A Case Report on the Treatment of Irvine-Gass Syndrome with Nonsteroidal Anti-Inflammatory Drugs

Lishi Deng, Limin Wang*
Department of Ophthalmology, The First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine, Guiyang, China
**Corresponding Author*

Abstract: Irvine-Gass syndrome, characterized by idiopathic macular edema following cataract surgery, is a common postoperative complication and a significant factor leading to recurrent visual deterioration after cataract extraction. The precise pathogenesis of this condition remains incompletely understood. While Irvine-Gass syndrome often exhibits self-limiting characteristics, a subset of patients may develop refractory macular edema. This persistent edema can cause long-term visual impairment. Clinically, an integrated approach combining traditional Chinese and Western medicine may be employed for treatment. This report presents one case of Irvine-Gass syndrome treated with Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), aiming to provide a reference for the future management of this condition.

Keywords: Irvine-Gass Syndrome; Macular Edema; Phacoemulsification Cataract Surgery; Pathogenesis; Integrated Traditional Chinese and Western Medicine Therapy

1. Clinical Data

Patient: A 69-year-old female with no significant medical history presented to the First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine due to "1+ year of decreased vision in both eyes". She was diagnosed with bilateral age-related cataracts and was planned for cataract surgery upon admission. Ophthalmologic examination revealed visual acuity of 1.0 in the right eye and 0.2 in the left eye, with bilateral lens opacity (C4N2 in the right eye and C2N2 in the left eye). Fundus examination of the right eye was unclear, while the optic disc margin was faintly visible in the left eye with a flat macula in the posterior pole. Intraocular pressure was 13 mmHg in the right eye and 12 mmHg in the left eye. Ocular B-scan ultrasound showed no significant abnormalities in both eyes. Macular optical coherence tomography (OCT) indicated epiretinal membrane in the left eye (imaging unclear in the right eye). Following comprehensive preoperative preparation, the patient underwent phacoemulsification with intraocular lens implantation under local anesthesia in the right eye. The procedure was uneventful, and the patient reported no specific discomfort postoperatively. Visual acuity in the operated eye on the first postoperative day was 0.3, with mild conjunctival injection, corneal edema, shallow anterior chamber, and a clear artificial lens in place, yet a fuzzy fundus examination. At the one-month postoperative visit, visual acuity in the operated eye improved to 0.8, with no conjunctival congestion, clear cornea, shallow anterior chamber, intact artificial lens, and a clear optic disc with a flat macula in the posterior pole. OCT findings revealed a normal macular structure in the right eye, without epiretinal membrane or vitreomacular adhesion. Three months postoperatively, the patient returned due to decreased visual acuity in the right eye. Ophthalmologic examination of the right eye indicated a visual acuity of 0.5, with no conjunctival congestion, clear cornea, shallow anterior chamber, intact artificial lens, a clear optic disc with peripheral color vision, and macular edema in the macular region. OCT revealed cystoid macular edema in the right eye, without epiretinal membrane or vitreomacular adhesion. Diagnosis: ① Right eye Irvine-Gass syndrome, ② Right eye pseudophakia. Treatment with sodium diclofenac eye drops was initiated for the right eye, administered three times daily. One week later, OCT follow-up showed resolution of macular edema in the right eye, with an improvement in visual acuity to 0.8. Subsequent follow-up visits revealed stable disease progression with no specific discomfort reported by the patient.

2. Discussion

Irvine-Gass Syndrome (IGS), characterized by idiopathic macular edema following cataract surgery, is a common complication encountered postoperatively. This condition typically manifests between 4 to 12 weeks after surgery, with varying incidence rates depending on the diagnostic modalities employed. While most patients exhibit mild symptoms, a minority may experience visual blurring and other manifestations. The syndrome tends to self-limit to some extent; however, the persistence of macular edema without timely intervention can lead to irreversible visual impairment.

2.1 Mechanisms of Onset

2.1.1 Mechanical traction theory

The exact etiology of Irvine-Gass Syndrome remains incompletely elucidated, with proposed theories primarily revolving around the mechanical traction theory and the disruption of the blood-retinal barrier. Irvine posited that surgical interventions impacting the vitreous body could lead to anterior membrane rupture, generating a certain level of traction on the macula's retinal structure [1]. Gass, on the other hand, proposed that following lens extraction, the vitreous body undergoes anterior displacement, exerting a degree of traction on the retina, thereby promoting the onset of edema.

2.1.2 Disruption of the blood-retinal barrier theory

Cataract surgery, being an invasive procedure, involves surgical manipulation of the iris during anterior chamber operations, causing irritation or entrapment at the surgical incision. This manipulation triggers the release of inflammatory factors such as cyclooxygenase and interleukin-6, augmenting prostaglandin production and inducing the upregulation of vascular endothelial growth factor. Consequently, this disrupts the blood-retinal barrier, heightens vascular permeability, leads to localized fluid accumulation, and initiates edema [2]. Sun Qian et al., through quantitative assessments of diabetic patients, pre and post cataract surgery, observed changes in macular retinal thickness and anterior chamber protein concentration. Their findings indicated that in diabetic eyes, the disruption of the blood-aqueous barrier post-cataract surgery precedes alterations in macular retinal thickness and reaches its peak earlier [3]. Another study revealed that even 30 weeks post small-incision cataract surgery, 50% of operated eyes manifested fluorescein leakage, setting the stage for subsequent fluid accumulation between retinal layers and the eventual formation of macular edema [4]. Additionally, the presence of a lens opacity to some extent obstructs UV light from entering the eye. Upon completion of surgery and removal of the cloudy lens, an increased amount of light penetrates into the eye, exposing the retina further to UV radiation, leading to the production of oxygen free radicals and initiating localized oxidative damage reactions [5,6]. During surgical procedures, disruption of the integrity of the eye's circle, coupled with intraocular pressure fluctuations, can create a pressure differential gradient between the retinal vascular perfusion pressure and intraocular pressure when the intraocular pressure is too low. This heightened gradient increases vascular permeability, elevating the incidence of macular edema [7].

2.2 Diagnosis

The primary symptoms of Irvine-Gass Syndrome include post-cataract surgery visual impairment, blurred vision, and metamorphopsia. Upon direct ophthalmoscopy or slit-lamp examination, petaloid macular edema in the macular area may be observed, typically unaccompanied by fundus hemorrhage, vitreous warts, or retinal vascular abnormalities. When edema is mild, OCT provides a more direct and precise visualization of the morphology and extent of retinal edema, enhancing the diagnostic accuracy of macular edema. Early fluorescein angiography of the fundus may reveal leakage of fluorescein from small vessels around the fovea, with leaked fluorescein gathering in an exudative pattern, forming the characteristic petaloid appearance. As macular edema is not an isolated condition, most fundus disorders may also manifest as macular edema, such as retinal vein occlusion and diabetic retinopathy. Therefore, in clinical practice, it is crucial to differentiate Irvine-Gass Syndrome through careful consideration of medical history, fundus presentation, OCT, and fundus fluorescein angiography (FFA) results.

2.3 Treatment

2.3.1 Traditional Chinese medicine approach

In Traditional Chinese Medicine (TCM), it is believed that "all dampness and swelling are related to the spleen". When the spleen's healthy

functioning is disrupted, internal dampness accumulates, leading to the occurrence of edema. Therefore, TCM treatment often involves strengthening the spleen and eliminating dampness. Director Xie Like proposed from a TCM perspective that macular edema is a manifestation of internal dampness accumulation, with the imbalance lying in the spleen. When water does not flow naturally, it indicates a dysfunction in qi transformation. Edema is considered a manifestation of excessive yin, which moves with yang and dissipates with warmth. Therefore, the prescription of herbs like Guizhi (Cinnamomi Ramulus) can be used to warm yang, transform qi, and promote fluid circulation effectively [8]. Zhang Xiaoyin et al. reported on 45 cases involving 65 eyes of post-cataract surgery patients with macular edema. A comparison was made between using corticosteroids or nonsteroidal anti-inflammatory drugs alone for treatment and using a combination of corticosteroids, nonsteroidal anti-inflammatory drugs, and TCM herbs for nourishing qi and promoting fluid circulation. The results indicated that the group receiving combined TCM treatment showed significantly better therapeutic effects compared to the group not using TCM [9]. Chen Yang et al. studied 106 post-cataract surgery patients with cystoid macular edema, comparing a group treated solely with Western medicine to a group undergoing integrated Chinese and Western medicine treatment. The results suggested that the combination of Chinese and Western medicine yielded better outcomes for post-cataract surgery cystoid macular edema [10]. Li Jiangling et al. included 46 post-cataract surgery patients with macular edema and explored the efficacy of using Modified Wuling Powder, an augmented formula based on Wuling San (Five-Ingredient Powder with Poria) with added Astragali Radix and Alismatis Rhizoma in treating macular edema following phacoemulsification surgery. Patients in the control group were treated with Pranoprofen eye drops and Tobramycin Dexamethasone eye drops, while patients in the research group received modified Wu Ling San orally in addition to the control group's treatment. The results indicated that the group receiving combined treatment with Modified Wuling Powder exhibited a shorter duration for the resolution of macular edema compared to the control group [11]. Yao Xueyun et al. administered intravitreal anti-VEGF therapy to the control group, while the observation group received intravitreal anti-VEGF therapy in conjunction with oral Shenling Baizhu Power (Chinese herbal formula containing Ginseng, Poria, Atractylodes macrocephala, etc.). After 30 days of treatment, the total macular volume and central macular thickness in the observation group were lower than those in the control group, and the resolution time of macular edema was shorter in the observation group, suggesting that the combined use of Shenling Baizhu Powder can effectively and rapidly control macular edema [12]. Wei Jiecheng et al. included 72 patients with post-cataract surgery macular edema, randomly assigning them to a Chinese medicine group of 36 cases and a control group of 36 cases. The control group received treatment with Pranoprofen eye drops, while the Chinese medicine group was given Sanren Tang (Three Kernels Decoction containing Semen Armeniacae, Semen Coicis, and Semen Amomi) combined with Linggui Zhugan Tang (Poria, Cinnamon, Atractylodes and Licorice Decoction) on the basis of the control group's treatment. After 30 days of treatment, the Chinese medicine group showed a lower macular edema diameter and central thickness than the control group, suggesting that the combination of Sanren Tang and Linggui Zhugan Tang with Pranoprofen eye drops can effectively improve post-cataract surgery macular edema[13].

2.3.2 Western medical treatment

Western medical treatment primarily focuses on anti-inflammatory measures and improving local vascular permeability: ①Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): By blocking the arachidonic acid pathway, NSAIDs reduce the expression of intraocular inflammatory factors and stabilize vascular permeability. Xu Xuejiao et al. reported in a meta-analysis on the prevention of post-cataract surgery cystoid macular edema with NSAIDs that pre- and post-cataract surgery treatment with NSAIDs significantly reduces the incidence of postoperative macular edema (OR=0.31, 95%CI:0.18-0.52, P〈0.01)[14]. In a study by Ma Yuansong comparing cataract surgery outcomes in diabetic patients with or without the use of Pranoprofen eye drops, it was observed that patients treated with Pranoprofen had improved postoperative visual acuity and lower incidence of macular edema, suggesting that NSAIDs can

effectively prevent the occurrence of macular edema[15].② Corticosteroids: The therapeutic mechanism of corticosteroids primarily involves the inhibition of arachidonic acid synthesis, resulting in a reduction in the release of inflammatory factors, thereby exhibiting both anti-inflammatory effects and decreased vascular permeability. Commonly used clinical preparations include triamcinolone acetonide and dexamethasone intravitreal implants. Feng Haixiao et al. employed intravitreal injections of modified low-dose triamcinolone acetonide in 12 typical patients suffering from cystoid macular edema post-cataract surgery. By replacing the TA suspension with an intraocular perfusion solution through a 0.22 μm filter, and administering 2 mg/0.05 mL of the substituted TA solution, they observed significant improvements in best-corrected visual acuity, reductions in central macular thickness, intraocular pressure, and no instances of local or systemic complications post-treatment. The results indicate that compared to pre-injection levels, all patients showed a significant improvement in visual acuity after medication administration. There was a significant decrease in central macular thickness ($P < 0.05$), and no ocular or systemic complications were observed in any of the patients [16]. Similarly, Xiu Liheng et al. treated 14 patients (16 eyes) with persistent cystoid macular edema with a 0.7 mg dexamethasone intravitreal implant and followed them for six months. The results indicated marked improvements in both best-corrected visual acuity and macular edema, with no complications associated with the medication or ocular treatment reported during the follow-up period [17]. Furthermore, Bai Xiaolong et al. included 15 patients (15 eyes) with cystoid macular edema following cataract surgery in their study, administering intravitreal triamcinolone acetonide therapy. They assessed best-corrected visual acuity and central macular thickness before treatment, as well as at one day, and one, three, and six month(s) post-treatment. The findings revealed that post-treatment best-corrected visual acuity was significantly superior to pre-treatment levels, with statistically significant reductions in central macular thickness occurring at one, three, and six months compared to baseline ($P < 0.05$). Throughout the study, no ocular or systemic complications were noted [18]. ③ Anti-VEGF Drugs: In diabetic patients with macular edema, heightened intraocular levels of VEGF contribute to the condition. Anti-VEGF medications counteract this by inhibiting intraocular VEGF activity, reducing neovascularization, enhancing vascular permeability, and effectively combatting macular edema. He Lin et al. observed a significant reduction in central macular retinal thickness in 75 patients (75 eyes) with post-cataract surgery macular edema following intravitreal anti-VEGF therapy[19]. Moreover, Deng Tongtong et al. divided 126 cataract patients with postoperative macular edema into two groups, administering intravitreal injections of either ranibizumab or conbercept for a treatment period of three months. They monitored intraocular pressure, central macular retinal thickness, corneal nerve fiber density and length, as well as the incidence of adverse reactions. The results indicated that both ranibizumab and conbercept effectively and safely improved macular edema. Ranibizumab may possess certain advantages in protecting corneal nerve fibers based on their findings[20]. ④ Laser Therapy: Subthreshold micropulse laser therapy focuses laser energy on the retinal pigment epithelial cells, inducing the expression of reparative factors and anti-angiogenesis properties, thereby aiding in the management of chronic retinal inflammations [21]. Zhong Wen et al. investigated the efficacy of full macular grid micropulse laser treatment in 21 patients (24 eyes) with refractory macular edema related to Irvine-Gass syndrome. When compared to pre-treatment measures, significant improvements were observed in best-corrected visual acuity (BCVA) at 1, 3, and 6 month(s) post-treatment ($t=5.060, 5.564, 6.466$), as well as a marked decrease in central macular thickness (CMT) ($t=4.854, 5.777, 7.349$), with all differences showing statistical significance ($P < 0.01$). The mean macular retinal volume (MRV) also significantly decreased for diameters of 1 mm and 6 mm, with statistical significance noted for both (1 mm diameter: $t=4.527, 5.394, 7.380$, $P < 0.01$; 6 mm diameter: $t=4.577, 7.980, 11.209$, $P < 0.01$). No macular scars related to laser therapy occurred during treatment, suggesting the safety and efficacy of full macular grid micropulse laser therapy for post-cataract surgery macular edema. However, given the study's small sample size, further data support is necessary. For diffuse macular edema without significant leakage, grid-like photocoagulation may be employed. This treatment modality

disrupts retinal photoreceptors, reduces outer retinal oxygen consumption, induces vascular constriction, and diminishes vascular leakage. A study involving 36 patients (41 eyes) compared the efficacy of intravitreal triamcinolone acetonide injections alone versus in combination with grid-like photocoagulation in the treatment of post-cataract surgery macular edema. The results indicated that the combination treatment group demonstrated superior outcomes in terms of best-corrected visual acuity and macular edema control compared to the monotherapy group [22]. ⑤Vitrectomy: For refractory macular edema following cataract surgery, it is essential to assess for the presence of vitreous traction. When vitreous traction is identified, vitrectomy can effectively relieve the traction and alleviate macular edema [23]. ⑥ In the case of patients with specific types of cataracts, such as those accompanied by uveitis, elevated intraocular pressure, diabetic retinopathy, or retinal vein occlusion, it is crucial to proactively manage these comorbidities prior to surgery in order to minimize postoperative inflammatory responses. For pediatric cataract patients, whose barrier functions are still immature and are prone to significant postoperative reactions, an approach involving capsulotomy with anterior vitrectomy, coupled with local and systemic corticosteroid treatments during surgery, can mitigate postoperative inflammation [24].

3. Conclusion

The increasing trend of population aging has led to a gradual rise in the prevalence of cataract surgeries. Among the common postoperative complications of cataract surgery is Irvine-Gass syndrome, which can result in varying degrees of vision deterioration in patients. Recent studies have highlighted the complex nature of the pathogenesis of Irvine-Gass syndrome, primarily characterized by alterations in vascular permeability that disrupt the integrity of the blood-retinal barrier. Despite the condition generally exhibiting a self-limiting course, some individuals may experience persistent macular edema over the long term, leading to irreparable harm to their vision. Consequently, it is crucial during clinical assessment and treatment to conduct a comprehensive evaluation of the patient's condition, develop individualized therapeutic approaches, and aim to optimize the postoperative visual outcomes for each patient.

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