DYSTHYROID OPHTHALMOPATHY ASSOCIATED WITH HYPOTHYROIDISM

OFTALMOPATÍA DISTIROIDEOA ASOCIADA A HIPOTIROIDISMO

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ABSTRACT

Case report: Graves’ ophthalmopathy (exophthalmos, muscular and eyelid infiltration) is associated almost systematically to hyperthyroidism. A female patient was diagnosed with subclinical hypothyroidism and treated with oral thyroxine. Months later she developed bilateral exophthalmos and was serum-positive for thyrotropin receptor antibodies. Thyroxine treatment was suspended, and it was verified that her condition had developed into primary hypothyroidism. A diagnosis of Graves’ disease with hypothyroidism was made.

Discussion: The diagnosis was based on the existence of ophthalmopathy and positive serum antibodies, both specific indicators of Graves’ disease. The coexistence of hypothyroidism with Graves’ disease is exceptional, but possible (Arch Soc Esp Oftalmol 2007; 82: 765-768).

Key words: Graves’ ophthalmopathy, hypothyroidism, thyrotropin receptor antibodies, thyroxine, therapeutics.

RESUMEN

Caso clínico: La oftalmopatía por enfermedad de Graves (exoftalmos, infiltración muscular y palpebral) se asocia casi sistemáticamente a hipertiroidismo. Paciente diagnosticada de hipotiroidismo subclínico y tratada adecuadamente con tiroxina oral. Unos meses después desarrolla un exoftalmos bilateral y simultáneamente presenta anticuerpos séricos anti-receptor de TSH positivos. Se suspende entonces el tratamiento con tiroxina, y se comprueba que el hipotiroidismo ha progresado hasta hacerse primario. Se establece el diagnóstico de enfermedad de Graves hipotiroida.

Discusión: El diagnóstico se basó en la existencia de la oftalmopatía y los anticuerpos positivos, ambos específicos de la enfermedad de Graves. La coexistencia de hipotiroidismo es excepcional, pero posible.

Palabras clave: Oftalmopatía por enfermedad de Graves, hipotiroidismo, anticuerpos anti-receptor de tirotropina, tiroxina, terapéutica.
INTRODUCTION

Ophthalmopathy due to Graves’ disease (GE) is characterized by a variable degree of (generally bilateral) ocular proptosis and infiltration signs of the extrinsic muscles of the eye or of the periorbital soft tissue. The clinically evident forms, which would develop with exophthalmos, chemosis, palpebral edema or ophthalmology, appear in 10-20% of patients with GE even though the subtle forms which appear (for instance) in a computerized axial tomography are a lot more prevalent (1). Infrequently, this ophthalmopathy may appear in the absence of hyperthyroidism, either associated to thyroid normofunction or —exceptionally— to hypofunction (2). This paper presents a case of GE with hypothyroidism and exophthalmos.

CASE REPORT

A healthy fifty nine year-old woman, non-smoker and without symptoms, was referred by primary care to the Endocrinology practice in August 2003 due to subclinical hypothyroidism. She had no goiter and two recent assessment of thyroid function had shown normal serum levels of free thyroxin (T4L) and high levels of thyrotropin (TSH) : 13.55 and 13.86 mcUI/mL (normal values —VN—: 0.25-4.22). The thyroid anti-peroxidase antibodies (Ac anti-TPO) were positive at high titers. With a diagnosis of self-immune subclinical hypothyroidism, either associated to thyroid normofunction or —exceptionally— to hypofunction, it was decided to begin treatment with 50 mcg/day of oral thyroxin (1 mcg/kg weight) and, after analyses carried out after six and twelve months, it was determined that this substitution dosage was correct (TSH normal). In December 2004 the patient returned spontaneously referring that in the last month she had noticed a protrusion of the eyes, conjunctival irritation and tearing. The exploration carried out by the Ophthalmology Service determined a moderate bilateral exophthalmos and normal ocular motility. We establish the diagnosis of ophthalmopathy with probable thyroid origin (no supplementary tests were considered to be pertinent). The patient was recommended to treat herself with artificial tears and the Endocrinology Section was asked to investigate a possible GE. Subsequently, the serum levels of T4L and TSH (normal with treatment), anti-TPO (positive) antibodies and anti-TSH antibodies receptor (anti-TSHr antibodies) were determined, with equally positive results: 40 U/L (VN below 10).

Considering that said antibodies are virtually pathognomonic to GE and that the normal function of the thyroid in this disease is less infrequent than a hypofunction, we suspended the thyroxin treatment to verify the status of the intrinsic thyroid function (which cannot be established in the presence of treatment). After two months without oral thyroxin, the T4L was of 0.47 ng/dL (VN: 0.7-1.7) and TSH of 54.01. Accordingly, the patient was diagnosed as primary hypothyroidism in a GE and substituting treatments was reintroduced. To this date (April 2006) the exophthalmos has remained unchanged (annual assessments in the ophthalmology practice) and the thyroid function remained normal with said treatment.

DISCUSSION

The GE diagnosis can be reached in two different ways: starting with the hyperthyroid patient who visits the Endocrinology practice, and with a patient suffering suggestive ophthalmopathy who visits the Ophthalmology practice. In the former case, the appearance of positive anti-TSHr antibodies in the serum confirms the diagnostic, as well as the existence of an ophthalmopathy. However, the letter condition is infrequent and does not usually appear in the absence of antibodies. Finally, we may also have a diagnostic of exclusion in hyperthyroid patients without antibodies or ophthalmopathy, but without goiter or with a diffuse goiter free of nodules (3).

In the cases in which the initial symptom is an ophthalmopathy we must always investigate the condition of the thyroid function. If hyperthyroidism is confirmed, Graves disease is a certainty. Otherwise, the diagnostic requires the anti-TSHr antibodies to be positive, in the absence of which (and even though this could be a technological limitation) it would be very bold to state GE with certainty. In some occasions, in the course of time, the patient begin to suffer hyperthyroidism or to express positive values for antibodies which were previously negative (4).

It is possible that an ophthalmopathy which suggests GE may coexist with positive anti-TSHr antibodies (i.e., GE) together with hypothyroidism. Some authors define and this situation as «hi Paul
thyroid Graves’ disease» due to its analogy with euthyroid GE. A study carried out in Singapore with over one thousand patients suffering this type of ophthalmopathy proved that only 1.9% were not hyperthyroid, and of these only 0.2% were hypothyroid (2). Isolated cases of this GE variant have been published on some occasions with severe forms of ophthalmopathy, marked hypothyroidism and very high titers of anti-TSHr antibodies (3). The physiopathological mechanism involved seems to be the thyroid inhibiting capacity of some type of anti-TSHr antibody: most of these antibodies are stimulants for the receptor, which translates in hypofunction and goiter. However, there may exist a non-stimulating subgroup which could block the receptor (4). With the analytical methods currently available in the usual clinical practice it is not possible to differentiate both subgroups.

In summary, GE with hypothyroidism exists but only exceptionally, and its diagnostic is always based on the thyroid function study of a patient suffering ophthalmopathy.

REFERENCES