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Dysthyroid orbitopathies: Review of 156 cases

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Abstract
The objective is to determine the frequency and clinical forms of dysthyroidian orbitopathies, in order to argue the current practical diagnostic and therapeutic attitude.
A retrospective study based on the analysis of 570 patient files is conduct from 2006 to 2015, in the Ophthalmology and Metabolic and Endocrine Diseases departments of the Teaching University Hospital of Brazzaville, Congo. All patients received a complete clinical and ophthalmic examination. Patients were classified according to EUGOGO staging. The hospital frequency of dysthyroid orbitopathies was 0.3% of all patients received in ophthalmology and 1.5% in Metabolic Diseases. The results indicated that 156 patients [9 males (5.8%) and 147 females (94.2%)] with hyperthyroidism had dysthyroid orbitopathy (27.3%) and 98 exophthalmia (17.2%). The mean age was 35.5 years (range: 16-72 years). The minimal impairment was dominated (61.5% of cases), including 62 patients with exophthalmia of less than 3 mm and 32 cases with soft tissue involvement. The moderate lesion was found in 38.5%, made of palpebral retraction (24 cases) and exophthalmos greater than or equal to 3 mm (36 cases). Any severe damage did'nt observed. Therapeutically, only medical treatment has been prescribed including synthetic antithyroid drugs, local lubricants and corticosteroid therapy. In conclusion, the dysthyroid orbitopathy observed in our daily practice is dominated by minimal and moderate forms. The treatment is multidisciplinary, the therapeutic modalities obey the recommendations of the European Study Group of EUGOGO.

Keywords: orbitopathy, dysthyroidism, exophthalmia

Introduction
Dysthyroid orbitopathy (OD) is an inflammatory pathology of the orbit associated or not with a disorder of the thyroid function. There are pure ophthalmic forms and the diagnosis is made in front of eyelid retraction, exophthalmia, oculomotor disorders, inflammatory signs and optic nerve damage [1]. It affects the quality of vision and life. About 5% of patients have a severe form with corneal involvement or optic neuropathy threatening visual function [2]. The ODs are associated with hyperthyroidism in 80% of cases. Five to 10% of patients developing an OD have autoimmune hypothyroidism (Hashimoto's thyroiditis) and for 5% there are no abnormalities of thyroid function [3]. Management was codified by European Group on Graves' Orbithopathy (EUGOGO); it is multidisciplinary, based on the balance of thyroid function, the removal of aggravating factors, management thyroid pathology is common in our environment. It is the second endocrine affection after a diabetes mellitus [5]. Thus, we purpose to determine frequency, clinical forms of dysthyroidian orbitopathies, in order to argue the current practical diagnostic and therapeutic attitude.

Material and Methods
Nature, scope and period of study
This study analyzed retrospectively 570 patient consulted respectively in Department of Ophthalmology and Department of Metabolic and Endocrine Departments study, from January 2006 to December 2015.

Patients
These were included all records of patients with a clinical examination performed by an endocrinologist and highlighting signs of dysthyroidism namely: hormonal assays of T3, T4 and ultra-sensitive TSH. Ophthalmologic examination was performed by 3 ophthalmologists and included visual acuity, exophthalmia with Hertel's exophthalmometer, eye tone with automatic tonometer. Examination of the eyelids was done with the inspection, the anterior segment of the slit lamp, the ocular motility in the 9 positions of the view in duction and version, from the fundus of the eye to the biomicroscope with a lens of 90° volk and the visual field at the Goldmann campimeter or the Octopus 300. Scan or MRI scan were used if possible. Dysthyroid orbitopathy was stadified by the clinical activity score described by EUGOGO [4], which quantifies the inflammatory nature of orbital involvement in three stages [6-7]:

- Severe impairment threatening the visual prognosis by optic neuropathy and / or corneal ulcer.
- Moderate to severe involvement with palpebral retraction greater than or equal to 2 mm, moderate to severe soft tissue involvement, exophthalmia greater than or equal to 3 mm beyond norms for gender and ethnicity, diplopia.

- Minimal impairment includes small soft tissue involvement, exophthalmia less than 3 mm, absent or transient diplopia, superficial keratitis.

Variables

The following variables were studied following the compilation of patient records:

- Type of ophthalmological events staged according to EUGOGO;
- Sex of patients;
- Age of patients;
- Biological aspects of ophthalmological events;
- Medical imaging aspects;
- Therapeutical aspects;
- Evolutive aspects.

Statistical analysis

The data was entered using Microsoft Excel 2010 for the calculation of the distribution frequencies of the various parameters and then transferred to the SPSS (Statistical Package for Social Sciences) version 17.0 software for appropriate analyzes. Traditional formula of statistics was used for comparing two percents [6]. p-value <0.05 defined statistical significance.

Results and Discussion

During the study period, out of 570 patient files compiled: 156 hyperthyroid patients had a dysthyroid orbitopathy (27.3%), of whom 98 had exophthalmos (17.2%). The hospital frequency of dysthyroid orbitopathies was 0.3% of all patients consulted in ophthalmology and 1.5% in Metabolic Diseases. There were 9 men (5.8%) and 147 women (94.2%), sex ratio equal to 0.06. There were 5 men (5%) and 93 women (95%) with exophthalmia. The mean age was 35.5 years (range: 16-72 years). Four patients were aged less to 20, 44 subjects with age comprised 20-40 years, 94 with age comprised 40-60 years and 14 patients were aged over 60 years old. Dysthyroid orbitopathy is a common condition. In the literature, it is present in 40% of patients with Graves' disease [3]. In our series the frequency seems underestimated, this could be explained by the inaccessibility of our populations to healthcare, hormonal and serological assays and medical imaging. Dysthyroid orbitopathy is especially seen in women. All ages can be affected with a peak between 40 and 50 years [3, 7]. Clinically, the palpebral signs are the most frequently encountered lesions with palpebral retraction in 90% of cases [1, 2, 3, 4, 6, 7, 8].

The main ophtamologycal events were (table 1): exophthalmos for 98 cases (62%), orbital and conjunctival oedema for 32 cases (20%), upper palpebral retraction for 24 cases (15%) and ocular motility disorder for 2 cases (1%).

Table 1: Ophthalmological events staged according to EUGOGO

Stade/ EUGOGO	Signs	Number	Pourcentage
Severe attack	Optic neuropathy	-	-
	and/or corneal ulcer	-	-
Moderate to severe impairment (n = 60)	Palptive retraction greater than or equal to 2 mm	24	15.4
	Moderate to severe impairment of soft tissues	-	-
	Exophthalmos greater than or equal to 3	36	23,1
	diplopia	-	-
Minimal damage (n = 96)	Small soft tissue involvement	32	20,5
	Exophthalmos less than 3 mm	62	39,7
	Absentee or transient diplomacy	2	1,3
	Superficial Keratitis	-	-

Exophthalmos were greater than 20 mm in (63.2%), between 22-25 mm in (29%) and greater than 25 mm (7%). It was bilateral in 79% of cases, axile and reducible in 97% of cases. Exophthalmitis is present in 40-90% of patients and appears as the most stable sign in time and rarely regressive spontaneously [1, 3]. The abnormalities of intrinsic motility were poorly represented in our series, whereas they are present in 60% of patients and are responsible for diplopia in the extreme looks and / or the primary gaze [1, 3]. We did not find complications such as exposure keratitis or compressive optic neuropathy that make the pathology serious.

The decrease in visual acuity was found in 92 cases (59%). Cardiac arrhythmias and neuromuscular manifestations were the main signs of hyperthyroidism. The decrease in visual acuity was moderate and due to the inflammatory signs present at the beginning of the evolution of the disease. Among the symptoms of hyperthyroidism, rhythm disturbances and neuromuscular manifestations were the main signs of appeal.

Biologically thyroid hormones were elevated in more than 98% of cases with TSH collapse in 95% of cases. The determination of thyroid hormones is essential for diagnosis, Graves' disease being an autoimmune disorder whose main target is the thyrotropin receptor (TSH). An abnormality in the recognition of this receptor results in the secretion of anti-TSH receptor autoantibodies that will stimulate TSH receptors and trigger increased secretion of thyroid hormones [9].

Computed tomography without contrast injection was performed in 25% of patients (Fig. 1) and two patients (1%) had MRI. Sectional imaging allows the analysis of the orbital content, it is often a supplement to the clinic. The CT scan measures the exophthalmos, evaluates the increase in the volume of the muscular body and visualizes the optic nerve. Computed tomography allows to distinguish the exophthalmos of muscular forms linked to the hypertrophy of the oculomotor muscles from those of the fatty forms related to a hypertrophy of the intra-orbital fat [10]. MRI improves the quality of images and allows evaluation of moderate and severe forms. It must

be systematic in case of heavy treatment with immunosuppressors or radiotherapy to adapt doses [11].

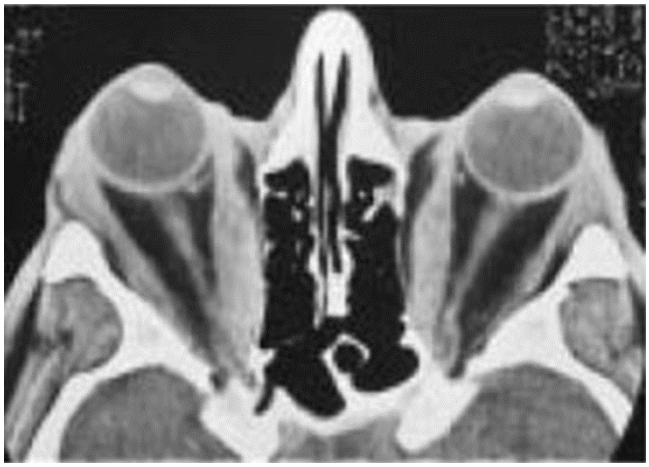

Fig 1: Computed tomography of OD. Neuro-ophthalmological plan. Large exophthalmos (1), eyeballs in front of the bicanthal line. Increase in the volume of internal rights (2)

Therapeutically, only medical treatment was prescribed including synthetic antithyroid drugs for 18 months and corticosteroid therapy at the dosage of 1 mg / kg / day for 10-15 days and progressive weaning for a total duration of less than 3 months. Boluses of weekly corticosteroid treatment of 500 mg were performed for 6 weeks in some patients in moderate to severe forms. With a follow-up of 5 years, 55% of patients had an exophthalmia regression of less than 18 mm, 25% had residual exophthalmia and 20% were lost to follow-up. Therapeutic modalities have been well codified by the EUGOGO European Study Group [2, 4]. The goal is to get euthyroidism by avoiding the transition to hypothyroidism. In our series the minimal forms were the most represented with 61.5% of the cases. Treatment with local lubricants, oral corticosteroids and synthetic antithyroid drugs were used to control inflammation. Moderate to severe forms require, in addition to synthetic antithyroid drugs, intravenous corticosteroid therapy [12, 13] with or without radiotherapy. Other immunosuppressive therapies are available in patients who do not respond to corticosteroids, but their use can be discussed [11, 14].

Surgical treatment with orbital decompression is indicated in severe forms when the visual prognosis is threatened and in case of sequelae. It reduces oculomotricity disorders, reduces exophthalmitis and is indicated immediately in case of compressive optic neuropathy.

Conclusion

Dysthyroid orbitopathy is observed in our daily practice, dominated by minimal and moderate forms. The treatment is multidisciplinary, the therapeutic modalities obey the recommendations of the European study group of EUGOGO. The treatment is aimed at anti-inflammatory at the initial stage and surgical in severe and sequential forms.

Declaration of interests

The authors declare that they have no conflict of interest in relation to this article.

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