SOMATOSTATIN ANALOGUE TREATMENT IN GRAVES' OPHTHALMOPATHY: A CASE REPORT

TRATAMIENTO DE LA ENFERMEDAD DE GRAVES CON ANÁLOGOS DE LA SOMATOSTATINA: CASO CLÍNICO

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ABSTRACT

Case report: The effect of a somatostatin analogue in a patient with Graves’ ophthalmopathy is presented, including data on the dose requirements and the results of therapy.

Discussion: There are few effective options for the management of Graves’ ophthalmopathy, a cell-mediated immune co-morbidity of thyroid disease. Somatostatin analogues inhibit lymphocyte proliferation and activation, and accumulate in the orbital tissue during the active ophthalmopathy. Because of this, such therapy is able to inactivate the ophthalmopathy without complications occurring (Arch Soc Esp Oftalmol 2007; 82: 51-54).

Key words: Somatostatin analogues, lanreotide, SOM230, Graves’ ophthalmopathy, octreoscan.

RESUMEN

Caso clínico: Se presenta la evolución de un paciente con oftalmopatía de Graves (OG) tratado con análogos de la somatostatina, así como las indicaciones, pauta y resultados obtenidos.

Discusión: Son pocas las opciones terapéuticas efectivas para el manejo de la oftalmopatía asociada a disfunción tiroidea de origen autoinmune. Los análogos de la somatostatina inhiben la proliferación y activación de los linfocitos, y se acumulan en el tejido orbitario durante la fase activa de la enfermedad oftálmica. Así, nos permitieron en el caso presentado llegar a la fase inactiva de la enfermedad sin secuelas importantes.

Palabras clave: Análogos de la somatostatina, lanreótido, SOM230, enfermedad de Graves, octreoscan.
INTRODUCTION

Graves ophthalmopathy (GO) is a self-immune inflammatory process associated to thyroid dysfunction, although there are euthyroid cases (Graves ophtalmic disease). It represents the most frequent extra-thyroid expression in Graves disease (10-25%) and affects more men than women between 20 and 45 years of age.

The natural history of GO comprises an rapidly progressing active or inflammatory phase followed by a partial regression and inactive phase in which residual expressions hardly show any substantial change and become subsidiary to surgery, mainly muscular and palpebral.

The therapeutic management for GO is estab-

lished according to the degree of activity and severity (table I), with high dosage corticoids and/or orbitary radiotherapy being the most effective options for severe cases in the active phase (1).

Recently, with the use of ocreotide scintography (Octreoscan, Mallinckrodt, St. Louis, MO, USA) the existence of somatostatine receptors in the orbitary tissue during the active phase of the disease has been proved. This would make these patients subsidiary to treatment with analogues of somatostatine (2).

CASE REPORT

A 42 year-old man referred to our hospital due to recurring conjuncti vitis and episcleritis episodes which refused to improve with conventional treat-

ment. He did not refer personal or ophthalmological history of interest, only a smoking habit of about 20 cigarettes per day.

Upon ophthalmological exploration, corrected visual acuity (VA) was of 1 in both eyes; biomicroscopic findings comprised injection and conjunctival chemosis, superior palpebral edema and inferior superficial dotted keratitis. He did not exhibit palpebral retraction or exophthalmos, and intraocular pressure (IOP) was of 13/11 mmHg. Classification as per the NONSPECS index: 2-b, 5-a.

The basic analyses (biochemistry and hemogram) gave normal results, but thyroid hormones (T₃, T₄, TSH) were high. The patient was referred to the endocrinologist with a diagnostic of slight-moderate GO in active phase. Said specialist established anti-thyroid treatment together with topical ophthalmological treatment.

Subsequent revisions revealed the progression of the eye disease to a moderate-severe stage (fig. 1) with worse biomicroscopic signs, development of 3 mm superior palpebral retraction in both eyes and 2 mm inferior retraction in right eye (RE) as well as 1 mm retraction in left eye (LE), Hertel exopthalmometry of 25 mm in RE and 24 mm in the LE and increase of IOP (24/22 mmHg). An octreoscan was performed, consisting in a 6 mg IV injection of In¹¹¹-octreotide, together with planar images with photon emission tomography after 4 and 24 hours. Said images revealed the presence of activity at the orbitary level, utilizing a contrast qualitative method to compare the retention vis-à-vis- the background (occipital bone tissue) (fig. 2). Treatment was initiated with 90 mg lanreotide

Table I. Therapeutic management of thyroid ophthalmopathy per activity and severity

<table>
<thead>
<tr>
<th>Ocular involvement</th>
<th>Degree of activity</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-severe</td>
<td>Active</td>
<td>Support measures</td>
</tr>
<tr>
<td>Non-severe</td>
<td>Inactive</td>
<td>Support measures</td>
</tr>
<tr>
<td>Severe</td>
<td>Active</td>
<td>Consolidated: ↑ glucocort.</td>
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<td></td>
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<td>Dosage, Rt and Qx</td>
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<tr>
<td></td>
<td></td>
<td>In study: somatostatin analogues, Ig IV</td>
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<tr>
<td></td>
<td></td>
<td>Not consolidated: Cyclosporine, plasmapheresis</td>
</tr>
<tr>
<td>Severe</td>
<td>Inactive</td>
<td>Orbital decompression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Strabismus surgery</td>
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<tr>
<td></td>
<td></td>
<td>Palpebral surgery</td>
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</tbody>
</table>

Fig. 1: The patient before treatment.
every 3 weeks for 2 months, followed by 60 mg intramuscularly every 15 days for an additional 2 months.

After the treatment the test was repeated, verifying a reduction in orbital retention (fig. 3). Corrected VA was of 1 in the RE and 0.9 in the LE, with the persistence of a slight inferior corneal epitheliopathy. The IOP was of 17/14 mm Hg with hypotensor topical treatment in RE and trabeculectomy in LE (one month after initiating treatment) due to persistence of high IOP (≈36 mmHg) which did not respond to the medical treatment. Exophthalmometry of 22 mm BE and 2 mm superior palpebral retraction and 1 mm inferior BE are awaiting surgical correction.

**DISCUSSION**

The general evolution of our patient was good, reaching the inactive phase without important sequels. The VA remained between 1 and 0.9 with fluctuations only after a trabeculectomy in the LE due to intraocular pressures which could not be controlled with pressure-reducing topical treatment. Inflammatory signs and symptoms responded positively to the treatment. The exophthalmometric values went down 2-3 mm while the palpebral retraction hardly evidenced any changes (1 mm) just like the muscle restriction.

Our results match those observed in previous studies and, in our view, are promising because they show the possible effect that this type of treatment could have on parameters such as proptosis which are not influenced by other treatments in use.

In addition, the side effects of somatostatine analogues (local unease in injection area, slight glucemia alterations and digestive trouble such as nausea, diarrhea and less frequently gall stones and gastritis) are of lesser relevance than those related to corticoids and radiotherapy, both resources widely employed for managing this type of patients.

Taking into account that somatostatine analogues inhibit the proliferation of lymphocytes and fibroblasts (cells which play a leading role in Graves disease), as well as the production of cytokines and the action of IGF-I, the utilization thereof acts on the factors which give rise and perpetuate the process, halting it and not only at the level of its effects.

In this case we utilized the first and only therapeutic option of lanreotide following a suggestion of the distributors because the patient was not in critical condition. However, further studies are needed to prove that the therapeutic effect is in fact due to the treatment and not the result of the natural evolution of the process towards remission (3). In addition, further studies would also prove the combination of these with other treatments such as corticoids and the new analogues which have appeared recently (SOM230) with greater affinity.
for somatostatine receptors present in orbitary tissue (4).

As drawbacks for this therapeutic option, we identified the need of owning or having access to the Octreoscan equipment (5).

REFERENCES