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Bilateral exorbitism revealing thymic hyperplasia: Case report and review of the literature

Bellamlih Habib, Ayouche Othman, Meriem Fikri, Mohammed Jiddane, Moulay Rachid El Hassani

ABSTRACT

Introduction: Graves' thyroiditis is an autoimmune disease, commonly associated with other autoimmune disorders, such as myasthenia gravis, autoimmune gastritis, Type 1 diabetes, vitiligo, and Addison's disease. There is a well-documented association between Graves' disease and thymus hyperplasia. The knowledge of this association makes it possible to avoid a risky and unnecessary surgery of a thymus mass in patients with Graves' disease. Case Report: We report the case of a patient with bilateral exophthalmos. The biological and radiological assessment was in favor of a grave disease associated with thymus hyperplasia. A medical treatment was administered with a favorable evolution. There were no sign of malignancy in the follow up exam. Conclusion: Knowledge of the association between Graves' disease and thymus hyperplasia is necessary. For there is some authors that preconize thymus surgery in cases of resistant grave disease. The favorable evolution under medical treatment makes it possible to avoid unnecessary, even dangerous, thymus mass surgery in patients with Graves' disease by proposing a simple radiological monitoring.

Keywords: Computed tomography, Exorbitism, Grave's disease, Thymic hyperplasia, Ultra-sound

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INTRODUCTION

Graves' disease is an autoimmune disease, commonly associated with other autoimmune disorders, such as myasthenia gravis, autoimmune gastritis, type 1 diabetes, vitiligo, and Addison's disease [1].

There is also a rare but well-documented association between Graves' disease and thymic hyperplasia that was described in 1914 and confirmed in the 1960s [2]. The knowledge of this association makes it possible to avoid a risky and unnecessary surgery of a thymic mass in patients with Graves' disease [3].

In this work, we report the case of a patient with bilateral exophthalmos. The biological and radiological assessment was in favor of a grave disease associated with thymic hyperplasia. A medical treatment was administered with a favorable evolution. There were no sign of malignancy in the follow up exam.

CASE REPORT

A 20-year-old patient, with no personal or family history of disease, who had bilateral exophthalmos associated with a progressive decrease in the left eye visual acuity. Clinical examination found signs of thyrotoxicosis associated with anterior cervical swelling. Ophthalmological examination revealed, in addition

to the decrease in visual acuity, a central corneal defect measuring 2x2 mm on the left. Examination of the appendix showed non-reducible, non-pulsatile axillary exophthalmoses with bilateral palpebral retraction. There was an optic atrophy with poor macular reflection on the left eye and a papillary hyperemia on the right. An initial biological assessment confirmed hyperthyroidism with a braked TSH at 0.002U / mL, high free T4 54pmol/l and free T3 15pmol/l. Anti-TSH receptor antibodies are positive at 4 IU / L. Cervical sonographic findings revealed a globally hypoechoic heterogeneous thyroid gland with color doppler revealing global hyperemia (Figure 1). Therefore, the diagnosis of a Graves' disease exophthalmos is related to the association of bilateral exophthalmia, clinical and biological hyperthyroidism, goiter and the presence of anti-TSH receptor antibodies. Ultrasound was completed with an orbital and a cervicothoracic computed tomography. At the orbital level there was a bilateral exophthalmia grade III, with a fusiform thickening of the right muscles and hypertrophy of the intra and extra conal fat (Figure 2). The thyroid gland was enlarged in volume and homogeneous density (Figure 3). At the thoracic level, there was a well delineated homogeneous soft-tissue mass, without invasion of neighboring structures, measuring 63 mm in transverse diameter, 27 mm in anteroposterior diameter and 78 mm in height (Figure 4). Initially, treatment with synthetic antithyroid drugs was started in combination with corticosteroids bolus of methyl-prednisolone (1 g, three days in a row) and prednisone 2 mg / kg / day for four weeks. Subsequently, the patient underwent bone decompression with lipectomy by the lower palpebral approach associated anterior position of the orbital rim. There were no complications in the post-operative and the two months follow up. Clinically, a clear improvement hyperthyroidism's clinical signs was obtained with a slight regression of exophthalmia. An eye exam showed a stability of the lesions. A cervical ultrasound was performed after two months of treatment, showing a clear thymic mass reduction.

DISCUSSION

Graves' disease is an autoimmune disease characterized by the presence of circulating immunoglobulins directed against thyrotropin receptors.

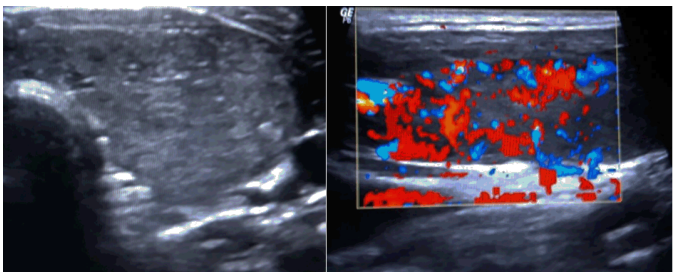

Figure 1: Cervical sonography: Hypoechoic heterogeneous thyroid gland with global hyperemia.

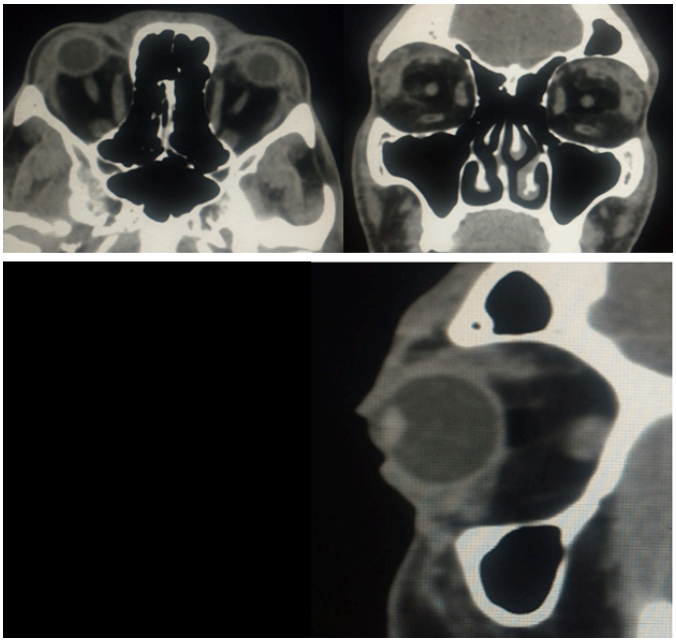

Figure 2: Contrast-enhanced CT in axial, coronal and sagittal plane shows a grade III bilateral exophthalmia with enlarged extraocular muscles and extra conal fat infiltration.

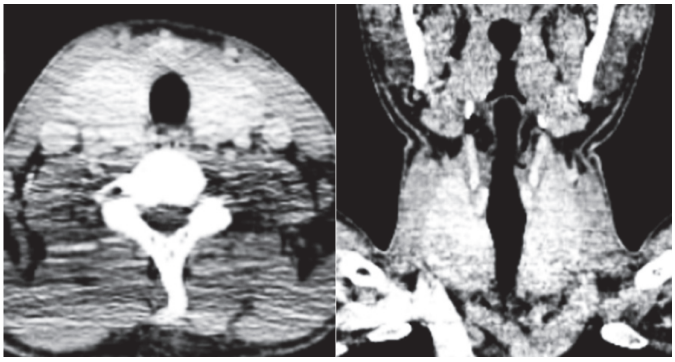

Figure 3: Contrast–enhanced CT in axial and coronal plane: Thyroid hypertrophy.

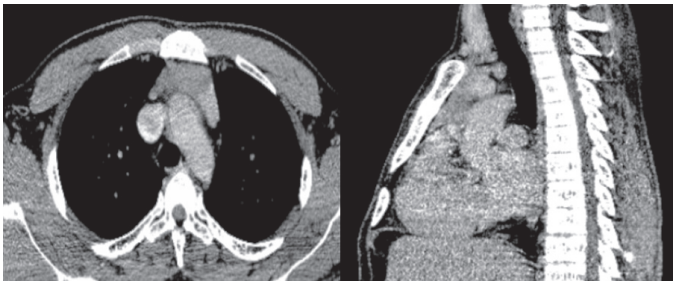

Figure 4: Axial and sagittal contrast-enhanced CT: Thymic hyperplasia.

These autoantibodies have a stimulating effect on the thyroid gland. The incidence of the disease in the population is 16 women and 3 men per 100 000 inhabitants / year [4].

The association between Graves' disease and myasthenia is not uncommon. Yet the association of Graves' disease and simple thymic hyperplasia does not seem to be fortuitous, as reported in the literature [3].

The first cases were reported at the beginning of the 20th century [5]. However this association remains little known.

In addition to the 92 cases discussed by Deforges-Bullet et al., we found 16 other cases of thymic hyperplasia associated with Grave's disease. Only 4 of these 108 cases were diagnosed as malignant thymomas. However, these results are minimal and radiological evidence is rarely reported [6]. Michie and Gunn demonstrated histological changes in the thymus in 38% of patients with thyrotoxicosis [7].

In most cases, thymic hypertrophy is minimal and unapparent. Therefore, radiologically detectable thymic hyperplasia with thyrotoxicosis has rarely been reported. Its association mechanisms are still poorly understood, as we did not discover a link as to why some patient develop thymic hyperplasia in association with Grave's disease. The pathophysiology of this association seems to be based on the action of antireceptor TSH antibodies present in Graves' disease. These antibodies are known to be responsible, by stimulation of the TSH receptor, for thyroid hyper function and the increase in thyroid size [8]. Expression of TSH receptors in extra thyroidal tissues (retro-orbital and pretibial fibroblasts) is higher in patients with Graves' disease than in other patients.A Japanese team has demonstrated the presence of TSH receptors in human thymic tissue [9].

In addition, Wortsman et al. reported the case of a patient with Graves' disease and thymic hyperplasia whose IgG immunoglobulins stimulated her thymocytes in vitro. Stimulation by TSH antibodies of intrathymic TSH receptors could therefore be responsible for thymic hyperplasia in patients with Graves' disease [10].

Popoveniuc et al. suggest two different pathogenic mechanisms. The hyperplasia of the thymic cortex appears to be due to a state of hyperthyroidism involving high levels of thymulin, a protein involved in lymphocyte function and differentiation [6], While lymphoid hyperplasia appears to correlate with abnormalities in the lymphocyte, underlying immune system in the context of Grave's disease. Radiologically, the study of the particularities of this association could avoid unnecessary invasive diagnostic procedures. Indeed, the thymus generally decreases in thickness with age. It also has the same as that of muscles on CT; this density tend to gradually decrease to near the fat density in older patients. Akari et al. recently demonstrated that the CT density of the thymus is significantly higher in lymphoid hyperplasia than in true hyperplasia [11]. MRI also seems to help in the differentiation between the thymic hyperplasia of a real tumor [12]. It has been reported that the chemical shift ratio in MRI is useful for distinguishing the normal thymus from the hyperplastic. This ratio is also significantly lower in patients with thymic hyperplasia than in thymic tumors (0.614 ± 0.13 vs. 1.026 ± 0.039, $p < 0.001$) [13]. Nevertheless, the discovery of anterior mass mediastinal mass justifies a precise differential diagnosis to exclude the possibility of a malignancy.

Once the diagnosis is made, the majority of authors are in favor of a simple radiological monitoring, no diagnostic or therapeutic procedure is necessary in most cases. In some cases invasive method, such as thymic biopsy or total thymectomy, may be necessary for masses that continue to grow or do not regress despite biological euthyroidism, or where the possibility of malignancy cannot be ruled out [14]. In the literature, the decrease in thymic volume under medical treatment varies considerably and is difficult to predict. Generally the delay is two years with an average of 6 months [4, 6].

CONCLUSION

Knowledge of the association between Grave's disease and thymic hyperplasia is necessary. Although there are some authors that preconize thymic surgery in cases of resistant Grave's disease. The favorable evolution under medical treatment, makes it possible to avoid unnecessary, even dangerous, thymic mass surgery in patients with Grave's disease by proposing a simple radiological monitoring.

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Author Contributions

Bellamlih Habib – Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Ayouche Othman – Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Meriem Fikri – Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Mohammed Jiddane – Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
Moulay Rachid El Hassani – Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.