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CYSTOID MACULAR OEDEMA. ETIOLOGY. DIAGNOSIS. EVOLUTION AND TREATMENT

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SUMMARY

Cystoid macular oedema (CMO), also known as Irvine-Gass syndrome, is the most common cause of decreased central visual acuity (CVA) in different clinical and postoperative eye conditions.

Clinical conditions include certain predominantly vascular alterations (diabetic retinopathy, arterial hypertension, retinal vessel obstructions, etc.). Clinical CMO also occurs in various inflammatory conditions (Behçet's disease, chronic uveitis, etc.), drug-induced, iatrogenic or toxic disorders (topical epinephrine, systemic nicotinic acid, talc retinopathy, etc.), hereditary degenerative diseases (retinitis pigmentosa and related conditions) and tumours (malignant choroid melanoma, choroid hemangioma, etc.).

The postsurgical forms of CMO mainly comprise intracapsular aphakia, posterior capsulotomy with YAG laser in implantology, refractive surgery, penetrating keratoplasty in aphakic eyes, suprascleral implants or exoplants plus cryotherapy in the surgical management of retinal detachment, *pars plana* vitrectomy, peripheral iridectomy, etc.

A retrospective study has been made of 29 cases subjected to intracapsular cataract extraction (ICCE) in the *Centro de Oftalmología Barraquer (COB)* (Barcelona, Spain) between 1981 and 1994, with a presentation of our results and suggestions following strict patient follow-up over 13 years.

KEY WORDS

Cystoid macular oedema.
Photocoagulation.
Visual acuity.
Fluorescein angiography.

INTRODUCTION

Cystoid macular oedema (CMO) has always been closely associated to conventional intracapsular cataract extraction (ICCE) surgery for, as will be seen below, the first findings of the syndrome were reported precisely in patients undergoing this surgical procedure.

Nevertheless, CMO is not exclusively related to ICCE, since it is also diagnosed in routine practice in various ocular conditions, both surgical and clinical; the latter particularly include some inflammatory, degenerative, vascular and other disorders (Tables 1-6).

Surgical procedures
— Intracapsular cataracts.
— Extracapsular cataract extraction + intraocular lens (IOL).
— Following posterior capsulotomy with YAG laser in implantology post-phacoemulsification.
— Penetrating keratoplasty in aphakic eyes.
— Refractive surgery.
— Peripheral iridectomy.
— Filtering surgery for glaucoma.
— Hypotony.
— Cyclocryotherapy.
— Suprascleral implants in retinal detachment surgery.
— Cryotherapy.
— *Pars plana* vitrectomy.
— Use of hyaluronidase in surgery under local anaesthesia... C.D.H.G.

TABLE 1. *Causes of cystoid macular oedema (CMO).*

Hereditary degenerative diseases
— Sex-linked (chromosome X) hereditary retinoschisis*.
— Dominant autosomal macular dystrophy*.
— Retinitis pigmentosa.
— Wagner's disease.
— Goldmann and Favre disease.
— Familial hereditary vitreoretinopathy, etc.
* Without dye leakage. C.D.H.G.

TABLE 2. *Causes of cystoid macular oedema (CMO).*

Drug induced, iatrogenic or toxic disorders
— Epinephrine instillation.
— Nicotinic acid*.
— Griseofulvin*.
— Talc retinopathy.
— Phototoxicity (induced by coaxial illumination of the surgical microscope).
— Idiopathic...
* Without dye leakage from the perifoveal retinal capillaries. C.D.H.G.

TABLE 3. *Causes of cystoid macular oedema (CMO).*

Tumours
— Choroid hemangioma.
— Malignant choroid melanoma (primary and secondary).
— Postoperative following melanoma excision.
— Ecto- and mesodermal phakomatosis.
— Coats' disease.
— Choroidoretinal angiomatosis... C.D.H.G.

TABLE 4. *Causes of cystoid macular oedema (CMO).*

Vascular disorders
— Retinal vessel obstructions.
— Diabetic retinopathy.
— Panretinal photocoagulation for diabetic retinopathy.
— Retinal aneurysms and telangiectasias.
— Vascular collagenosis.
— Arterial hypertension.
— Arteriosclerosis... C.D.H.G.

TABLE 5. *Causes of cystoid macular oedema (CMO).*

Inflammatory conditions
— Chronic uveitis.
— Peripheral uveitis or *pars planitis.*
— Toxoplasmosis.
— Histoplasmosis.
— Nematode-induced endophthalmitis.
— Sarcoidosis.
— Behçet's syndrome.
— Birdshot choroidoretinopathy.
— Neurosyphilis.
— Accidental ocular contusion.
— Sympathetic ophthalmia... C.D.H.G.

TABLE 6. *Causes of cystoid macular oedema (CMO).*

From the historical perspective, the first biomicroscopic observation of changes in the macular area in patients undergoing ICCE was made by Hruby in 1950.

In 1953, Irvine confirmed the findings reported by Hruby in 1000 cases subjected to the same surgical procedure (22).

This author described the symptoms of the clinical condition, i.e., photophobia, loss of central visual acuity (CVA), metamorphopsia, conjunctival hyperaemia, aqueous humour turbidity due to the accumulation of cells (leukocytes) with flare or the presence of proteins, papillitis, vitreitis, retinal phlebitis, miosis, increased intraocular pressure, vitreous prolapse in the anterior chamber due to delayed breakage of anterior hyaloid membrane, etc.

Irvine added that the condition occurs during the late postoperative period, i.e., after one to three months, and never or only rarely earlier, particularly in eyes pre-

viously having an excellent anatomic and functional outcome, as confirmed by other authors (5,8,21).

In 1966, Gass and Norton reported that the macular changes described by Hruby, Irvine and later Chandler (absence of the foveolar reflex and a peculiar blurriness in the macular region) are difficult to visualize ophthalmoscopically but can be easily seen by slit lamp examination using the Goldmann lens (retroillumination with a fine oblique slit, with visualization of the thickening and alteration of the anterior profile line of Busacca's parallelepiped) as the clinically significant swelling or oedema typical of the condition described (36).

These latter authors subsequently reported the first results of fluorescein angiogram (FA) studies that allowed a more careful and detailed observation of the syndrome and constituted a valuable contribution to the establishment of a precise diagnosis (5,8,13,14,37).

Thanks to FA, the incidence of CMO diagnosed in patients undergoing ICCE increased from 3% to 54%, with an average of 40% (23).

The fluorescein angiographic image is very typical and suggestive, since it shows a petal-shaped accumulation of dye in late phase angiograms, corresponding to contrast leakage due to the hyperpermeability of the dilated perifoveal capillaries (Figure 1).

This gradual fluorescein oozing eventually results in dye accumulation in the circumfoveal cystoid spaces. The retinal cystoid spaces are pathognomonic of CMO and, according to some authors, originate from the degenerating Müller cell layer (intracellular theory); according to others, however, the origin is to be found between the external plexiform layer (or Henle's fibre layer) and the internal granulosa (extra-

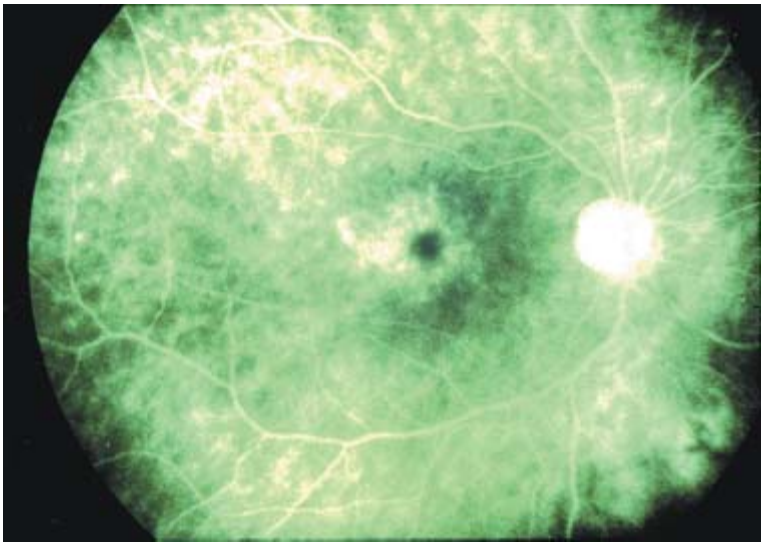


FIGURE 1. *Late phase fluorescein angiogram. Cystoid macular oedema. Typical petal-shaped or stellate image. The former is the generally used term. Right eye (R.E.).*

cellular theory). In any case, there is general agreement on the existence of breakage of the blood-aqueous and blood-retinal barriers and/or local anoxia (1).

Extravasation or loss of dye from the capillary network of the second cranial nerve (papillary hyperfluorescence) is sometimes seen, as well as the presence of fluorescein in the anterior chamber (aqueous humour) arising from the anterior and middle uvea (12,14)(Figure 2).

CMO can also be confirmed by optical coherence tomography (OCT) and A-B ultrasonography (33)(Figure 2A).

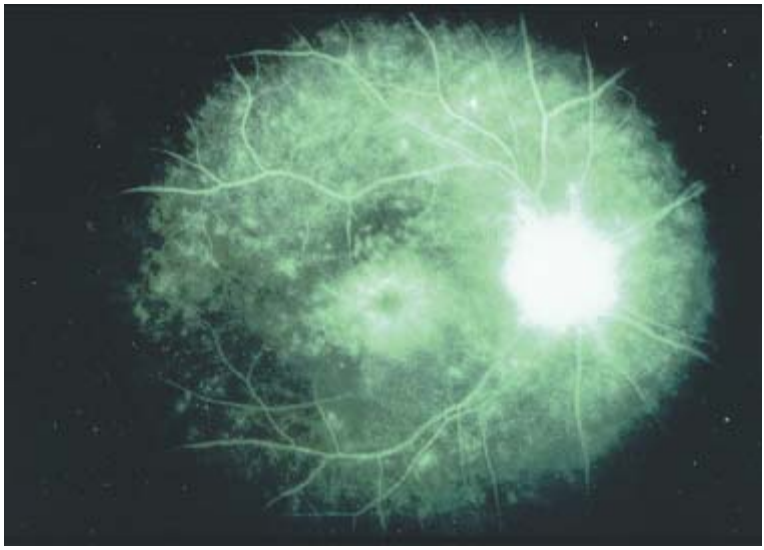


FIGURE 2. *Papillary hyperfluorescence. R.E.*

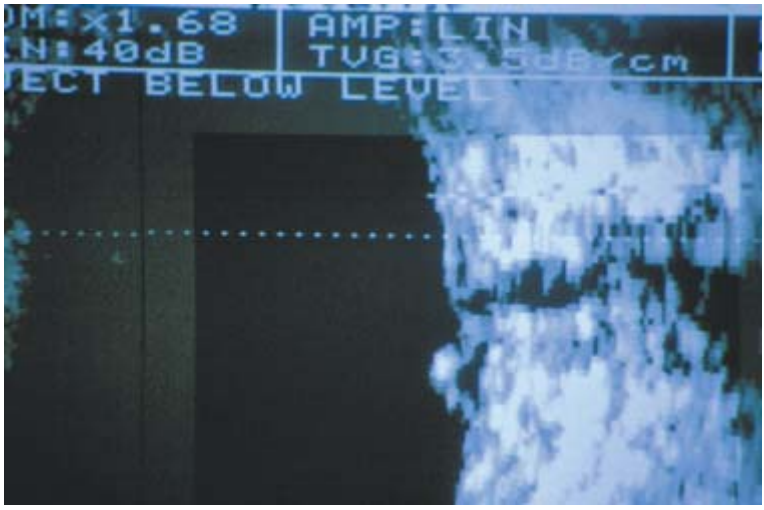


FIGURE 2A. *A-B ultrasonography. Cystoid macular oedema.*

The intracellular theory proposes the development of cystic or pseudocystic retinal cavities from degenerated Müller cells; histopathologically, an initial oedema of these cells would subsequently lead to the formation of vacuoles that would fill the cell cytoplasm and give rise to a burst secondary to cell wall rupture. Cysts or cystoid formations would then result, particularly following effraction of the neighbouring cells (42).

The extracellular theory is in turn based on the findings of electron microscopic studies. According to this theory, cyst formation would be the result of serum exudation distending the extracellular space between the internal nuclear and external plexiform or Henle retinal layers (15).

Other pathogenetic hypotheses have also been proposed, of which only a few are described below for the sake of brevity. Nevertheless, no single all encompassing etiological theory has been developed to date.

The tractional, vascular and inflammatory theories will be discussed.

The hypothesis of vitreous traction associated to surgery is based on the presence of webs of the gel incarcerated within the corneal wound following ICCE, at a time when no alternative technique was favoured (3).

In addition to the above described symptoms, these fibres would be responsible for the discoria (pearl shaped pupil) resulting from wedging in the corneoscleral incision with traction upon the base of the vitreous and the macula. This latter event would be the cause of CMO, due to mechanical traction by the fibres in the adhesion areas, particularly during pupil dilatation and contraction, and in endophthalmodonesis or iris movement on the vitreous adhered to the macula, or trembling motion of the eye (ophthalmodonesis)(Figures 3, 4 and 5).

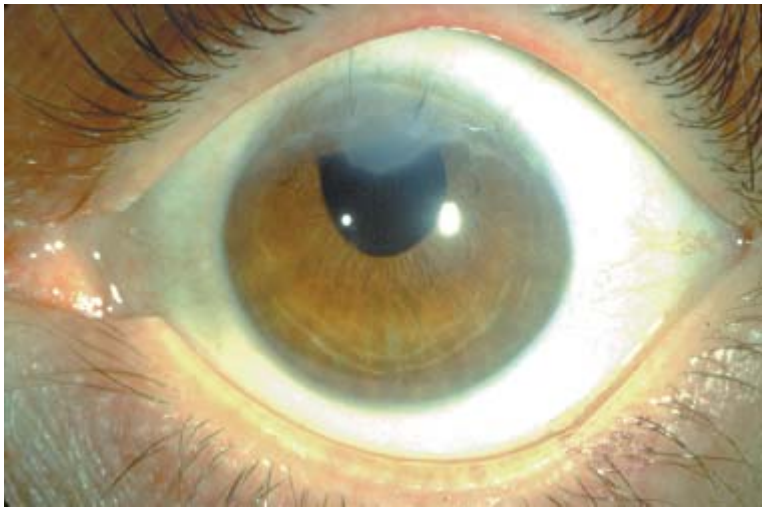


FIGURE 3. *Cystoid macular oedema. Biomicroscopy of the anterior segment. Vitreous wedged in corneoscleral incision. ICCE. Tractional theory R.E.*

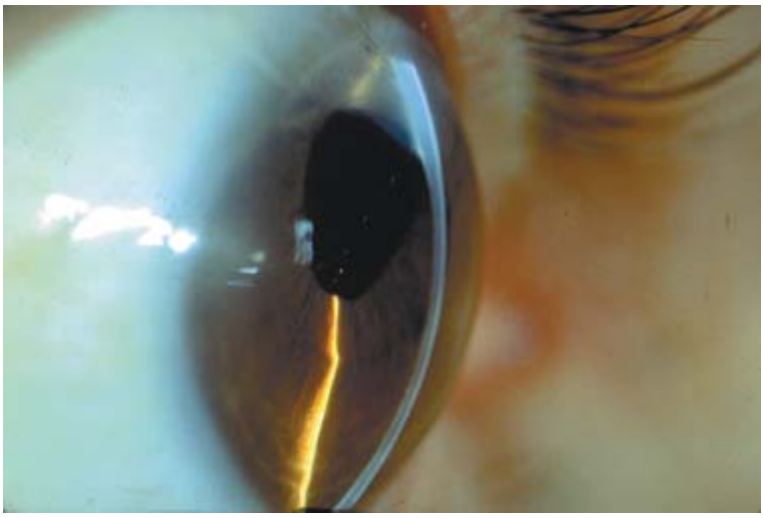


FIGURE 4. *Lateral view. Photograph of the same case (discoria). Tractional theory.*

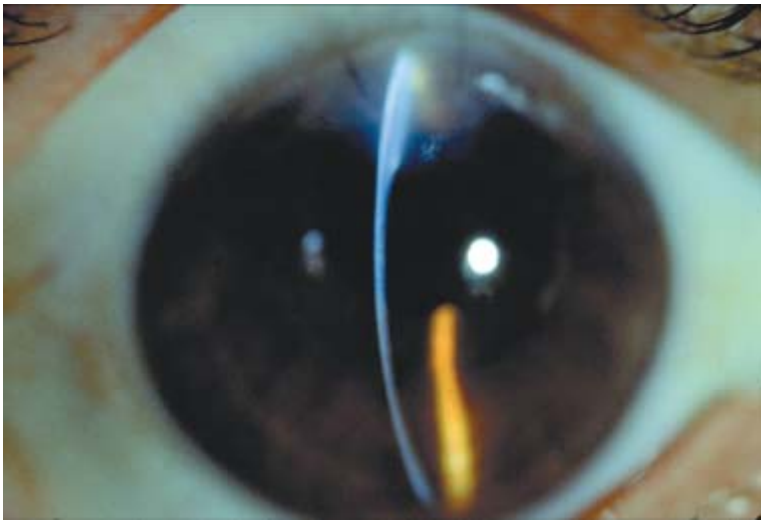


FIGURE 5. *Narrow slit, anterior plane. Same case as in Figures 3 and 4.*

In addition to the inclusion of vitreous tufts in the scar, changes in secondary biochemical activity occur, as well as the presence according to some authors of a premacular or posterior precortical vitreous bursa where different substances with toxic effects upon the macula, such as oxygen free radicals, cytokines, etc., are deposited. In this context, age-related posterior vitreous detachment (PVD) results in the formation of a hole in the posterior cortex of the gel through which these toxic substances —previously stored and retained within the *bursa premacularis*— are now able to diffuse to the macula (25,38,41).

The vascular theory in turn attributes the pathogenesis of CMO to cardiovascular disease, systemic arterial hypertension, diabetes mellitus, arteriosclerosis and other organic conditions involving marked instability of the chorio-retinal vascularization, leading to increased perimacular capillary permeability (16,28) Table 5.

The inflammatory effect of surgery must be summed to the above considerations. Thus, according to some authors a mixed inflammatory and vascular theory should be proposed, while others (as shown below) advocate the pure inflammatory hypothesis.

Support of the inflammatory theory comes from the clinical signs that typify the syndrome: conjunctival hyperaemia, the Tyndall effect or cells and flare in the aqueous humour (the Tyndall effect being the result of cell concentrates —mainly leukocytes— that cross the vascular endothelium, causing active inflammation; the flare effect is caused by proteins resulting from the vascular hyperpermeability secondary to wall alteration), vitreous turbidity, photophobia, CVA impairment, micropsia, and dysmegalopsia - in sum, anterior and posterior polaritis (Figure 6).

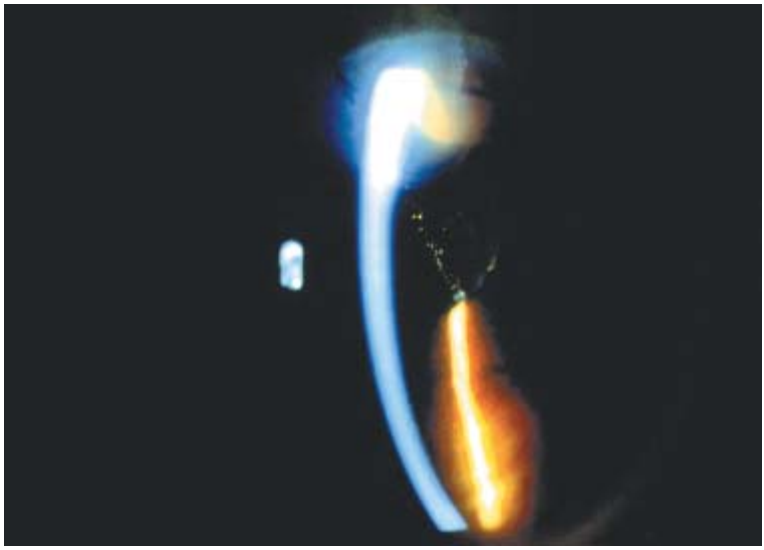


FIGURE 6. *Anterior polaritis secondary to ICCE with CMO.R.E. (Flare).*

Substances causing ocular inflammation have a predominant role in the postoperative inflammatory mechanism leading to CMO. These include prostaglandins (PGE and PGF2), leukotrienes, neuropeptides (particularly substance P), lysosomal enzymes, histamine, endotoxins, interleukins, immune complexes, bradykinin, serotonin, acetylcholine and other less important vasoactive substances that nevertheless influence the changes in biochemical activity (2,29).

These biotoxic elements from the anterior uvea migrate as a result of the surgical insult towards the macular area via two pathways: (a) Rupture of the blood-aqueous barrier and anterior aspect of the vitreous or anterior hyaloid membrane (which acts as a physiological-mechanical barrier when intact), reaching the perifoveal capillaries

to cause local dilatation and hyperpermeability by altering the zonulae occludens, or junctional complexes of the capillary endothelial cells (internal blood-retinal barrier), and the resulting transudate leakage into the retinal thickness (17,18,40) (Diagrams 1 and 2).

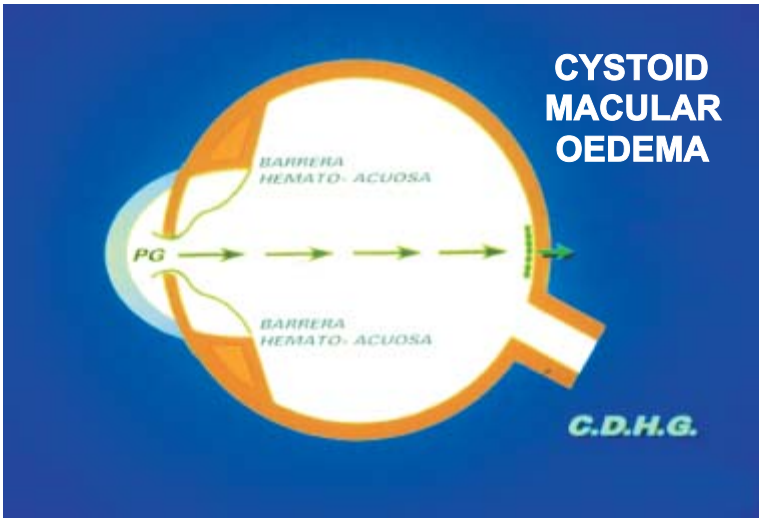


DIAGRAM 1. *Anteroposterior passage of inflammatory mediators (prostaglandins, immune complexes, lysosomes, endotoxins, interleukins, etc.).*

Postoperative damaging, inflammatory action.
—
Causes
—
release of prostaglandins, leukotrienes, toxins, immune complexes, etc., within the anterior chamber (aqueous humour) due to rupture of the blood-aqueous barrier (shown by fluorophotometry).
—
These cross the vitreous to reach
—
the perifoveal capillaries (leading to rupture of the blood-retinal barriers)
—
thus resulting in
—
cystoid macular oedema, (shown by FA).

DIAGRAM 2. *Schematic representation of the inflammatory-vascular hypothesis of CMO pathogenesis following ICCE, (relationship between prostaglandins, other inflammatory mediators and blood-eye barriers).*

(b) Passage of the inflammatory mediators towards the macula as a result of PVD, which causes dehiscence of the posterior vitreous cortex (25,38,41).

The inflammatory theory, hypothesis or doctrine has been confirmed by a number of authors using fluorophotometric methods (7,30,35).

Prostaglandins (PG) are synthesized in all tissues from arachidonic acid which, under the action of two enzymes (endoperoxide isomerase and prostacyclin synthase), forms PGH2 - a biologically active substance that in turn yields PGG2 and thus also the forms PGE2, PGF2 alfa, and PGD2, which are released locally and act *in situ* (31).

In turn, leukotrienes are derived from arachidonic acid contained within leukocytes by the metabolic pathway of lipooxygenases **5, 12 and 15** (4,6).

PGE2 and PGF2 are involved, along with leukotrienes B4 and E4, in the pathogenesis of CMO (according to the inflammatory theory)(32).

Recently, the release of other inflammatory mediators such as interleukins has also been suspected to be involved in the development of CMO (10).

MATERIAL AND METHODS

A total of 29 cases corresponding to the period 1981-1994 were retrospectively studied in the *Centro de Oftalmología Barraquer (COB)*(Barcelona, Spain).

This patient group consisted of 18 men and 11 women (Graph 1).

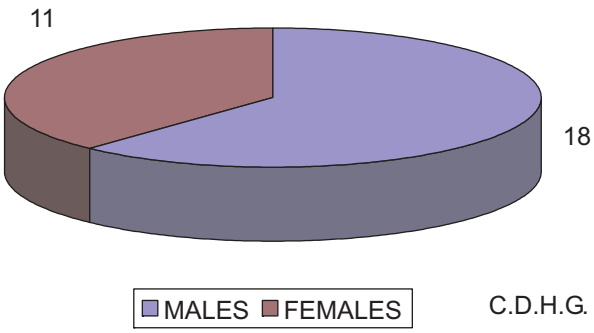
The mean patient age was 65.5 years, with a range of 51-85 years.

The development of CMO spanned an average of 3 months (range 1-5.5 months).

All cases but one were subjected to ICCE under general anaesthesia (GA), in the awareness that CMO is less frequent with GA than when locoregional anaesthesia (LRA) is given, since administration of hyaluronidase at retrobulbar level when LRA is used explains the pathogenesis and occurrence of some CMO (37).

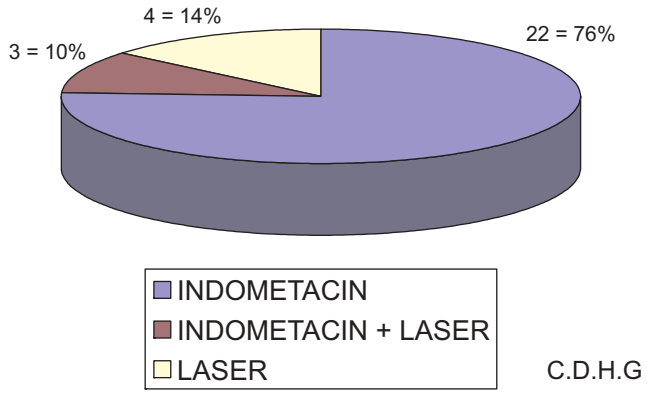
Actually concepts and behaviour have been widely changed.

A group of 22 patients (76%) received medical treatment only, in the form of topical indometacin (10 mg/ml eyedrops) in fractionated doses: one drop every 8 hours.



GRAPH 1. *Cystoid macular oedema. Sex distribution.*

Three patients (10%) were treated in the same way though adding laser photocoagulation, while the remaining four patients (14%) received only laser therapy. One of these four individuals showed marked hypersensitivity to both systemic and topical indometacin, thus warranting increased emphasize on laser therapy (Graph 2).



GRAPH 2. *Cystoid macular oedema. Percentage distribution by treatment.*

In all cases an accurate diagnosis was basically established by decreased CVA, metamorphosia with Amsler´s test, posterior pole biomocroscopy, ophthalmoscopy, FA, OCT…

Where necessary, when no angiogram is available, it is possible to perform angioscopy using indirect ophthalmoscopy, or also by biomicroscopy with cobalt blue filter, after oral administration or sodium fluorescein (27,34).

All patients were followed-up on by the same examiner physician over 2, 4 and 6 months of treatment. All cases that failed to comply with the established protocol were discarded (Figures 7 to 30).

All cases that failed to comply with the established protocol were discarded.

Photocoagulation was carried out using a monochromatic green wavelength argon device in four cases, delivering between 150 and 155 shots to a 200 µm spot (time 0.2 s, power 130 mW, approximately). In the remaining three cases the yellow dye wavelength was used, delivering 130 to 140 shots to a 200 µm spot (time 0.2 s, power 200 mW). (Figures 7, 8, 9 and 10).

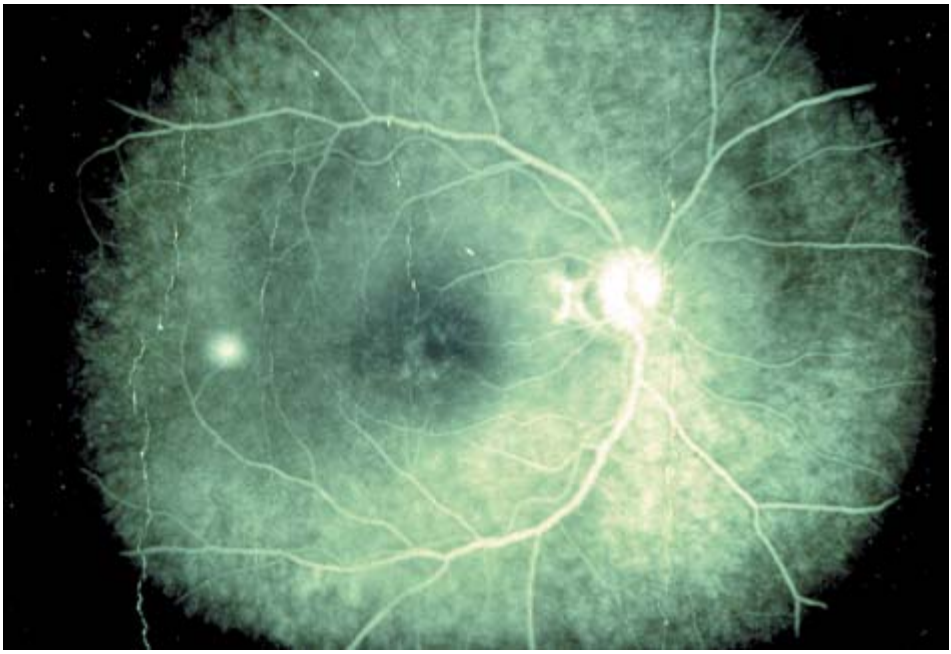


FIGURE 7. *CMO secondary to ICCE. FA. R.E.*

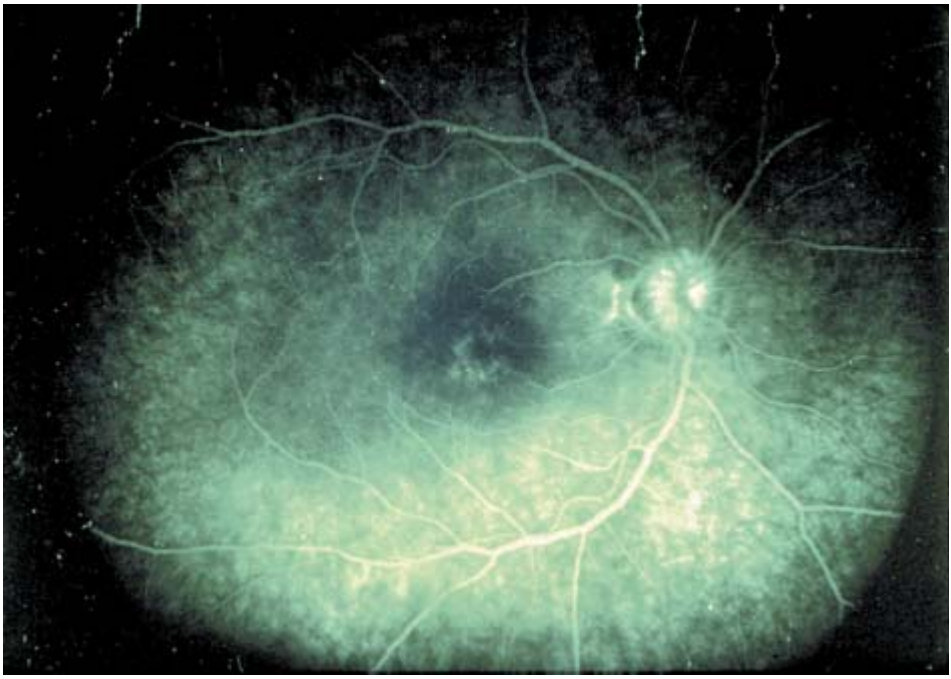
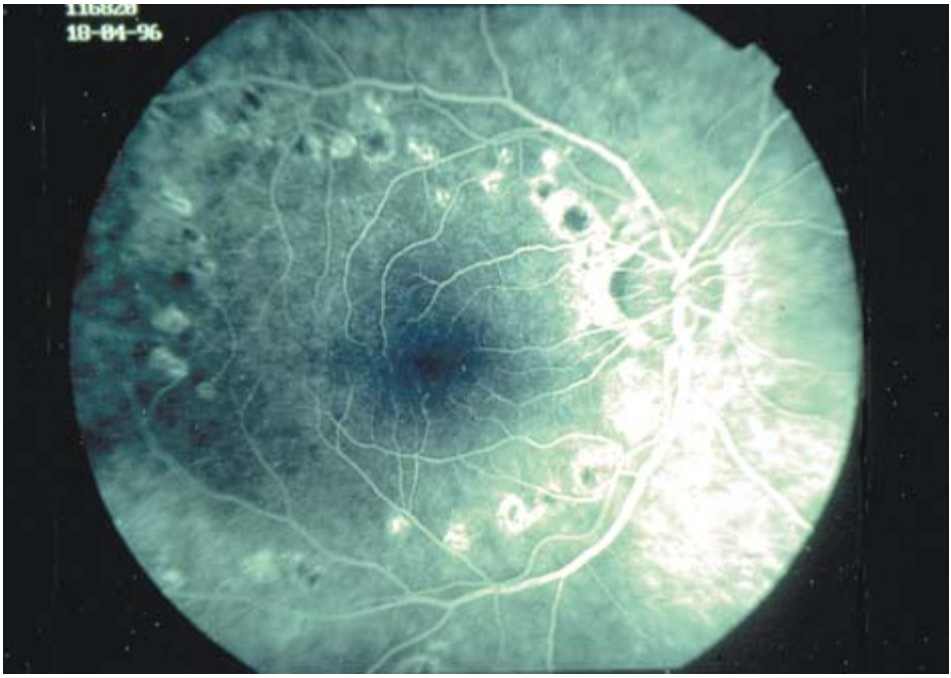
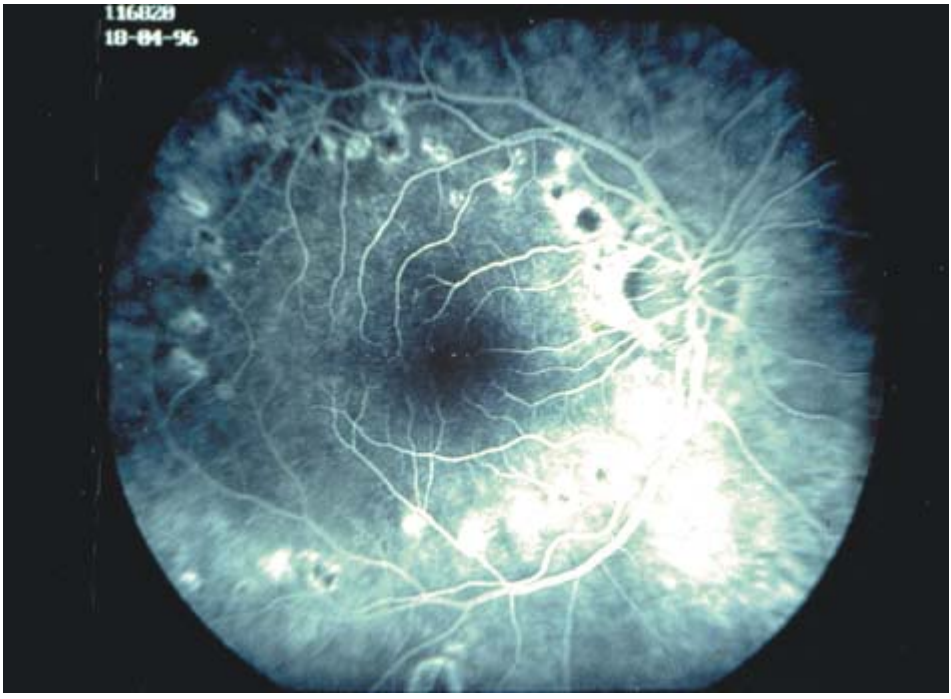


FIGURE 8. *CMO secondary to ICCE. FA. R.E.*





FIGURES 9 AND 10. *FA. Late phases (R.E.). Six months after atypical laser photocoagulation of the posterior pole, without NSAID's. CVA. Initial. R.E. = 0.3 No. 2 with refractive correction(C). Without metamorphopsia (WM). CVA. Final. R.E. = 0.9 No. 1 C. WM.*

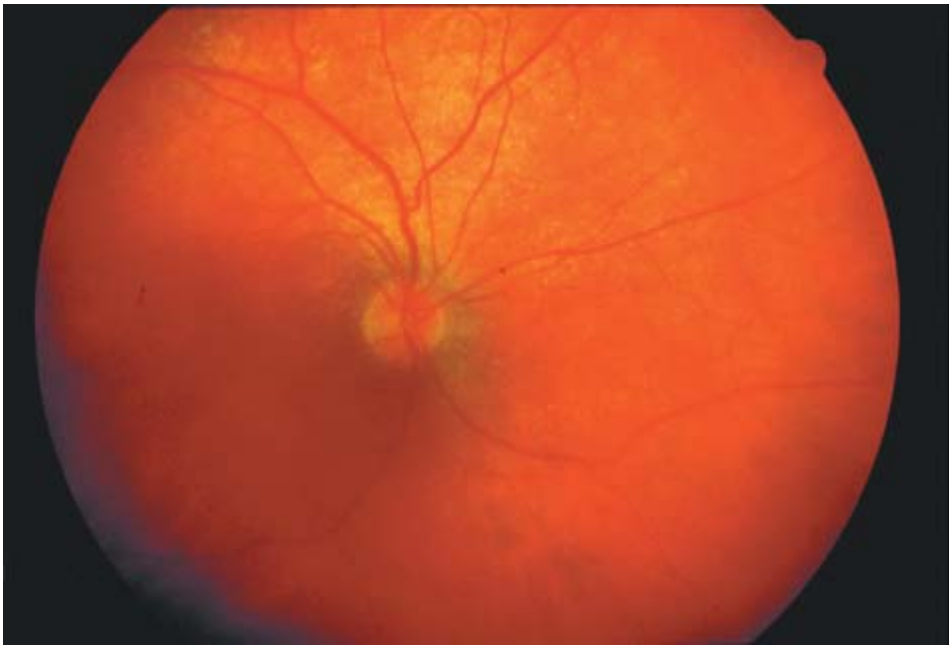


FIGURE 11. *CMO. Simple colour retinography. R.E.*

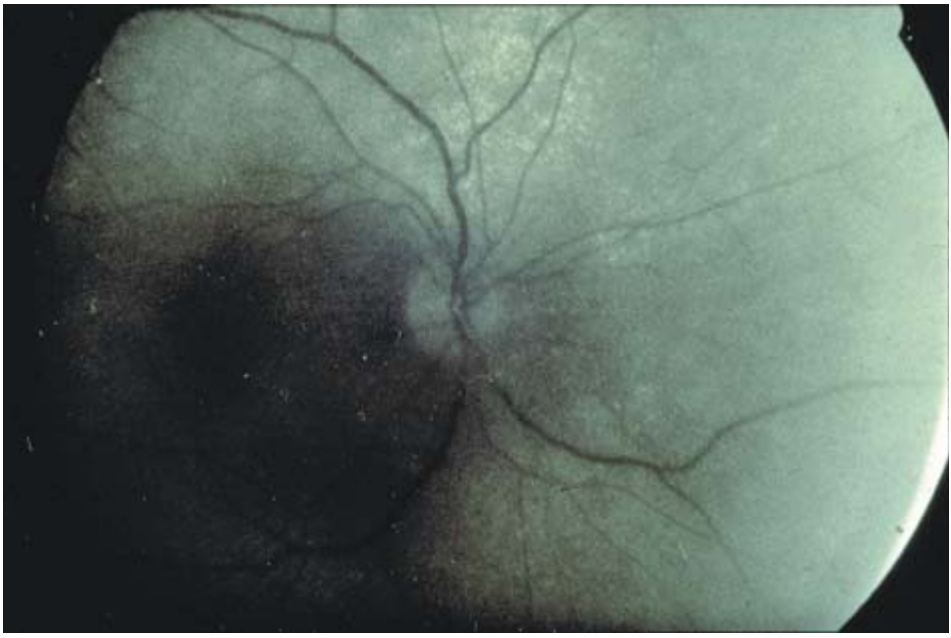


FIGURE 12. *CMO. Retinography with anerythral light. R.E.*

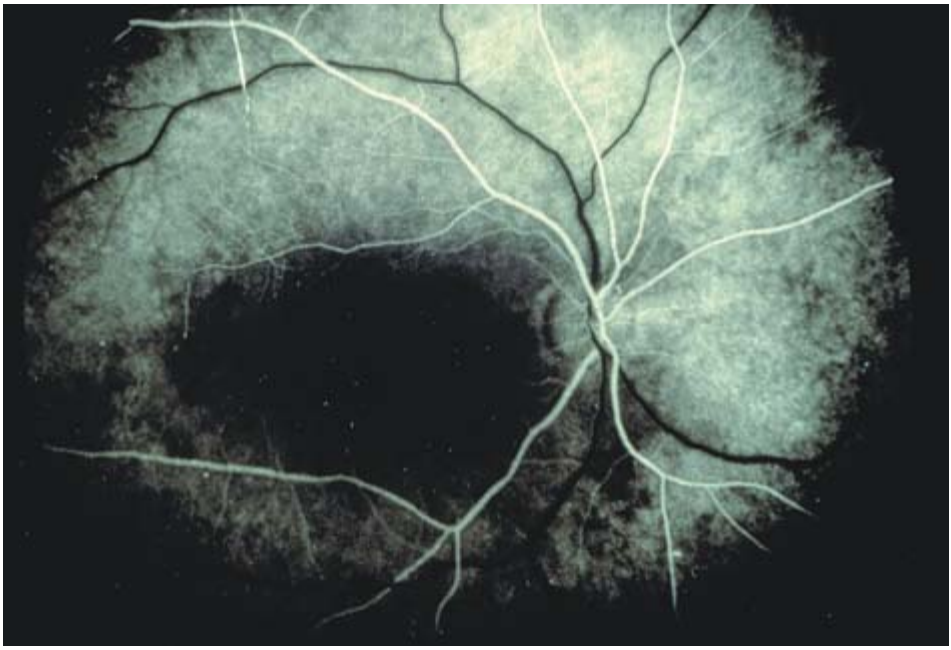


FIGURE 13. *CMO. Arteriovenous phase. FA. R.E.*

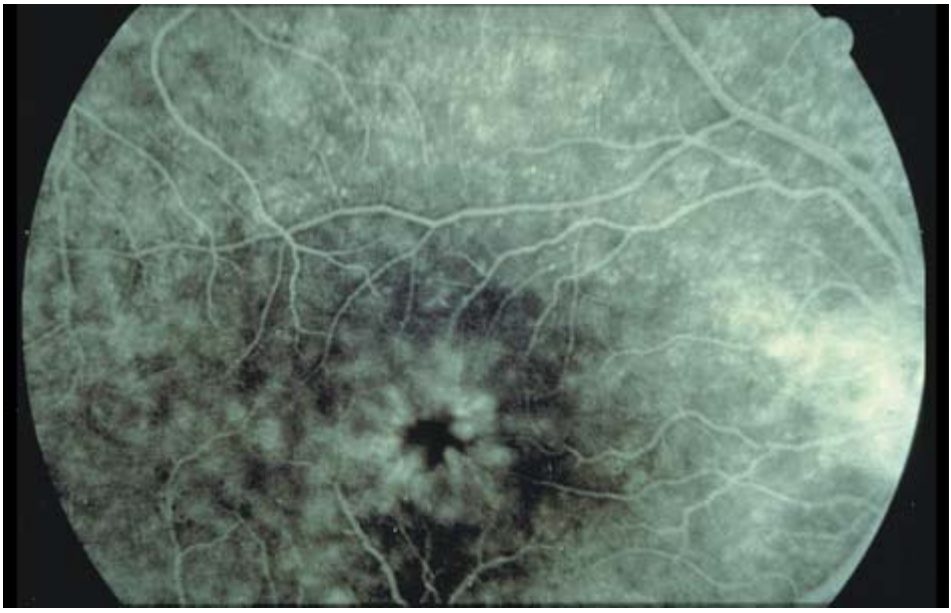


FIGURE 14. *CMO. Typical. Late phases. FA. R.E.*

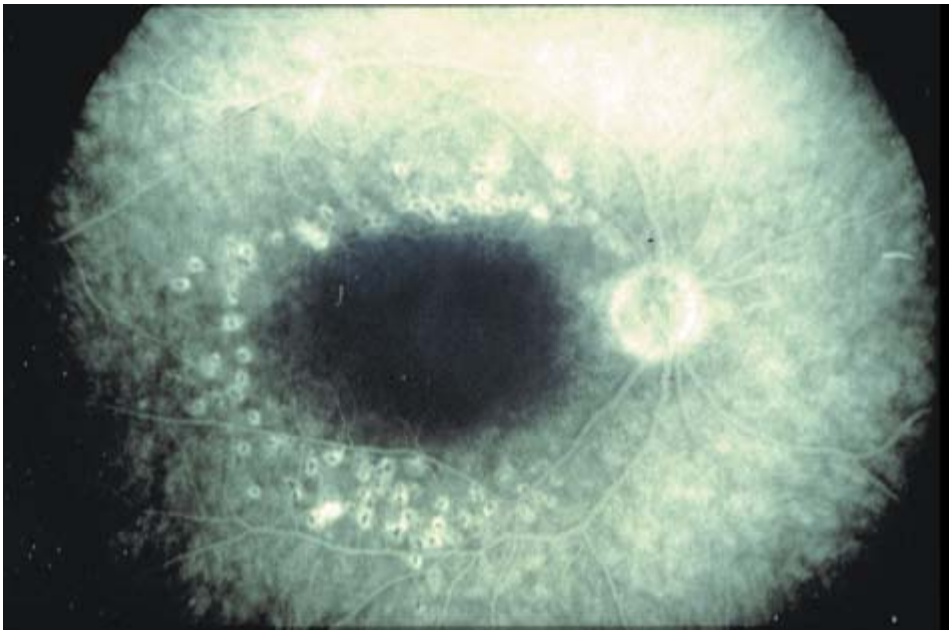


FIGURE 15. *CMO. Laser photocoagulation. Four months later. Same case as before. FA. Late phases. R.E.*

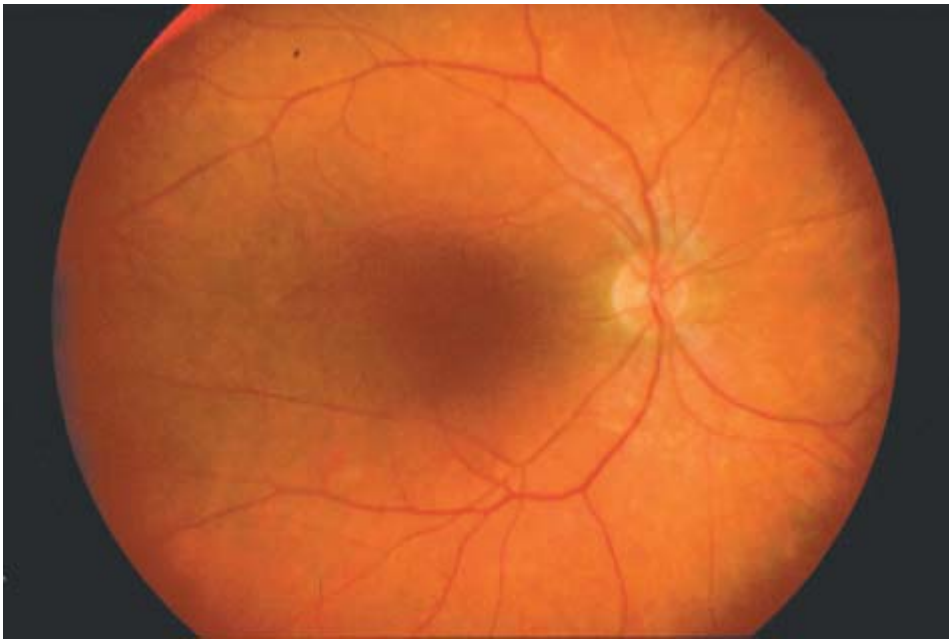


FIGURE 16. *CMO. Simple colour retinography. Previous case. R.E.*
CVA. Initial. R.E. = 0.5 No. 1 C. WM.
CVA. Final. R.E. = 0.65 No. 1 C. WM.

CASE TREATED ONLY WITH TOPICAL INDOMETACIN (NSAID)

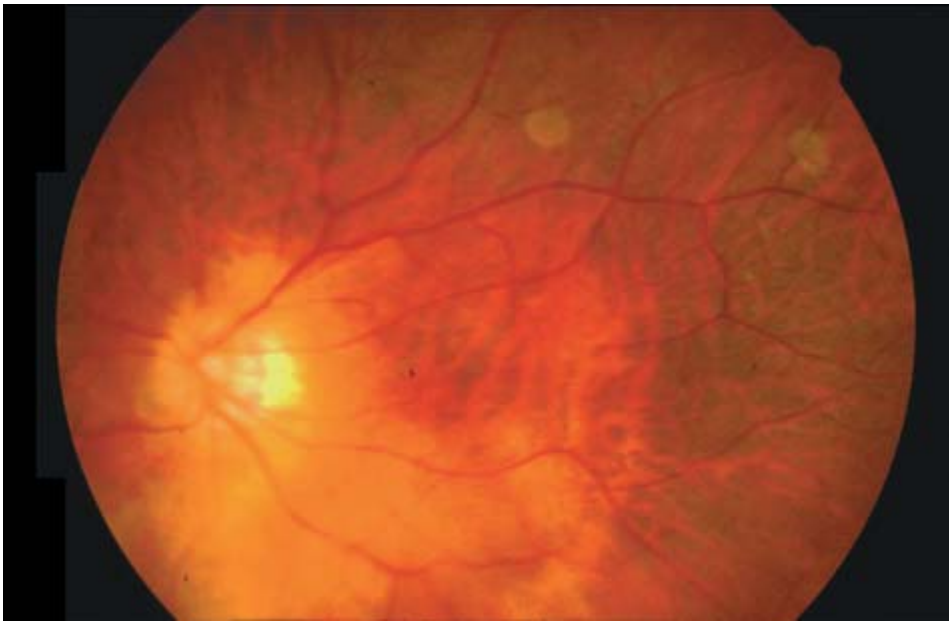


FIGURE 17. *Simple colour retinography. CMO. Left eye (L.E.).*

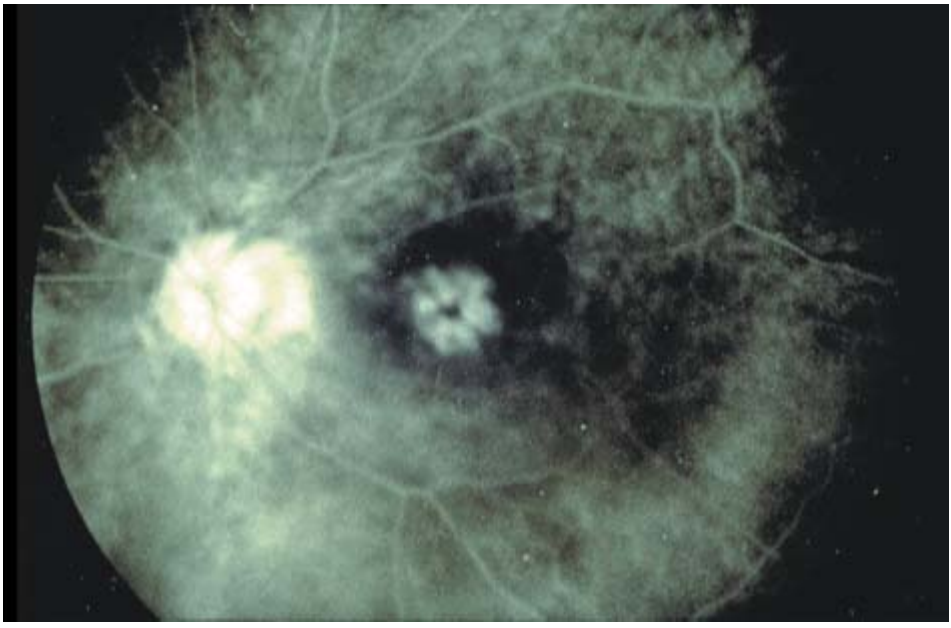


FIGURE 18. *Retinography with FA. Late phases. CMO. L.E.*

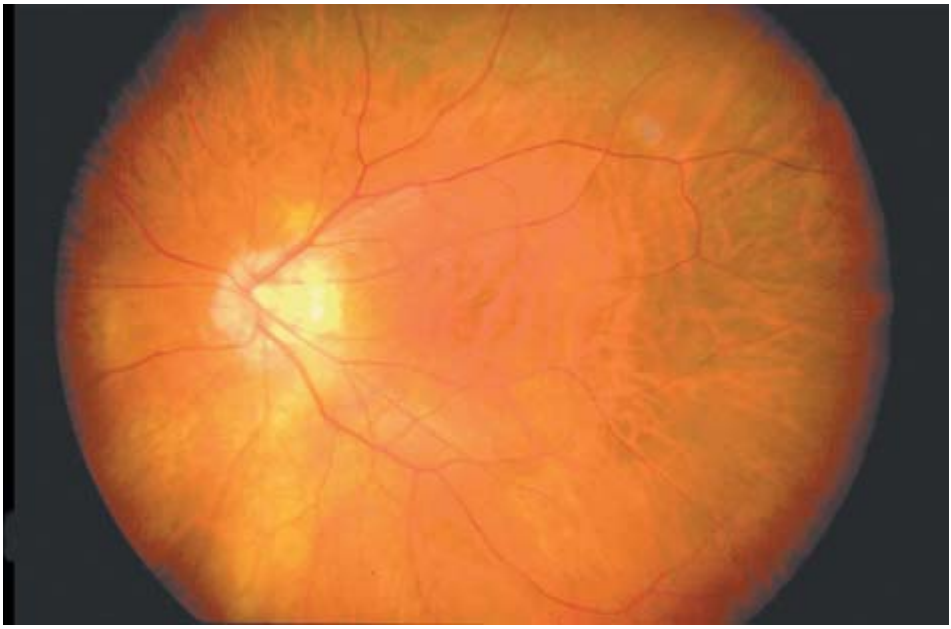


FIGURE 19. *Simple colour retinography. Previous case. Four months after starting local treatment. L.E.*

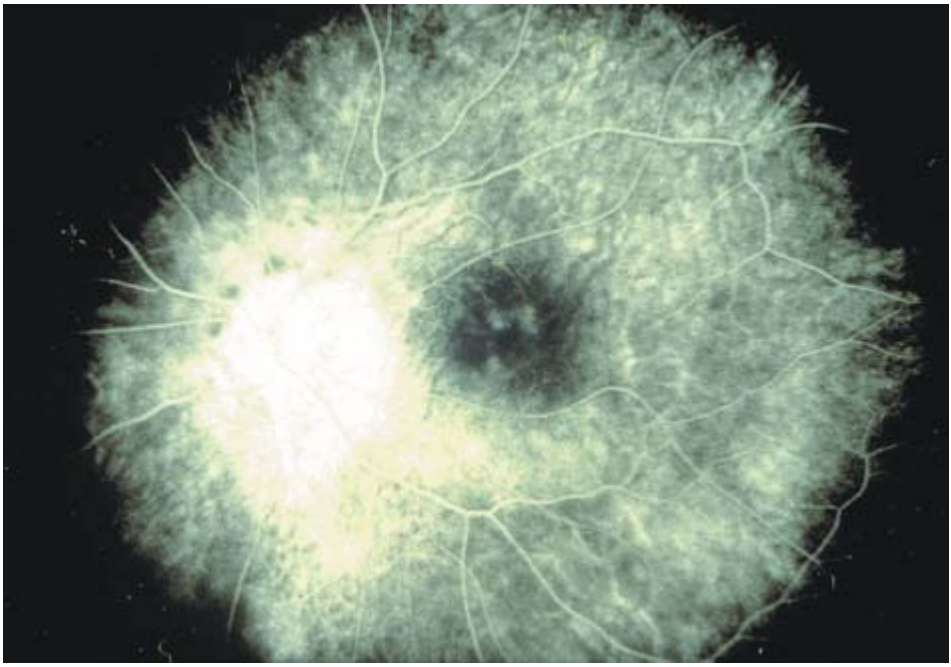


FIGURE 20. *Retinography with FA of same case. L.E.*
CVA. Initial. L.E. = 0.4 No. 1 C. WM.
CVA. Final. L.E. = 0.95 No. 1 C. WM.

ANOTHER CASE TREATED ONLY WITH TOPICAL NSAID'S

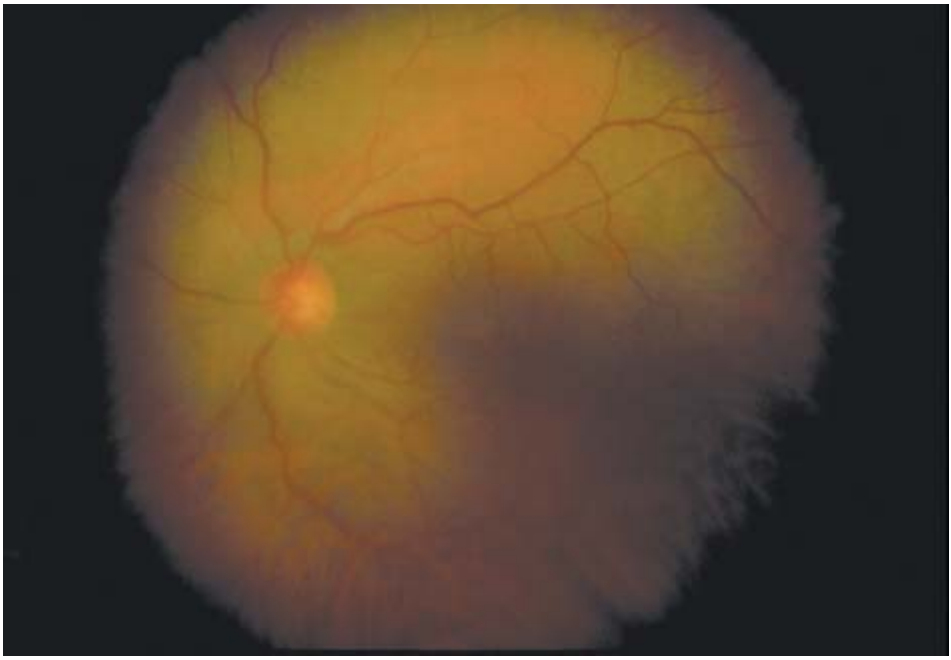


FIGURE 21. *Simple colour retinography. CMO. L.E. Macula with typical yellowish appearance.*

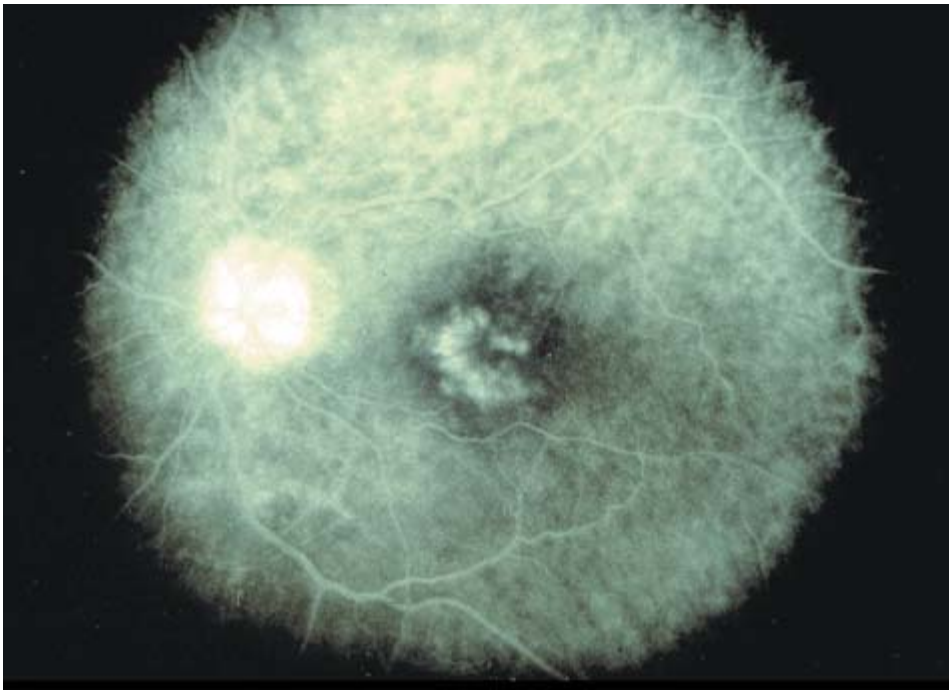


FIGURE 22. *Retinography with FA. Late phases. CMO. L.E.*

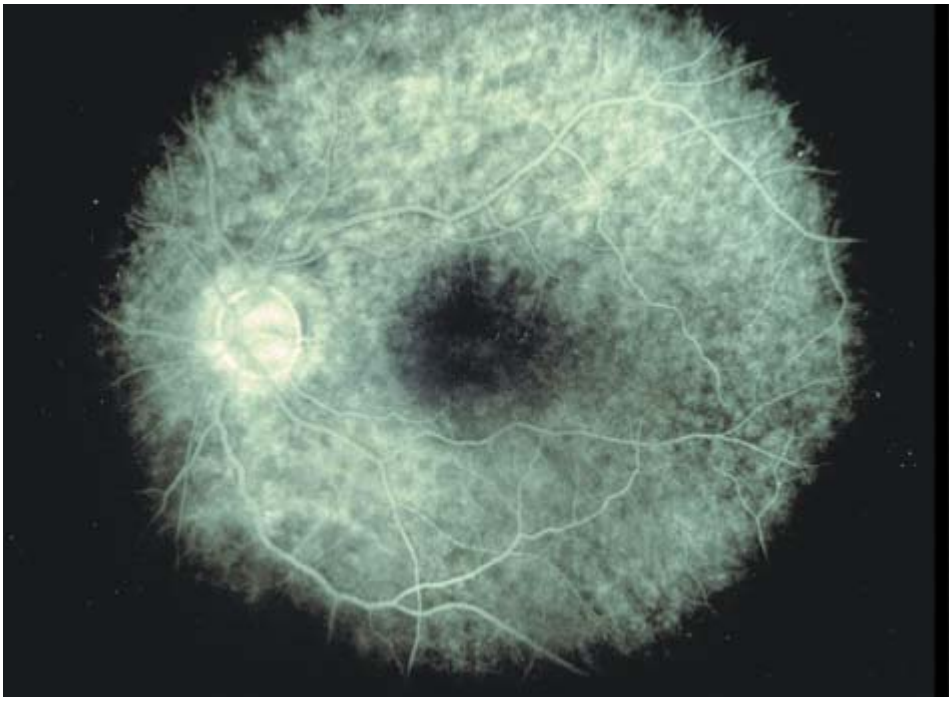


FIGURE 23. *FA. Late phases. Previous case. Four months after starting local treatment. CMO. L.E.*

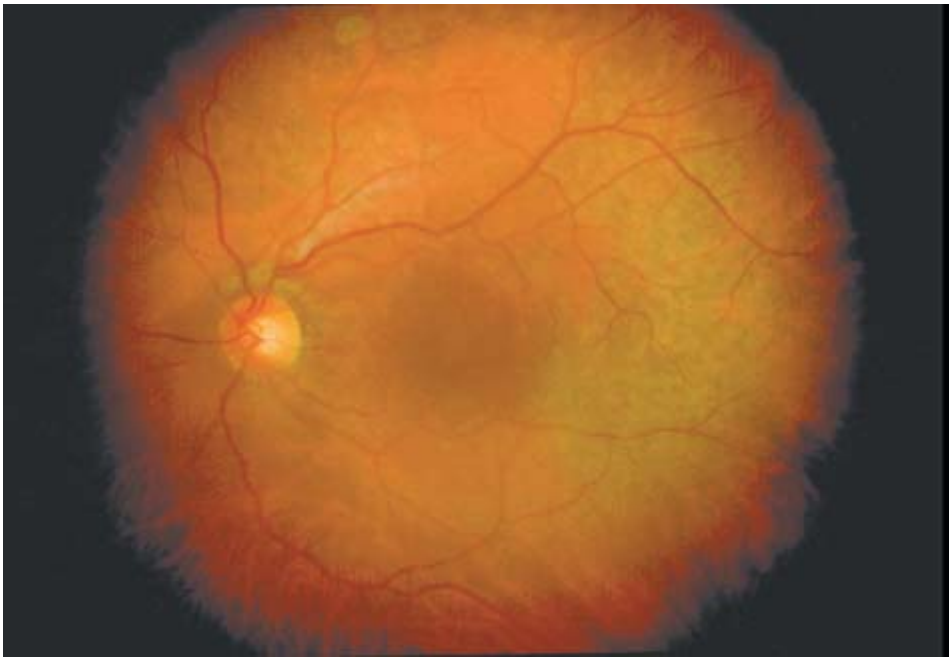


FIGURE 24. *Simple colour retinography in the same case. CMO cured by topical indometacin. L.E. CVA. Initial. L.E. = 0.4 No. 2 C. WM. CVA. Final. L.E. = 0.9 No. 1 C. WM.*

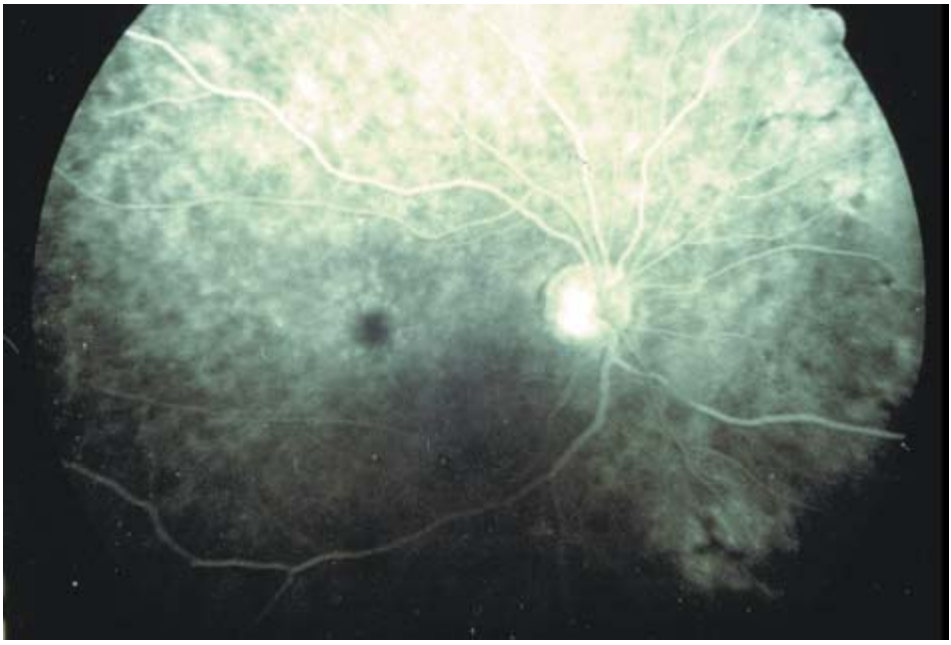


FIGURE 25. *FA. Late phases. Typical CMO. R.E.*

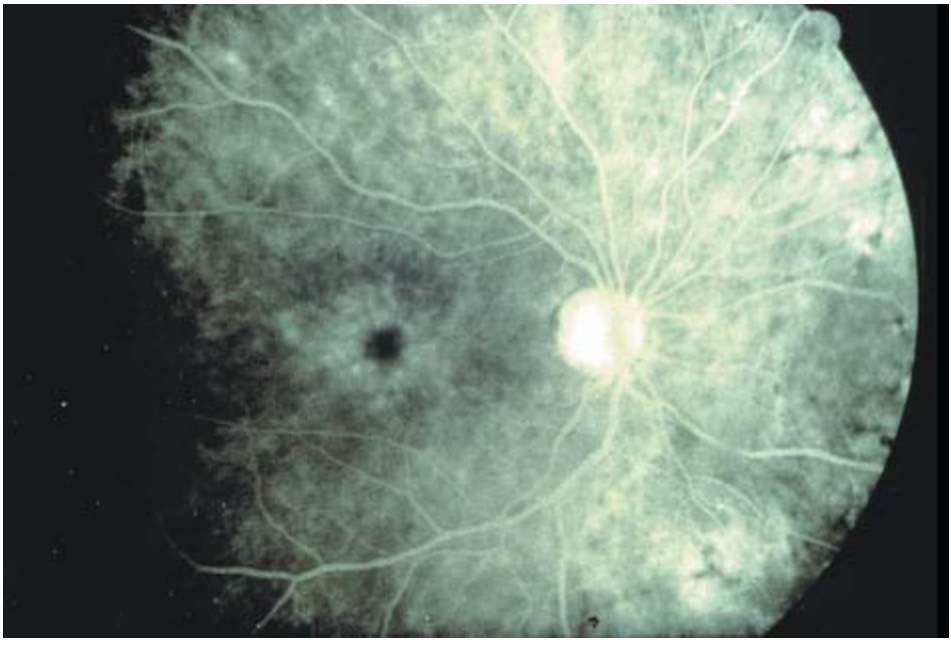


FIGURE 26. *Late phases. Typical CMO. R.E.*

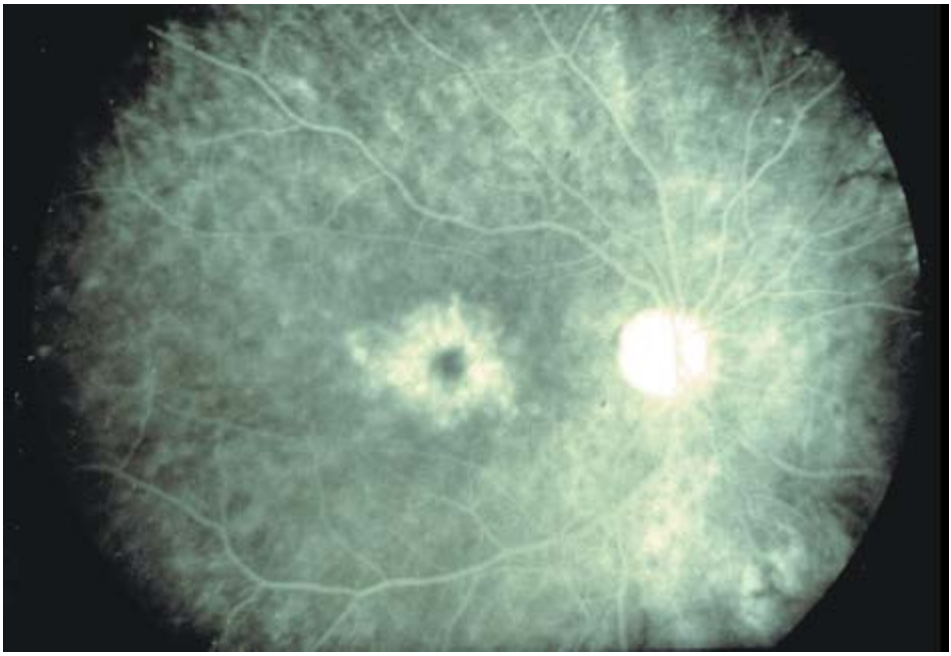


FIGURE 27. *Late phases. Typical CMO. R.E.*

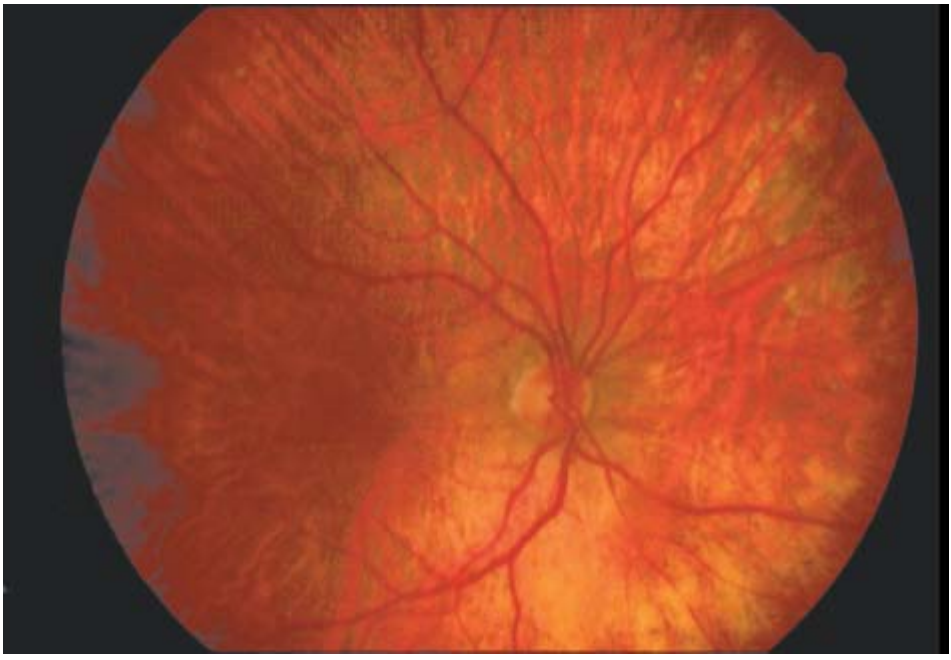


FIGURE 28. *Simple colour retinography of the same case, healed after three months with daily instillation of NSAID's (one drop every 8 hours). R.E.*

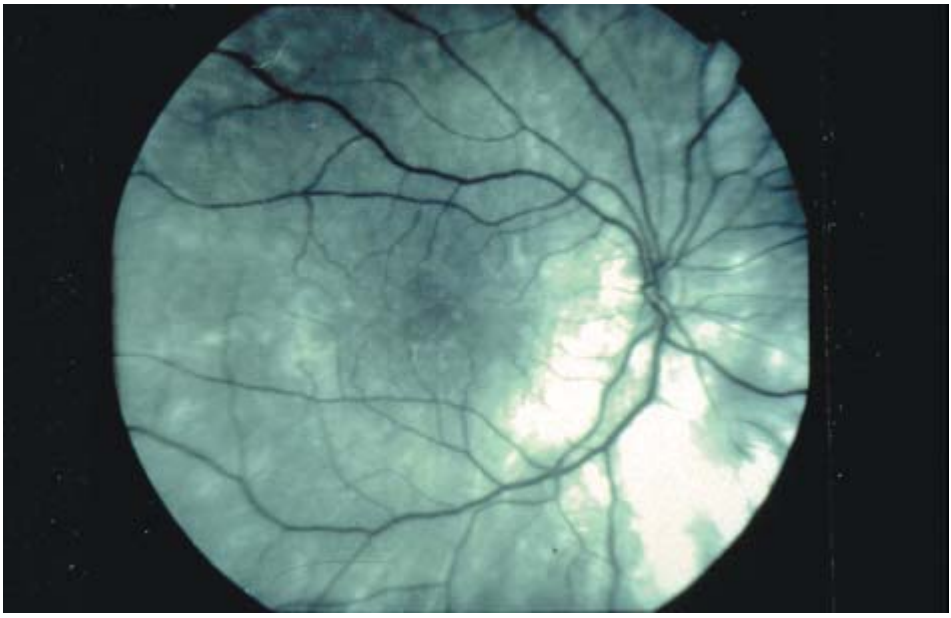


FIGURE 29. *Retinography with anerythral light. Previous case. CMO healed with topical treatment. R.E.*

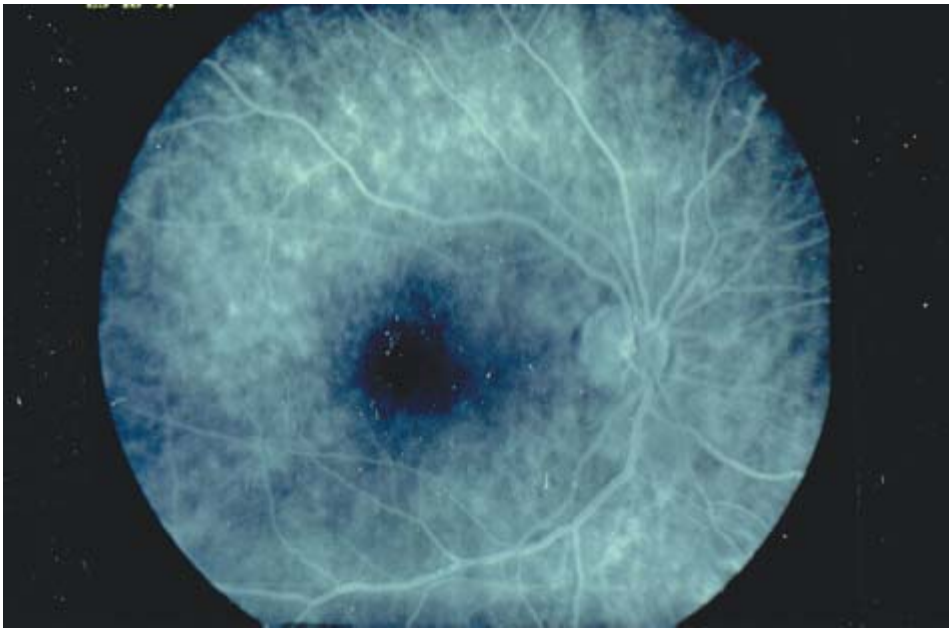
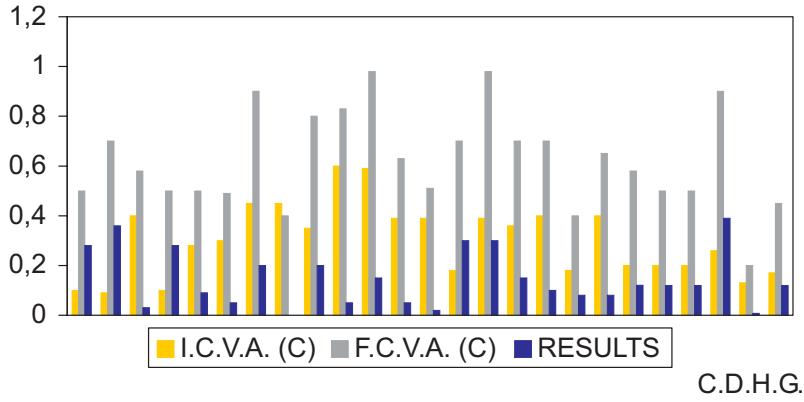


FIGURE 30. *FA. Late phases in the same case. R.E.*
CVA. Initial. R.E. = 0.09 No. 6 C. WM.
CVA. Final. R.E. = 0.5 No. 1 C. WM.

RESULTS

The biostatistical tests applied to the CVA variables were only performed in the most numerous group, i.e., the one treated with topical indometacin (22 cases = 76%). For this, Pearson's test was used (chi-squared = 0.5074) for N = 1 and K = 2, with a significance level $\alpha = 0.10$, and a theoretical N distribution (mean = 0.330; σ = 0.1475).

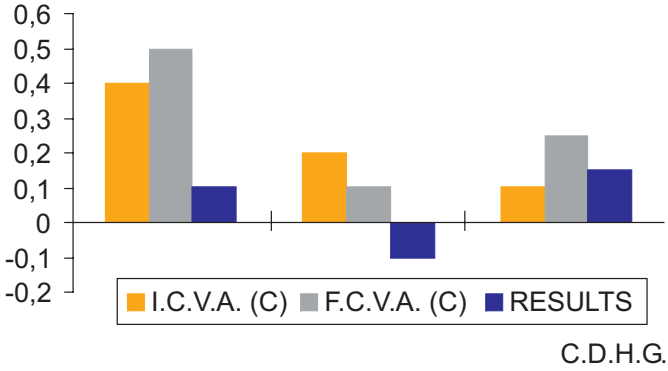
Improvement in CVA in under 6 months after topical NSAID's instillation was 0.330 ± 0.1 - yielding a value of 0.13, which is clinically and statistically significant based on the test used. The 95% confidence interval corresponded to an upper and lower limit of 0.3878 and 0.221, respectively (Graph 3).



GRAPH 3. *Indometacin treatment (according to Pearson's test). ICVA: Initial central visual acuity. FCVA: Final central visual acuity. C: With refractive correction.*

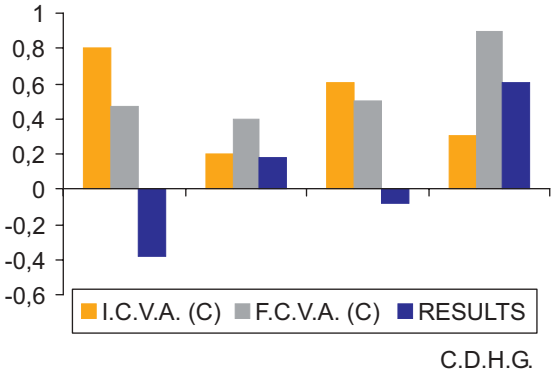
It should be added that in this first group, CVA continued to improve in subsequent controls.

The second group, treated with indometacin plus laser photocoagulation, showed an improvement of 0.05 (Graph 4).

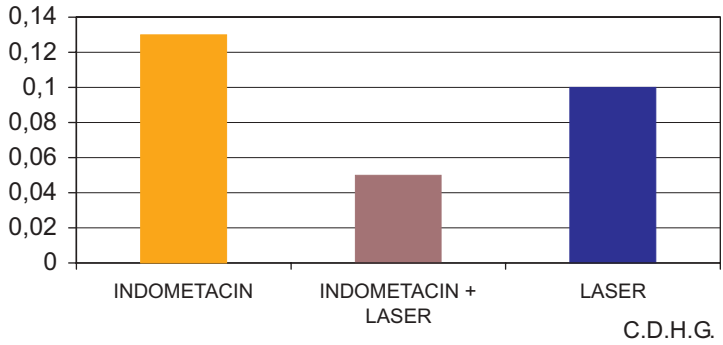


GRAPH 4. *Treatment with indometacin and laser.*

The third group, given only confluent laser therapy, showed an improvement of 0.10 (Graphs 5 and 6).



GRAPH 5. *Laser treatment.*



GRAPH 6. *Cystoid macular oedema. Total cases and treatments.*

DISCUSSION

No single aetiology is able to fully account for the development of cystic or cystoid macular oedema; consequently, the condition should be regarded as having a multifactorial origin.

Despite spontaneous resolution of the clinical picture in many cases (in up to 80% according to some authors), in a large and significant number of cases the course of the disease does not lead to *ad integrum* restitution, and a foveal perforation, macular epiretinal membrane or disc-shaped scar may eventually result in some cases. The two latter conditions occur when the syndrome becomes chronic, and require immediate and selective treatment (9,39).

Transudate accumulation within the Henle fibre or external plexiform layer surrounding the fovea is explained in histopathological terms by the fact that this thick

retinal membrane may collect relatively large amounts of fluid within its multiple cavities - with edematization occurring in response to minimal stimuli.

The avascular nature of the macular area substantially limits fluid and oedema absorption by the Henle and internal nuclear layers. This condition explains the application of physical therapy (laser photocoagulation) in certain specific cases, based on the concept that laser therapy stimulates the release of inhibitory factors from the pigmentary epithelial cells to increase the reabsorption of fluid deposited within the retinal layers after pumping towards the choroid; this is an adjuvant mechanism for the resolution of CMO. However, not all authors readily accept this latter postulate, and some reject the idea.

Preventive drug treatment (particularly topical) is widely used, since the blood-retinal barriers (particularly the external) hinder passage into the posterior segment when drugs are administered systemically (19,26,32).

Nevertheless, oral carbonic anhydrase inhibitors (specifically, acetazolamide 250 mg every 12 hours) are commonly prescribed, for they also increase the absorption capacity of the choroid and pigmentary epithelial cells, thus initially contributing to remove the intra-retinal fluid by stimulating active ion transport pump. In theory, this is the way in which all transudates typically found in CMO are removed.

The use of conventional topical corticoids was once very widespread. However, although such drugs do exert potent anti-inflammatory effects, their side effects (immune suppression, delayed healing, secondary glaucoma, enhancement of bacterial and fungal overinfection, etc.) advise against their use. Furthermore, the conventional corticoids only inhibit the leukotrienes, regardless of the administration route employed.

Non-steroidal anti-inflammatory drugs (NSAIDs) are very effective, as reflected by the results of the present study.

In this context, both indometacin and sodium diclofenac eyedrops readily penetrate inside the eyeball, causing marked inhibition of prostaglandin synthesis without the untoward effects elicited by these same drugs when administered systemically. Early CMO remission is thus achieved by blocking of the inflammatory reaction mediators. Moreover, sodium diclofenac, which is also analgesic and acts only upon the anterior segment, can be combined with indometacin, since the latter acts upon the posterior pole - thereby avoiding possible incompatibilities between both two drugs.

The formulation of the indometacin preparation used in the present study includes two alcoholic preservatives (benzyl and phenylethyl alcohol), which in addition to the alkaline nature (pH 9) of the solution account for the burning sensation referred by some patients after instillation.

This very mild symptom has been little reported in our series, for we recommended rubbing the eyedrop bottle before use, and storage in the home refrigerator door compartment between local treatments.

We likewise observed no cases of intraocular hypertension, bullous keratitis or iatrogenic miosis. Surgery was not required (*pars plana* vitrectomy), since among

other parameters patient response to medical treatment was excellent and the duration of the process was under 6 months in all cases. Moreover, significant improvements in CVA have been recorded over time (after 1-2 years).

In pseudophakic eyes even by extracapsular cataract extraction (ECCE), the incidence of CMO is much lower - as also occurs when the intraocular lens (IOL) is placed into the capsular sac (CS) instead of the anterior chamber (AC). However, the development of CMO has occasionally been reported in patients subjected to cataract extraction with IOL implantation in the CS (24,39).

In our opinion, this latter observation is due to age-related PVD, which causes the hole in the central posterior hyaloid (*bursa premacularis*) through which the vasoactive substances described by Kishi, Shimizu and Worst diffuse towards the macula. (25,41).

Authors such as Hitchings suggest that in cases of ICCE the incidence of CMO can reach 50%, both when the conventional technique is used and when the IOL is implanted in the AC (20).

One aspect that remains to be addressed is why the fundamentally inflammatory condition develops in late phases rather than suddenly or during the early postoperative period. This supports the immune hypothesis of the syndrome, for it accounts for the presence of autoantigens which could induce an immune reaction when slowly released or deposited in the vitreous (10).

CONCLUSIONS

Although the natural history of CMO tends towards spontaneous resolution in 80% of cases (particularly in subclinical presentations), immediate therapeutic measures relieves the troublesome symptoms, prevents potential chronic complications and contributes to ensure prompt vision recovery.

The intact posterior capsule in phacoemulsification or ECCE plus IOL prevents the inflammatory mediators from reaching the posterior pole, however, if in these pseudoaphakic eyes capsule photocoagulation is performed (e.g., capsulotomy with YAG laser) due to opacification of the latter, with the subsequent reduction in visual acuity, the incidence of CMO increases for obvious reasons - reaching the proportion observed for ICCE.

We have no long experience with the administration of other inhibitors such as aspirin, carbonic anhydrase inhibitors or with the instillation of eyedrops composed of flurbiprofen or ketorolac tromethamol in CMO (11). Nor with intravitreal and subtenon‘s injections of steroids (triamcinolone acetonide), neither by sustained release of intraocular implants.

The high frequency of CMO has decreased with the increasing performance of ECCE and phacoemulsification, particularly when the IOL is implanted into the CS, because of the reasons given above.

OCT is supremely useful as diagnostic method.

In some cases, laser photocoagulation is quite successful.

In selected cases a surgical approach ought to be done.

Recently intravitreal injection of triamcinolone acetonide is being used as a adjunct therapeutic option for long-standing cystoid macular oedema and several macular diseases including age-related macular degeneration. Our clinical results should be soon published.

As stressed in this study, for the moment we consider topical medical treatment with indometacin to be superior to the other management options in full-blown postoperative CMO. On the other hand, attention is drawn to the importance of prophylaxis with this same drug, in compliance with the recommendations of many authors who consider the topical route to afford global stabilization of the blood-aqueous barrier.

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