Euthyroid Ophthalmopathy: A Rare Case Report and a Brief Review of Literature

Dr. Mahendra Wawhal¹, Dr. Vajed Mogal², Dr. Pratik Patil³, Dr. Preetam Ahire⁴, Dr. Sushant Yadav⁵

¹Associate Professor and Consultant (M.D. Medicine), ²Senior Resident, ³,⁴,⁵Junior Resident, all are in department of medicine, M.G.M. Medical college and Hospital, Aurangabad-431003, Maharashtra, India

Abstract: Thyroid-associated ophthalmopathy usually occurs in a close temporal relationship with hyperthyroidism. It is rare in patients with normal thyroid function (euthyroid ophthalmopathy) and in patients with hypothyroid forms of thyroid autoimmune disease (hypothyroid ophthalmopathy)¹. A 43-year-old male, known case of hypertension presented with involuntary jerky movements and protrusion of eyes since 2 months with normal thyroid functions, diagnosed to have euthyroid ophthalmopathy & responded very well to steroids. It is currently believed that euthyroid ophthalmopathy reflects the underlying autoimmune process and it is not a consequence of alternations in thyroid function².

Keywords: Euthyroid, Thyroid eye disease (TED), Thyroid-associated ophthalmopathy (TAO), TSH receptor antibodies (TRAb).

1. Introduction

Euthyroid Graves' disease is an autoimmune condition that causes the characteristic eye symptoms of Graves' ophthalmopathy, which is more commonly known as thyroid eye disease (TED), in the absence of thyroid dysfunction. Most patients with euthyroid Graves' disease go on to develop thyroid disease within 12-18 months after eye symptoms develop. Most of these patients develop Graves' disease, an autoimmune thyroid disorder, although a smaller number of patients may develop autoimmune hypothyroidism³. Thyroid-associated ophthalmopathy (TAO), frequently termed Graves ophthalmopathy, is part of an autoimmune process that can affect the orbital and periorbital tissue, the thyroid gland, and, rarely, the pretibial skin or digits (thyroid acropachy)⁴. Graves 'ophthalmopathy is the most common orbital disease and affects 25-50% of the patients with Graves’ disease. It’s more common in females, between the second and fifth life’s decade. The disease has an acute and a chronic stage, slowly progressing until it stabilizes, with rare cases of spontaneous resolution. The treatment depends on the stage and the disease is mainly treated with oral or intravenous corticosteroids with or without radiotherapy⁵. Here, we present a rare case where there is severe Anti-TPO related autoimmune ophthalmopathy in a euthyroid patient.

2. Case Report

A 43-years-old male, presented with the chief complaints of involuntary jerky movements and protrusion of eyes (fig:1) since past 2 months. He was treated by local doctor, and artificial tears and eye ointments were prescribed for his symptoms. 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. The patient was non diabetic. He is a known case of hypertension and hypercholesterolemia controlled on Tab. Telmisartan 40mg and Tab. Stator 40mg. The family history was without any significance.

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. No evidence of cyanosis, clubbing, lymphadenopathy, oedema , and pallor was seen. Higher functions were normal. Systemic examinations were within normal limits. Fundus examination and eye movements were normal. On ophthalmological examination patient had eyelid retraction. Upper eyelid retraction. This finding is associated with lid lag on inraduction (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.

Routine investigations including hemogram (Hb-15gm/dl, TLC-7500/cumm, Platelet count-147,000/cumm), liver function tests and kidney function tests & serum electrolytes were normal. Lipid profile showed serum
cholesterol-208mg/dl, serum triglycerides-96mg/dl. His serum thyroid levels (TSH-1.37(0.490-4.670), T3-84.2(70-130) and T4- 5.70(4.5-12.5) were normal. Ultrasonography (USG) of thyroid was normal. The anti thyromosomal antibody titre (TPO) was too high (371.65 IU/ml). MRI Brain (Plain) showed no significant abnormality. CT Orbit showed increased retrobulbar fat more on left side and mild bilateral proptosis slightly more on left side. We suspected of severe Anti-TPO related autoimmune ophthalmopathy in a euthyroid and started on Intravenous Methylprednisolone 1gm/day for three days, followed by 40mg daily which was tapered to a maintenance dose of 10mg after six weeks. After pulse therapy, his jerky movements slow down and protrusion of eyes disappear gradually. Simultaneously lubricants such as carboxy-methyl cellulose 1% eye drop at day time and ointment at night along with topical NSAIDS was prescribed. The patient was following up after one month. The general condition of the patient improved and without any complaints. Here, we report a rare case where there is severe Anti-TPO related autoimmune ophthalmopathy in a euthyroid patient.

3. Discussion

Euthyroid ophthalmopathy is much less common; occurring in approximately 10% of patients with Graves' ophthalmopathy. Euthyroid ophthalmopathy is defined as ophthalmopathy without any present or past history of hyperthyroidism and is reported in 0.7% of patients in a large series of Graves' ophthalmopathy. TSAb positivity has been shown in 10 of 11 patients with euthyroid Graves' ophthalmopathy by Ealey et al. by a cytochemical bioassay. In 1995, two patients with euthyroid Graves' ophthalmopathy showing no thyroid abnormalities except positive TSAb were reported by Watanabe et al. The annual incidence rate of TAO has been estimated at 16 cases per 100,000 women and 2.9 cases per 100,000 men. There appears to be a female preponderance in which women are affected 2.5-6 times more frequently than men; however, severe cases occur more often in men than in women. In addition, most patients are aged 30-50 years, with severe cases appearing to be more frequent in those older than 50 years. Although most cases of TAO do not result in visual loss, this condition can cause vision-threatening exposure keratopathy, troublesome diplopia, and compressive optic neuropathy. Therefore, although the prognosis is generally favorable for patients with this condition and most patients do not require surgical intervention.

The thyroid gland itself does not cause TAO, and regulation of thyroid function does not affect this condition. Rather, the thyroid gland, eye muscles, and pretibial skin are especially subject to the autoimmune attack. Many patients with TAO are hyperthyroid, but euthyroidism, Hashimoto thyroiditis, thyroid carcinoma, and neck irradiation are also associated with TAO. TAO is associated strongly with smoking; the more severe the eye disease, the stronger the association. Autoimmune diseases such as myasthenia gravis, Addison disease, vitiligo, and pernicious anemia have been described with TAO. In simplest terms, the underlying pathophysiology of TAO is thought to be an antibody-mediated reaction against the TSH receptor with orbital fibroblast modulation of T-cell lymphocytes. T-cell lymphocytes are believed to react against thyroid follicular cells with shared antigenic epitopes in the retro-orbital space. An active phase of inflammation is initially present. Lymphocytic infiltration of the orbital tissue causes a release of cytokines (e.g., tumor necrosis factor [TNF], interleukin-1 [IL-1]) from CD4+ T-cells stimulating the orbital fibroblasts to produce mucopolysaccharides, which, by hyperosmotic shift, cause tissue edema in the extraocular muscles. Patients with euthyroid Graves' disease typically have high levels of both stimulating and blocking TSH receptor antibodies (TRAb). While stimulating TRAb, which are also known as thyroid stimulating immunoglobulins or TSI, stimulate thyroid cells to produce excess thyroid hormone in Graves' disease, the blocking TRAb in euthyroid Graves' disease prevent TSI from causing hyperthyroidism. Each of these antibodies cancels out the effects of the other on thyroid function. However, because they are both capable of eliciting an immune response in eye muscle (orbital) tissue, they contribute to signs and symptoms of TED.

Several studies have investigated the relationship between different antibody profiles and hyperthyroidism and Graves' ophthalmopathy in Graves' disease.

In two previous studies, TSAb positivity correlated with ophthalmopathy and TBII was related to hyperthyroidism. In the study by Goh et al., ophthalmic dominant patients also had significantly lower TPOAb and TgAb levels. Regarding the correlation between the presence, type or levels of TRAb and Graves' ophthalmopathy, there are studies that report both TSAb and TBII to be closely correlating with Graves' ophthalmopathy clinical activity score. Weaker but significant correlation was also noted between antibody levels and proptosis. In a study by Khoo et al., in patients with severe ophthalmopathy, an unexpectedly high prevalence of TPOAb and TgAb negativity and high TSAb positivity was reported. Conversely, two studies by Kim et al. demonstrated TSAb positivity was significantly associated with the presence of Graves' ophthalmopathy.

Euthyroid Graves' disease is a self-limited disorder. During the active disease phase, this can last from several months to 5 years or longer, symptoms typically wax and wane, sometimes worsening over time. The active phase is followed by a resolution phase. During the resolution phase, much change associated with TED resolve spontaneously. However, if scar tissue forms or permanent changes occur, surgery known as orbital decompression may be required. This surgery should not be performed during the active disease phase since surgical changes can interfere with the normal healing process.

Thyroid ophthalmopathy is classified into acute or inflammatory disease, progressive and histologically associated to lymphocytic infiltration and edematous changes, and in chronic or inactive disease associated with fibrotic changes and fat infiltration in the retro-orbital tissues, especially the extraocular muscles. The acute

Volume 4 Issue 10, October 2015

www.ijsr.net
Licensed Under Creative Commons Attribution CC BY

Paper ID: SUB158699
phase of the disease presents as main symptoms: pain, conjunctival hyperemia, edema and eyelid hyperemia, proptosis, caruncle edema, chemosis, diplopia and blurred vision. The involvement is bilateral in 80% of cases; and usually manifests in patients with hyperthyroidism, involving two or more extracocular muscles without tendon involvement.

In screening for thyroid disease, the combination of free T4 (thyroxine) and TSH or serum TSH (thyrotropin) are highly sensitive and specific. Assays that measure the binding of TSH to a solubilized receptor are thyroid receptor antibody (TRAb), TSH receptor binding immunoglobulins (TBI), and long-acting thyroid stimulator assays. TPO antibodies (antimicrosomal antibodies) and antibodies to thyroglobulin may be useful when trying to associate eye findings with a thyroid abnormality, such as euthyroid Graves’ disease. Patients with euthyroid Graves’ disease may also have high levels of thyroglobulin and/or TPO antibodies. Imaging tests, especially MRI or CT scans, may also be used to assess orbital congestion, and an exophthalmometer may be used to measure proptosis. An orbital ultrasound may also be used to measure enlargement of orbital muscles. Ultrasounds may be followed over time to assess disease progression and treatment response.

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, 20 that more than 90 % of patients with active Graves’ ophthalmopathy were associated with hyperthyroidism. Another recent review 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 triiodothyronine, and TSH levels within normal range with absent of serum TRAb. However, radioactive iodine treatment, hyper and/or hypothyroidism elevated TRAb level, which were considered as risk factors for the development of Graves’ Ophthalmopathy. 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. This result is evidence of a significance of TSAb in the development of Ophthalmopathy.

The treatment is based on the phase in which the disease is (acute or chronic). In the acute phase, the anti-inflammatory treatment of choice is the corticosteroid therapy orally or intravenously. Corticosteroid therapy is associated with the use of radiation, using the linear accelerator in ten continuous sessions in the most severe cases or ten weekly sessions with total doses of 2000cGy. Another drug treatment option is the use of colchicine, with a dosage of 0.5 to 1.5 mg/day, alone or combined with radiotherapy and/or corticosteroids, with good therapeutic response.

Treatment for euthyroid Graves’ disease involves therapies designed to reduce the immune response and promote immune system healing. Most patients with TAO can be observed; the follow-up interval depends on disease activity. Monitor for visual loss from corneal exposure and optic neuropathy and for strabismus development. If a patient has dry eye symptoms, consider having them use artificial tears during the day, lubricating ointment at night, and punctual plugs. In addition, encourage patients to stop smoking to decrease the risk of congestive ophthalmopathy. Sleeping with the head of the bed elevated may decrease morning lid edema. Systemic steroids are usually reserved for patients with severe inflammation or compressive optic neuropathy in TAO. Adjunctive cyclosporine, ocreotide, and intravenous immunoglobulin are less common modalities of medical treatment for optic nerve compression. Orbital irradiation is sometimes prescribed for moderate to severe inflammatory symptoms, diplopia, and visual loss in patients with TAO. Approximately, 5% of patients with TAO may require surgical intervention. Unless compressive optic neuropathy or severe corneal exposure is present, surgery is generally delayed during the active inflammatory phase of TAO. Surgery is usually performed during the quiescent cicatricial phase of the disease. Patients who show a favorable response to corticosteroids usually show a good response to orbital radiotherapy. Nutrient-rich diets, stress reduction techniques, and an avoidance of environmental triggers including excess dietary iodine and stress, are also essential steps in the healing process.

4. Conclusion

This is a rare being 3rd case report in literature known to us of thyroid related severe ophthalmopathy / orbitopathy in a structurally and functionally normal thyroid gland related to very high titre (Anti-TPO =371.6) of Anti-TPO antibodies. Thyroid ophthalmopathy is a feature of thyroid illness with deranged thyroid function and radiologically normal thyroid gland.

References

population representing the gene contribution from several ethnic backgrounds. Thyroid. 2001;1:31-35.


