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Major review

Management of pseudophakic cystoid macular edema

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ABSTRACT

Pseudophakic cystoid macular edema (PCME) is a common complication following cataract surgery. Acute PCME may resolve spontaneously, but some patients will develop chronic macular edema that affects vision and is difficult to treat. This disease was described more than 50 years ago, and there are multiple options for clinical management. We discuss mechanisms, clinical efficacy, and adverse effects of these treatment modalities. Topical non-steroidal anti-inflammatory agents and corticosteroids are widely used and, when combined, may have a synergistic effect. Intravitreal corticosteroids and anti-vascular endothelial growth factor (anti-VEGF) agents have shown promise when topical medications either fail or have had limited effects. Randomized clinical studies evaluating anti-VEGF agents are needed to fully evaluate benefits and risks. When PCME is either refractory to medical therapy or is associated with significant vitreous involvement, pars plana vitrectomy has been shown to improve outcomes, though it is associated with additional risks.

1. Introduction

Pseudophakic cystoid macular edema (PCME) was first described in 1953 by A. Ray Irvine, Jr., in patients with unexplained visual loss following intracapsular cataract extraction.[64] The cause of the visual loss was later identified by Gass and Norton as marked macular edema with a classic perifoveal petalloid pattern of staining and late leakage from the optic nerve on intravenous fluorescein angiography (IVFA, Fig. 1).[46] The incidence of angiographic PCME has decreased with the transition from intracapsular cataract extraction (~60%) to extracapsular cataract surgery (~20%) and again with the development of small-incision phacoemulsification.[39,117] An estimated 20–30% of patients undergoing phacoemulsification, however, have PCME on IVFA.[50,123] New diagnostic tools such as optical coherence tomography (OCT)

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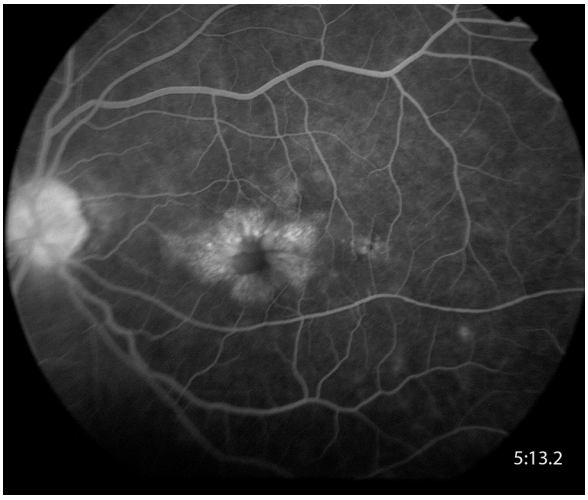

Fig. 1 – Intravenous fluorescein angiography demonstrating classic perifoveal petalloid staining with late leakage from the optic nerve head consistent with pseudophakic cystoid macular edema.

suggest that the rate may be as high as 41%.[75] The majority of patients with PCME on imaging do not experience visual disturbances.[23,123] The incidence of clinical PCME, defined as symptomatic vision loss 20/40 or worse, is much lower with today's surgical techniques—approximately 0.1% to 2.35%.[57,76]

Most patients with PCME have spontaneous resolution of the macular edema within 3–4 months.[15] One year after surgery, a small minority of patients (<1%) in the absence of treatment may still have decreased visual acuity from PCME. A better understanding of the condition and its causes, as well as more aggressive treatment of PCME, however, has considerably altered the course of the disease.[111]

1.1. *Pathogenesis*

Various factors and many presumed mechanisms may be involved in the pathogenesis of PCME, including the release of mediators of inflammation such as prostaglandins, light toxicity, and mechanical irritation.[29,60,106] Inflammatory mediators disrupt the blood–aqueous barrier (BAB) and blood–retinal barrier (BRB), leading to increased vascular permeability resulting in macular edema. Breakdown of the BAB and BRB may be associated with diabetes, glaucoma, and uveitis.[134] Surgical manipulation of the anterior segment may lead to the release of arachidonic acid from cell membranes, with production of either leukotrienes via the lipooxygenase pathway or prostaglandins via the cyclooxygenase pathway.[29,60] These inflammatory biomarkers result in increased retinal vessel permeability and the development of PCME. Alternatively, contraction of the posterior hyaloid as a result of inflammation may lead to mechanical traction onto the perifoveal retinal capillaries and result in PCME. Iridovitreal adhesions and traction may contribute to PCME.[106]

1.2. *Incidence and risk factors*

Following extracapsular cataract extraction, the incidence of clinical PCME in uncomplicated, low-risk patients varies from 2% to 12%.[15] Following phacoemulsification the rate is even lower, ranging from 0.1% to 2.35%.[57,76] The incidence of angiographic CME 1–2 months postoperatively is as high as 20% to 30%.[126] PCME as seen on OCT after modern phacoemulsification may range from 4% to 11%,[12,93] though there may be up to a 41% incidence of subtle macular alterations.[75] The peak incidence of PCME occurs at 6 weeks after surgery. Incidence increases in patients with high-risk characteristics—including diabetes mellitus, hypertension, history of central retinal vein occlusion, recent history of uveitis, preexisting epiretinal membrane, or following complicated cataract surgery.[39,57] Perioperative glaucoma has been implicated as a risk factor for PCME, though a recent large retrospective study showed no increased incidence of clinical PCME in glaucoma patients undergoing uncomplicated cataract extraction.[72] Although that study found no relationship between the use of prostaglandin analogs for the treatment of glaucoma and the development of PCME, other studies have found that prostaglandins, synthesized by the uvea and lens epithelial cells, may be one of the inflammatory mediators associated with PCME.[87] Arcieri et al randomized 80 patients and demonstrated glaucoma patients on prostaglandin analogs were more likely to develop PCME (by IVFA) compared with controls.[3] Henderson et al also reviewed a series of 1,659 cataract surgeries and demonstrated that prostaglandin analog use was one risk factor for developing PCME. They also correlated the presence of epiretinal membrane and prior history of retinal vein occlusion with an increased risk for PCME.[57]

1.3. *Diagnosis and treatment options*

PCME most often develops 4–6 weeks after cataract surgery. Acute PCME occurs within 6 months postoperatively; chronic PCME is present more than 6 months after cataract surgery. PCME is diagnosed by decreased visual acuity, by fluorescein angiography with the classic appearance of perifoveal petalloid staining with or without late leakage from the optic disk, or by OCT. Characteristics of PCME on OCT include macular thickening and cystic spaces in the outer plexiform layer, occasionally with subfoveal fluid (Fig. 2).[69,134] Once PCME is confirmed by clinical findings, fluorescein angiography, and/or OCT, initial treatment includes the use of topical nonsteroidal anti-inflammatory medications (NSAIDs), which inhibit the production of prostaglandins via inhibition of the COX pathway. Several studies have documented the use of NSAIDs in the treatment and prophylaxis of PCME, although

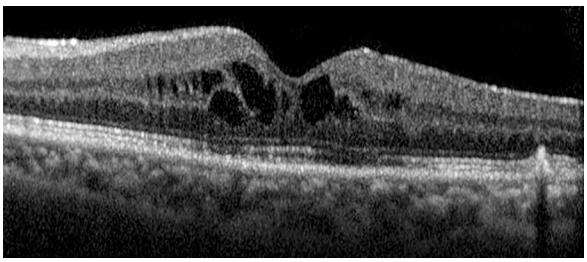

Fig. 2 – Characteristic macular thickening and cystic intraretinal spaces typical of PCME on OCT.