	Fine Needle Aspiration Cytology of Thyroid Gland			
	Features suggestive of Hyperthyroidism	2		
	Features suggestive of Normal Thyroid Gland	1		

TREATMENT OF THROID

1. Medical Treatment:

Antithyroid Drugs Eltroxin

1. 20 patients is on antithyroid drugs and 6 on eltroxin.

2. Radio ablation for 1 patient was given at Nuclear Medicine Department

3. 2 patients have undergone thyroidectomy for hyperthyroidism

Majority of my patients (twenty) were treated with antithyroid drugs and six of them were treated with thyroxine.

SURGERY

Cosmetic Eyelid Surgery

'Z' MYOTOMY in 5 patients

In our special clinic patients, especially young females complained of cosmetic problems due to lid retraction and they did not have visual impairment. These patients were selected for 'Z' myotomy after their thyroid disease has been non-progressive for atleast 6 months. After the satisfaction of selection criteria, 5 of my patients underwent 'z' myotomy for lid retraction with excellent results.

DISCUSSION:

In my study simple conservative measures like lubricating drops was applicable to all my 30 patients (J5). All my male patients were advised to stop smoking as it is known to aggravate the condition (J9). 19 patients were treated with oral prednisolone and they showed good response with decreased (or) static exophthalmos¹¹. Immunosuppressants are reserved for those not responding to steroids because of its toxicity¹¹ (J2). In my study it was started for a single patient but unfortunately the patient was lost for follow up. As it was reported literature (J7) patients not responding to steroids show poor response to radiotherapy. It was not tried for steroid, unresponsive patients. Orbital decompression is indicated for compressive optic neuropathy and for disfiguring exophthalmos¹¹ (J2) in thyroid related orbitopathy which was not noted in any of our cases.

CONCLUSION

1. Most of the patients who come for ophthalmic department with TRO are females belonging to 30 – 50 yrs of age.
2. Though many of them had toxic thyroid symptoms and swelling, even enlargement of EOM on USG, 'B' scan orbit and CT scan the proptosis was mostly minimal.
3. Many of them were on medical treatment. Associated with proptosis required systemic steroids for arresting progression of ophthalmic disease.
4. Simple procedure of marginal 'z' myotomy gives good acceptable cosmetic results especially in females patients and there is no requirement for special instruments and sutures. However, long term effect and results of this procedure are to be evaluated.

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