

CASE REPORT

GRAVES' OPHTHALMOPATHY IN A EUTHYROID PATIENT - A RARE CASE REPORT

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ABSTRACT: Purpose: To present a case of Graves' Ophthalmopathy, with normal thyroid profile and negative Thyrotropin receptor antibody (TRAb) with elevated thyroid stimulating antibody (TSAb) level in an elderly individual. **METHODS:** A 60years-old man presented with a complaint of prominence of both eyes for 5months and swelling and pain for last 15days, was examined with thyroid function test, Thyrotropin receptor antibody (TRAb) and thyroid stimulating antibody (TSAb) along with computed tomography (CT) brain and orbit. He was started on IV methyl Prednisolone 1gm/day for 3 days/week and tapered off. **RESULTS:** The patient was with normal thyroid profile, negative Thyrotropin receptor antibody (TRAb) with elevated thyroid stimulating antibody (TSAb) level. CECT orbit revealed fusiform swelling of recti muscles with sparing of tendinous insertion in both eyes suggestive of bilateral Grave's ophthalmopathy. **CONCLUSION:** In this case study, we reported a case of Graves' Ophthalmopathy with normal thyroid profile and negative TRAb. The only laboratory basis for diagnosing this patient as having Graves' disease was his elevated TSAb level. The patient had remarkable improvement in his eye symptoms following steroid therapy.

KEYWORDS: Graves' Ophthalmopathy, Proptosis, Thyrotropin receptor antibody, Thyroid stimulating antibody.

INTRODUCTION: Thyroid eye disease or thyroid ophthalmopathy is one of the severe complications of hyperthyroidism, which has a detrimental effect on the patient's quality of life. It almost runs parallel with the disease process. It is an organ-specific autoimmune process with strong association with dysthyroidism. In the medical literature, Thyroid ophthalmopathy was formally described by Graves in 1835 and by Von Basedow in 1840. The panorama of eye disease can range from mild gritty sensation due to induced dry eye syndrome to even loss of vision contributed by Exposure Keratitis and compressive optic neuropathy [1]. Here we report a patient with Graves' Ophthalmopathy, in euthyroid status and negative Thyrotropin receptor antibody (TRAb) with elevated thyroid stimulating antibody (TSAb) level.

CASE REPORT: A 60years old male attended eye OPD at Agartala Govt. Medical College and G B Pant Hospital on 05.12.13, with a complaint of prominence of both eyes for last 5months followed by swelling and pain for last 15days. He noticed the prominence of both eyes, which was more on the right eye than the left eye. It was insidious in onset, progressive in nature and worsens more in the morning hours after getting up from the bed. The prominence was associated with mild discomfort and grittiness of the eyes for which he frequently needs to give water splashes. The patient then developed swelling of both upper and lower eyelids, more on the right than the left, followed by pain and redness which was progressive in nature and worsen in the morning hours. The pain was dull aching in nature, mostly behind the eye and subjected a sense of something pushing behind the eyes.

CASE REPORT

The pain was localized, non radiating, present both at rest and with movements of eyes. There was no associated ocular motility disorder or doubling of vision or postural variations. The patient denies for any loss of weight in spite of good appetite, sweating, tremor or palpitation. There was no history of any trauma. There is no preceding history of defective vision or blackouts or transient loss of vision or defective color perception. The patient also denies for any skin discoloration or any neck swelling or exposure to radiation therapy or chemotherapy. There was no history of dysphagia, dysphonia, easy fatigability, drooping of eyelids. The patient was non diabetic. He is a known case of systemic hypertension under regular medication for last 8years. He is a chronic smoker. The family history was without any significance.



Fig. 1: Patient on first visit

On examination, he was averagely built and well nourished. Sleeping pulse rate 86 per minute, regular in rhythm and volume. Blood pressure 140/90 mm Hg in right upper arm in supine position. Higher functions were normal. Systemic examinations were within normal limits.

On Ocular examination, he had a staring look (Kocher's sign). His vision was 6/18 right eye and 6/24 left eye. Bilaterally there was axial proptosis, periorbital edema around the lids; Conjunctiva was congested nasally and temporally, with mild chemosis, Decreased tear film height. Cornea was clear and sensation was intact. Anterior chamber was of normal depth. Iris was brown in color and normal in pattern. Pupil was 4 mm in diameter and reacting briskly to both direct and consensual reflex. There was inability of both eyes to converge (Moebius sign).

On inspection, in primary position there was proptosis in both eyes. The proptosis was axial. Nafziger's sign (Protrusion of the eye beyond the orbital rim when examined from above and behind the patient) was positive bilaterally. Eyebrows were normal with no evidence of madarosis. Lid revealed periorbital edema of both upper lids (Vigouroux sign) and lower lids (Enroth's sign). There was upper lid lag on down gaze (Von Graefe's sign) with upper eyelid retraction (Dalrymple's sign).

Lid margins were 3 mm from superior and inferior limbus suggestive of moderate lid retraction. Temporal flare was present. No variation of proptosis was observed with posture especially on bending forwards or stooping and with valsalva's manoeuvre. Lid lag was present on down gaze. There was minimal lagophthalmos with good Bell's phenomenon in both eyes. Proptosis was non pulsatile. There was no evidence of engorged veins or corkscrew vessels.

CASE REPORT



Fig. 2: Ocular findings before steroid therapy

On palpation, orbital margins were intact. There was resistance to retropulsion was present. Proptosis was non compressible and non reducible. No thrill or pulsation felt. There was no evidence of warmth or tenderness over both eyes.

On auscultation, no bruits were heard in both eyes.

Measured by Hertel exophthalmometer, 20 mm of proptosis was found in right eye and 22 mm in left eye. On Applanation tonometry, tension was 19 mm Hg in right eye and 18 mm Hg in left eye in primary gaze. While in up gaze, tension was 24 mm Hg in right eye and 26 mm Hg in left eye.

Schirmer's test by Whatmann's filter paper, at the end of 5 mins revealed 15 mm wetting in right eye and 13 mm wetting in left eye suggestive of mild dry eye.

The patient was advised for thyroid function test. Serum levels of free Tri iodothyronine and free Thyroxine were 3.3 pg/mL (2.47-to-4.34 pg/mL) and 1.33 ng/dL (0.97-to-1.79 ng/dL), respectively, and his Thyrotropin receptor antibody (TRAb) level was 0% (<15%). simultaneously, we measured his thyroid stimulating antibody (TSAb) and found that it was positive (240%; reference range <180 %). With this test results, he was finally diagnosed as having Graves' Ophthalmopathy.

CECT orbit was done which revealed outward protrusion of left orbital globes with fusiform swelling of all recti muscles of left orbit and superior and lateral rectus muscle of right side with sparing of tendinous insertion. Retro orbital fatty tissue was seen normal. Optic nerve sheath complex was seen normal. There was no evidence of intra or extra ocular mass lesions. Both lacrimal glands were normal. The CECT orbits were suggestive of bilateral Graves's ophthalmopathy. CECT Brain was done which revealed normal study.



Fig. 3: CECT orbit showing fusiform swelling recti muscles with Sparing of tendinous insertion before steroid therapy

CASE REPORT

The patient was advised to stop smoking. He was started on IV Methyl Prednisolone 1gm/day for 3 days/week and tapered off. Simultaneously lubricants such as Carboxymethyl cellulose 1% eye drop at daytime and ointment at night along with topical NSAIDS Nepafenac 0.1% was prescribed. The patient was advised for head elevation.



Fig. 4: Patient on 2nd visit after steroid therapy

The patient was followed up after 1 month. The general condition of the patient improved. The prominence of both eyes regressed along with subsidence of orbital swelling and pain. A repeat CECT orbit was done which showed regression of the fusiform swelling of extra ocular muscle bellies than what were seen previous CECT reports.



Fig. 5: CECT orbit showing regression of fusiform swelling recti muscles after steroid therapy

DISCUSSION: Thyroid associated ophthalmopathy is an organ specific auto immune process that is strongly associated with dysthyroidism. Although thyroid ophthalmopathy can occur rapidly over a few weeks, in most cases it is gradual and insidious.

Being an organ-specific autoimmune reaction, a humoral agent (IgG antibody) produces inflammation of extra ocular muscles characterized by pleomorphic cellular infiltration associated with increased secretion of glycosaminoglycans and osmotic imbibition of water. This lead to enlargement of muscle thereby compressing the optic nerve. Subsequent degeneration of muscle fibres eventually leads to fibrosis, which exerts a tethering effect on the involved muscle, resulting in

CASE REPORT

restrictive myopathy and diplopia. On the other side, inflammatory cellular infiltration in orbital fat and lacrimal glands with accumulation of glycosaminoglycans and retention of fluid causes an increase in the volume of orbital contents and secondary elevation of intra orbital pressure.^[2] This might be the cause of raised IOP on Applanation tonometry in our patient. The same pathogenesis is responsible for the clinically obvious Proptosis and the swelling of the extra ocular muscles in CECT in our case.

Multiple named signs are known in thyroid eye disease, as attribute to the pioneers in the field. Eyelid signs include: Kocher's sign – staring look, Vigouroux sign – eyelid fullness or puffiness. Von Graefe's sign – upper lid lag on down gaze. Dalrymple's sign – upper eyelid retraction. Stellwag's sign – incomplete and infrequent blinking. Grove sign – resistance to pulling the retracted upper lid. Boston sign – uneven, jerky movements of the upper lid in inferior gaze. Gellinek's sign – Abnormal pigmentation of the upper lid. Gifford's sign – difficulty in everting the upper lid. Means sign – Increase superior sclera show on up gaze. Enroth's sign – edema of lower lid. Griffith's sign – lower lid lag on upward gaze. The extra ocular movement signs include: Moebius sign – unable to converge eyes. Ballet's sign – restriction of one or more extra ocular muscles. Suker's sign – poor fixation on abduction. Jendrassik's sign – Paralysis of all extra ocular muscles. Most of those signs were found in our patient as mentioned in the literature.

The diagnosis of Thyroid Eye Disease was based on the presence of ophthalmopathy and confirmed by positive serum thyroid stimulating antibody, both being specific indicators of Graves' disease. In one of the largest series reported in the literature,^[3] that more than 90 % of patients with active Graves' ophthalmopathy were associated with hyperthyroidism. Another recent review ^[4] reported that 10% of Graves' ophthalmopathy patients are euthyroid, but made no comment as to the natural history of the euthyroid state. In addition our patient had serum free thyroxine, free tri iodothyronine, and TSH levels within normal range with absent of serum TRAb. Smoking is considered as risk factors for the development of Graves' Ophthalmopathy which is found in our patient. However, radioactive iodine treatment, hyper and/or hypothyroidism elevated TRAb level, which were considered as risk factors for the development of Graves' Ophthalmopathy^[5, 6] were not observed in our patient.

The only abnormal laboratory finding in our patient was elevated TSAb. Nishikawa M, et al. in their study evaluated the association between eye changes and thyroid-associated auto antibodies. They concluded that TSAb in Graves' patients with Graves' Ophthalmopathy was significantly higher than that in patients without Graves' muscles measured using MRI.^[7] This result is evidence of a significance of TSAb in the development of Ophthalmopathy. They also found that the level of stimulating activity in Graves' patients with Graves' Ophthalmopathy was significantly positively correlated with the sum of the swelling ratios of the individual eight eye Graves' Ophthalmopathy.

CONCLUSION: In this case study, we reported a case of Graves' Ophthalmopathy with normal thyroid profile i.e. euthyroid status and negative TRAb. The only laboratory basis for diagnosing our patient as having Graves' disease was his elevated TSAb level. The patient had remarkable improvement in his eye symptoms following steroid therapy. However, the case study needs the evaluation of level of TSAb in other patients with hypothyroidism and other euthyroid, TRAb-negative Graves' Ophthalmopathy patients.

CASE REPORT

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