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GRAVES DISEASES WITH SEVERE PROGRESSIVE OPHTHALMOPATHY AFTER THYROIDECTOMY. CASE REPORT.

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Abstract

Graves' disease is an autoimmune disease that may consist of hyperthyroidism, goiter, orbitopathy, and occasionally a dermopathy referred to as pretibial or localized myxedema. Graves' disease is caused by autoantibodies that bind to the thyrotropin receptor, stimulating growth of the thyroid and overproduction of thyroid hormone. Clinical manifestations of Graves' disease include diffuse goiter and symptoms and signs resulting from hyperthyroidism.

Thyroid hormones excess affects several different body systems, and for this reason, signs and symptoms associated with Graves' disease can vary strongly, and significantly influence the general well-being. Common symptoms are: tremor, heat sensitivity and warm, weight loss even if with normal eating habits, anxiety and irritability, enlargement of the thyroid gland, alterations in menstrual cycles, erectile dysfunction or decreased libido, fatigue, frequent bowel movements, palpitations, and others. Graves' orbitopathy is present in about 30-50% of patients with Graves disease. Graves' orbitopathy is an autoimmune disease of the retroocular tissues occurring in patients with Graves' disease.We present the clinical case report with progressive ophthalmopathy after a total thyroidectomy. In our case after surgery his ophthalmopathy did not regress and, in fact, was progressive. In the vast majority of cases of Grave's ophthalmopathy, the periorbital edema regresses significantly after a total thyroidectomy. This patient's ophthalmopathy did not regress after surgery even the ophtalmopathy progressed. Only after initiation of pulsatile therapy of 500 mg of methylprednisolone weekly did the ophthalmopathy regress noticeably.

Keywords: *Graves disease, ophtalmopathy, hyperthyroidism, thyroid gland.*

Introduction

Graves' disease is an autoimmune disease that may consist of hyperthyroidism, goiter, eye disease (orbitopathy), and occasionally a dermopathy referred to as pretibial or localized myxedema. Graves' disease was originally described by the Irish physician, Robert James Graves in 1835. Prevalence of Graves' disease is relatively high compared to other hyperthyroidism causes *[McLeod DS et al.,2015]*.

Graves' disease is caused by autoantibodies that bind to the thyrotropin receptor (TSHR-Ab), stimulating growth of the thyroid and overproduction of thyroid hormone. Clinical manifestations of Graves' disease include diffuse goiter and symptoms and signs resulting from hyperthyroidism. Graves' disease is often associated with ophthalmopathy, which is not found in other etiologies of hyperthyroidism and is not caused by the high serum thyroid hormone concentrations [*Smith TJ, Hegedus L, 2016*].

Genetic factors strongly influence the predisposition to Graves' disease, as shown in a population-based study of Danish twins, which estimated that approximately 80 percent of the risk of Graves' disease is attributable to genetic factors [*Brix TH et al.,2001*]. The cellular actions of thyroid hor-

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mone are mediated by T_3, the active form of thyroid hormone. T_3 binds to two specific nuclear receptors (thyroid hormone receptor α and β) that regulate the expression of many genes. Nongenomic actions of thyroid hormone include regulation of numerous important physiologic functions. Thyroid hormone influences almost every tissue and organ system. It increases tissue thermogenesis and basal metabolic rate and reduces serum cholesterol levels and systemic vascular resistance. Some of the most profound effects of increased thyroid hormone levels occur within the cardiovascular system [*Alexander I, 2022*]. Untreated or partially treated thyrotoxicosis is associated with weight loss, osteoporosis, atrial fibrillation, embolic events, muscle weakness, tremor, neuropsychiatric symptoms, and rarely cardiovascular collapse and death [*Taisuke U et al., 2022*]. Only moderate correlation exists between the degree of thyroid hormone elevation and clinical signs and symptoms [*Michela B, 2022*]. Symptoms and signs that result from increased adrenergic stimulation include tachycardia and anxiety and may be more pronounced in younger patients and those with larger goiters[*Klein I, Ojamaa K,1994*].

The signs and symptoms of mild, or subclinical, thyrotoxicosis are similar to those of overt thyrotoxicosis but differ in magnitude [*Li Y et al., 2020*]. Measurable changes in basal metabolic rate, cardiovascular hemodynamics, and psychiatric and neuropsychological function can be present in mild thyrotoxicosis [*Raymond S, 2022*].

Thyrotoxicosis rarely can cause thyrotoxic periodic paralysis (acute muscle paralysis and severe hypokalaemia), with a higher incidence in Asian men with thyrotoxicosis and is often a consequence of infection, alcohol, high carbohydrate load, or a hard physical activity. Patients with thyrotoxicosis rarely manifest a life-threatening condition called thyroid storm, that is associated with deranged liver function, altered mental state, fever, agitation, features of cardiac failure, and tachycardia [*Margret E et al.,2019*]. Different events such as surgery, childbirth, infection, trauma or a poor compliance to the treatment, are able to precipitate the condition [*Yotsapon T et al.,2021*].

Pretibial myxedema, also known as Graves' dermopathy or thyroid dermopathy, is a rare infiltrative dermopathy complication of Graves' disease, whose incidence rate is about 1-5%. This complication usually follows the ocular signs found in Graves' disease. It appears as a waxy, discolored induration of the skin (described as having a so-called peau d'orange appearance) on the anterior aspect of the lower legs, that spreads to the dorsum of the feet; or as a non-localised, non-pitting edema of the skin in the same areas. In advanced cases, it can reach the upper trunk as well as upper extremities (face, neck, back, chest and ears). Acropachy resembles clubbing of the fingers or toes and is present only in patients with dermopathy.

Graves' orbitopathy is present in about 30-50% of patients with Graves' disease. Graves' orbitopathy is an autoimmune disease of the retroocular tissues occurring in patients with Graves' disease [*Bahn RS, Heufelder AE, 1993*]. Although it has often been referred to as Graves' ophthalmopathy, or simply thyroid eye disease, it is primarily a disease of the orbit and is better termed Graves' orbitopathy. Thyroid-associated orbitopathy may precede, coincide, or follow the systemic complications of dysthyroidism [*Minghong T et al.,2021*].

In Graves' disease, the main autoantigen is the thyroid-stimulating hormone (TSH) receptor, which is expressed primarily in the thyroid but is also expressed in adipocytes, fibroblasts, and a variety of additional sites and appears to be closely aligned with the insulin-like growth factor 1 (IGF-1) receptor. TSH receptor antibodies and activated T cells also play an important role in the pathogenesis of Graves' orbitopathy by activating retroocular fibroblast and adipocyte TSH receptor and IGF-1 receptors and initiating a retro-orbital inflammatory environment[*Terry F et al.,2020*].

Risk factors for thyroid-associated orbitopathy include increased age of onset, duration of Graves hyperthyroidism, and smoking [*Yann-Sheng L et al.,2017*]. The ocular manifestations of thyroid-associated orbitopathy include eyelid retraction, proptosis, chemosis, periorbital edema, and altered ocular motility with significant func-

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

tional, social, and cosmetic consequences. Of affected patients, 20% indicate the ocular morbidity of this condition is more troublesome than the systemic complications of dysthyroidism [*Tauseef N, Nadeema R, 2022*] Ophthalmopathy is characterized by inflammation of the extraocular muscles and orbital fat and connective tissue, which results in proptosis (exophthalmos), impairment of eye muscle function, and periorbital edema. Patients with these findings almost always have Graves disease. Patients with ophthalmopathy may have a gritty feeling or pain in their eyes, and they may have diplopia caused by extraocular muscle dysfunction. Corneal ulceration can occur as a result of proptosis and lid retraction.

Diagnosis of Graves' disease made based on signs, symptoms, and the result of the ancillary laboratory tests. Clinically, Graves' disease can be diagnosed based on the signs and symptoms of thyrotoxicosis.

Case presentation

A 58 yr old male, presented to the department of endocrinlology of Muratsan University hospital with progressive ophthalmopathy after a total thyroidectomy. A 57 year-old male presented to his local outpatient clinic in 2021 with unexplained fever, chills, aches, weight loss, and heat intolerance. It is noteworthy to mention that he had COVID-19 in 2020 and reports experiencing severe stress during the pandemic which was established by phychologist. There was goiter and the patient described a sense of dysphagia. Total volume of thyroid gland was 35 *ml*. After testing, TSH 0.002 *mU/L* (N 0.4-4.0), free T4 16.8 *ng/dl* (N 0.9-2.3), free T3 12.4 *pmol/l* (N 2.0-7.0) and high level of TSH receptor antibodies 36.2 *IU/I* (N <1.5) a diagnosis of Grave's disease was confirmed and he was prescribed methimazole 30 *mg* daily. Hi has no family history of thyroid diseases. The first signs of ophthalmopathy began while receiving antithyroid medication and the patient reported changes in vision, tearing, and diplopia around the months of June-July of 2021. Considering the remaining compression of the neck, overactive hyperthyroidism, high level of TSH receptor antibodies and taking into account that medication treatment was not satisfactory, total thyroidectomy was recommended. Post-operation, he was prescribed 175 *mkg* of levothyroxine and was stable. However, after surgery his ophthalmopathy did not regress and, in fact, was progressive. His symptoms of Craves eye disease include redness of the conjunctiva, severe swelling of the eyelids, incomplete closure of the eye and double vision (See Figure 1 A.). A magnetic resonance imaging was done and revealed eye protrusion, increased orbital fat with compression on the optic nerve and increased volume of the extraocular muscles. He came to our hospital on February with complaints of progressive of ophthalmopathy. He was prescribed 500 *mg* of methylprednisolone which he has taken a total of 8 times (total dose 4 *g*). Opthalmopathy began to regress after initiation of methylprednisolone (See Figure 1B.). The patient reports his vision has gotten better, but it is not at pre-diagnosis level. Reports loss of depth perception and sensitivity to wind and dust. He reports no family history of thyroid or any other autoimmune disease. The patient reports bowel incontinence. He has regained his lost weight.

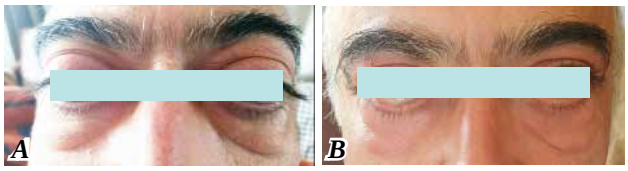

FIGURE 1*. Graves ophthalmopathy after surgery (A) and before treatment with methylprednisolone (B)*

Conclusion. It was interesting that in the vast majority of cases of Grave's ophthalmopathy, the periorbital edema regresses significantly after treatment especially after total thyroidectomy. Our patient's ophthalmopathy did not regress after surgery even the ophtalmopathy progressed. Only after initiation of pulsatile therapy of 500 *mg* of methylprednisolone weekly did the ophthalmopathy regress noticeably.

REFERENCES

1. *Alexander Iwen (2022).* Schilddrüsenfunktionsstörungen im Alter. Geriatrie up2date 04:02, 77-89. DOI: 10.1055/a-1561-9335
2. *Brix TH, Kyvik KO, Christensen K, Hegedüs L (2001).* Evidence for a major role of heredity in Graves‘ disease: a population-based study of two Danish twin cohorts. J Clin Endocrinol Metab ; 86:930.doi.org/10.1210/jcem.86.2.7242
3. *Bahn RS, Heufelder AE (1993).* Pathogenesis of Graves‘ ophthalmopathy. N Engl J Med 329:1468. DOI: 10.1056/NEJM199311113292007
4. *Klein I, Ojamaa K (1994).*Thyroid hormone and the cardiovascular system: from theory to practice. J Clin Endocrinol Metab 78:1026. DOI: 10.1210/jcem.78.5.8175954
5. *McLeod DS, Cooper DS, Ladenson PW, et al. (2015).* Race/Ethnicity and the prevalence of thyrotoxicosis in young Americans. Thyroid ; 25:621.DOI: 10.1089/thy.2014.0504
6. *Michela Bottani, Aasne K. Aarsand, Giuseppe Banfi, Massimo Locatelli, Abdurrahman Coşkun, Jorge Díaz-Garzón, Pilar Fernandez-Calle, Sverre Sandberg, Ferruccio Ceriotti, Anna Carobene (2022).* European Biological Variation Study (EuBIVAS): within- and between-subject biological variation estimates for serum thyroid biomarkers based on weekly samplings from 91 healthy participants. Clinical Chemistry and Laboratory Medicine (CCLM) 60:4, 523-532. DOI: 10.1515/cclm-2020-1885
7. *Minghong Tong, Jun Ding, Biao Huang, Jindan Chen, Xin Wei, Zhiming Li, Jie Shu, Zhigang Hu, Xiaohong Jiang, Huiming Sheng (2021).* Evaluation of the application of TSH receptor stimulating autoantibodies and the optimization of detection strategy in Graves’ disease. Clinica Chimica Acta 521, 34-39. DOI: 10.1016/j.cca.2021.06.017
8. *Margret Ehlers , Matthias Schott, Stephanie Allelein (2019).* Graves’ disease in clinical perspective. Front Biosci (Landmark Ed). Jan 1;24(1):35-47. DOI: 10.2741/4708
9. *Li Y, Cui X, Yang Y, Liang Y, Chai F, Sun YC, Shao C, Mo H, Yin S, Yang Z, Zhang F.(2020)* Surgical treatment of children Graves‘ disease with huge goiter-a case report and literature review. Gland Surg. Apr;9(2):467-473. doi: 10.21037/gs.2020.02.19
10. *Smith TJ, Hegedus L(2016).*Graves’ Disease. N Engl J Med ;375:1552-65. DOI: 10.1056/NEJMra1510030
11. *Taisuke Uchida, Hideki Yamaguchi, Takayuki Kawabata, Hiroyuki Tanaka, Fumiaki Kawano, Kazuya Shimoda (2022).* Longitudinal changes in an autonomously functioning thyroid nodule with coexisting follicular thyroid carcinoma over 14 years. Oxford Medical Case Reports 2022:4. doi.org/10.1093/omcr/omac041
12. *Tauseef Nabi, Nadeema Rafiq. (2022).* Comment on “factors associated with severity of orbitopathy in patients with Graves‘ disease. Taiwan Journal of Ophthalmology 12:1, 118. DOI: 10.4103/tjo.tjo_3_21
13. *Terry F Davies , Stig Andersen , Rauf Latif , Yuji Nagayama , Giuseppe Barbesino , Maria Brito, Anja K Eckstein, Alex Stagnaro-Green, George J Kahaly(2020).* Graves’ disease Nat Rev Dis Primers. Jul 2;6(1):52. DOI: 10.1126/scisignal.aah4120
14. *Raymond S. Douglas, Andrea L. Kossler, Jody Abrams, Cesar A. Briceño, David Gay, Andrew Harrison, Michael Lee, John Nguyen, Shannon S. Joseph, Dianne Schlachter, Jeremy Tan, Judah Lynch, Louisa Oliver, Richard Perry, Shoaib Ugradar (2022).* Expert Consensus on the Use of Teprotumumab for the Management of Thyroid Eye Disease Using a Modified-Delphi Approach. Journal of Neuro-Ophthalmology doi: 10.1097/WNO.0000000000001560
15. *Yotsapon Thewjitcharoen, Krittadhee Karndumri, Waralee Chatchomchuan, Sriurai Porramatikul, Sirinate Krittiyawong, Ekgaluck Wanathayanoroj, Nampetch Lekpittaya, Worawit Kittipoom, Tawee Anuntakulnatee, Somboon Vongterapak, Siriwan Butadej, Soontaree Nakasatien, Rajata Rajatanavin, Thep Himathongkam. (2021).* Practice patterns and outcomes in the management of Thai patients with Graves’ disease. Thyroid Research 14:1.
16. *Yann-Sheng Lin, Jen-Der Lin, Chih-Chieh Hsu, Ming-Chin Yu (2017).* The long-term outcomes of thyroid function after subtotal thyroidectomy for Graves‘ hyperthyroidism. J Surg Res . Dec;220:112-118. DOI: 10.1016/j.jss.2017.06.091

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