Our Patient has Large Protruding Eyes: Is it Related to the Thyroid Gland? (Thyroid Eye Disease)

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Proptosis, or abnormal protrusion of the eyeballs in relation to the skull, remains a common presenting complaint for a wide variety of orbital and systemic conditions. When the offending lesion is 'intraconal' or within the muscle cone, it leads to axial proptosis. On the other hand, eccentric proptosis may be caused by orbital lesions outside the muscle cone, or lesions in the adjacent structures such as the paranasal sinuses, the cranial cavity etc. Oftentimes, the exact causative mechanism leading to proptosis may be difficult to delineate, due to the inaccessibility of the structures in the orbit. It may be due to a variety of inflammatory, infectious, vascular, neoplastic or traumatic causes.[1]

Thyroid associated orbitopathy (TAO) is the most common cause of unilateral and bilateral proptosis (Fig. 1), although 90% of the cases present bilaterally. In the setting of thyroid disease, this proptosis is referred to as 'exophthalmos'.

It is essential to distinguish it from mimicking conditions, also called 'pseudoproptosis' - such as contralateral enophthalmos, upper eyelid retraction and conditions causing actual enlargement of the eyeball including degenerative myopia and buphthalmos (congenital glaucoma).[2] Exophthalmos is the most frequent extrathyroidal manifestation of Graves' disease, presenting in almost 50% of the cases. Approximately 5% of these patients are likely to progress to severe disease with dysthyroid compressive optic neuropathy (DON). Severe cases may also progress to exposure keratopathy, corneal ulceration (Fig. 2) and even perforation in rare cases.[2,3]

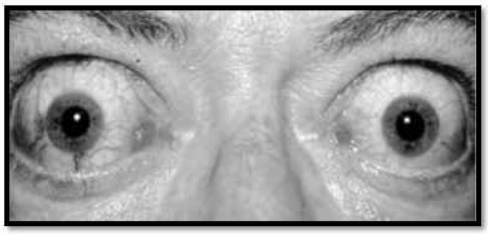

Fig. 1: Bilateral symmetrical proptosis

Reference:

Bowling B. (2016). Orbit. In: Bowling B. Kanski's Clinical Ophthalmology: A systematic approach (pp. 85). Edinburgh: Elsevier Limited

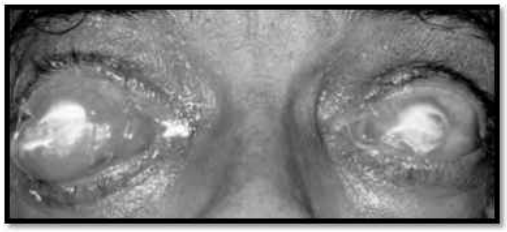

Fig. 2: Bilateral bacterial keratitis due to severe exposure

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The mechanism behind the involvement of the orbits and orbital structures, is believed to be autoimmune. Thyroid disease is associated with the presence of circulating autoantibodies against the thyroid-stimulating hormone receptor (TSHR). As the thyroid gland and the orbital tissues share a common antigen, these antibodies cross-react with orbital fibroblasts, causing their activation. Chemokines released from these activated fibroblasts, cause recruitment of T-lymphocytes into the orbit. T cells, in concert with the orbital fibroblasts, promote the deposition of extracellular matrix, proliferation of fibroblasts and adipogenesis, thus perpetuating thyroid eye disease. While 80% of the cases of TAO are found to occur in association with hyperthyroidism, 5-10% of the patients may be euthyroid and 10% may have autoimmune hypothyroidism. Moreover, in hyperthyroid cases, the condition may present before or during thyroid dysfunction, and also when the patient is euthyroid following therapy.[4]

Exophthalmos in these patients is accompanied by a variety of other ophthalmic manifestations. Patients commonly present with symptoms such as dryness and stinging sensation, photophobia, watering, diplopia and a feeling of pressure behind the eyes. Soft tissue involvement may lead to redness, swelling and pain, while impaired visual function and difficulties in colour vision may be encountered in case of optic nerve involvement.[4]

Bartley et al conducted a study involving 120 patients of TAO and concluded that upper eyelid retraction was the most common sign observed, which frequently varied with gaze (Kocher's sign). It was found in 90% of the patients and is multifactorial - increased sympathetic stimulation to the Muller's muscle, contraction of the levator muscle and scarring between the levator muscle and lacrimal fascia, are all factors that contribute to it. The scarring typically gives rise to a temporal flare in the contour of the retracted upper lid, a sign which is almost pathognomonic for TAO.[4,5]

Additionally, other clinical signs documented are proptosis (62%) and restrictive extraocular myopathy (43%). The latter may be due to inflammatory oedema of the extraocular muscles in the active stage of the disease, and due to fibrotic contracture and scarring during the quiescent phase. Optic nerve dysfunction is noted in 6% and is thought to be due to pressure of the enlarged muscles on the optic nerve. Fundus examination shows optic disc oedema, choroidal folds or optic disc pallor in these patients. 5 The degree of involvement can be assessed by the Clinical Activity Score as per the American Thyroid Association (ATA)/American Association of Clinical Endocrinologists (AACE) guidelines. (Table 1)[6]

TABLE 1

1: Active disease: Clinical Activity Score ? 3/ 10

ELEMENTS ASSESSED ON EACH VISIT	**SCORE**
Spontaneous retrobulbar pain	1
Pain on attempted up or down gaze	1
Redness of the eyelids	1
Redness of the conjunctiva	1
Swelling of the eyelids	1
Inflammation of the caruncle and/or plica	1
Conjunctival oedema	1
ELEMENTS COMPARED WITH PREVIOUS VISIT	**SCORE**
Increase in proptosis ≥2 mm	1
Decreased eye movements ≥5 degrees in any direction	1
Decreased visual acuity ≥1 line on Snellen chart	1

Computed Tomography (CT) is the most commonly used technique used for evaluation of TAO and is used along with Magnetic Resonance Imaging (MRI) for evaluation of enlarged extraocular muscles. It is required especially when surgical intervention is planned, in order to define the degree of involvement. Commonly noted features on CT include tendon-sparing enlargement of extraocular muscles (Fig. 3), crowding of the optic nerve at the orbital apex and apparent increase in the volume of orbital fat.[7]

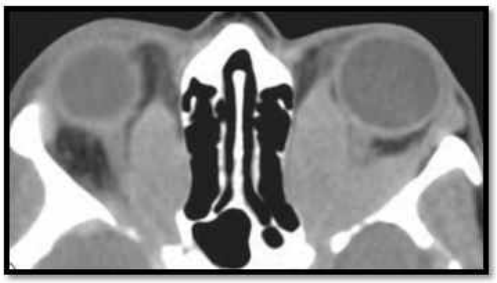

Fig 3: CT scan showing tendon-sparing muscle belly enlargement in thyroid eye disease - axial view.

Reference:

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While mild and non-progressive involvement is seen in most patients, may resolve spontaneously with control of the systemic disease, medical or surgical treatment may be warranted in some patients. In mild cases, local supportive measures may be provided, such as artificial tears to keep the ocular surface moist, sunglasses to reduce photophobia and head elevation to reduce periorbital oedema. Active form of the disease requires medical management, of which achievement of euthyroid status forms the cornerstone. While this may be achieved by antithyroid drugs, thyroidectomy or radioactive iodine (RAI), studies have shown development of new ophthalmopathy or exacerbation of existing ophthalmopathy with RAI. Furthermore, cessation of smoking is mandated, as it is the greatest risk factor for the development of TAO.[8]

Steroids continue to be the best medical treatment for active disease. High-dose oral steroids (60-100 mg/day or higher prednisolone) are usually required. The dose can be gradually reduced (5-10 mg/week) based on the response of the patient. Alternatively, intravenous pulse steroids (0.5 - 1 gm/day) may be administered for a duration of three days, followed by oral treatment. In patients showing no response or exaggerated side effects to steroids, immunosuppressive drugs such as azathioprine, cyclosporine or cyclophosphamide may also be considered.[8] Orbital radiotherapy may be

considered in patients with active disease and recent progression. A cumulative dose of 20 Gy per eye is delivered over a two-week period, at times supplemented with steroids. Due to the anti-inflammatory effect of this treatment and the reduced risk of cataract, retinopathy or secondary malignancies with modern techniques, this form of treatment is also widely used.[9,10]

Surgical treatment for rehabilitation can commence six months after stabilisation of active signs and symptoms. Techniques include decompression for reduction in proptosis, followed by surgical correction of any residual strabismus. Since vertical muscle recession can affect the position of the upper and lower lid, strabismus correction needs to be undertaken prior to any surgery for lid repositioning.[11]

Although a majority of the cases of TAO are mild and do not require active intervention, all patients require careful and timely follow-up with timing of intervention directed by its potential impact on the patient's quality of life. The chronic and persistent nature of this condition may lead to permanent visual impairment and disfigurement. A multidisciplinary approach with active coordination between the physician and the ophthalmologist, becomes essential in order to avoid complications arising due to inadequate treatment, leading to blindness or deformity, and those arising from aggressive treatment, such as side-effects due to steroid use.

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