Severe sight-threatening thyroid-associated orbitopathy successfully treated with combined systemic glucocorticosteroids and intravitreal injections of antibiotics

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Title: Severe sight-threatening thyroid-associated orbitopathy successfully treated with combined systemic glucocorticosteroids and intravitreal injections of antibiotics

Short title: Severe thyroid-associated orbitopathy and schizophrenia

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Competing interests
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Thyroid-associated orbitopathy (TAO) is an inflammatory autoimmune response directed to orbital tissues. It is the most frequent extra-thyroidal manifestation of Graves’ disease (GD), while severe form affects 3-6% of patients [1].

A 59-year-old non-smoking woman was admitted due to vision deterioration and purulent secretion from the eyes observed for one week. She was clinically and biochemically hyperthyroid, with undetectably high anti-TSH-R antibodies and features of GD on thyroid ultrasound. Personal history revealed schizophrenia treated by intramuscular injection of zuclopenthixol-depot (200 mg/21 days) due to noncompliance.

Clinical examination and MRI suggested active TAO (Fig.1A,B,C). Regarding the criteria of dysthyroid optic neuropathy, bilateral apical crowding of the optic nerve on MRI and deteriorated visual acuity (0.1 by Snellen chart) in the right eye, but without optic disc edema and only light perception on the left were detected (left optic disc edema could not be evaluated due to corneal lesions) [2].

The patient received interdisciplinary care of endocrinologists, ophthalmologists and psychiatrists. Firstly, propranolol (3x20 mg/day) and thiamazole (3x20 mg/day) were introduced. For TAO, methylprednisolone 3 g i.v./3 days and then 40 mg p.o./day with ciprofloxacin 2x200 mg i.v. were administered. A decision on continuation of glucocorticosteroid therapy via oral route was made hoping for better compliance following discharge from the hospital, while olanzapine (10 mg/day) was added as a prevention of psychosis induction. Intravitreal antibiotics (1 mg vancomycin and 2.25 mg ceftazidime) were administered. Artificial tears during the day and eye patches with retinol and dexamethasone ointment overnight and eye ointment with antibiotics (ofloxacin, moxifloxacin) were used under moist chambers. Once biochemical euthyroidism was achieved, the patient underwent radioiodine therapy, but denied to give consent for tarsorrhaphy or orbital decompression.
At 6-weeks follow-up a significant improvement was observed (Fig.1D,E,F). Improvement in hydrostatic pressure and vascular perfusion, as well as a reduction in orbital congestion was observed. Asymmetric bilateral proptosis was 16 mm (right eye) and 21 mm (left eye). Motion restriction was still observed (left eye), while in the right eye a small limitation in extreme gazes was present.

In patients with GD and TAO, restoration of euthyroidism is essential. Although radioiodine is not the first line therapy, it was applied in our patient due to concern about future compliance on pharmacotherapy and lack of consent for thyroidectomy. The risk of TAO exacerbation is lower in non-smokers [3], and might be alleviated with glucocorticosteroids [4]. The management of bacterial keratitis is not widely covered in TAO guidelines. To the best of our knowledge, this is the first report on application of intravitreal injection of antibiotics in the management of bacterial complications of TAO. Optic neuropathy often requires urgent orbital decompression [1]. Novel option for such patients include rituximab or tocilizumab [5], but then unavailable.

In conclusion, we demonstrated treatment difficulties in a schizophrenic patient with GD, hyperthyroidism and sight-threatening TAO complicated with bacterial keratitis, where multidisciplinary therapy and individualized approach allowed to avoid enucleation and prevent from complete sight loss. It is recommended that such treatment is performed only in specialized referral centers.
Declarations

Ethics approval and consent to participate

All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This is a case report, retrospectively describing the course of the diagnostics and therapy, thus does not require the local Bioethical Committee approval.

Consent for publication

Written informed consent was obtained from the patient for publication of this report and any accompanying images.

References


Figure 1 A, B, D, E
Figure 1 C

Figure 1 F
Slit-lamp examination on admission (A - right eye, B - left eye), and at six weeks follow-up (D - right eye, E - left eye). An asymmetric bilateral proptosis (more severe on the left), eyelids retraction and swelling, bilateral lacrimal caruncle swelling, conjunctival congestion, redness of conjunctivae and chemosis were detected - 7/7 points in Clinical Activity Score (A,B). The cornea was bilaterally involved: microbial keratitis on the right, corneal ulceration with perforation and secondary fibrosis on the left. Episcleral vessels were dilated. Intraocular pressure in the right eye was 19 mm Hg by applanation tonometry, while the left eyeball was tense on palpation. The proptosis was 19 mm (right eye) and 23 mm (left eye). Upper lid retraction, lower lid displacement and significant eyeball motion restriction were observed bilaterally. Significant improvement was observed at follow-up (Clinical Activity Score 4, D,E). Visual acuity in the right eye was 0.5 (Snellen chart), but in the left eye no light perception was present. The right conjunctiva was almost normal with only locally dilatated episcleral vessels. Corneal inflammation was cured in the right eye. C - bilateral anterior bulging of the eyeballs and the thickening (medial, inferior and superior rectus muscles on both sides) and enhanced signal from extraocular muscles suggesting an active phase of thyroid associated orbitopathy on magnetic resonance imaging. F - Optical coherence tomography images of the cornea in the right eye. Upper scan taken before treatment demonstrate observed distortion of cornea surface with destroyed epithelium and stroma. Lower scan obtained after treatment demonstrate good healing of the cornea.