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Chapter 16

Uveitic Glaucoma

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Additional information is available at the end of the chapter

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1. Introduction

Uveitis is the third leading cause of preventable blindness worldwide although its incidence is relatively infrequent. Over 2 million people worldwide may be affected by uveitis. Its prevalence in the States is estimated as 15 per 100,000 and worldwide as 38-730 per 100,000. [1], [2] Females have a higher prevalence and the prevalence in both genders increases with increasing age. [3]

Uveitis may be accompanied by normal, low or high intraocular pressure (IOP). If the IOP is higher than 21mmHg, it is defined as glaucoma and as all the secondary glaucomas, the optic disc and the visual field may be normal. This is in contrast to primary glaucomas, where the high IOP should be accompanied by either abnormal optic disc or visual field or both.

Uveitic glaucoma refers to glaucoma that develops in uveitic patients. The glaucoma in these cases is secondary to or concurrent with uveitis. This is a narrow definition of uveitis and glaucoma even if since it does not include cases of uveitis that develop in glaucoma patients. Uveitic glaucoma is composed of different ocular diseases of different causes and mechanisms. Between 10% and 20% of the uveitis patients develop glaucoma. [4]-[6] The development of glaucoma is more common in chronic than in acute uveitis glaucoma and may reach 46%. [7] There is no predilection to race or gender.

Any uveitis may be accompanied by glaucoma. Nevertheless, in glaucomatocyclitic crisis or Posner Schlossman disease, both intraocular inflammation and high IOP always concur while in others such as Fuchs' heterochromic iridocyclitis they appear in high association or with lesser association.

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2. Pathogenesis of uveitic glaucoma

Imbalance between aqueous humour secretion and clearance due to the intraocular inflammation may result in change in IOP. The IOP is often reduced because of hyopsecretion in conjunction with increased uveoscleral outflow. However, the IOP may be also increased due to increase in outflow resistance.

Several mechanisms are involved in the pathogenesis of glaucoma and this group of diseases may be divided to open and closed angle. Open angle is the largest group. In open angle glaucoma, increased outflow resistance is caused by obstruction of the trabecular meshwork by inflammatory cells, plasma proteins, fibrin and/ or debris. All of these are released from the blood vessels due to loss of aqueous-blood barrier and accumulate in the anterior chamber and the angle. Another mechanism is dysfunction of the trabeculocytes caused by toxicity of blood borne-products. This eventually may result in loss of trabeculocytes and scarring. Increased IOP may be caused by cytokines and prostaglandins. A role for the complement component C1qs has been implicated. [8] This component is part of the complement system, which is activated in uveitis. Rho kinases that are released in uveitis may also result in increased IOP. [9], [10]

Corticosteroid-induced glaucoma is another mechanism for open angle glaucoma. It may occur in up to one third of the patients but with impairment of the conventional outflow facility in uveitic patients, it may increase even to 70%. [11] Corticosteroids are being routinely used for uveitis and they can cause this type of open angle glaucoma in any form although it is more common with topical installation. The development of glaucoma depends on the subject susceptibility (corticosteroid responder), dose, duration, type of medication and route of administration. The glaucoma may develop at any time after the initiation of treatment, but usually within 6 weeks. The glaucoma develops due to multiple mechanisms. Trabecular cells have receptors for corticosteroids and they cause alternation of multiple gene expression leading to the production of extracellular glycosaminoglycans including fibronectin, laminin and collagen. [12] They also decrease the turnover of the extracellular matrix by inhibiting matrix metaloproteinases (MMPs) and tissue plasminogen activator and increasing plasminogen activator inhibitor 1 and tissue inhibitors of MMPs. Therefore, the glycosaminoglycans accumulate in the angle. The corticosteroids also cause inhibition of phagocytosis, proliferation and migration of the trabeculocytes, and formation of certain prostaglandins.

Secondary angle closure glaucoma may occur as chronic and acute forms. In chronic angle closure glaucoma, peripheral anterior synechiae (PAS) develop along the angle. They are being developed due to organization of inflammatory products in the angle. These PAS are broad base, trapezoid and highly pigmented bands that bridge the peripheral iris with the corneal periphery obstructing the angle. They may widen with time, resulting eventually in closure of the angle and increased IOP. Because the angle is progressively closing, the IOP increases gradually without causing an acute stage of increased IOP and without corneal edema. The acute form of angle closure glaucoma occurs secondary to papillary block because of 360° of posterior synechiae. These synechiae develop between the posterior margin

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of the iris and the crystalline (or intraocular) lens secondary to accumulation of fibrin and inflammatory precipitates over the lens. When the papillary margins are completely blocked, the aqueous humour is trapped in the posterior chamber, accumulates there, resulting in anterior iris displacement (iris bombe). The peripheral iris becomes appositioned against the peripheral cornea and obstructs the angle. The glaucoma in these cases develops abruptly and may be accompanied by ocular pain and corneal edema. A third, rarer mechanism includes the anterior rotation of the lens-iris diaphragm that results in angle closure. The forward rotation is caused by ciliary body and choroidal edema.

3. Uveitic entities associated with glaucoma

3.1. Glaucomatocyclitic crisis (Posner-Schlossman syndrome)

Glaucomatocyclitic crisis is characterized by recurrent episodes of increased IOP and anterior chamber inflammation. Therefore, the uveitis is always accompanied by glaucoma and vice versa. In between, the eye is quiet and the IOP is normal. The disease is usually unilateral and involves the same eye.

Patients complain of blurred or decreased vision and ocular discomfort. Minimal flare and cells (usually +1 or 5-10 cells per wide field magnification of X40) are found in the anterior chamber along with increase in IOP in the range of 40-60mmHg that may reach 70mmHg. Iris heterochromia may appear after recurrent attacks. The first attack is always the most challenging to diagnose. When subsequent episodes occur, the diagnosis is obvious and the patient is aware when they occur. The disease usually appears at the 3rdto 4th decade.

The pathogenesis of the disease is not well established. Viral infection by herpes and cytomegalic viruses, allergic factors and immunogenetic factors related to HLA-Bw54 have been suggested. [13-16] It may also be related to certain prostaglandins such as E released due to vascular incompetence. [17] Indeed, prostaglandin inhibitors, oral indomethacin and subconjunctival polyphloretin, a prostaglandin antagonist have been demonstrated to decrease the IOP. [17], [18]

The disease responds to medical treatment with topical corticosteroid (prednisolone acetate 1% qid) and anti-glaucoma medications such as beta-blockers (timolol 0.5% bid) and carbonic anhydrase inhibitors (acetazolamide 250mg bid or tid). [19] Topical IOP sparing corticosteroids and non-steroidal anti-inflammatory drugs may replace the classic corticosteroids. Prostaglandin inhibitors, oral indomethacin 75-150mg/day and subconjunctival polyphloretin, a prostaglandin antagonist, may also decrease the IOP. No preventive treatment during the remissions is known. In rare cases in which progression in optic disc and visual field damage is demonstrated, trabeculectomy or stenting procedure may be performed. The prognosis is good and some claim that the frequency of the attacks decreaseage. Unfortunately, no prophylactic treatment exists. The risk of developing optic disc and visual field damage is increased with the duration of the disease. Patients with 10 years or more of disease have a risk of 2.8 folds to develop damage than those with duration of less than 10 years.

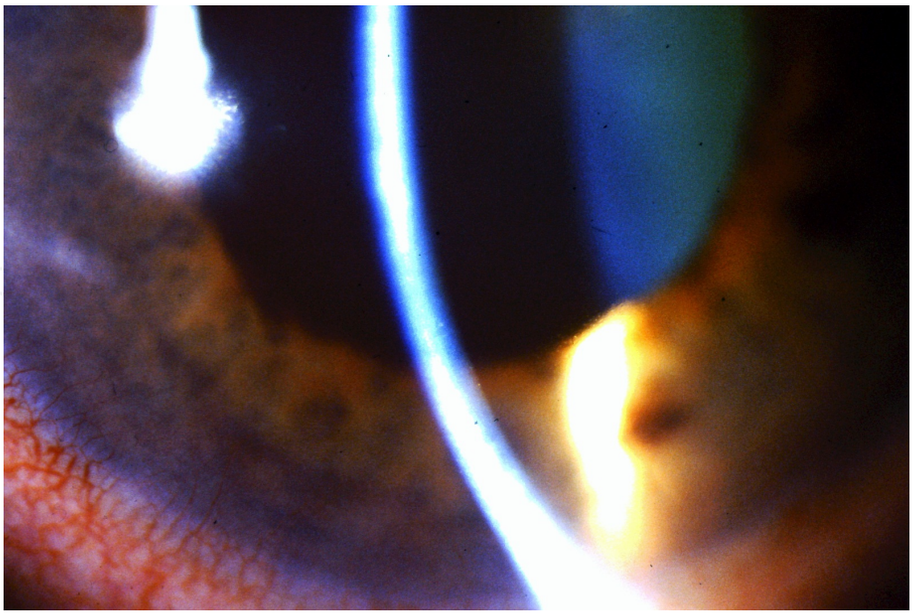


Figure 1. Posner-Schlossman syndrome. Note the few keraticprover the endothelium.

3.2. Fuchs' heterochromic iridocyclitis

The disease is characterized by iris heterochromia and chronic, low-grade iridocyclitis. It appears in the 2nd to 4th decade and is unilateral in 87% of the patients. [20]

The patients may be asymptomatic or may complain of a decrease in vision or change iris color. On examination, heterochromia along with low-grade anterior chamber reaction (flare and cells +1) are noted. Fine keratic precipitates may be noted as well. Secondary open angle glaucoma develops in 13-59% of the patients depending on the duration of the disease. It is more frequent in patients with bilateral disease and in African descends. Posterior subcapsular cataract may also develop.

Treatment for Fuchs' dystrophy without glaucoma is not required since it poorly responds to corticosteroids. The glaucoma may develop late in the course of the disease. Anti-glaucoma medications may be effective initially but later the medical treatment usually fails and filtration surgery is required. [21]



Figure 2. Fuchs' heterochromic iridocyclitis in the right eye. The differential diagnosis for a brighter involved iris is congenital and acquired Horner syndrome (with 2mm ptosis and miosis) and more rarely Posner Schlosmann syndrome and for darker involved iris, siderosis bulbi.

3.3. Glaucoma in juvenile idiopathic arthritic (JIA) uveitis

Secondary glaucoma may develop in 14-42% of the patients with JIA. [22]-[24] The glaucoma is usually open angle. However, papillary block glaucoma and chronic angle closure glaucoma may also develop.

The patient is usually asymptomatic and the eye is quiet. Therefore, any child with pauciarticular arthritis should be referred to ophthalmologic examination every 6 months. If uveitis presents, flare and cells will be present in the anterior segment. In cases of uveitis, measurement of the IOP and evaluation of the optic disc are mandatory. Both the uveitis and glaucoma should be treated early and aggressively. The uveitis is treated in a stepladder manner. The purpose of the treatment is to achieve remission but treatment should be continued even after its achievement. First, topical corticosteroid (prednisolone acetate 1% every 1-2 hours) and cycloplegic (cyclopentholate 1% tid) agent are being used. [25] Change to IOP-sparing or less potent corticosteroids should be performed only when the initial inflammation decreased. If treatment with corticosteroid fails, oral NSAID such as naprosyn (Naproxen®) 5mg/kg twice a day is being used and if this fails, immunosuppressive treatment with oral methotrexate 15mg/m^2 up to 30mg/m^2 (or 03-0.5mg/kg) once a week is employed. Common side effects of methotrexate include nausea, anorexia, stomatitis and transient elevation of serum aminotransferase. Alopecia, hematological toxicity, headache, dizziness, fatigue, and mood changes may also occur. A "post-dosing" reaction may occur within 24 hours of receiving methotrexate and is usually characterized by malaise, fatigue, gastrointestinal upset, and occasionally central nervous system manifestations. Liver cirrhosis is a long-term potential complication. Other immunomodulators, such as oral cyclosporine (2-5 mg/kg/day), azathioprine (1-2mg/kg per day), mycophenolate mofetil (300mg/m2 body surface area bid), or chlorambucil (0.10-0.16 mg/kg/day) may be used when methotrexate is not tolerable or when remission is not achieved.

3.4. Sarcoidosis

A multi-organ inflammatory disease that is prevalent in blacks. The patients have pulmonary hilar lymphadenopathy, peripheral lymphadenopathy and cutaneous non-caseating epithelioid granulomas. Ocular involvement occurs in 38% of the patients and may be the first manifestation of the disease. [26] Anterior uveitis is the most common ocular manifestation. At the beginning, the uveitis appears as acute iridocyclitis. A characteristic but not pathognomonicsign is large (mutton fat) keratic precipitates (KPs) over the endothelium. The disease may become chronic and bilateral. The mutton fat PKs are usually encountered at this stage along with Koeppe's nodules on the iris margins and Busacca's nodules on the iris surface. Nodules may also appear in the angle and over the ciliary body. Open angle glaucoma is present in 11%. The usual pathogenesis is obstruction of the angle by inflammatory cells and debris. The disease may mistakenly be considered as Fuchs' heterochromic iridocyclitis. Elevated serum angiotensin converting enzyme or a positive Kveim test will confirm the diagnosis of sarcoid. Additional tests include Gallium [67] scan that shows high intake in the lacrimal and parotid lymph nodes with or without submandibular lymph nodes and serum-lysozyme, which is increased. Treatment includes topical corticosteroid (prednisolone ace-

tate 1% every 1-2 hours) and cycloplegic agent. If the posterior segment is involved, sub-Tenon and or oral corticosteroids (see the section on medical treatment of uveitic glaucoma below) are added. The sub-Tenon injections of corticosteroids may be repeated weekly. However, they should be cautiously used if glaucoma exists. Immunosuppressive agents such as methotrexate should replace corticosteroids if there is no response or contraindications such as steroid-induced glaucoma. In resisting cases, anti-tumor necrosis factor alpha (TNFα) such as infliximab, etanercept, or adalimumab and intravitreal anti-vascular endothelial growth factor such as bevacizumab may be employed. Anti-glaucoma medications are indicated. Generally, the long-term prognosis is poor.

3.5. Herpetic keratouveitic glaucoma

Secondary open angle glaucoma may develop in herpetic keratouveitis in 10-54%. [27], [28] The disease appears weeks to years after recurrent episodes of keratouveitis with either stromal keratitis (96%) or metaherpetic ulcer (4%). The pathogenesis is probably a complex of direct injury to the trabeculocytes by the virus, inflammatory products and response to corticosteroids. The condition is responsive to medical treatment with topical corticosteroid and antiglaucoma medications such as β-blockers, α-agonists and topical and oral carbonic anhydrase inhibitors. In patients with several episodes of keratouveitis in a year, oral acyclovir 400 mg bid for a year or more may decrease the recurrences.

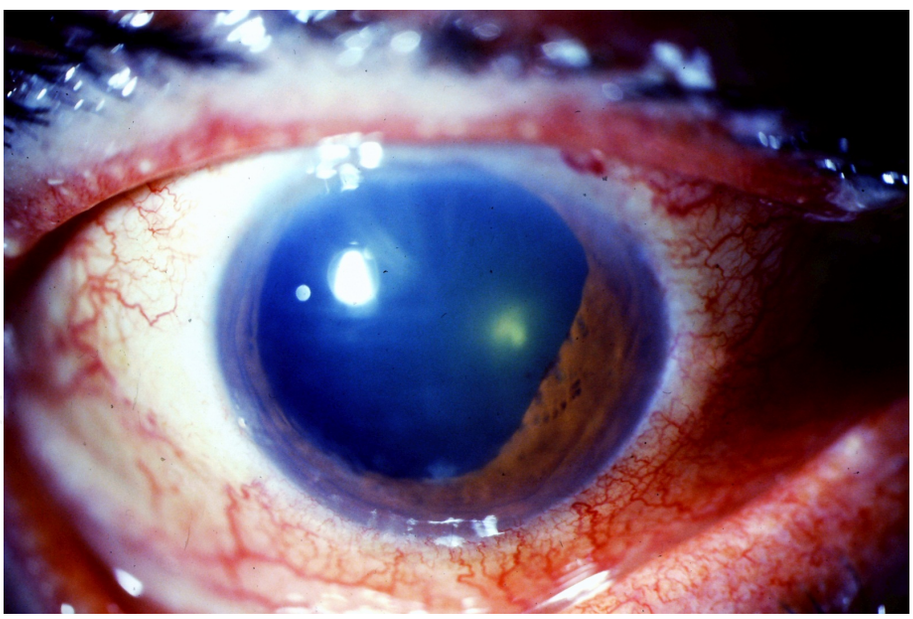


Figure 3. Glaucoma in herpetic keratouveitis. Note the mild stromal haze from stromal keratitis and posterior synechia.

3.6. Congenital rubella

Congenital rubella affects the heart, auditory system and the eye. It may cause cataract, retinopathy, glaucoma and microphthalmia in 30-60% of the affected children. Glaucoma ap-

pears in 2-15% and is frequently associated with cataract and microphthalmia. [29] The pathogenesis is multi-factorial. Congenital angle abnormalities, chronic iridocyclitis, papillary block and angle closure glaucoma from intumescent cataract or microphthalmia are implicated. The glaucoma may appear at any age and therefore routine follow-up that includes measurement of the IOP and evaluation of the optic disc is required for lifetime. It should be performed at least every 6 months. If glaucoma is diagnosed, treatment should be aggressive and follow-up should be frequent to prevent blindness since it may occur in 44%. A peripheral iridectomy should be performed if cataract surgery is performed to deepen the anterior chamber and to prevent papillary block glaucoma.

3.7. Glaucoma in idiopathic uveitis

Any patient with chronic or recurrent anterior uveitis from unknown cause may develop glaucoma. Thus, in all patients with chronic or recurrent uveitis, IOP measurements should be obtained. Independently, medical treatment for the uveitis and for the glaucoma should be initiated to achieve remission of the inflammation and control the IOP.

3.8. Phacoanaphylactic uveitis (phacoantigenic uveitis)

Phacoanaphylaxis is a granulomatous uveitis from liberated crystalline lens proteins and contact with blood circulation. This disorder may be classified also as part of the lens-induced glaucomas. [30] It is the result of cataract extraction or traumatic lens rupture. The disorder may occur any time after surgery or trauma. It may occur spontaneously usually in microphthalmic eyes. It is type III hypersensitivity (immune complex). It usually causes hypotony and rarely pupillary block glaucoma or angle closure glaucoma from peripheral anterior synechiae. Keratic precipitates may appear on the cornea and the intraocular lens (IOL), hypopion and numerous white cells in the anterior chamber and vitreous may be present. Remnants of the crystalline lens are always present, while cultures are negative. Anterior chamber tap reveals foamy macrophages (as seen in phacolytic glaucoma). A high suspicion index is required because the disease may be similar to infectious endophthalmitis (but without pain), sterile endophthalmitis and toxic anterior chamber reaction (fibrinoid reaction). The respond to corticosteroids is temporary and removal of the lens remnants is the treatment of choice.

3.9. Uveitis-glaucoma-hyphema (UGH) syndrome

Uveitis-glaucoma-hyphema (UGH) syndrome is a triad classically caused by subluxated or mal-positioned IOL (usually an anterior chamber IOL) rubbing against the iris and causing release of pigment and bleeding that result in open angle glaucoma. [31] If vitreous hemorrhage also presents, the condition is called UGH plus. Incomplete UGH is when uveitis and sometimes glaucoma are absent. The condition may also be caused by excessive movement of a small IOL. The patient complaints are sudden (within minutes to hours) decrease in vision that gradually improves over hours to days, and sometimes, ocular pain. The patient may describe his vision as “white-out” or having reddish tint (erythropsia). The condition occurs from one week to months after surgery. It is diagnosed by attacks of this triad and

the presence of iris transillumination corresponding to the rubbing site. The diagnosis is easiest during the attack. A blood cloth or hyphema may be observed. The diagnosis can be confirmed by ultrasound biomicroscopy (UBM) and anterior segment optical coherence tomography (AS-OCT) showing a contact between the optic or haptic and the iris. The complications include pseudophakic bullous keratopathy, corneal staining and cystoid macular edema (CME). The differential diagnosis includes amaurosis fugax and vertebrobasilar insufficiency. Amaurosis fugax occurs more rapidly (within seconds to minutes) and loss of light perception in at least one quadrant. Loss of light perception never occurs in UGH syndrome and there is always a history of cataract extraction and IOL implantation or iris device implantation. The differentiation between the two is crucial because patients with amaurosis fugax may be treated with anti-coagulants that may increase the bleeding in UGH syndrome. Patients may respond to topical corticosteroids and anti-glaucoma medications. The definite treatment of UGH is replacement or repositioning of the IOL.

4. Other uveitic glaucomas

Glaucoma has been reported in patients with pars planitis (8%), uveitic from Reiter's syndrome (1%), ankylosing spondylitis, hemorrhagic fever with renal syndrome (nephropathia epidemica) and epidemic dropsy from ingestion of sanguinarine in Argemone mexicana oil. Bilateral acute angle closure glaucoma due to uveal effusion has been described in acquired immunodeficiency syndrome (AIDS) and responded to medical treatment with cycloplegics, topical corticosteroids and anti-glaucoma medications. [32]

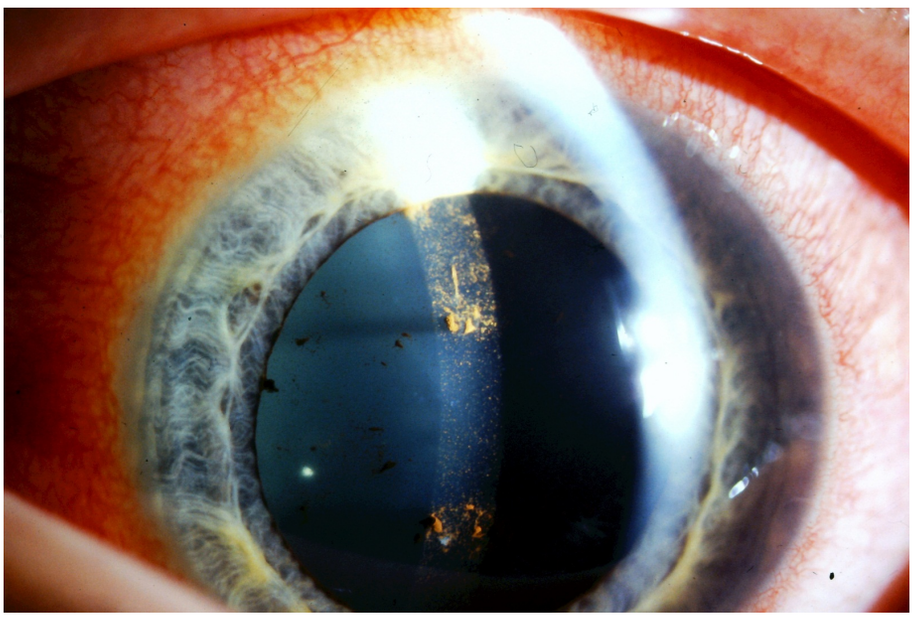


Figure 4. Reiter's syndrome. Note the pigment over the crystalline lens after pupil dilation and release of posterior synechiae.

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5. Diagnosis

Patients with acute closed-angle glaucoma may present with ocular and brow ace, blurred vision, halos, photophobia and even nausea and vomiting. Patients with open or chronic angle closure glaucoma are asymptomatic.

All uveitis patients should be routinely evaluated for IOP, which is elevated (>21mmHg) in uveitic glaucoma. In acute closed angle glaucoma, the cornea may be edematous and ciliary and conjunctival congestion may be present. Gonioscopy should be performed to define the type of glaucoma. Topical glycerin 50-100% would clear corneal edema for evaluating the angle and posterior segment. Otherwise, the corneal epithelium may be removed with a blade or 70% alcohol on a cotton-tipped applicator. If the cornea is still cloud, UBM or AS-OCT may replace gonioscopy in evaluating is performed the angle. Optic disc evaluation by slit lamp biomicroscopy and other imaging techniques (OCT, scanning laser polarimetry (GDx) or Heidelberg retinal tomography (HRT)) when the cornea is clear. Visual fields should be obtained in patients with cup/disc ratio of 0.6 or more for baseline and follow-up documentation of the progression of the glaucoma. In patients with cup/disc ratio of less than 0.6, the visual field is usually normal. The visual field may be abnormal due to CME (central relative scotoma) and retinitis or retinal scarring (defects corresponding to these areas). CME and macular atrophy may be confirmed by OCT. Differentiation should be made between steroid responder (the IOP returns to normal upon discontinuation of the corticosteroids) and corticosteroid-induced glaucoma (the IOP remains high). Differentiation between increased IOP due to increased inflammation and steroid responder may be performed by replacing the corticosteroids with IOP-sparing corticosteroids. The IOP should decrease.

6. Medical treatment

Treatment is aimed to control both the uveitis and IOP. The uveitis is treated by topical and/or systemic corticosteroids and/ or immunosuppressive drugs to achieve resolution or remission. Sub-Tenon corticosteroids such as triamcinolone acetonid (Kenalog®) 20-40mg (0.5-1ml) or methylprednisolone acetate (Depo-medrol®) 40-80mg may be given to treat noninfectious uveitis and macular edema. Intravitreal implants such as Ozurdex®, a copolymer of glycolic and lactic acid with 700μg of dexamethasone may be injected through the pars plana with 22G injector. It dissolves gradually over 6 months to H_2O and CO_2 and releases the dexamethasone. However, they all and especially those that cannot be removed (sub-Tenon and intravitreal) should be used cautiously in patients with glaucoma and are contraindicated in steroid responders and steroid-induced glaucoma. In cases of steroid responders orcorticosteroid-induced glaucoma, topical corticosteroids may be replaced by IOP-sparing corticosteroids such as such as loteprednol etabonate 0.5% (Lotemax®) or rimexolone 1%(Vexol®) but because of low potency, they may be more frequently required. These agents are especially useful for maintenance. Alternatively, topical non-steroidal anti-

inflammatory (NSAID) such as nepafenac 0.1% (Nevanac®), ketorolac tromethamine 0.5% (Acular® or Tradol®), diclofenac sodium (Voltaren® (0.1%), Solaraze® (3%)) or indomethacin 1% (Indoptic®) may be used. Topical immunosuppressive agent such as cyclosporine A 0.5-2% and systemic immunosuppressive drugs may be alternatives for corticosteroids and NSAID. The dosage of corticosteroids depends on the severity of inflammation and is titrated according to the response to treatment. The corticosteroids are gradually tapered according to the response since abrupt discontinuation may cause flare-up. Topical cycloplegic agents such as cyclopentholate HCl 1% (in neonates 0.5%) tid are added to control pain that originates from the ciliary body and to prevent the formation of posterior synechiae.

The preferred anti-glaucoma medications include topical alpha agonists, carbonic anhydrase inhibitors and beta-blockers. Prostaglandins may be added in a quiet eye but should be avoided in an inflamed eye and herpetic keratouveitis because they may exacerbate the intraocular inflammation and cause CME. [33]- [35] Oral or intravenous carbonic anhydrase inhibitors (acetazolamide 500mg) and hyperosmotic agents (oral glycerol 50% or IV mannitol 20% 1gr/kg) should be added if the reduction in IOP is not to the normal range. The efficacy of prostaglandins and alpha adrenergic agonists may decrease with concurrent use of topical or systemic NSAID. [36], [37] The glaucoma is controlled by medical treatment in 26% of the children and 24% of the adults. [6] In near future, ocular implants containing slow release IOP sparing corticosteroids may improve the visual outcome of patients with macular edema secondary to uveitis without inducing steroid-induced glaucoma. In future, new drugs such as Rho kinase inhibitors may replace existing medications.

7. Laser treatment

7.1. Laser iridotomy

Laser iridotomy is indicated for all cases of secondary papillary block glaucoma, chronic angle closure glaucoma and prophylactically when progressive anterior synechiae are being formed. [38] It is performed either to allow aqueous humour access into the anterior chamber in papillary block glaucoma or increase in the depth of the anterior chamber in chronic angle closure glaucoma. In some cases of papillary block glaucoma, the glaucoma may not resolve because the entrapment of aqueous in several compartments behind the iris. In such cases, more than one iridotomy is required.

The first treatment modality, which is usually the simplest, if the cornea is clear, is peripheral laser iridotomy. It is usually performed with Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser. Topical glycerin may be placed over the cornea before the procedure if it is edematous. After instillation of topical pilocarpine 2% or 4% and topical analgesic (e.g., oxybuprocaine HCl 0.4% or proparacaine HCl 0.5%) eye drop, a spot of 10mJ is placed over the peripheral iris. Two pulses may be used simultaneously. The size of the spot is constant depending on the instrument (50-70μm). The spot is placed at the periphery of the iris in the superior half to avoid glare, and over a thin part of the iris (usually a crypt) avoiding blood vessels. If bleeding occurs, the cornea is pressed by a contact lens until bleeding ceases. The

procedure may be performed with contact lens such as Abraham (+66D), Wise (+103D), CGIor without it. The advantages of a contact lens are additional magnification, focusing the beam, absorbing part of the heat, stabilizing the eye and keeping the eyelids open. Topical apraclonidine (Iopidine®) 0.5%-1.0% or other alpha 2 agonist (e.g., brimonidine tartrate) is administered following the procedure to decrease IOP spikes and corticosteroids such as prednisolone acetate 1% qid are prescribed for a week to decrease intraocular inflammation and risk of synechiae formation. Additional anti-glaucoma medications may be added. This procedure facilitates aqueous flow from the posterior into the anterior chamber and may result in deepening of the anterior chamber and lowering the IOP. The major complication is acceleration of cataract. If Nd:YAG laser is unavailable, Argon laser iridotomy may be performed. The parameters for this procedure depend on the iris pigmentation. For brighter iris, the power is lower than for darker ones. The preparatory stretch burns are of 200-600mW, 0.2-0.6 sec, 200-500 μ m. The penetration burns are of 800-1000mW, 0.2 sec, 50μm. The iridotomy size should be increased to 150-500μm. The position of the Argon iridotomy in this case is preferably supero-nasal to prevent injury to the macula. Argon laser may increase the intraocular inflammation because it releases pigment due to a different mechanism of action (plasma creation by ionizing in cases of ND:YAG versus coagulation in Argon). The treatment before and after the procedure is identical to Nd:YAG laser iridotomy. Perforation of the iris is confirmed when aqueous mixed with pigment is flowing from the posterior to the anterior chamber through the iridotomy. The lens should be visible through the iridotomy, since positive transillumination is not reliable. When laser iridotomy is not feasible or is impossible to perform, surgical peripheral iridectomy should be performed. Complications include visual disturbances such as halo and glare, development and progression of cataract, transient corneal burns, temporary increase in IOP, intraocular inflammation and rarely retinal injury, CME and malignant glaucoma.

Argon laser trabeculoplasty has no role in uveitic open-angle glaucoma because of its low success rate. It may increase the intraocular inflammation and alter the angle structure. Some authors found selective (ND:YAG) laser trabeculoplasty to be effective in 20% of the patients, [39] but the follow-up was limited and the effectiveness is expected to decline. Therefore, it is not an ideal solution. The reason is that both procedures do not prevent the obstruction of the open angle by inflammatory products.

7.2. Surgical treatment

Surgical procedures are reserved for patients who fail to respond to medical treatment. Surgical intervention is required in 56% of the children and in 35% of the adults with uveitic glaucoma. [6] Any intraocular intervention should be performed on a quiet eye for at least 3 months. Topical corticosteroids or other medications as indicated above should be administrated two weeks preoperatively and postoperatively to control the uveitis. Systemic corticosteroids may be added. Any intervention on an inflamed eye may result in exacerbation of the uveitis, failure of the procedure and complications. When increased postoperative intraocular inflammation is anticipated, enoxaparin (Clexan®) (40mg/500 balanced salt solution (BSS)), a low-weight molecular heparin decreases the intensity of such inflammation in sur-

gery for uveitic eyes as it does in congenital cataract surgery. [40] Glaucoma surgery may be combined with cataract extraction. The data on the newer procedures in uveitic glaucoma are limited. Detailed description of the newer devices can be found in chapter 19 in this book, chapter 20 in Rumelt S. Ed. Glaucoma – basic and clinical concepts. Rijeka, Croatia: Intech 2011 and chapter 17 in Rumelt S. Ed. Advances in ophthalmology. Rijeka, Croatia: Intech 2012.

7.3. Trabeculectomy

As for all secondary glaucomas, uveitic glaucoma that does not respond to medical treatment should be treated with trabeculectomy and mitomycin C (MMC) or other shunting procedure. [41]-[46] Without MMC, trabeculectomy may fail. Trabeculectomy with MMC is indicated for open and closed angle glaucomas. MMC decreases the risk of scarring of the filtering bleb, which is higher in uveitic glaucoma than in primary glaucomas, because of the increased postoperative inflammation. MMC 0.04% may be applied for 3 min under the scleral flap (or the conjunctiva) avoiding the conjunctival margins. Copious BSS irrigation is performed to remove the free MMC.

The cumulative probability for success of trabeculectomy with MMC or 5-fluorouracil at 1 and 2 years was 78 and 68% respectively. [4] Risk factors for failure include male gender and young age. [47] The use of spacers such as collagen matrix (Ologen®) or other biodegradable material may prove to be beneficial as well as injection of subconjunctival bevacizumab 2.5mg/0.1ml.These should be evaluated for uveitic glaucoma.

8. Non-Penetrating Glaucoma Surgery (NPGS)

Non-penetrating glaucoma surgery (NPGS) is a filtration procedure in which the anterior chamber is not penetrated. [48]- [50] It is based on creation of a partial thickness scleral flap and a deep pocket in the area of the outer wall of the Schlemm's canal. It involves the Schlemm's canal without penetrating its inner wall. Three variations of the procedure exist: canaloplasty, viscocanalostomy and deep sclerostomy. In the first procedure, a 10-0 nylon is passed through the Schlemm's canal while in the second, viscoelastic agent such as hyaluronic acid (Healon®) is injected into the canal. The aqueous flows through the trabeculo-Descemet's membrane into scleral pocket and from there to surrounding blood and aqueous vessels. The NPGS with intraoperative MMC is promising showing good short-term (between one and three years) success, but a long follow-up is required.

9. Glaucoma drainage implants

Drainage implants drain the aqueous humour to the subconjunctival space. They are considered if one or two trabeculectomies with MMC fail or if extensive conjunctival scarring exists. [51] Some authors who have favorable outcomes with glaucoma drainage implant select

it as the procedure of choice in uveitic glaucoma. [52], [53] Two types of drainage implants exist. The first type is with control of the flow (with a "valve" or flow resistance) and includes Ahmed (New World Medical, Rancho Cucamonga, CA) and Krupin-Denver (Hood Laboratories, Pembroke, MA) drainage implants. The second type is without pressure control (no valve) and includes Molteno single or double plate (IOP, Inc., Costa Mesa, CA, USA, and Molteno OpLimited, Dunedin, New Zealand), Baerveldt (Advanced Medical Optics, Santa Ana, California, USA), Shocket (self-assembled) and Eagle Vision (Eagle Vision, Inc. Memphis, TN, USA) implants. The later require blocking the aqueous flow for a few days externally by temporary suture or internally passing a suture through the lumen of the tube or injecting viscoelastic agent. The implantation may also be performed as a two-stage implantation, to decrease the risk for postoperative hypotony. Ahmed and Krupin implants should be preferred over the implants without a valve, because the risk for postoperative overflow and hypotony that may result in endothelial-iris and lens touch. This is more prevalent in patients with uveitis than without it because the aqueous production is usually low. Ahmed valve has convenient plate of variable sizes including for pediatric population.

The success rate of Ahmed implant in uveitic glaucoma at one year is 77-94% and at 4 years 50%. [54]- [56] The success rate of Baeveldt implant at 1 year is 92%. [47] A decrease in corneal endothelial cell count has been observed with glaucoma drainage devices (Ahmed) in comparison with non-valved implanted eyes. The decrease in endothelium is related to the age of the patient, duration of the uveitis and presence of the implant and corneal-valve touch. [57]

9.1. ExPress shunt

It is expected that this device will have the advantages of trabeculectomy (guarded filtration) and other glaucoma drainage device (uniform internal opening) as long as it will not be blocked by inflammatory products. We have found that it is beneficial in secondary glaucomas including uveitic glaucoma (in publication). The only exceptions are neovascular glaucoma and iridocorneal endothelial syndrome where it usually fails. No other data are available on the outcome of ExPress implantation in uveitic glaucoma.

9.2. IStent

IStent is a titanium device that is placed into the Schlemm's canal through the anterior chamber. This device may be effective in secondary glaucoma and may decrease the requirement for postoperative hypotensive medications. It has not been proven yet to be effective in uveitic glaucoma.

9.3. Trabectome

Trabectome is a micro-electrical device that removes the trabecular meshwork and unroof the Schlemm's canal under gonioscopy to decrease the resistance to aqueous outflow. No results of this device in uveitic glaucoma are available. It is expected that it will have only a

temporary effect if the uveitis persists, since new inflammatory products may gradually obstruct the surgical site.

9.4. Solx Gold shunt and CyPass

These devises are placed into the suprachoroidal space. Based on other devises with similar principle, it is expected that these devices will fail due to obstruction by uveal tissue especially in eyes with uveitis.

9.5. Cycloablation

Cycloablation, preferably with 810nm infrared diode laser may be applied in uncontrolled glaucoma with no potential for improvement in visual acuity in which other anti-glaucoma procedures failed. [58], [59] The reason is that it is difficult to predict the outcome of the treatment (final IOP) and to control the post-treatment intraocular inflammation, which is usually, exacerbate. Such inflammation may result in CME with decrease in visual acuity and central scotoma, papillary and retropupillary membranes and phthisis bulbi. The initial settings for trans-scleral cyclophotocoagulation with this laser is 1,250mW, 2sec. Following topical anesthesia and additional peribulbar lidocaine 2% 2ml, the probe is placed 1.2mmbehind the limbus. The power is increased in 150mW increments but not over 2250mW until a "pop" sound is heard. Then it is decreased in 150mW until no "pop" is heard and treatment begins. Eighteen spots are delivered to 270° avoiding 3:00 and 9:00 positions where the long posterior ciliary nerves enter the eye. Prevention of CME may be possible by topical NSAID such as diclofenac sodium (Voltaren®) 0.1% qid for 6 months. Decrease in visual acuity mayoccur from CME if prophylactic treatment is refrained or in cases of advanced visual field loss (splitting of the fixation or high mean deviation) as in other surgical procedures.

10. Follow-up

The follow-up intervals depend on the severity of the uveitis and glaucoma. Patients with quiet eyes and controlled IOP should be observed at least every 6 months. If the uveitis is active or the glaucoma is uncontrolled, the follow-up interval should be decreased. The follow-up examinations include IOP measurement, complete anterior and posterior segments for activity of the uveitis, optic disc cupping and other means as necessary (e.g., visual fields and OCT).

11. Prognosis

The prognosis depends on the etiology of the uveitis and severity of the inflammation and the glaucoma. Early medical and surgical interventions may improve the visual outcome and obtain resolution or long-term remission of the uveitis.

12. Summary

Uveitic glaucoma is a heterogeneous group of diseases in which glaucoma develops secondary to uveitis. The diagnosis is based on elevated IOP. Periodic evaluation of the optic disc should be made, and in patients with cup/disc ratio of 0.6 or more, visual field evaluations should be obtained. The management includes treating the uveitis, glaucoma and the underlying disorder. Most of the uveitis types should be treated although uveitis in juvenile rheumatoid arthritis requires minimal medical treatment to obtain remission and the uveitis in Fuchs' heterochromic iridocyclitis does not require any treatment. In contrary, glaucoma should always be treated aggressively. If medical treatment for glaucoma fails, surgical intervention should be promptly applied. Evaluation of the newer procedures and implants is required to determine the best approach.

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