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## Original article

# Response to tocilizumab treatment in Graves' ophthalmopathy by measuring rectus muscle thickness and chemosis using optical coherence tomography<sup>☆</sup>



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## ABSTRACT

**Purpose:** To assess the extraocular muscle thickness and chemosis after treatment with tocilizumab in patients with active Graves' ophthalmopathy by optical coherence tomography.

**Methods:** Case series of five patients with active Graves' ophthalmopathy (clinical activity score  $\geq 4/10$ ) treated with 4 doses of tocilizumab. These patients had been previously treated with corticosteroids with no response. Spectral-domain optical coherence tomography was employed to determine lateral and medial rectus muscle thickness and chemosis before and after 4 doses of tocilizumab given monthly. Scanning was performed at 3 and 9 o'clock (nasal and temporal).

**Results:** The study included four women and one man with a median age of 52 years (range: 38–73). Median Graves' ophthalmopathy activity duration was 17 months (12–18). Median medial rectus and lateral rectus thicknesses pre-treatment were 249  $\mu\text{m}$  (174–366) and 337  $\mu\text{m}$  (142–443), respectively. Median chemosis was 409  $\mu\text{m}$  (290–610). After tocilizumab treatment, median muscle thicknesses reduced to 157  $\mu\text{m}$  (88–187) and 197  $\mu\text{m}$  (99–290), respectively ( $p = .043$ ; Wilcoxon) and chemosis to 59  $\mu\text{m}$  (0–78). Median clinical activity score decreased from 5 (4–8) to 1 (0–3).

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**Conclusions:** A reduction in extraocular muscle thickness and chemosis was observed after treatment with tocilizumab in Graves' ophthalmopathy patients using an optical coherence tomography, so this technique could be a useful complementary technique to assess the therapeutic responses.

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## Evaluación del grosor de los músculos extraoculares y la quemosis tras tocilizumab en oftalmopatía de Graves mediante tomografía de coherencia óptica

### R E S U M E N

#### Palabras clave:

Músculos extraoculares  
Oftalmopatía de Graves  
Grosor muscular  
Tomografía de coherencia óptica  
Orbitopatía tiroidea  
Tocilizumab

**Propósito:** Evaluar el grosor de los músculos extraoculares y la quemosis tras el tratamiento con tocilizumab en pacientes con oftalmopatía de Graves activa mediante tomografía de coherencia óptica.

**Métodos:** Serie de 5 casos con oftalmopatía de Graves activa (escala de actividad clínica  $\geq 4/10$ ) tratados mediante 4 dosis de tocilizumab. Estos pacientes habían sido tratados previamente con corticoides sin mejoría. Se empleó una tomografía de coherencia óptica de dominio espectral para determinar el grosor del recto lateral y del recto medial, y la quemosis antes y después de 4 dosis de tocilizumab administradas mensualmente. Se realizó el escaneado a las 3 y 9 h (nasal y temporal).

**Resultados:** Se estudiaron 4 mujeres y un hombre con una edad mediana de 52 años (rango: 38–73). La duración mediana de la actividad fue de 17 meses (rango: 12–18). El grosor muscular mediano del recto medial y del recto lateral pretratamiento fue 249  $\mu\text{m}$  (174–366) y 337  $\mu\text{m}$  (142–443) respectivamente, siendo la quemosis mediana 409  $\mu\text{m}$  (290–610). Tras el tratamiento con tocilizumab el grosor muscular disminuyó a 157  $\mu\text{m}$  (88–187) y 197  $\mu\text{m}$  (99–290) respectivamente ( $p = 0,043$ ; Wilcoxon), y la quemosis a 59  $\mu\text{m}$  (0–78). La escala de actividad clínica disminuyó de 5 (4–8) a 1 (0–3).

**Conclusiones:** Se observó una reducción en el grosor muscular de los rectos horizontales y en la quemosis en pacientes con oftalmopatía de Graves tras el tratamiento con tocilizumab mediante tomografía de coherencia óptica, por lo que esta técnica podría ser útil para la valoración de la respuesta al tratamiento.

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## Introduction

Graves' ophthalmopathy (GO) is a self-immune disease that affects 0.4% of the population.<sup>1</sup> Up to 90% of cases exhibit subclinical form, with 30–50% of patients exhibiting the symptomatic form of the disease.<sup>2</sup> GO is characterized by thickening of extraocular muscles and retrobulbar fat deposits. Muscular thickening occurs due to the expansion of connective tissue but does not compromise muscle fibers.<sup>3</sup> In addition, veins are compressed due to increased intra-orbital pressure, giving rise to chemosis.

In the active phase of the disease, treatment is based on anti-inflammatories or immunosuppressant therapies. At present, the first line treatment consists in corticosteroids administered with intravenous boluses. However, 20–30% of patients with GO do not respond to corticoids and exhibit relevant systemic adverse effects.<sup>4</sup> For these reasons new therapeutic agents have been assessed including tocilizumab, a monoclonal antibody against interleukin receptor 6 (IL-6) that has demonstrated effectiveness in the deactivation of GO.<sup>4</sup>

Nuclear magnetic resonance (NMR) and computerized tomography (CT) are the most widely used technologies for assessing muscular thickening of the rectus, with NMR being more precise.<sup>5,6</sup> The chemosis that arises in the course of the disease is assessed at this date with slit lamp.

Recently, the use of optical coherence tomography (OCT) has been described for visualizing extraocular muscles.<sup>7–10</sup> In addition, by means of this technique Häner et al. observed greater thickness of the medial rectus muscles in patients with GO.<sup>10</sup>

However, to date there are no studies assessing muscular thickness and chemosis in GO patients before and after treatment. The purpose of the present study is to analyze with OCT changes occurring after treatment with tocilizumab.

## Materials and methods

A prospective series of cases of 5 patients with GO between January and June 2017 at the San Carlos Clinic Hospital of Madrid, Spain. The study protocol included full clinic records

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