A RARE CASE OF THYROID ASSOCIATED ORBITOPATHY IN A PATIENT WITH ANTI-TSH RECEPTOR ANTIBODY NEGATIVE HASHIMOTO'S THYROIDITIS

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PRESENTATION OF CASE

Thyroid-associated orbitopathy (TAO) is characterized by immune-mediated inflammation of the extraocular muscles surrounding orbital connective tissue and adipose tissue. It often occurs in patients with Grave's disease, but is rare in patients with Hashimoto's thyroiditis, being reported in only 5% of the patients.

We report a 33 year old lady with Type I Diabetes Mellitus, who had incidentally noticed progressive increase in prominence of her eyeballs and increased tearing for 2 years. She denied having clinical symptoms suggestive of thyroid disease in the past. There was no thyroid swelling on clinical examination. Eye examination showed bilateral proptosis with lagophthalmos. Lateral eyeball movements were restricted and other signs consistent with thyroid associated ophthalmopathy were present. MRI scan of orbit revealed generalized prominence of bilateral extraconal and retrobulbar orbital fat with bilateral resultant proptosis and bilateral enlarged extraocular muscles and features suggestive of optic neuropathy. The patient had sufficiently high TSH levels, low Free T4 levels, high thyroglobulin antibody and anti-TPO antibody titers to substantiate a diagnosis of Hashimoto's thyroiditis. Several studies have noted a strong correlation between the levels of antibodies to Anti-TSH receptor antibodies and TAO in Graves' disease. But patients with Hashimoto's thyroiditis can test negative for TSH-r antibodies as in our case. So other pathogenetic mechanisms may be responsible for the orbitopathy in Hashimoto's thyroiditis. We report a case of Hashimoto's disease with TAO being the only clinical manifestation of the disease.

We report a 33-year-old lady with Type I Diabetes Mellitus, who had incidentally noticed progressive increase in prominence of her eyeballs and increased tearing for 2 years. She denied having clinical symptoms suggestive of thyroid disease in the past. Thyroid gland was not enlarged clinically. Systemic examination was unremarkable. Showed bilateral proptosis measuring 25 mm with lagophthalmos. Visual acuity, pupillary reaction to light and fundus examination were normal. She was found to have features consistent with Grave's ophthalmopathy like hyperpigmentation of both eyelids (Jellinek's sign), Lid lag on infraduction (Von Graefe's sign), eye globe lag on supraduction (Kocher's sign), a widened palpebral fissure during fixation (Dalrymple's sign) and an incapacity of closing the eyelids completely (lagophthalmos), thin tremors were observed on the eyelids when closed (Rosenbach's sign), lack of convergence (Mobius Sign), restriction of movements of bilateral lateral recti (Ballet's sign), infrequent blinking (Stellwag sign), inability to maintain fixation on extreme lateral gaze (Sulker's sign).

Images 1 and 2

CLINICAL DIAGNOSIS

Thyroid Associated Orbitopathy.

DIFFERENTIAL DIAGNOSIS

Thyroid associated ophthalmopathy is commonly encountered in hyperthyroidism and Grave's disease, and rarely in those with euthyroid and hypothyroid Graves' disease who test positive for Anti-TSH receptor antibodies.[1] When patients who are euthyroid and hypothyroid patients with orbitopathy but Anti-TSH receptor antibodies negative, other diseases such as cavernous carotid fistula, sphenoid meningioma, orbital lymphoma, idiopathic orbital myositis and IgG4 related disease can be entertained.[2] Orbital and pre-septal cellulitis are differential diagnosis that need to be kept in mind before making a diagnosis of Thyroid associated Orbitopathy but, patients with the former conditions will have more acute onset proptosis accompanied by fever and leucocytosis. Orbital inflammatory syndrome (orbital pseudotumor) is another painful condition that can cause proptosis and has to be ruled out and it is associated more often with ptosis than lid retraction.

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PATHOLOGICAL DISCUSSION

Her complete hemogram was normal and RBS was 549 mg/dl. Thyroid hormone profile by radioimmunoassay TSH - 20.8 mU/l (normal 0.5-3.5 mU/l), Free T4 - 0.2 ng/dl (0.7 to 1.9 ng/dl). Anti-TPO antibody titres were more than 600 IU/ml (normal <34 IU/ml) and Anti-Thyroglobulin Antibodies were 278.9 IU/ml (Normal Upto 115 IU/ml). Anti TSH Receptor Antibodies were negative. USG thyroid gland revealed a thyroid volume of 9 ml and was non-nodular. The patient had sufficiently high thyroglobulin antibody titers and anti-TPO antibody titres to substantiate the diagnosis of Hashimoto's thyroiditis. MRI scan of orbit revealed generalized prominence of bilateral extraconal and retrobulbar orbital fat with bilateral resultant proptosis with subtle T2 hyperintense signal at bilateral optic disc region suggestive of optic neuropathy.

Thyroid-associated orbitopathy is characterized by autoimmune processes that involves swelling of extraocular tissues leading to exophthalmos either caused by hypersecretion or accumulation of hydrophilic glycosaminoglycans and cellular proliferation involving orbital tissues.[3] These alterations in normal architecture of the orbit can result in eyeball motility disturbances, keratopathy, and pressure on the optical nerve leading to optic neuropathy. Thyroid-associated orbitopathy accompanies Graves' disease in most cases, whereas it's occurrence is rare in Hashimoto's disease being reported in only 5% of the patients.[4,5] We are reporting a case with a rare coexistence of thyroid orbitopathy and Hashimoto's disease. This case is being reported primarily to draw attention to the fact that infiltrative ophthalmopathy may appear as the first manifestation in hypothyroid individuals without a previous history of thyroid disease.

Immunologic cross reactivity of sensitized T lymphocytes and/or autoantibodies against thyroid and orbit may trigger the inflammatory process. In both of Graves' and Hashimoto's disease, antithyroglobulin, anti-thyroid peroxidase antibodies and Anti TSH Receptor antibodies can be detected. Although Graves' disease and Hashimoto's thyroiditis were considered to be different entities, currently both are considered to be autoimmune processes leading predominantly over excitation of thyroid tissue in the former and suppression of thyroid hormone secretion in the former.A common factor linking thyroid disease and ocular mal conditioning is the TSH-receptor antigen that is shared between the thyroid and the orbital tissues in Graves' disease, which could hold the answer for extra thyroidal manifestation of the disease.[6] TSH receptor expression in also high in orbital preadipocytes.[7] Hence sensitized T Lymphocytes cross react with TSH receptor along with various cytokines and stimulate fibroblast proliferation has been postulated as a possible mechanism of Graves' ophthalmopathy. TSH Receptor Antibody is of stimulating type in Grave's disease, though the blocking variety has been also described in literature. Kasagi et al examined five patients of hypothyroid Graves' disease and reported presence of stimulating and not blocking variety of TSH Receptor Antibody in all the cases[8] and it was also reported that hypothyroidism in these cases was not secondary to presence of blocking type antibodies. It was hypothesised that hypothyroidism in these cases might have been associated with high antibody titres against thyroglobulin and resultant destructive changes in the thyroid, as evidenced by ultrasound and histological changes suggesting simultaneous presence of Hashimoto's thyroiditis. Several studies have noted a strong correlation between the levels of antibodies to Anti-TSH receptor antibodies and TAO in Graves' disease. But patients with Hashimoto's thyroiditis can test negative for TSH-r antibodies. So in such scenarios the TSH-r hypothesis cannot successfully explain the eye muscle involvement in Hashimoto's thyroiditis. Awareness of this atypical form of ophthalmopathy is important, as prompt recognition and monitoring and steroids if indicated can result in favorable outcomes.

DISCUSSION OF MANAGEMENT

Our patient was initiated on thyroxine supplementation and her thyroid associated orbitopathy was conservatively managed and is on regular observation.

Most patients with Thyroid Associated Orbitopathy can be managed conservatively but they need to be regularly monitored for vision loss from corneal exposure and development of optic neuropathy and strabismus.[9]

Colour vision testing and visual field charting may aid in earlier detection of visual loss. Patients with dry eye symptoms or corneal exposure should be prescribed artificial tears. Though not warranted if clinical suspicion of TAO is high, MRI Orbit could aid in identifying optic nerve compression. Patients should be educated about the possibility of worsening of TAO with exposure to tobacco smoke. Systemic steroids can be used in patients with severe inflammation or compressive optic neuropathy in thyroid-associated orbitopathy (TAO). If patient responds well with systemic steroids, orbital irradiation can be considered. In severe cases, combined steroids, radiation, and surgery may be required. In patients with worsening TAO despite surgical intervention like orbital decompression, intranasal steroids can be tried.

FINAL DIAGNOSIS

Thyroid Associated Orbitopathy in a patient with Anti-TSH Receptor Antibody Negative Hashimoto's Thyroiditis.

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