



## RESEARCH ARTICLE

### OCULAR MANIFESTATION OF GRAVE'S DISEASE: A CASE REPORT OF GRAVE'S OPHTHALMOPATHY IN A PEDIATRIC PATIENT

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#### ABSTRACT

Grave's disease (GD) is an autoimmune disorder characterized by the presence of autoantibodies that bind to the thyrotropin receptor (TR) in the gland, leading to excess production of thyroid hormones maintaining a state of hyperthyroidism. Also this autoantibodies recognize the TR present on orbital fibroblasts, which produce the tissue changes of Grave's ophthalmopathy (GO): eyelid retraction and swelling, proptosis, orbital congestion (chemosis), exposure keratopathy, extraocular motility dysfunction, as well as compressive optic neuropathy in more severe cases. The case of a 14-years-old patient with bilateral proptosis is presented.

#### INTRODUCTION

GD is an autoimmune disorder in which there are autoantibodies that bind to the TR in the thyroid gland activating it, leading to excess production of thyroid hormones maintaining a state of hyperthyroidism, (Sadeghi, 2015). It's involvement goes not only the thyroid gland, also orbital and periorbital tissue, mixedema or pretibial edema. The initial clinical manifestations are nonspecific: tachycardia, diarrhea, increased appetite with or without weight loss, asthenia, sleep disorders, thermo phobia, irritability, tremors, palpitations and behavioral disorders (Ibañez L, 2017). Unlike adults, ophthalmopathy occurs in a minority of patients, a low incidence has been recorded with 1.7 to 3.5 cases per 100 000 children per year (Jankauskiene, 2017). GO is manifested by an increase of the volume of extraocular muscles, also the connective tissue and retroorbital adipose due to the inflammatory process and the accumulation of Glycosaminoglycans (GAGs), secreted by fibroblast as a consequence of the cytokines activity after binding of autoantibodies to TR (Santos M., 2013).

#### CASE REPORT

14-year-old male patient, originally from Mexico City. Diagnosis of myopia for 2 years ago. His condition begins in February with excessive food intake, weight loss, distal fine tremor in arms, mood swings, irritability and difficulty falling asleep.

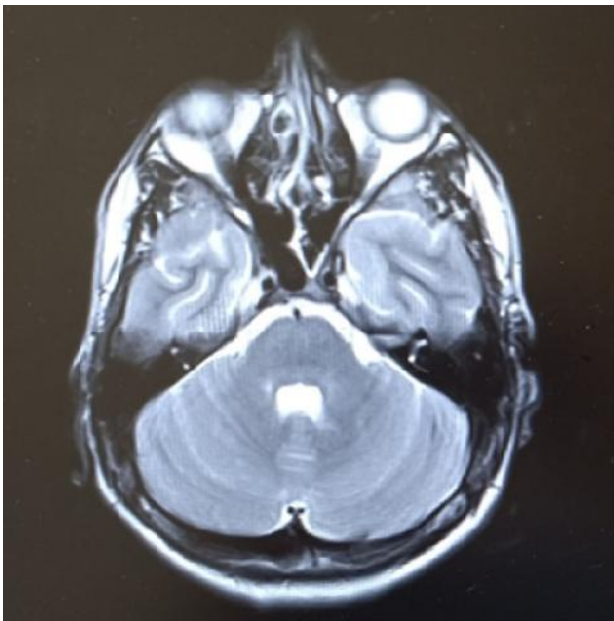
In May, he noted bilateral proptosis with a predominance in the right eyeball, decreased visual acuity and increased body temperature without reaching fever. Two months later, he went to the emergency service to notice an increase of right - side proptosis. Ophthalmological examination: -right eye: visual acuity 20/40, intraocular pressure 15mmHg, anterior segment and retina without alterations. -left eye: visual acuity 20/30, intraocular pressure 15 mmHg, anterior segment, and retina without alterations. It was suspected in tumor or thyroid disease. Laboratory studies were performed. Aspartate aminotransferase 23 UI/l, alanine aminotransferase 25.2 UI/L, leukocytes 4.8%, hemoglobin 15.3 mg/dl, platelets 218 000, lymphocytes 41.4%, monocytes 7.9%, neutrophils 48%, eosinophils, 2.4%, calcium 9.6, phosphorus 4.9 mg/dl, magnesium 1.7 mg/dl, sodium 137mg/dl, chlorine 104.9 mg/dl, potassium 3.8 mg/dl. Glucose 74.7 mg/dl, creatinine 0.59mg/dl, lactic dehydrogenase 145 UI/l. Altered thyroid profile: Total triiodothyronine 1.81 ng/ml, Free thyroxine 2.56 ng/dl (0.99-1.81 ng/dl), Thyroid Stimulating Hormone (TSH) 0.0mUI/ml(0.53-5.16UI/ml), Total Thyroxine T4 14.67mcg/dL(5.08-10.58 mcg/dL), Free T35.76pg/ml(2.5-3.9pg/ml). Thyroglobulin antibodies (TgAb) 38.2 U/ml(0-4 U/ml), Thyroglobulin 1.16ng/ml (1.15-130.7 ng/ml), Myeloperoxidase Antibodies 3.88 URL/ml (<20URL/ml), Thyroid Stimulating Immunoglobulin (TSI) 8.38u/L(0-15 U/L), Thyroid Stimulating Hormone Receptor Antibody (TRAb) 49 U/ml (0-1.8 U/ml). Chest X-ray without pathological images. Skull Contrast MRI: negative for intracranial or orbital tumor, predominantly right exophthalmos, increased volume of extraocular muscles with abnormal enhancement in the right eye, data of thyroid orbitopathy.

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**Figure 1. Bilateral proptosis and eyelid retraction predominantly in right eye**

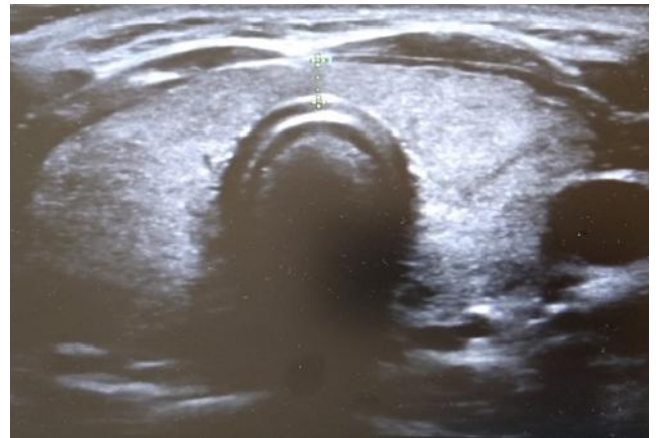


**Figure 2. Skull Magnetic Resonant Imaging with an increase in the volume of extraocular muscles with abnormal reinforcement in the right eye**

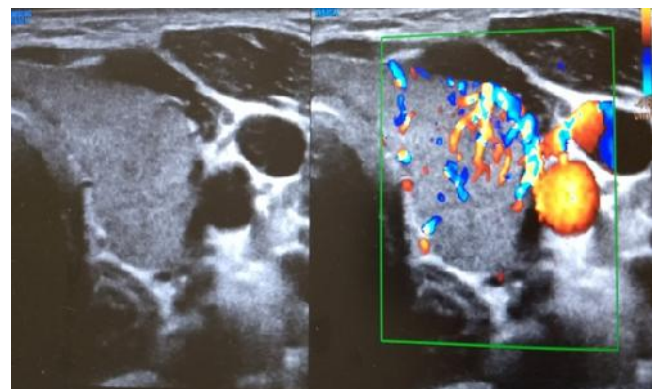


**Figure 3. Orbits Simple Computed Axial Tomography that shows bilateral exophthalmos with increased volume of the right extraocular muscles**

Simple orbital Computed Tomography with report of right bilateral exophthalmos, increased volume of right extraocular muscles. Thyroid ultrasound reported a thyroid gland in a usual situation with defined borders, preserved morphology, but with an increased dimension of both lobes. The diagnosis of GD and GO was integrated due to being with hyperthyroidism, low TSH levels, high T3 and T4 levels, TRab and TgAb positive and ophthalmological involvement, rejected previously suspected orbital tumor.



**Figure 4. Ultrasound of the thyroid gland with an increased dimension of both lobes, micronodular pattern**



**Figure 5. Color Doppler ultrasound: Thyroid gland in habitual situation with increased vasculature**

Treatment was given with Thiamazole 15 mg orally every 12 hours and Propanolol 5 mg orally every 8 hours. Symptomatic treatment with artificial tears. The patient showed gradual improvement of the symptoms, propranolol was discontinued three months after treatment and did not require corticoid or surgical treatment for ocular involvement.

**DISCUSSION**

GO is a rare entity in pediatric patients, reporting an incidence of 1.7 to 3.5 cases per 100,000 children each year. (Jankauskiene J.,2017). It predominates in girls with a ratio of 5:1 and occurs more frequently in adolescents (11-18 years 68.2%) than in children under 11 years (Uribe M, 2012).The accumulation of GAGs in the endomysium, predominantly highly hydrophilic hyaluronate, leads to an excessive accumulation of water in the tissues of the orbit and muscles, in addition to the infiltration of inflammatory cells: IL-1 , IL-1 , IL-6, IL-8, transforming growth factor (TGF- ). The most frequent symptoms in children are eye pain, foreign body

sensation, hypersensitivity to light, epiphora, occasionally diplopia, eyelid retraction and proptosis (Szczapa, 2016). There are no specific biochemical determinants for the diagnosis of GO, however, measurement of TSI levels has been used as a marker of GO activity (Acuna O., 2007). Treatment of GD is crucial for the improvement of GO. This patient must be treated by pediatric endocrinology and ophthalmology. Antithyroid drugs generally improve the eye condition. Reserving the major intervention in those cases that don't present improvement after reaching the euthyroid state. In this case, the therapy used is the use of corticosteroids. Descompressive surgery is rare. (Penta, 2018).

## Conclusion

Grave's disease is a rare pathology in children, even more the appearance of ophthalmopathy with serious manifestation. Although its course is less aggressive than in the adult population, it is important to make the early diagnosis to avoid complications.

## Glossary of abbreviations

GD: Grave's disease  
 GO: Grave's ophthalmopathy  
 TR: Thyrotropin receptor  
 GAGs: Glycosaminoglycans  
 TSH: Thyroid Stimulating Hormone  
 TSI: Thyroid stimulating immunoglobulin  
 MRI: Magnetic Resonance Imaging

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