Combined mechanism glaucoma asociated with Grave's Ophtalmopathy. Case report

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Abstract

A 69-year-old female presented marked vision loss in both eyes, intense photophobia and ocular pain. The patient had long history of uncompensated glaucoma, Graves ophtalmopathy, treated for several years with topical medication without normalizing the intraocular pressure. The patient undergo orbital decompression for Grave's ophtalmopathy which ameliorated the exophthalmia. Visual assessment showed 0,08 best corrected visual acuity (BCVA) in the right eye respectively 0 in the left eye, posterior chamber pseudophakic implant both eyes, posterior capsular opacification left eye. The intraocular pressure was 18-25 mmHg in the right eye, respectively 14-19 mm Hg under topical medication. The cup-disc ratio was 0.8 in the RE respectively 0.9-1 in the LE. The visual field assessment in the RE showed relative central scotoma, complete lower arcuate (Bjerrum) scotoma, generalized depresion of VF. We performed RE trabeculectomy with 5 fluorouracil and collagen implant (OLOGEN®), with good postoperative evolution. The Visual Acuity improves significantly to 0.1, the IOP after a month was 15 mm Hg. The onset, symptomatology and general clinical context of the patient determined the focus on the neuro-ophthalmological aspect of the case, even if that meant that the control of the glaucoma, at times obviously inefficient, would remain second, from the perspective of its importance.

Keywords: combined mechanism glaucoma, compressive ischemic optic neuropathy, Grave's orbitopathy, collagen implant.

Thyroid orbitopathy is an immunological disorder that affects the orbital muscles and fat. Hyperthyroidism is seen with orbitopathy at some point in most patients, although the two are commonly asynchronous. Middle-aged adults (30–50 years) are affected most frequently, the disease is seen in women more commonly than in men, in a ratio of 3-4:1, it is always a bilateral process but is often asymmetrical and multiple muscles are involved simultaneously, most commonly the inferior and medial rectus.[10]

Symptoms and signs include dry eyes, conjunctival injection, lid retraction, exophthalmos, diplopia, corneal exposure, and rarely optic nerve compression. Graves'

disease usually runs a progressive course for 3–5 years and then stabilizes.

Primary open angle glaucoma is associated with Graves ophthalmopathy (GO) in 5-24% of the cases. There are studies who support the association of GO with normal tension glaucoma.

Case report

A 69-year-old female presented marked vision loss in both eyes, intense photophobia and ocular pain.

The history shows that the patient was diagnosed in May 2001 with hypothyroidism, treated with levothyroxinum (Eutirox®). In march 2003 she presented with signs of exophthalmia, the analyses certified the Hyperthyroidism. In may 2003 the patient complained of visual loss in left eye (LE), over a two month period associated with moderate exophthalmia, visual loss in right eye (RE) with slower progression.

In July 2003 the patient was diagnosed with Basedow Grave's disease and thyroid ophthalmopathy. The visual assessment showed best corrected visual acuity (BCVA) 0.04 in the RE, respectively hand motion (HM) in the LE. The computer-tomography: bilateral exophthalmia with hypertrophy of ocular extrinsic muscles and infiltration of the retrobulbar fat tissue. The intraocular pressure (IOP) was 30 mm Hg in both eyes. The ophtalmoscopy revealed precise contour optic disk with normal coloration. The patient presented marked ophtalmoplegia with extremely limited ocular motility. The patient was recommended Latanoprostum, Brinzolamide and Timolol (Xalatan®, Azopt® and Timolol®). For the Thyroid Ophthalmopaty the patient received repeated Methylprednisolone therapy (SoluMedrol®).

In September 2003, the patient with Basedow Grave's disease was treated with antithyroid drugs, the BCVA was 0.04, respectively HM. The IOP remained 30 mm Hg even under topical medication: Latanoprostum, Brinzolamide and Timolol (Xalatan®, Azopt® and Timolol®).

In October 2003 for marked visual loss and following the CT scan which revealed marked optic nerve tumefaction at the level of the bilateral optic channel, the patient undergo surgery treatment, RE decompression of the optic nerve in the optic channel and orbital fat resection, which led to the amelioration of exophthalmia. In November 2003, the follow-up mentions "a slight sight improvement", without specifying any particular values, after the serious sight aggravation, immediately after the surgery.

In February 2004 the patient's diagnostics were malignant Basedow Grave's disease, Grave's ophtalmopathy, compensated glaucoma both eyes, optic atrophy, left eye total optic atrophy, incipient cortisone cataract both eyes, iatrogenic Cushing's syndrome, diabetes mellitus, dyslipidemic syndrome. The visual assessment showed the BCVA 0.06, in the RE respectively no perception of light (NPL) in the LE. The IOP was 18 mm Hg, respectively 19 mm Hg under treatment with Latanoprostum, Brinzolamide and Timolol (Xalatan®, Azopt® and Timolol®). The ophthalmoscopy revealed discolored, moderately swollen optic disks, no cupping. The visual field (VF) assessment showed isolated areas of light sensitivity in the 300 central area. This seems to be a glaucoma via orbital compression: Latanoprostum

(Xalatan®) is no longer used for the treatment. The IOP continues to be treated with Timolol and Brinzolamide (Timolol® and Azopt®), remaining at the same values. The general recommended treatment was Piracetam® and Difrarel®.

In March 2004, the BCVA was 0.016, the IOP 19-20 mm Hg under Timolol and Brinzolamide (Timolol® and Azopt®), constriction of the visual field. One tablet of Acetazolamidum (Ederen®) and two tablets of Nicergoline (Sermion®) were added. The MRI exam revealed muscular hypertrophy, more important in the posterior half of the muscular body, at which level the optic nerves are compressed in their trajectory to apex of orbit.

In June 2004, the BCVA was 0.033 and NPL, the IOP 17-31 mm Hg under Timolol and Brinzolamide (Timolol® and Azopt®). An interdisciplinary examination concluded that this is a compression glaucoma ("Pseudo-glaucoma"), for which the recommended treatment is: Acetazolamidum, Timolol and Brinzolamide (Ederen®, Timolol®, Azopt®), Prednisone 80mg/day for 3 weeks, after which the dose will be decreased.

In August 2004 the right eye cataract undergo surgery, was performed phacoemulsification with posterior chamber pseudophakic implant (PC IOL), with favorable evolution.

In November 2004, the patient presented dysthyroid orbitopathy, secondary glaucoma, ischemic optic neuropathy in both eyes, antiphospholipid syndrome and dyslipidemia. The patient continues the same treatment, with Timolol and Brinzolamide (Timolol®, Azopt®) – the IOP values are not measured. The MRI exam revealed optic nerve with reduced thickness (≈2 mm RE, ≈1.5 mm LE); hypertrophy of the extrinsic muscles. The successive hospitalizations of April 2005, June 2005, and July 2005 confirm the antiphospholipid syndrome as being secondary to toxoplasmosis. The patient is under periodic treatment with Cerebrolysin®, Sulodexide (VesselDueF®). In Aprilie 2005 the patient was operated for cataract, with a PC pseudofakic implant in the left eye.

Over the period 2005-2008, the patient was treated with Cerebrolysin®, Sulodexide (VesselDueF®). Treatment with Timolol and Brinzolamide continues, without the monitorization of IOP.

In May 2008 the patient was examined at the Rothschild Clinic. The BCVA in the RE was 0.02 and HM in the LE. The patient presented exotropia of the left eye. The IOP was 19 mm Hg in the right eye, respectively 23 mm Hg in the left eye. In both eyes the patient presented pseudofakic implant. The ophtalmoscopy revealed white optic disks. The visual field revealed a paracentral residual island, only in the right eye. The visual evoked potentials showed a persistency of a flash response in the right eye, a low VEP in the left eye. The OCT scan, performed in October 2008 revealed in the right eye: major optic atrophy with a retinal nerve fiber layer less than 50 μ thickness. The MRI scan showed thick and non-inflamed extraocular muscles in both eyes, with discrete compression at the level of the apex.

The main conclusions at the Rothschild Clinic were: considering the serious nature of the disease and its long history, a orbital decompression might be useful, without a guaranteed favorable outcome; it is necessary to reduce the IOP, the recommended treatment was

Latanoprostum (Xalatan®) and Brinzolamide (Azopt®). Although a surgical orbital decompression was recommended, the clinic where the patient was hospitalized refused to perform the surgery.

Over the period 2008-2009, the patient continues the treatment with: Sulodexide (VesselDueF®), Cerebrolysin® and topical treatment with Latanoprostum (Xalatan®), Dorzolamide and Timolol (Cosopt®). Visual discomfort becomes more intense, being dominated by marked photophobia.

In November 2009 the patient was examined in an ambulatory department. The BCVA was 0.02 in the RE and NPL in the LE. The IOP was 40 mm Hg, in the right eye, respectively 24 mm Hg in the left eye under the treatment with Latanoprostum (Xalatan®), Dorzolamide and Timolol (Cosopt®). It was recommended for the patient to be hospitalized, and the topical treatment was changed with Bimatoprost and Timolol (Ganfort®).

The patient arrived in our department in December 2009. The visual assessment revealed the BCVA in the right eye 0.02, the left eye 0 (NPL). At the slit lamp exam: PC pseudofakic implant in both eyes, posterior capsular opacification in the left eye. Intraocular pressure in the right eye was 18-25 mm Hg, respectively 14-19 mm Hg in the left eye (circadian curve) under Bimatoprost and Timolol (Ganfort®). The IOP correction was -1 mm Hg (pachymetry=551 μ, Herndon formula, Ocuscan RXP®)

The gonioscopy: open angle – lower third degree, 2nd-3rd degree nasal and temporal, upper second degree. Ophtalmoscopy: cup-disc ratio 0.8 in the right eye and 0.9-1 in the left eye, choroidal folds at the posterior pole in the left eye.

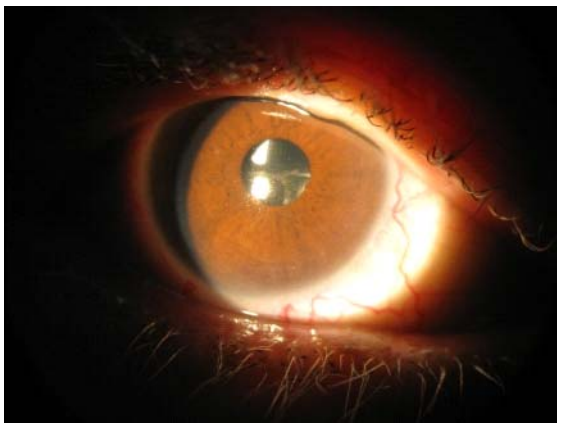


Figure 1 Slit lamp photo of the right eye

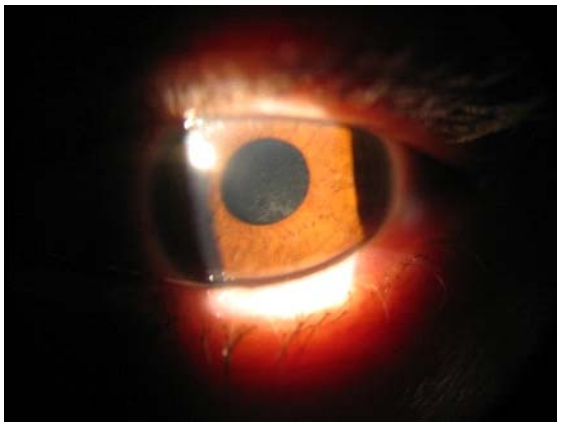


Figure 2 Slit lamp photo of the left eye

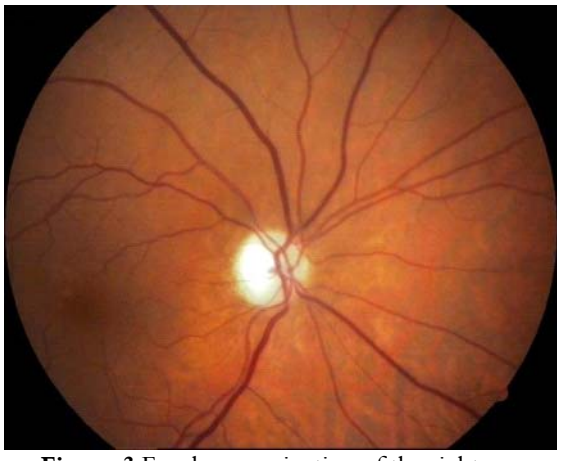


Figure 3 Fundus examination of the right eye

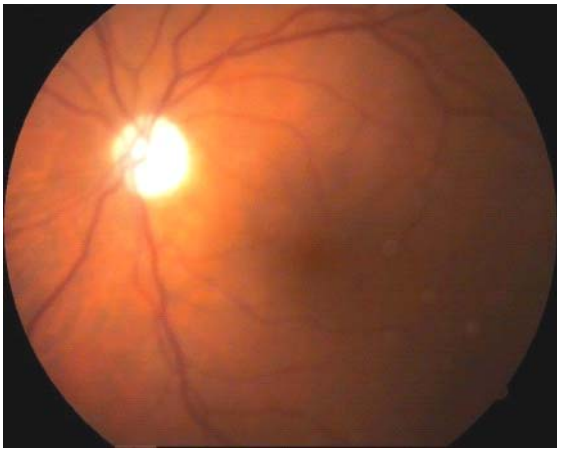


Figure 4 Fundus examination of the left eye

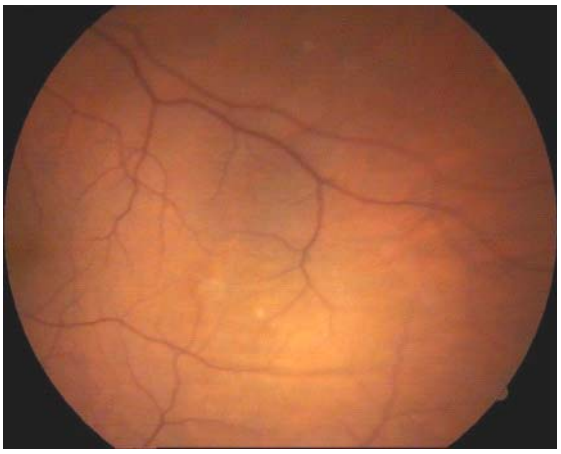


Figure 5 Choroidal folds in the left eye

The perimetrical assessment: the right visual field revealed relative central scotoma, complete lower arcuate (Bjerrum) scotoma, generalized depresion of VF.

The general examination revealed the associated diseases: arterial hypertension, painless chronic ischemic cardiopathy, first degree of obesity and hypothyroidism.

The ophthalmic diagnoses were: combined mechanism glaucoma both eyes, compressive ischemic optic neuropathy, optic atrophy, total left eye optic atrophy.

We decided to perform a trabeculectomy with addition of 5-fluorouracil and collagen implant (OLOGEN™).

Ologen™ is a biodegradable and implantable scaffold Collagen Matrix Implant. It's function is to induce a regenerative non-scarring wound healing process without the use of anti-fibrotic agents. The Matrix improves regeneration and tissue re-modeling, preventing scar formation. The implantation of Ologen™ is a simple process requiring that the ophthalmologist perform the operation based on traditional methods and techniques with minimal changes to suture techniques (such as the trabeculectomy). Ologen™ is implanted over the scleral flap, with the surgeon making sure to carefully suture both Tenon's capsule and conjunctiva over the Ologen making a water tight seal of the wound.

Before surgery we maintained the ocular hypotonia with topical medication Bimatoprostum and Timolol (Ganfort®) and systemic osmotic Manitolum (Manitol®). We also began the neuroprotective treatment with Pentoxifyllinum (Pentoxifilin®) and Cerebrolysin®.

The surgery consists of subconjunctival anaesthesia at 10-11 mm posterior to the limbus, we perform the lift of the conjunctiva. The incision is made at 9 mm posterior to the limbus, having a length of 9 mm. We make a square conjuctival flap with the length of 9 mm. We perform a carefully diathermia and clean the sclera of any tissue (Tenon's capsule or episclera). The 5 fluorouracil is then applied for 2 or 3 minutes. After this we make the scleral flap, the trabeculectomy and peripheral iridectomy. We suture the sclera and apply 5 fluorouracil 1 or 2 minutes. The collagen implant (OLOGEN ™) is implanted over the sclera flap with tight seal of the wound.

For the next day the patient wear a slightly compressive patch.[4]

Immediately after the surgery the BCVA in the RE was 0.02, and IOP was 14-16 mm Hg under Dorzolamidum and Timolol (Cosopt®). The BCVA in the LE was 0 and the IOP was 17 mm Hg under Bimatoprost and Timolol (Ganfort®). The patient was administered Pentoxifyllinum and Cerebrolysin and, at discharge the patient was recommended treatment with: Nicergoline (Sermion®), Lutein, Omega 3 (Lutein-Omega 3®), and she remained under treatment with topic hypotensors (Cosopt® and Ganfort®) and also Indomethacin (Indocollyre®). The patient was treated, at home, with Cerebrosylin.

The patient's follow-up after a month revealed the BCVA in the RE 0.1. At the slit lamp exam: discreetly congestive filtration bleb, minor corneal oedema, average depth of the anterior chamber, free iridectomy; functional filtration bleb at gonioscopy. The fundus exam revealed a discrete macular oedema. The IOP was 15 mm Hg, corrected with a - 4 mm Hg factor (pachymetry was 586 μm). The visual field shows extension of the deficit, with increase in the density of the central scotoma (aspect of altitudinal visiual fiel defect).

We recommended topical treatment with Bimatoprost (Lumigan®), Indomethacin (Indocollyre®) and systemic treatment with Pentoxifyllinum for 10 days and Cerebrolysin for 5 days.

In March 2010 the BCVA in the RE was 0.125, the IOP 16-17 mmHg under treatment with Bimatoprost (the internist advised against the use of Timolol because the patient registered cardiac side effects), a reduction of the density of the central scotoma, free central zone and reduction of the extension of the altitudinal VF defect.

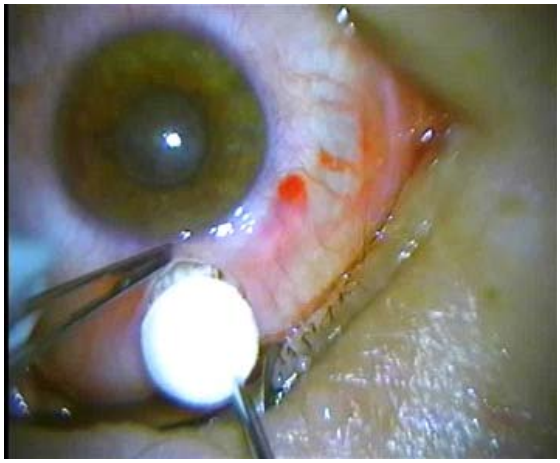


Figure 6 Ologen ™ Implant

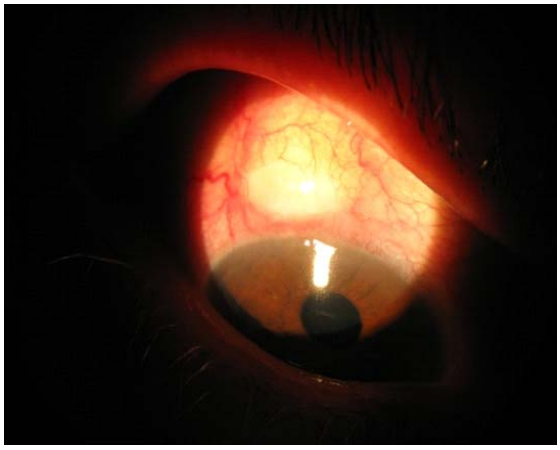


Figure 7 Slit lamp exam: filtration bleb

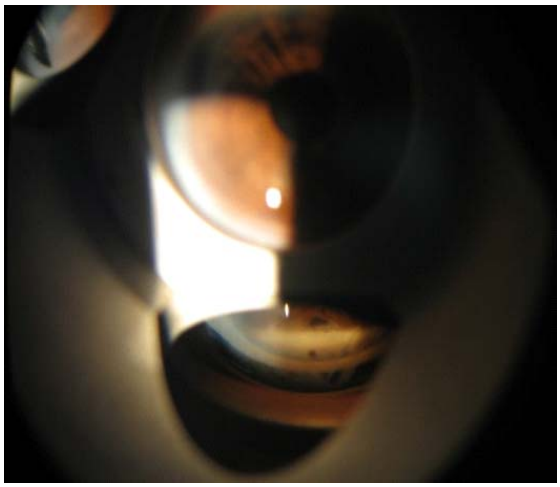
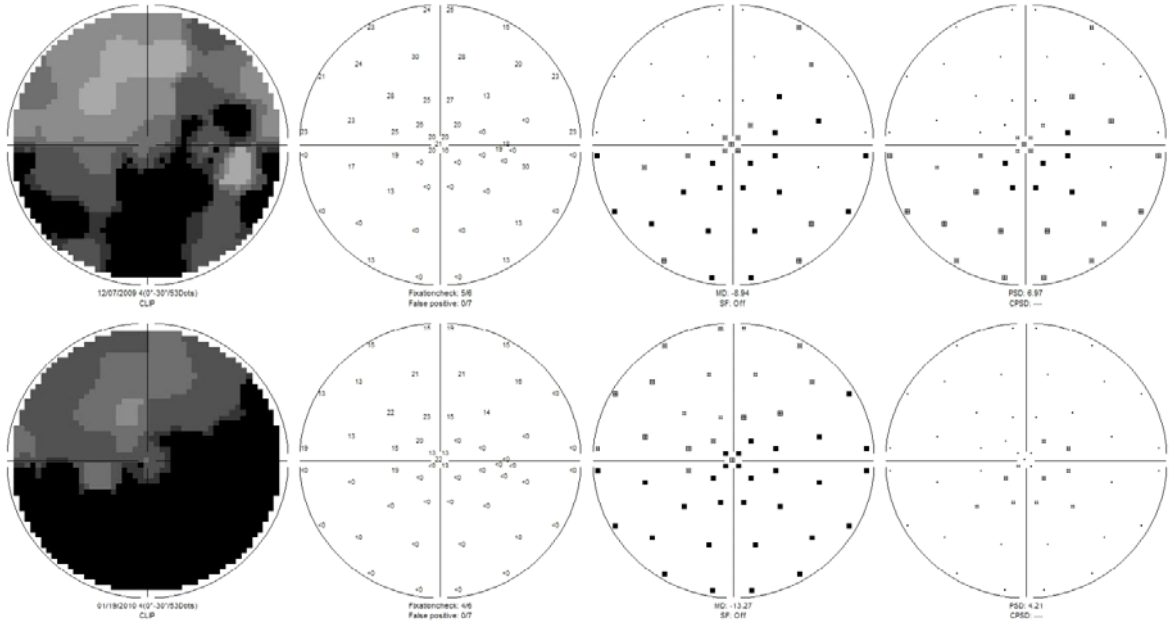
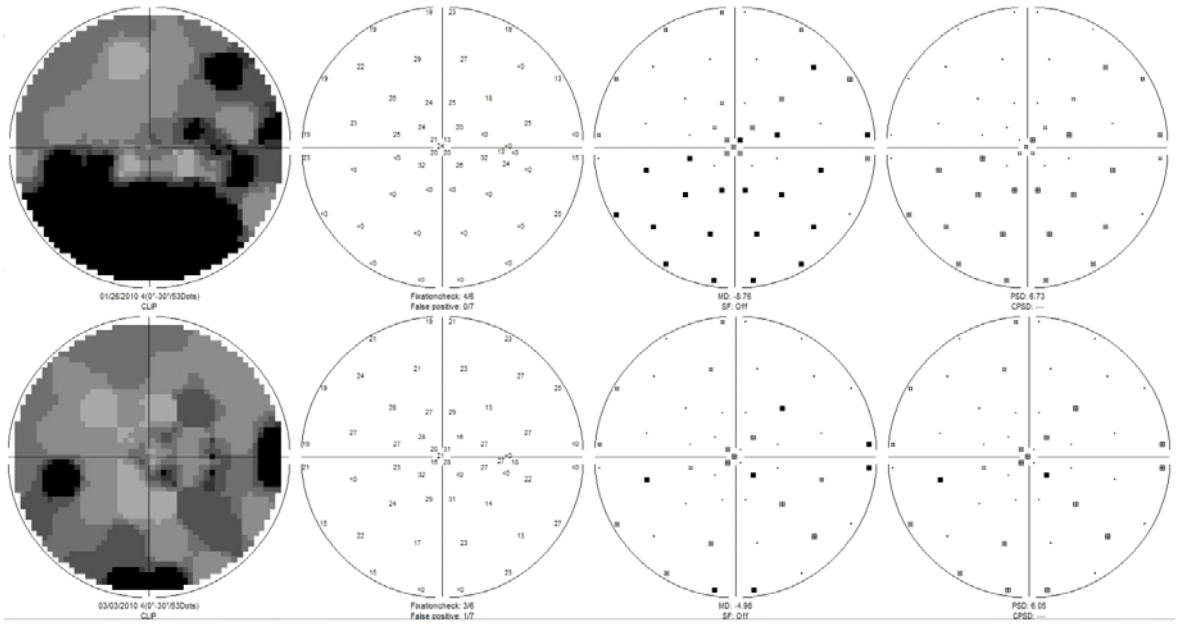


Figure 8 Gonioscopy: patent filtration bleb



9 A



9 B

Figure 9 Visual field evolution

We recommended Interruption of the anti-glaucoma topical medication, continuation of the treatment with Nicergoline (Sermion®) and Lutein-Omega3®, periodical treatment with Cerebrolysin and Pentoxifyllinum, topical treatment with Indomethacin (Indocollyre®), if necessary, examination after a 3 months period.

A. The diagnosis

• Combined Mechanism Glaucoma
• Via compression
• Primary Open Angle Glaucoma
• Compressive Ischemic Optic Neuropathy

B. The treatment

• Medical
• Surgical

C. Therapeutic strategies

• Priority of treatment of the diseases

D. Behavior in the cases with multiple risk factors

A. Combined mechanism Glaucoma

It is known that the 1 mm Hg increase of the pressure in the episcleral veins determines the increase of IOP by approximately 1 mm. [5] Graves ophthalmopathy is the most frequent cause of obstructive mechanisms that generate the pressure increase in the episcleral veins. The IOP also increases via the pressure rise in the episcleral veins and via the trabecular blockage, through the increased deposit of muccopolysaccharides in the trabecular system. [2] The compression of the globe is also exercised via the fibrotic extraocular muscles, with increased volume, in certain positions of the sight. The pressure increase in the episcleral veins is a sure fact, for the MRI and the CT scans revealed modifications of the orbital elements (oculomotor muscles, orbital fat). At present, the LE seems to suffer from a certain extent of orbital compression (revealed by the choroidal folds at the posterior pole) and the eye is more seriously affected.

Primary Open Angle Glaucoma

Primary open angle glaucoma is associated with Graves ophthalmopathy in 5-24% of the cases.6 There are studies who support the association of GO with the normal pressure glaucoma. [1] We thought about the existence of a POAG either simultaneously with or before the thyroid disease, because of the following reasons:

- The existence of relatively high IOP values (even if measured with the Schotz tonometer) from the occurrence of the disease.
- The severe decrease of visual acuity made us think about the preexistence of a disease at the level of the optic nerve.
- We must not forget that the IOP also increases in GO via the trabecular blockage, and that the patient also suffered from insufficiently controlled thyroid disease, about 2 years before the triggering of the acute phenomena.
- There is a genetically related predisposition between glaucoma and thyroid diseases.

Counter-arguments:

- Lack of documentation related to the assessment of the aspect of the optic disk (C/D ratio)
- Lack of documentation related to the modifications of the VF

Compresive Ischaemic Optic Neuropathy

In this case, severe orbital compression determined, on the one hand, the increase of intraocular pressure, with the impairment of the perfusion of optic nerve head and on the other hand, the impairment of the blood flow in the orbit, at the level of the optic nerve. The optic nerve oedema may have not occurred following the increased values of IOP. Anyhow, the stasis of the axoplasmic flow compressed the ON in the optic channel.

B. Treatment

Medical treatment of glaucoma

It seems that, in these circumstances, the topical medication did not manage to

control the evolution of the glaucoma and not even the IOP values.

Surgical treatment of glaucoma

The therapeutic target should have been established at a lower level and the surgical intervention should have occurred earlier. The surgery (in the absence of an artificial drainage device) was meant to be as radical as possible, but also safe.

Medical treatment of Compressive Ischemic Optic Neuropathy

Treatment with Cerebrolysin (especially) and vasodilator drugs, in association with Sulodexide (not performed after the surgery) proved its efficiency. The sustained neuroprotective treatment contributed to the post-operative improvement of VA and VF. We consider that such a neuroprotective treatment is of great interest in all the diseases that target the ON, either directly or indirectly. Anti-edematous treatment with intravenous Acetazolamide would have also been useful.

Surgical treatment of compressive ischemic optic neuropathy

The first decompression had a relatively limited effect. The intervention was the only viable solution in the given situation. The subsequent evolution of the disease seems to have shown that a second decompression would have not had better results. This was also the decision of the neurosurgeons that were requested to perform a second intervention. We must underline the importance of neuroprotective medication as adjuvant therapy in all these situations.

C. Therapeutic strategies

We consider that an equidistant approach of the components of eye impairment would have been appropriate in this case. If, in the case of the ON, the surgical intervention was choosen hastily, maybe this is how it should have with the glaucoma. There may have been constraints as concerns the decision of performing the glaucoma surgical intervention, associated with the discovery and exposure of the filtration bleb because of the exophthalmia; an artificial drainage system would definitely have been a good solution at any given time. The modest result of the laminectomy may have reduced the hopes, associated with the benefits of glaucoma surgery.

D. Behavior in the cases with multiple risk factors

- Analysis of each disease, with the evaluation of the impact on the target segments.
- Analysis of the interactions of the diseases and of the most exposed areas following the combined action of risk factors.
- Overall analysis of the general etiopathogenic context.

Conclusions

The open-angle glaucomas are chronic, progressive optic neuropathies, that have in common characteristic morphological changes at the optic nerve head and retinal nerve fibre layer in the absence of other ocular disease or congenital anomalies. Progressive retinal ganglion cells death and visual field loss are associated with these changes. [8,9]

It is much easier to make accurate assessment by analyzing at the end, a long sequence of data and information that become complete and clear, along the way.

Unfortunately, most of the times we have to choose the best solution at that very

moment and we can only hope that there will be only few cases, when this solution does not turn out to be the best.

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