

CYSTOID MACULAR EDEMA

ELLEN N. YU, M.D.

CASE REPORT

A 41 year old white female presented with a history of recurrent anterior uveitis. The patient was diagnosed with anterior uveitis eighteen months prior to presentation when she consulted her local ophthalmologist for right eye redness, slight pain and blurring of vision. The uveitis resolved with topical steroids, but recurred twice over the past year and a half.

There were no associated systemic symptoms. Past medical history and family medical history were unremarkable.

On examination, visual acuities were 20/100 on the right and 20/20 on the left. Slit lamp exam of the right eye showed white and quiet conjunctiva, few fine keratic precipitates on the posterior corneal surface and +1/2 cells in the anterior chamber. There was no synechiae or cataract. Slit lamp exam of the left eye was normal.

Dilated eye exam of the right eye showed clear vitreous, cup disc ratio of 0.3, no retinal lesions were noted except for a dull foveal reflex (Figure 1). The left fundus was normal. Fluorescein angiogram was done (figures 2 & 3) which revealed the presence of cystoid macular edema. Transeptal steroid injection was administered and oral non-steroidal anti-inflammatory drug was initiated for the macular edema.

Systemic work-up was negative except for HLA-B27 positivity.

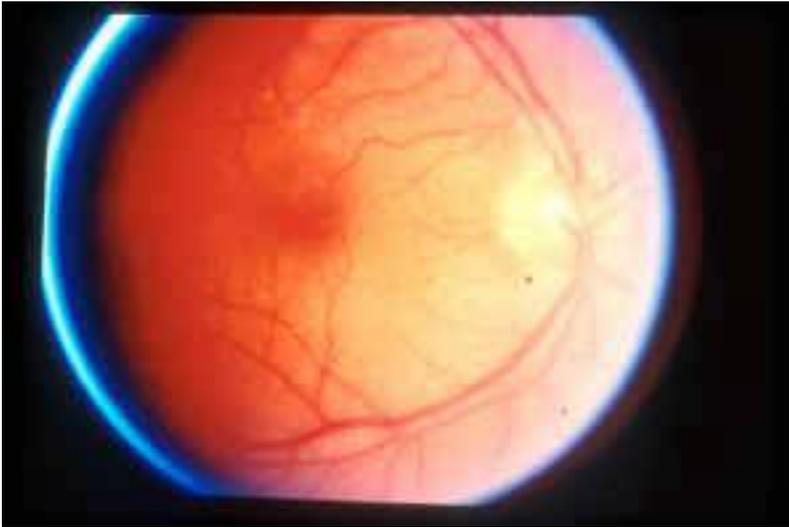


Figure 1. Color photo of right fundus showing dull foveal reflex.

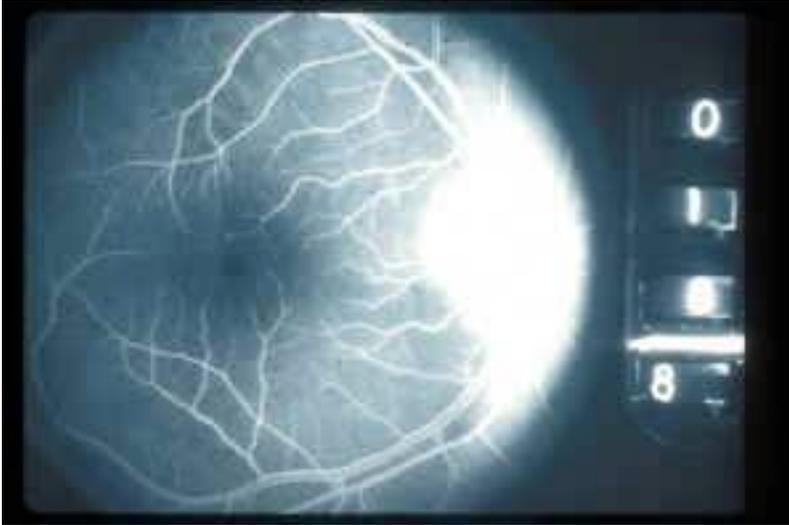


Figure 2. Early phase of fluorescein angiogram of the right eye.



Figure 3. Late phase of fluorescein angiogram of the right eye showing dye leakage in a petalloid pattern at the macular area.

INTRODUCTION

The macroscopic changes of cystoid macular edema (CME) was first described by Irvine in 1953. A loss of the foveolar reflex in the macula was noted in a patient with decreased visual acuity associated with prolapse of vitreous in the anterior chamber after intracapsular cataract extraction (ICCE). Since that time, macular edema has been identified as a common cause of decreased vision in many ophthalmic diseases. In fact, it is the most common macular alteration associated with uveitis. Although it may occur in any type of ocular inflammation, the types of uveitis most commonly associated with macular edema are: pars planitis, iridocyclitis, birdshot retinochoroidopathy, sarcoid uveitis and HLAB27 uveitis

PATHOPHYSIOLOGY

Macular edema is caused by disruption in the normal permeability barrier of the retina, the blood-retinal barrier (BRB). The BRB is responsible for restricting movement of plasma constituents into the retina and in maintaining homeostasis. The BRB has 2 components: the inner BRB is composed of the endothelial cells of the retinal blood vessels; the outer BRB is composed of the tight junctions between retinal pigment epithelial (RPE) cells.

When the BRB is disrupted, the volume of the extracellular space of the retina expands due to unrestricted entry of protein and water from plasma. Why the macula is predisposed to accumulation of fluid causing cystoid macular edema is not known.

Inflammation is among the factors implicated in BRB breakdown. Other factors include metabolic alterations (diabetes, retinitis pigmentosa), ischemia (severe hypertension, toxemia of pregnancy, collagen vascular disease, disseminated intravascular coagulopathy), increased capillary pressure (venous occlusive disease, systemic hypertension), severe ocular hypotension, mechanical forces (epiretinal membrane), and toxicity (epinephrine, betaxolol, latanoprost).

In ocular inflammation, increased production of inflammatory mediators such as prostaglandins lead to increased permeability of the parafoveal capillaries and exudation in the macular area. Non-steroidal anti-inflammatory drugs (NSAIDs) and steroids are thus utilized to target the arachidonic acid pathway in prostaglandin synthesis.

The following soluble factors have also been implicated in promoting BRB breakdown leading to macular edema: adenosine, prostaglandin E1 (PGE1), tumor necrosis factor a (TNF a), interleukin-1 b (IL-1 b), vascular endothelial growth factor(VEGF), and vasoactive peptides such as bradykinins or kallikreines. When given intravitreally, these mediators have been noted to cause morphological and functional opening of the retinal vascular endothelium (RVE) tight junctions and upregulation of vesicle-mediated transport across the RVE. The effect of these mediators in the outer BRB is less clear.

HISTOPATHOLOGY

Light microscopy has shown the presence of fluid accumulation in intraretinal cysts in the inner nuclear and outer plexiform layers of the retina. The cysts are located around the fovea producing a petalloid pattern. With increased severity and chronicity, deeper and larger cysts were noted. Whether these represent smaller cysts that have coalesce has not been mentioned.

Other researchers believe that disruption of muller cell function by ischemia and other factors lead to the development of CME and that the cystic spaces observed were swollen Muller cells. The accumulation of fluid in the outer plexiform layer is said to be a late phenomena following breakdown of the Muller cells. However, some authors argue that these findings may be secondary to ischemic changes after cessation of blood flow to the retina during specimen collection.

Macular changes may be reversible, and restoration of vascular permeability may occur after resolution of the edema. However, after chronic edema, retinal thinning with photoreceptor damage and progressive fibrosis may occur. The length of time required to produce permanent damage is not known.

DIAGNOSIS The patient may complain of decreased visual acuity, metamorphopsia and micropsia. To document these, visual acuity testing and amsler grid should be performed. Under the slit lamp using a 78- or 90- diopter aspheric lens, areas with thickening or cystic accumulation of fluid may be detected. Indirect ophthalmoscopy can be utilized to visualize whether there are other areas of thickening or when evaluation is difficult due to hazy media and/or cataract. When changes are very subtle, fluorescein angiography is an important tool in the diagnosis of CME.

FLUORESCEIN ANGIOGRAM Fluorescein angiogram (FA) will show progressive hyperfluorescent leakage of dye in the macular area with late accumulation in the parafoveal cystic spaces resulting in the characteristic petalloid pattern (Figure 3).

Studies have shown a poor correlation between dye leakage and visual acuity. In some patients, leakage can occur without decrease in vision. FA is not helpful in predicting the present VA nor the ultimate outcome of therapy.

OPTICAL COHERENCE TOMOGRAPHY In optical coherence tomography (OCT), a laser slit beam is projected into the retina and a high-resolution cross-section image is obtained. Localized accumulation of fluid can be seen with increase in retinal thickness.

Studies have compared OCT and FA with regards to detection of macular edema and macular thickening has been shown to correlate better with visual acuity. Moreover, OCT has been shown to detect macular thickening even before any angiographic evidence of CME. Thus OCT seems to be a very promising tool.

TREATMENT

Currently, there is still no accepted treatment modality for uveitis-associated CME. This is due to the fact that there has been no success in producing macular edema experimentally in animals. Data has been based on clinical studies, and many agents are used with variable response. Since there is a constant release of inflammatory mediators when there is active uveitis, the first and most important step is to control the uveitis.

(1) Corticosteroids. Steroids have been used to treat uveitis-associated cystoid macular edema since studies have shown that inflammatory mediators lead to increased vascular permeability. Steroids may be given topically, by periocular injection, or orally. Topical steroids can be given to aphakics where it has been shown to reach the posterior pole. Periocular injections can produce high levels in the posterior segment of the eye with a lower risk of systemic side effects than oral steroids.

(2) Non-steroidal anti-inflammatory drugs (NSAIDs). NSAIDs also affect prostaglandin synthesis and may be given topically or orally. Whether steroids and NSAIDs affect macular edema other than prostaglandin synthesis i.e. whether they act directly on cells, or whether they help them in pumping out fluid more efficiently, is not known.

(3) Carbonic anhydrase inhibitors (CAIs). CAIs increase the active transport of fluid from the retina to the choroids by pumps in the pigment epithelial cells. However, recurrence of edema after discontinuation has been reported.

(4) Hyperbaric oxygen, vitrectomy and laser photocoagulation. These treatment modalities are still controversial at this point. Mechanism of action of hyperbaric oxygen in improving visual acuity in CME is not known.

PROGNOSIS CME requires many months of treatment. It may disappear with resolution of the uveitis. However, even with complete resolution of the inflammation, macular changes secondary to chronic CME may lead to permanent visual loss. Visual acuity improvement is more commonly seen in patients with CME of less than 6 months duration.

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Cystoid Macular Edema

Ellen Yu, M.D.

1. The following have been implicated in promoting blood-retinal barrier breakdown leading to macular edema EXCEPT:
 - a. metabolic alteration
 - b. increased capillary pressure
 - c. mechanical forces
 - d. inflammation
 - e. none of the above

2. Which of the following tools enables one to measure retinal thickness:
 - a. Fluorescein angiogram
 - b. Visual acuity
 - c. Amsler grid

- d. Optical coherence tomography
 - e. Indirect ophthalmoscopy
3. Which of the following medications acts by increasing the pumping action of RPE cells, aiding in the treatment of CME?
- a. NSAIDs
 - b. Corticosteroids
 - c. Carbonic anhydrase inhibitors
 - d. Vitrectomy
 - e. Laser photocoagulation
4. True of cystoid macular edema:
- a. may disappear with resolution of uveitis
 - b. may not disappear with resolution of uveitis
 - c. may lead to permanent visual loss when chronic
 - d. all of the above
 - e. none of the above
5. Fluorescein angiography is helpful in predicting the visual acuity in a patient with CME. True or False?
6. The best therapy for CME in phakic patients is topical steroid drops. True or False?
7. CME only occurs in posterior uveitis and never with anterior uveitis. True or False?
8. Retinal thinning with photoreceptor damage and progressive fibrosis may occur in chronic CME. True or False?

ANSWERS:

1. E 2. D 3. C 4. D

5. False. Studies have shown a poor correlation between dye leakage and visual acuity

6. False. Topical steroids may be used in aphakics where it has been shown to reach the posterior pole.

7. False. CME can accompany anterior, intermediate or posterior uveitis.

8. True. These findings lead to permanent vision loss in chronic CME.