Ophthalmol Ther (2023) 12:35–53
https://doi.org/10.1007/s40123-022-00601-z

REVIEW

Medical Therapy and Scleral Windows for Uveal Effusion Syndrome: A Case Series and Literature Review

Henry H. Li · Kaitlyn C. Hunter · Andrew C. Thomson · Allan A. Hunter

Received: July 29, 2022 / Accepted: October 16, 2022 / Published online: November 21, 2022

ABSTRACT

Introduction: Uveal effusion syndrome (UES) is a rare ocular disease causing idiopathic uveal effusion, often with associated ciliochoroidal and retinal detachment. UES diagnosis is challenging because of overlapping features with other ocular inflammatory, neoplastic, iatrogenic, and drug-induced causes of uveal effusion. While several successful surgical treatments have been described, such as full-thickness or partial-thickness sclerectomy, medical therapies may also have a therapeutic role.

Objective: To provide an updated review of the published literature on the course of the disease, medical and surgical management strategies, as well as newer treatment modalities.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40123-022-00601-z.

H. H. Li
Case Western Reserve University School of Medicine, Cleveland, OH, USA

A. C. Thomson
McGovern Medical School, The University of Texas Health Science Center, Houston, TX, USA

H. H. Li (✉) · K. C. Hunter · A. C. Thomson · A. A. Hunter
Oregon Eye Consultants, LLC, 1550 Oak Street, Suite 7, Eugene, OR 97401, USA
e-mail: Hhl19@case.edu

Keywords: Uveal effusion syndrome; Choroidal effusion; Scleral windows; Literature review

Key Summary Points

Uveal effusion syndrome (UES) presents a diagnostic and therapeutic challenge for vitreoretinal surgeons.

Varied success with initial medical treatment has been reported in the literature, with many cases requiring surgical intervention.

Initial medical therapy was started in our patients with UES; however, both patients required scleral window surgery to resolve the choroidal effusion and retinal detachment.

Several successful surgical therapies have been described, including the creation of sclerotomies and sclerectomies, alone or in combination.

DIGITAL FEATURES

This article is published with digital features, including videos, to facilitate understanding of the

article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.21342852.

INTRODUCTION

Uveal effusion, or choroidal effusion, refers to fluid accumulation in the suprachoroidal space, often secondary to intraocular surgeries, trauma, malignancy, medication adverse effects, inflammatory and infectious diseases [1]. Reported causes of uveal effusion are listed in Table 1. Uveal effusion syndrome, also referred to as idiopathic ciliochoroidal effusion, is a rare disease and diagnosis of exclusion.

UES was first described by Schepens and Brockhurst in 1963; they noted uveal effusion without an obvious cause in 17 patients, almost exclusively male with one female patient [2]. Patients presented with superior visual field loss, blurred vision, and metamorphopsia [3]. Notable clinical features included gradually progressing choroidal elevation and detachment starting in the periphery, often associated with a serous retinal detachment. Deep retinal and subretinal exudates commonly appeared prior to the serous detachment, along with optic nerve edema and mild to moderate vitreous cell [3]. Hyper- and hypopigmented lesions in the retinal pigment epithelium (RPE), termed leopard spots, are common during the UES disease course and remain after treatment. These lesions contribute to permanent visual acuity loss with chronic disease [4]. Though the exact incidence and prevalence of UES are unclear, a recent surveillance study in the UK estimated the annual incidence to be 1.2 per 10 million [5].

As a result of its rarity and shared features with other inflammatory, neoplastic, and ocular disorders, UES is a diagnostic and therapeutic challenge. In fact, only 16% of patients were correctly diagnosed initially with UES in one report [6]. This has significant implications, as patients may be ineffectually treated for other causes of retinal detachment or choroidal effusion, which fails to improve vision and may limit visual outcomes. UES classification (Table 2) has also been shown to affect management. Type 3 UES, for example, was

Table 1 Differential diagnosis of ciliochoroidal effusion

Inflammatory
Uveitis
Posterior scleritis
Chorioretinitis
Myxedema/multiple myeloma
Trauma and intraocular surgery (e.g., glaucoma surgery)
Orbital cellulitis
Idiopathic orbital inflammation
Cardiovascular
Diabetes
Hypertension retinopathy
Arteriovenous fistula
Genetic/oncologic
Tumor metastases
Uveal melanoma, lymphoma
Paraneoplastic syndromes
Vogt–Koyanagi–Harada syndrome
Hunter syndrome
Sturge–Weber syndrome
Iatrogenic
Wound leak
Laser photocoagulation, cryotherapy
Drug therapy
Sulfa drugs (e.g., topiramate, acetazolamide, hydrochlorothiazide, methazolamide) [6, 69, 73–78]
Bupropion
Mefenamic acid [70]
Phendimetrazine tartrate [79]
Ephedrine

Table 2 Uveal effusion syndrome classification and associated features

	Type 1 UES (nanophthalmic)	Type 2 UES (non-nanophthalmic)	Type 3 UES (non-nanophthalmic)
Anterior segment exam	Dilated episcleral blood vessels	Minimal to no anterior chamber cell	
	Blood in Schlemm's canal		
	Minimal to no anterior chamber cell		
Posterior segment exam	Ciliochoroidal detachment/elevation		
	Subretinal fluid		
	Retinal folds		
	Leopard spot changes in RPE		
	Optic nerve swelling		
	Mild to moderate vitreous cells		
Axial length	Short axial length (< 20.5 mm)	Normal or slightly short axial length (> 20 mm)	Normal or slightly short axial length (> 20 mm)
Refractive error	Hypermetropic	Non-hypermetropic	Non-hypermetropic
Scleropathy	Thickened/abnormal sclera on imaging and histology	Thickened/abnormal sclera on imaging and histology	Normal sclera on imaging and histology
Treatment efficacy	Surgery effective	Surgery favorable	Surgery non-favorable
			Medical treatment favorable

previously reported to be unresponsive to surgery, though results have been mixed in recent cases [7].

Current management approaches for UES recommend scleral thinning procedures, creation of scleral flaps or windows to decrease scleral resistance and allow for effusion drainage. Often, patients require surgery in the contralateral eye, as bilateral involvement occurs in more than 65% of patients [8]. Comparatively, medical therapies have had varied success in the literature, a majority reported in case studies and series owing to disease rarity. These include corticosteroids, carbonic anhydrase inhibitors, prostaglandin analogues, non-steroidal anti-inflammatory drugs (NSAIDs), and anti-vascular endothelial growth factor (VEGF) injections, which will be discussed further in this article.

This article presents a case series of patients with UES seen at our eye center and reviews relevant literature regarding UES pathophysiology, diagnosis, therapeutic and management options. The PUBMED and MEDLINE library databases were searched for all literature published in the English language before June 2022. Manuscripts included the following keywords: uveal effusion, choroidal effusion, suprachoroidal, retinal detachment, nanophthalmos, leopard spot, scleral windows, sclerotomy, sclerectomy, carbonic anhydrase inhibitor, anti-VEGF, corticosteroid, prostaglandin. Relevant manuscripts and respective bibliographies were carefully reviewed for inclusion in this article. The patients involved provided written consent for publication of the cases. The study did not require ethics approval, and was conducted in accordance with the Helsinki Declaration.

CASE SERIES PRESENTATION

A 70-year-old female patient presented with choroidal effusion with associated retinal detachment in her left eye. The patient reported left eye pain prior to experiencing sudden onset blurry and distorted vision. She then noted a "curtain" over her left temporal visual field and intermittent flashes. The left fundus exam revealed central macular edema with diffuse leopard spot retinal pigmentation, choroidal effusion, and serous retinal detachment (relevant clinical data presented in Table 3). There was no evidence of intraocular inflammation in either eye. Ocular oncology evaluation found no choroidal lesions. Fundus photos, fundus autofluorescence (FAF), optical coherence tomography (OCT), and fluorescein angiography (FA) were obtained (Fig. 1). B-scan ultrasonography (US) confirmed retinal detachment and choroidal effusions and revealed borderline nanophthalmos bilaterally with an axial length of 20.5 mm OD (right eye) and 20.65 mm OS (left eye). She was started on orally administered prednisone and topical difluprednate, with the addition of orally administered acetazolamide and topical latanoprost at the 1-month visit. Prednisone was discontinued after 2 months and acetazolamide after 1 month because of medication intolerance and malaise. Subtenon's Kenalog was also administered without improvement. After no significant improvement with medical therapy, superonasal and inferonasal scleral windows surgery was performed. Each window consisted of a 50–75% thickness sclerectomy measuring 4–6 mm by 4–6 mm in area, with the anterior edge at the insertion site of the extraocular muscles. A central sclerotomy was created in each site by carefully dissecting down to choroid and using a Kelly punch to open a 0.75-mm hole (Videos 1 and 2). Postoperatively, the exudative detachment greatly improved after 1 month, with complete resolution of subretinal fluid after 6 months. Persistent pigmentary changes (leopard spots) likely limited vision potential in this patient.

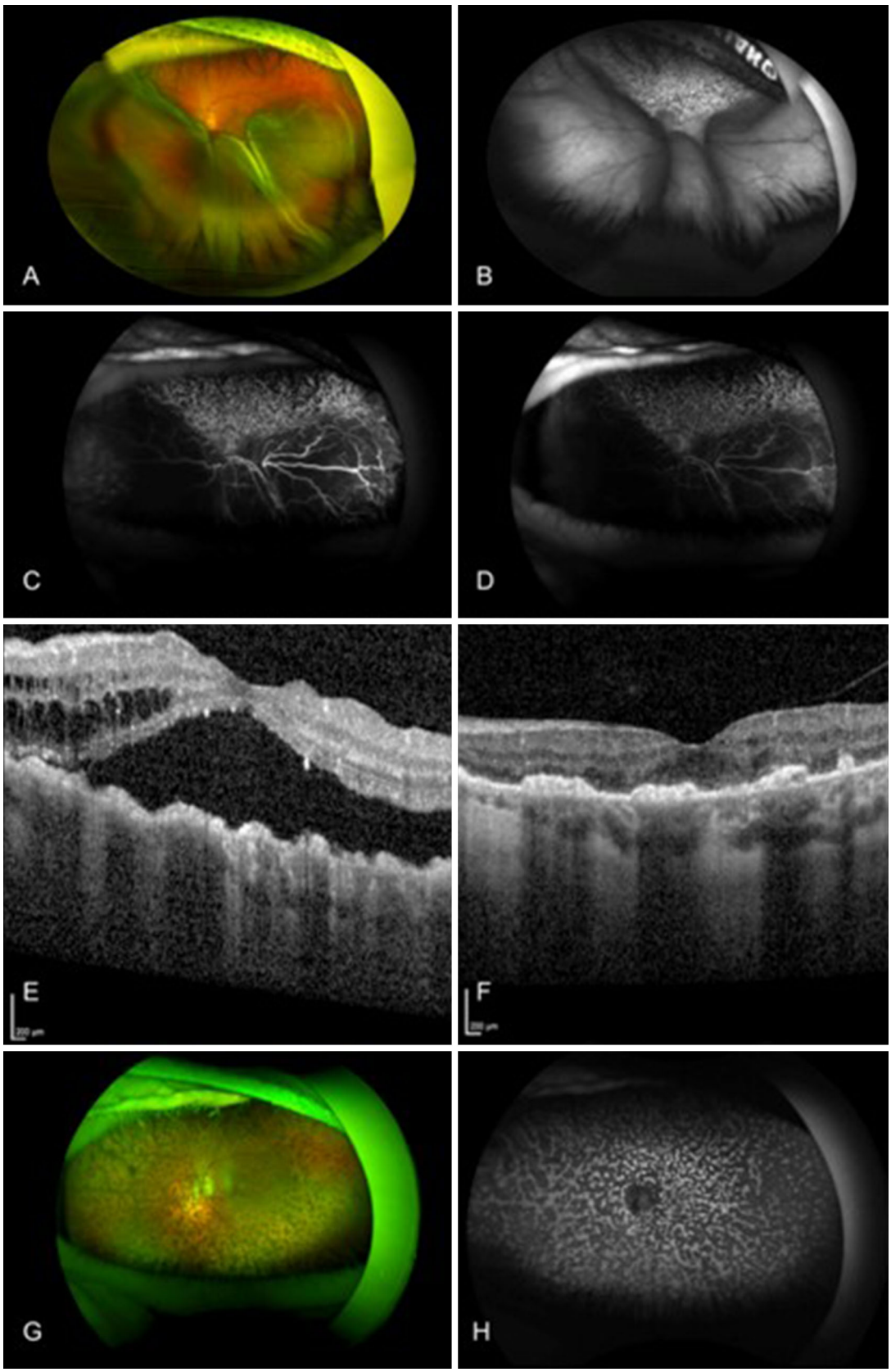
Case 2 is a 63-year-old male patient with history of type 2 diabetes without diabetic retinopathy, surgically treated basal cell carcinoma, mild primary open angle glaucoma, hyperopia, cataract surgery, referred to the retina clinic for exudative retinal detachment. At presentation, the patient reported blurry vision in the temporal visual field of his left eye and flashes. Slit lamp examination revealed no sign of anterior chamber inflammation in both eyes. Fundus exam revealed a choroidal effusion temporally and nasally with overlying retinal detachment and inferior subretinal fluid in the left eye. No retinal breaks or evidence of diabetic retinopathy were seen on exam. Fundus

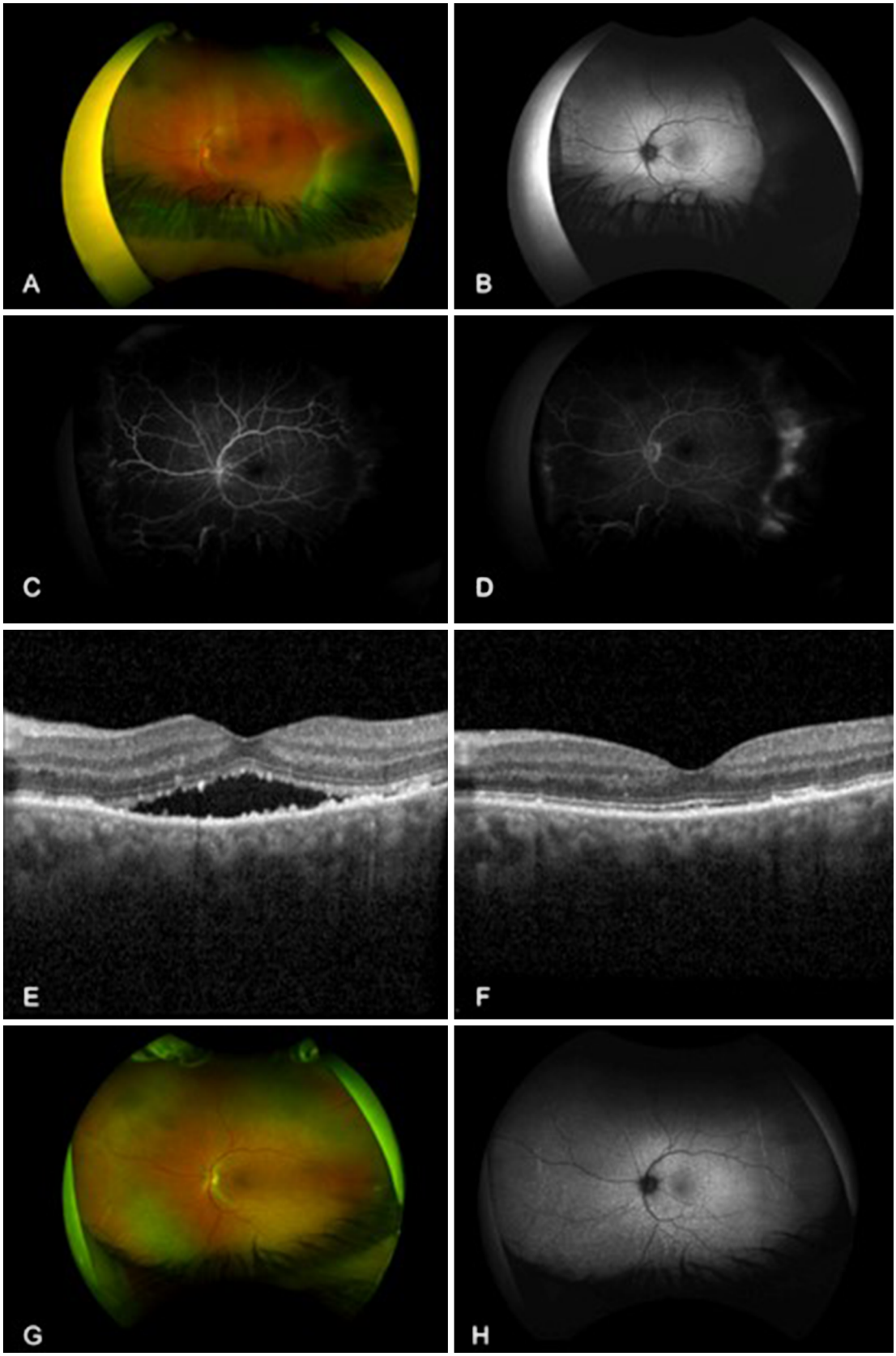
Fig. 1 **a** Preoperative fundus photos in patient 1 OS demonstrates inferior bullous retinal detachment nasally and temporally without choroidal mass lesions. **b** Preoperative fundus autofluorescence OS showing diffuse leopard spot appearance and corresponding patchy hypo-fluorescence on FA early and late-phase images (**c**, **d**). Preoperative (**e**) and postoperative 3-month OCT (**f**) demonstrating resolved detachment with persisting RPE changes. Postoperative fundus (**g**) and autofluorescence images (**h**) showing resolved choroidal effusion with remaining diffuse mottled hyper and hypo-AF changes (leopard spots) suggestive of chronic retinal pigment epithelium damage

Table 3 Preoperative and postoperative visual acuity in this case study

Case	Age (years) sex	Eye	Axial length (mm)	Refraction (spherical error)	Preoperative BCVA (Snellen)	Postoperative BCVA (Snellen)	Follow-up (months)
1	70 F	OS*	20.57	+ 3.00	20/400	20/70–2	12
2	63 M	OS*	20.31		20/400	20/30	8

*Operative eye


A
B
C
D
E
F
G
H


A
B
C
D
E
F
G
H

◀**Fig. 2** **a** Preoperative fundus photos in patient 2 OS demonstrates inferior bullous retinal detachment nasally without choroidal mass lesions. **b** Preoperative fundus autofluorescence OS showing mild pigmentary change and hypofluorescence on FA early and late-phase images (**c**, **d**). Preoperative (**e**) and postoperative 3-month OCT (**f**) demonstrating resolved detachment with mild RPE changes. Postoperative fundus (**g**) and autofluorescence images (**h**) showing resolved choroidal effusion with remaining mild pigmentary changes

photos, FAF, OCT, and FA images were obtained (Fig. 2). B-scan US showed choroidal effusion with thickened sclera, no obvious sub-Tenon's fluid, and no mass lesions. Axial length was measured to be 20.62 mm OD and 20.31 mm OS. Lab tests for antinuclear antibody (ANA), rheumatoid factor, antineutrophil cytoplasmic antibody (ANCA), angiotensin-converting enzyme (ACE), lysosome, QuantiFERON TB Gold, syphilis were negative. Initial medical treatment with orally administered prednisone and topical difluprednate was started and continued for 3 months. Latanoprost was started per glaucoma specialist recommendation. Subretinal fluid appeared to be only slightly resolving over the course of 1 month and thus sub-Tenon's Kenalog was also administered. At 3-month follow-up, the patient felt his left eye vision was regressing, and there was minimal change of the subretinal fluid, choroidal effusion, and serous retinal detachment on exam. The patient opted to proceed with scleral windows surgery, as described above. Postoperatively, he showed continued improvement with resolving serous detachment and fluid. Follow-up examination at 8 months showed resolved choroidal effusion and detachment with residual mild retinal pigmentary changes.

PATHOGENESIS

Aqueous humor leaves the anterior chamber via either the trabecular meshwork or uveoscleral outflow pathways. Unlike the trabecular meshwork pathway, aqueous humor in the uveoscleral pathway passes through structures diffusely rather than through distinctive channels. In the uveoscleral pathway, the aqueous humor passes through the ciliary muscle to enter the supraciliary and suprachoroidal spaces. Scleral outflow accounts for a part of this pathway as well, either directly or via the scleral emissaries, then into the choroidal vessels and vortex veins [9].

UES is hypothesized to be a result of decreased scleral permeability from scleropathy or vortex vein and emissary channel compression, resulting in impaired uveal outflow. The scleropathy component in UES appears to be driven by the accumulation of glycosaminoglycan-like (GAG) deposits, leading to scleral thickening [7, 10]. Further histologic evidence in UES eyes suggests that the reduced scleral permeability leads to protein accumulation, higher colloid osmotic pressure, and subsequent serous choroidal effusion [10–13]. In fact, in nanophthalmic eyes, the subretinal fluid contains 2–3 times greater concentration of albumin and other proteins than healthy eyes, suggesting impaired transscleral exit of protein [8, 14, 15]. Possibly stimulated by high protein concentrations and RPE phagocytosis, foci of RPE migration into the subretinal space produce the characteristic leopard spot pattern [16].

UES is associated with a clinical phenotype of microphthalmos, nanophthalmos. Nanophthalmos, a rare and potentially blinding disease, is characterized by a small eye with shortened anterior and posterior axial lengths with no other deformities. Predominantly bilateral with either dominant or recessive patterns of inheritance, nanophthalmos results from arrested growth of the eye during the embryonic stage [11, 17]. While the axial length threshold for nanophthalmos has been actively debated, most literature references suggest an upper axial length of 19–20 mm [18]. Nanophthalmos is accompanied by thickened and abnormal sclera according to histological studies, suggesting a predisposing factor to the development of UES due to impaired venous drainage from the eye [17]. According to a registry of 23 nanophthalmic patients, 26.1% had uveal effusions and 17.4% had subclinical effusions [19].

Vortex vein compression is an alternative hypothesis of UES pathogenesis. Each human eye usually comprises of 3–8 vortex veins, while

Johnson and Gass recorded a range of 2–4 in their UES cases [4, 20]. As an important choroidal drainage system, vortex veins and their compression could explain impaired uveal outflow. Authors studying vortex vein occlusion in rhesus monkeys noted marked and immediate venous congestion, though it is to be noted that vortex veins in monkeys follow a segmental distribution and do not communicate freely [21]. In UES, Brockhurst noted that absence of vortex veins or increased resistance of these veins could limit fluid evacuation, following a report of 10 nanophthalmic eyes undergoing vortex vein decompression and sclerotomy. Further support was provided by authors reporting improvement in choroidal effusion in nanophthalmic UES eyes [13, 22].

DIAGNOSIS

On slit lamp examination, the anterior segment may present with minimal to no anterior chamber cell, dilated episcleral blood vessels, and blood in Schlemm's canal [23]. The intraocular pressure is usually normal. On retinal examination, associated ciliochoroidal detachments appear solid and brown/orange in color. The serous nature of the fluid can be appreciated with transillumination. With ocular movements, the serous detachments do not undulate, unlike rhegmatogenous detachments. Annular or lobular choroidal detachments are seen as progression occurs, and a four-lobed configuration can form in worsening cases [24]. Other posterior segment features include subretinal fluid, retinal folds, leopard spot appearance from RPE changes, optic nerve swelling, and mild to moderate vitreous cell. Various clinical features of UES are presented in Table 2.

The classification of UES is often distinguished by eye size phenotype and evidence of scleropathy. Uyama et al. were the first to describe three different types of UES based on ocular anatomy, histology, and response to treatment [7]. Type 1 UES is nanophthalmic, characterized by a small eye with shortened anterior and posterior axial lengths, with hypermetropia and scleral thickening. Type 2 is non-nanophthalmic with hypermetropia and scleral thickening. Type 3, or idiopathic UES, is non-nanophthalmic without hypermetropia or scleral thickening.

The sclera in type 1 and 2 UES appears thickened under B-scan US and MRI imaging, while histologic examination of amputated scleral flaps shows scleropathy. Tissue sampling and histological examination reveal disorganized collagen and proteoglycan deposition in the extracellular matrix of affected eyes and thickened sclera [10]. Protein-rich exudative deposits are also present in the choroid. Detachment of the choroid, ciliary body, retina, and expansion of the subarachnoid space surrounding the nerve can be appreciated [3, 4, 10, 17].

IMAGING MODALITIES

The imaging modalities used for investigating and diagnosing UES have progressed over the years, including US, ultrasound biomicroscopy (UBM), indocyanine green angiography (ICG), OCT, FA, and MR imaging. Relevant imaging features of UES are listed in Table 4.

Ultrasound

US may be used to evaluate the presence of retinal and choroidal detachment, eye size phenotype, and scleral abnormalities. Type 1 and type 2 UES will demonstrate scleral thickening on US. In fact, in healthy subjects the sclera is 0.95 mm ± 0.18 mm, while in UES it is 1.3 mm (1.3–1.4 mm) in patients without intraoperative scleral thickening and 2.3 mm (1.5–2.9 mm) in those with intraoperative scleral thickening [15]. Earlier and more subtle changes in UES, such as ciliochoroidal effusion, may be detected using UBM. US has also been used to provide preoperative assessment of areas of maximal swelling to guide scleral thinning procedures [25]. Further, US may provide important evidence for excluding other causes of choroidal effusions and retinal detachment such as choroidal tumors or posterior scleritis [25, 26]. For example, areas of relative hypo-reflectivity may indicate infiltration due to inflammation or neoplastic process.

Table 4 Uveal effusion syndrome features on imaging

Fundus photography
Mottled hyper- and hypopigmented areas (leopard spot appearance)
Fluorescein angiography
Acute—granular hyperautofluorescence areas
Chronic—mixed granular hyper- and hypoautofluorescence areas (leopard spot appearance)
Little to no leakage on late phase
Indocyanine green
Increased choroidal flush in early and late phases
Diffuse early hypercyanescence
Dilated choroidal vasculature
Ultrasonography/ultrasound biomicroscopy
Ciliochoroidal thickening
Retinal and/or choroidal detachment (often peripherally)
Suprachoroidal space fluid
Optical coherence tomography
Focal choroidal thickening on lesions
Subretinal space hyperreflectivity
Subretinal fluid and deposits
MRI
Thickened sclera (type 1 and 2)
Histology
Disorganized scleral collagen and proteoglycan deposits

OCT

OCT imaging provides detailed assessment of retinal anatomy and has made large advances in diagnosing retinal diseases. In UES, OCT images demonstrate choroidal swelling at the posterior pole and macular folds. Enhanced-depth OCT may provide better detection of increased choroidal thickness compared to normal eyes, as well as the presence of hypo-reflective areas corresponding to engorged choroidal veins or expansion of the suprachoroidal space [27]. Focal thickening of the RPE through leopard spots can also be seen using OCT. Interestingly, pachychoroid features have been identified in cases of type 3 UES on OCT [28–30]. The exact relationship with type 3 UES and pachychoroid spectrum disease remains unknown.

Fluorescein Angiography

FA evaluates the extent of vascular pathology in the choroid and retina. In UES, FA demonstrates areas of hypo-fluorescence within hyperfluorescence corresponding to leopard spot pigmentation, without angiographic leakage [3, 4]. FA also rules out other causes of exudative retinal detachment, inflammatory or neoplastic processes. Unlike Vogt–Koyanagi–Harada syndrome or central serous chorioretinopathy, UES does not show distinct leakage [23].

Indocyanine Green Angiography

IGA is similar to FA but uses indocyanine green dye, which when fluoresced in infrared light, allows assessment of choroidal vasculature [31]. In UES, early phase IGA (10–15 s) demonstrates diffuse granular hyperfluorescence in the choroid and confirms the presence of dilated choroidal vessels [27, 32–34]. The hyperfluorescence typically increases over time and persists until the late phase (15–20 min), showing marked choroidal fluid accumulation. The late phase choroidal hyperfluorescence in both type 1 and type 2 UES is further indicative of choroidal vessel hyperpermeability in UES [7].

MRI

MRI facilitates UES diagnosis and classification. In UES, MRI demonstrates abnormal scleral thickness on T1- and T2-weighted images, which may help exclude other causes of uveal effusion, such as intraocular tumors [7, 35–38]. MRI findings may also disclose abnormal globe size and subretinal fluid accumulation. MRI with contrast can also help exclude scleritis or carotid-cavernous fistula [25]. Lam et al.

reported on measuring scleral thickness in five patients with uveal effusion syndrome and five matched controls using MRI and UBM [36]. In type 1 and type 2 UES, MRI identified markedly thickened sclera, compared to normal appearing sclera in type 3. However, scleral thickness measurements using MRI were less accurate and precise compared to UBM, likely as a result of movement artifacts.

SURGICAL TREATMENT METHODS

Full-thickness and partial-thickness sclerectomy is the preferred surgical approach for most vitreoretinal specialists. Gass et al. first described this method in 1983 after an unsuccessful vortex vein decompression [3]. Vortex vein decompression was described by Brockhurst in 1980 and involved unroofing vortex veins via sclerectomy [39]. This technique, however, had a high risk of vortex vein amputation and hemorrhage. Gass proposed that the presence of large scleral flaps created during vortex vein decompression was responsible for positive outcomes. In 1990, Gass and Johnson performed quadrantic partial-thickness sclerectomy without vortex vein decompression in 23 eyes with UES. The technique was the same as described in 1983 and involved $5 \times 7\ mm^2$ rectangular one-half to two-thirds thickness sclerectomies, approximately 1–2 mm anterior to the equator to avoid the vortex vein exit sites. A scleral punch was used to make a linear 2-mm sclerostomy in each sclerectomy site. They reported improvement of effusion in 83% and 96% of eyes after a single and second sclerotomy procedure, respectively, after a 6-month period [4]. Of the five eyes with recurrent effusions, three resolved spontaneously and three resolved after reoperation. Using the same method, Jackson et al. reported improvement in 7 of 14 eyes after 3 months, with 4 eyes requiring more than one operation [8]. Resolution of UES-associated effusion following sclerectomy suggests that reduced scleral thickness improves protein outflow and fluid accumulation.

Several successful iterations of this technique have also been described. Schneiderman and Johnson described a case of UES in a 73-year-old patient successfully treated with a pars plana vitrectomy and internal drainage of subretinal fluid with C_3F_8 gas tamponade combined with quadrantic partial thickness sclerectomies [40]. Mansour et al. described an extensive sclerectomy technique to treat UES due to extreme nanophthalmos, involving 90% depth scleral windows over the superior-nasal, inferotemporal, and inferonasal quadrants [19]. The superior-temporal quadrant was excluded to avoid the superior oblique muscle. The authors reported resolution of uveal effusion in seven of eight eyes, with one recurrent effusion needing additional surgery. Further studies have reported on the success of scleral-thinning surgeries in nanophthalmic and idiopathic UES [4, 41, 42]. Table 5 presents surgical methods and outcomes in recent studies.

Selective sclerectomy procedures may also be used to treat localized subretinal fluid. This allows the option to pursue additional sclerectomy and/or sclerostomy procedures in persistent cases. Avoiding larger resections may also reduce risks for potential complications such as scleral ectasia or traumatic expulsive hemorrhage. Uyama et al. performed subscleral sclerectomy in 19 eyes of 16 patients with UES [7]. In these patients, $4 \times 5\ mm^2$ two-thirds thickness scleral flaps were created in the inferonasal and inferotemporal quadrants, with the remaining sclera excised (3×4 mm) to expose the choroid. However, additional scleral thinning procedures were required for persistent or recurrent cases. Upper quadrant sclerectomies were performed in seven persistent cases and full-thickness upper quadrant sclerectomies were required in three recurrent cases. Of the patients requiring additional procedures, 2 of 6 eyes had type 1 UES and 5 of 11 eyes had type 2. In two eyes with type 3 UES, however, surgery was not effective despite two-quadrant sclerectomy. The optimal surgical management for type 3 UES is still elusive, however, and has varied success in the literature [28, 29, 43]. Some authors hypothesize that quadrantic sclerectomy may be required to reduce overall choroidal fluid resistance because of the global nature of the condition [42].

Topical mitomycin C can be used during the surgical procedure for UES. This is suggested to

Table 5 Literature review of surgical methods used for patients with UES

Authors	Cases	Surgical treatment	Outcome
Gass et al. [3]	2 eyes of 1 patient with UES without nanophthalmos	Four quadrant partial thickness sclerotomy	Stable at 5-month postoperative follow-up
Johnson and Gass [4]	23 eyes of 20 patients with UES (at least 14 of which were type 1 and 2 UES)	Four quadrant partial thickness sclerotomy	19 cases (83%) stable at 6 months after one procedure, 22 cases (96%) stable at 6 months after two procedures
Sabrosa et al. [45]	1 patient with nanophthalmic UES (deep sclerectomy surgery revision)	Scleral punch	Stable at 6-month postoperative follow-up
Kong et al. [80]	5 eyes in 4 patients with UES with or without nanophthalmos	Full-thickness sclerotomy (2–4 quadrants)	Stable at > 1-month postoperative follow-up
Wang et al. [42]	1 patient with idiopathic UES	Four quadrant sclerotomy (inferior nasal/temporal, followed by superior nasal/temporal)	Stable at 1-month postoperative follow-up
Ozgonul et al. [81]	6 eyes of 4 patients with nanophthalmic and/or idiopathic UES	Partial-thickness sclerotomy ± punch sclerostomy ± vortex vein decompression ± mitomycin C	Stable at > 18-month postoperative follow-up
Guo et al. [71]	3 patients with intractable UES	Four quadrant partial thickness sclerotomy + anti-VEGF	Stable at 4–10-month follow-up visits
Ghazi et al. [25]	6 eyes in 4 patients with idiopathic UES	Single sclerostomy in involved quadrant	Stable at 6 months postoperative follow-up
Mansour et al. [19]	8 eyes of 5 patients with nanophthalmic UES	Extensive circumferential partial thickness sclerotomy	Stable at 12-month postoperative follow-up, with recurrent effusion in one eye
Khatri et al. [82]	2 patients with nanophthalmic UES	Quadrantic vortex vein decompression	Stable at > 2-month postoperative follow-up
Konrad et al. [83]	1 patient with idiopathic UES	Deep posterior sclerotomy	Stable at 16-month postoperative follow-up

prevent recurrent fibrosis and blockage of transscleral outflow, particularly in patients needing repeat scleral thinning. Suzuki et al. described the use of topical mitomycin C with partial-thickness scleral flap and deep sclerostomy for the treatment of one case of type 1 UES [44]. Mitomycin C has also been used to successfully revise a failed deep sclerectomy [45].

Ultrasound has also been used for the therapeutic management of UES. Ghazi et al. described a modified technique where a preoperative B-scan was used to identify areas of maximal scleral thickening in each involved quadrant, to target sclerostomy placement using a Kelly punch [25]. This approach was successful in resolving choroidal effusion even in cases where conventional surgery failed. Maggio et al. reported treatment of one patient with type 1 UES, two patients with type 2 UES, and one patient with type 3 UES, with scleral thinning procedures using guiding ultrasound [35]. The thinning procedure depended on degree of involvement, which ranged from two sclerectomies at involved quadrants to four sclerectomies at the equator.

A new approach using an Ex-PRESS shunt presents a promising approach to UES [46]. Ex-PRESS shunts are commonly used in minimally invasive glaucoma surgery, designed to lower intraocular pressure by shunting aqueous fluid from the anterior chamber to the sub-conjunctival space through a scleral flap. Yepez et al. performed the Ex-PRESS shunt technique on three eyes with type 2 UES, through a conjunctival incision and oblique sclerotomy. Resolution of choroidal effusion was documented after 48 h and no recurrence after 1–2-year follow-up [46].

UES RISK AND PROPHYLAXIS IN NANOPHTHALMIC PATIENTS

Additional precautions are required when treating nanophthalmic eyes with concomitant ocular conditions. Cataract surgery in these patients is challenging, and may result in poor visual outcomes and complications such as uveal effusion, retinal detachment, and corneal decompensation [47]. In one study of 114 nanophthalmic eyes undergoing cataract surgery, 29 eyes had complications, of which uveal effusion accounted for half [48]. The current approach is to perform scleral thinning procedures prior to, or along with cataract surgery to reduce the occurrence of uveal effusions [11, 49, 50]. A randomized control trial comparing outcomes with and without prophylactic sclerostomy demonstrated lower complication rates with prophylaxis, reducing iatrogenic choroidal effusion by 80% [51]. On the other hand, advances in phacoemulsification have improved intraoperative eye pressure stability, which have improved visual outcomes in nanophthalmic patients [49, 52–54].

EMERGING MEDICAL THERAPIES

While surgical therapies have been the mainstay of UES treatment, medical approaches can be successful, according to recent reports. A population surveillance study from the British Ophthalmological Surveillance Unit (BOSU) revealed that of the 29 reported UES cases from 2009 to 2011, seven were managed non-surgically, including observation (one case), topical steroids (two cases), systemic steroids (three cases), and cyclodiode laser (one case) [5]. Thus, it is important to discuss medical management approaches in UES. Table 6 presents outcomes of various medical therapies to treat UES in recent reports. This includes steroids, topical NSAIDs, prostaglandin analogues, carbonic anhydrase inhibitors, anti-VEGF, or a combination of medical therapies [55–58].

Corticosteroids

Steroids inhibit both cyclooxygenase and lipoxygenase pathways to exert their anti-inflammatory effects [59]. Fledelius et al. reported on 16 UES cases, 12 of which received initial systemic prednisone, 3 resolved with only prednisone, 1 resolved in combination with NSAIDs, and others required further surgery [60]. Shields et al. reported control in 95% of type 3 UES eyes using corticosteroids, either oral, periocular, topical, or in combination [6]. The remaining 5% required surgery, but in these patients, a surgical approach may be ineffective because of the absence of scleropathy [7]. These findings perhaps point to an underlying inflammatory process contributing to uveal effusion that corticosteroids may help improve. As such, initial therapy with corticosteroids may be reasonable to rule out other causes, despite no apparent scleritis or inflammatory

Table 6 Literature review of medical therapy and/or in combination with surgery for patients with UES

Authors	Cases	Therapy	Treatment duration	Outcome
Kumar et al. [33]	2 patients with idiopathic UES	Oral NSAID (indomethacin) + topical NSAID + laser photocoagulation	6–9 months	Stable at 9-month follow-up visit
Derk et al. [58]	3 patients with bilateral UES	Topical PA (latanoprost) + oral carbonic anhydrase inhibitor (acetazolamide) ± partial sclerectomy	3 months	Stable at 12 months, one patient received partial sclerectomy in one eye
Pautler et al. [57]	1 patient with UES + hypermetropia	Oral carbonic anhydrase inhibitor (acetazolamide), later switched to topical (dorzolamide)	≥ 8 weeks	Stable at 1-year follow-up visit
Park et al. [56]	1 patient with bilateral nanophthalmic UES	Topical PA (latanoprost) + oral carbonic anhydrase inhibitor (acetazolamide) + additional topical NSAID (bromfenac)	2 months	Stable at 6-month follow-up visit
Guo et al. [71]	3 patients with intractable UES s/p sclerectomy	Anti-VEGF injection (ranibizumab, bevacizumab)	2–3 injections at 4–8-week intervals	Stable at 4–10-month follow-up visits
Tong et al. [61]	1 patient with intractable UES s/p sclerectomy	Topical NSAID	1 month	Stable at 3-month follow-up visit
Song et al. [72]	1 patient with nanophthalmic UES	Anti-VEGF injection (ranibizumab)	2 injections at 4-week intervals	Stable at 2-year follow-up visit
Anguita et al. [55]	3 patients with UES (1 nanophthalmic, 2 idiopathic)	Oral carbonic anhydrase inhibitor (acetazolamide) ± partial sclerectomy	3 months	Stable at 1–2-month follow-up visits, one patient treated with acetazolamide only, two patients received partial sclerectomy

features. Steroids may elevate intraocular pressure; thus, frequent monitoring is recommended.

NSAIDs

Topical NSAIDs are commonly used in ophthalmology for postsurgical pain, inflammation, and cystoid macular edema. As cyclooxygenase inhibitors, NSAIDs (in the

nonselective form) act on COX-1 and COX-2, reducing prostaglandin synthesis in the inflammatory response. Additionally, NSAIDs inhibit neutrophil migration and act as free radical scavengers. As demonstrated by uses in pseudophakic CME, NSAIDs decrease vascular permeability to reduce fluid accumulation.

In UES, Kumar et al. reported resolution of retinal detachment in two eyes with idiopathic UES following long-term indomethacin. ICG findings demonstrated dilated, tortuous choroidal vessels and late-phase choroidal hyperfluorescence, suggestive of choroidal hyperpermeability [33]. The authors postulate that the choroidal hyperpermeability indicates nonspecific inflammation, for which NSAIDs may have a beneficial effect. However, since laser photocoagulation was also performed in these cases, NSAIDs' effects cannot be completely isolated. Tong et al. also reported a case of rapid resolution of recurrent UES-associated retinal detachment following topical NSAIDs after 7 days [33, 61].

Prostaglandin Analogues

Prostaglandin analogues (PA) are used to reduce intraocular pressure by increasing outflow facility, such as in glaucoma. In the trabecular outflow pathway, prostaglandin analogues achieve outflow effects through EP receptor stimulation, resulting in increased contractility of the trabecular meshwork and decreased contractility of Schlemm's canal [62]. In the uveoscleral pathway, PGF2a and prostaglandin analogues bind to prostanoid EP and FP receptors in ciliary muscle to stimulate aqueous humor outflow [63–65]. The scleral response to prostaglandins has been observed to increase scleral metalloproteinase levels and reduce scleral collagen levels, resulting in enhanced scleral macromolecular permeability [66]. Therefore, PAs may theoretically improve fluid outflow through abnormal sclera. In UES, Derk et al. successfully treated three eyes with bilateral UES with a combination of topical latanoprost and orally administered acetazolamide. Similarly, Park et al. treated one case with the same regimen [58].

Carbonic Anhydrase Inhibitors

Carbonic anhydrase (CA) inhibitors act on CA, found in blood cells and the kidney, leading to excess water excretion and resulting pressure reduction systemically, intracranially, and intraocularly [67]. Acetazolamide is known to inhibit aqueous production and stimulate outward fluid removal in the RPE by at least one pump mechanism, which is the presumed therapeutic mechanism in UES [68]. There have been some reports of complete resolution of UES-associated choroidal detachment with acetazolamide alone or in combination with a topical PA or partial sclerectomy [55, 56, 58]. Paradoxically, acetazolamide and other sulfa medications have been implicated in rare cases of uveal and transient myopia following ocular surgery or altitude sickness treatment; thus, close monitoring is recommended [69, 70].

Anti-VEGF

Intravitreal anti-VEGF injections are often used to treat wet age-related macular degeneration, macular edema, diabetic retinopathy, and retinal vein occlusion. The molecular target is vascular endothelial growth factor, which upregulates new blood vessel growth, and pathological vasculature formation. While the exact therapeutic mechanism of anti-VEGF agents in UES remains unclear, Guo et al. reported resolution of three intractable cases of UES, and Song et al. reported success in one case of nanophthalmic UES [71, 72]. One hypothesis is that the increased expression of interleukin (IL)-6, IL-8, and VEGF in UES affects vessel permeability and choroidal congestion.

CONCLUSION

UES presents a diagnostic and therapeutic challenge for ophthalmologists. Other etiologies of uveal effusion should be ruled out prior to diagnosing true UES, such as inflammatory disease, malignancy, medication-related, or prior intraocular surgery. Evidence of scleropathy, eye size phenotype, and history of

hypermetropia may help further classify UES and direct therapy. In both cases presented, oral and topical corticosteroids as well as topical latanoprost were started as initial medical therapy. Acetazolamide was also used in patient 1; however, this was discontinued because of undesirable medication side effects. Sclerotomy was performed in both cases resulting in resolution of choroidal effusion and retinal detachment.

According to a review of the current literature, medical therapy with or without surgery has had varied success. Further investigation to optimize treatment regiments is limited owing to disease rarity. Despite this, medical therapy can be a reasonable first step before proceeding to surgery in many cases, particularly those of the type 3 presentation.

ACKNOWLEDGEMENTS

Funding. No funding was obtained for this study. The journal's Rapid Service Fee was funded by the authors.

Author Contributions. Concept and Design: Allan A. Hunter. Draft of manuscript: Henry H. Li and Andrew C. Thompson. Revision of manuscript: Allan A. Hunter. All authors read and approved the final manuscript.

Disclosures. Henry H. Li, Kaitlyn C. Hunter, Andrew C. Thomson and Allan A. Hunter have nothing to disclose.

Compliance with Ethics Guidelines. The patients provided written consent for publication of the cases. The above study did not require ethics approval, and was conducted in accordance with the Helsinki Declaration. We thank the patients for their involvement.

Data Availability. Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

REFERENCES

1. Besirli C, Johnson M. Uveal effusion syndrome and hypotony maculopathy. Schachat A, editor. Elsevier; 2017.

2. Schepens CL, Brockhurst RJ. Uveal effusion: 1. Clinical picture. Arch Ophthalmol. 1963. https://doi.org/10.1001/archopht.1963.00960050191010.

3. Gass JDM. Uveal effusion syndrome: a new hypothesis concerning pathogenesis and technique of surgical treatment. Retina. 1983. https://doi.org/10.1097/00006982-198300330-00003.

4. Johnson MW, Gass JDM. Surgical management of the idiopathic uveal effusion syndrome. Ophthalmology. 1990. https://doi.org/10.1016/S0161-6420(90)32511-3.

5. Sharma R, Foot B, Jackson TL. A prospective, population-based, surveillance (BOSU) study of uveal effusion syndrome in the UK. Eur J Ophthalmol. 2021. https://doi.org/10.1177/1120672120969369.

6. Shields CL, Roelofs K, di Nicola M, Sioufi K, Mashayekhi A, Shields JA. Uveal effusion syndrome in 104 eyes: response to corticosteroids—the 2017 Axel C. Hansen lecture. Indian J Ophthalmol. 2017;65(11):1093–104. https://doi.org/10.4103/ijo.IJO_752_17.

7. Uyama M, Takahashi K, Kozaki J, et al. Uveal effusion syndrome: Clinical features, surgical treatment, histologic examination of the sclera, and

pathophysiology. Ophthalmology. 2000. https://doi.org/10.1016/S0161-6420(99)00141-4.

8. Jackson TL, Hussain A, Hodgetts A, et al. Human scleral hydraulic conductivity: age-related changes, topographical variation, and potential scleral outflow facility. Investig Ophthalmol Vis Sci. 2006. https://doi.org/10.1167/iovs.06-0362.

9. Weinreb RN. Uveoscleral outflow: the other outflow pathway. J Glaucoma. 2000. https://doi.org/10.1097/00061198-200010000-00001.

10. Ward RC, Gragoudas ES, Pon DM, Albert DM. Abnormal scleral findings in uveal effusion syndrome. Am J Ophthalmol. 1988. https://doi.org/10.1016/0002-9394(88)90825-2.

11. Brockhurst RJ. Nanophthalmos with uveal effusion: a new clinical entity. Arch Ophthalmol. 1975. https://doi.org/10.1001/archopht.1975.01010020923001.

12. Trelstad RL, Silbermann NN, Brockhurst RJ. Nanophthalmic sclera: ultrastructural, histochemical, and biochemical observations. Arch Ophthalmol. 1982. https://doi.org/10.1001/archopht.1982.01030040915009.

13. Yue BYJT, Duvall J, Goldberg MF, Puck A, Tso MOM, Sugar J. Nanophthalmic sclera: morphologic and tissue culture studies. Ophthalmology. 1986. https://doi.org/10.1016/S0161-6420(86)33704-7.

14. Jackson TL, Hussain A, Salisbury J, Sherwood R, Sullivan PM, Marshall J. Transscleral albumin diffusion and suprachoroidal albumin concentration in uveal effusion syndrome. Retina. 2012. https://journals.lww.com/retinajournal/Fulltext/2012/01000/TRANSSCLERAL_ALBUMIN_DIFFUSION_AND_SUPRACHOROIDAL.26.aspx.

15. Jackson TL, Hussain A, Morley AMS, et al. Scleral hydraulic conductivity and macromolecular diffusion in patients with uveal effusion syndrome. Investig Ophthalmol Vis Sci. 2008. https://doi.org/10.1167/iovs.08-1980.

16. Forrester J, Lee WR, Kerr PR, Dua HS. The uveal effusion syndrome and trans-scleral flow. Eye (Basingstoke). 1990. https://doi.org/10.1038/eye.1990.48.

17. Gass JDM. Uveal effusion syndrome: a new hypothesis concerning pathogenesis and technique of surgical treatment 1983. Retina. 2003;23(6 Suppl).

18. Yang N, Jin S, Ma L, Liu J, Shan C, Zhao J. The pathogenesis and treatment of complications in nanophthalmos. J Ophthalmol. 2020. https://doi.org/10.1155/2020/6578750.

19. Mansour A, Stewart MW, Shields CL, et al. Extensive circumferential partial-thickness sclerectomy in eyes with extreme nanophthalmos and spontaneous uveal effusion. Br J Ophthalmol. 2019. https://doi.org/10.1136/bjophthalmol-2018-313702.

20. Kutoglu T, Yalcin B, Kocabiyik N, Ozan H. Vortex veins: anatomic investigations on human eyes. Clin Anat. 2005. https://doi.org/10.1002/ca.20092.

21. Hayreh SS, Baine JAB. Occlusion of the vortex veins: an experimental study. Br J Ophthalmol. 1973. https://doi.org/10.1136/bjo.57.4.217.

22. Casswell AG, Gregor ZJ, Bird AC. The surgical management of uveal effusion syndrome. Eye. 1987;1(1):115–9. https://doi.org/10.1038/eye.1987.17.

23. Waheed NK, Mendonça LSM, Young LH. Choroidal effusions and detachments. Albert Jakobiecs Princ Pract Ophthalmol. 2020. https://doi.org/10.1007/978-3-319-90495-5_125-1.

24. Schachat AP. Uveal effusion syndrome and hypotony maculopathy. In: Besirli CG, Johnson MW, editors. Ryan's Retina. 6th edn. 2018; p. 1484–1495.

25. Ghazi NG, Richards CP, Abazari A. A modified ultrasound-guided surgical technique for the management of the uveal effusion syndrome in patients with normal axial length and scleral thickness. Retina. 2013. https://doi.org/10.1097/IAE.0b013e3182790eb8.

26. Elagouz M, Stanescu-Segall D, Jackson TL. Uveal effusion syndrome. Surv Ophthalmol. 2010;55(2):134–45.

27. Harada T, Machida S, Fujiwara T, Nishida Y, Kurosaka D. Choroidal findings in idiopathic uveal effusion syndrome. Clin Ophthalmol. 2011. https://doi.org/10.2147/opth.s26324.

28. Jin S, Francisconi CLM, Wong DT. Pachychoroid findings in a case of uveal effusion syndrome. Can J Ophthalmol. 2020. https://doi.org/10.1016/j.jcjo.2019.08.002.

29. Terubayashi Y, Morishita S, Kohmoto R, et al. Type III uveal effusion syndrome suspected to be related to pachychoroid spectrum disease: a case report. Medicine. 2020. https://doi.org/10.1097/MD.0000000000021441.

30. Onoe H, Shimada H, Kawamura A, et al. Bilateral pachychoroid disease with type 3 uveal effusion syndrome in one eye and central serous chorioretinopathy in contralateral eye: a case report. BMC Ophthalmol. 2022. https://doi.org/10.1186/s12886-022-02316-y.

31. Yannuzzi LA, Slakter JS, Sorenson JA, Guyer DR, Orlock DA. Digital indocyanine green videoangiography and choroidal neovascularization. Retina. 1992. https://doi.org/10.1097/00006982-199212030-00003.

32. Wu C, Dong FT, Zhang H, Chen YX, Dai RP, Tan K. Diagnosis and treatment of uveal effusion syndrome: a case series and literature review. Chin Med Sci J. 2011. https://doi.org/10.1016/S1001-9294(12)60006-6.

33. Kumar A, Kedar S, Singh RP. The indocyanine green findings in idiopathic uveal effusion syndrome. Indian J Ophthalmol. 2002;50(3):217–9.

34. Kaewsangthong K, Thoongsuwan S, Uiprasertkul M, Phasukkijwatana N. Unusual non-nanophthalmic uveal effusion syndrome with histologically normal scleral architecture: a case report. BMC Ophthalmol. 2020. https://doi.org/10.1186/s12886-020-01581-z.

35. Maggio E, Polito A, Prigione G, Pertile G. Uveal effusion syndrome mimicking severe chronic posterior uveitis: a case series of seven eyes of four patients. Graefes Arch Clin Exp Ophthalmol. 2016. https://doi.org/10.1007/s00417-015-3176-y.

36. Lam A, Sambursky RP, Maguire JI. Measurement of scleral thickness in uveal effusion syndrome. Am J Ophthalmol. 2005. https://doi.org/10.1016/j.ajo.2005.02.014.

37. Markan A, Moharana B, Dogra M, Singh R. Multimodal imaging to aid in diagnosis of uveal effusion syndrome type 3. BMJ Case Rep. 2021. https://doi.org/10.1136/bcr-2020-239556.

38. Valmaggia C, Helbig H, Fretz C. Uveal effusion syndrome. Klin Monbl Augenheilkd. 2007;224(4):317–9. https://doi.org/10.1055/s-2007-962839.

39. Brockhurst RJ. Vortex vein decompression for nanophthalmic uveal effusion. Arch Ophthalmol. 1980. https://doi.org/10.1001/archopht.1980.01020040839008.

40. Schneiderman TE, Johnson MW. A new approach to the surgical management of idiopathic uveal effusion syndrome. Am J Ophthalmol. 1997. https://doi.org/10.1016/S0002-9394(14)71049-9.

41. Faulborn J, Kölli H. Sclerotomy in uveal effusion syndrome. Retina. 1999. https://doi.org/10.1097/00006982-199919060-00004.

42. Wang BZ, Clark B, McKelvie P, Matthews BJ, Buttery RG, Chandra A. Four quadrant sclerotomies for uveal effusion syndrome. Eye (Basingstoke). 2015. https://doi.org/10.1038/eye.2014.291.

43. Jin W, Xu Y, Wang W, Yang A. Diagnosis and a minimum effective management for nanophthalmic uveal effusion syndrome. Indian J Ophthalmol. 2016;64(8):593–4.

44. Suzuki Y, Nishina S, Azuma N. Scleral window surgery and topical mitomycin C for nanophthalmic uveal effusion complicated by renal failure: case report. Graefes Arch Clin Exp Ophthalmol. 2007. https://doi.org/10.1007/s00417-006-0403-6.

45. Sabrosa NA, Smith HB, MacLaren RE. Scleral punch method with topical mitomycin c for safe revision of failed deep sclerectomy in nanophthalmic uveal effusion syndrome. Graefes Arch Clin Exp Ophthalmol. 2009. https://doi.org/10.1007/s00417-008-1020-3.

46. Yepez JB, Fernando AJ. Ex-PRESS shunt for choroidal fluid drainage in uveal effusion syndrome type 2: a potentially novel technique. JAMA Ophthalmol. 2015. https://doi.org/10.1001/jamaophthalmol.2014.5913.

47. Rajendrababu S, Wijesinghe HK, Uduman MS, Kannan NB, Mishra C, Prajna L. A comparative study on endothelial cell loss in nanophthalmic eyes undergoing cataract surgery by phacoemulsification. Indian J Ophthalmol. 2021. https://doi.org/10.4103/ijo.IJO_956_20.

48. Rajendrababu S, Shroff S, Uduman MS, Babu N. Clinical spectrum and treatment outcomes of patients with nanophthalmos. Eye (Basingstoke). 2021. https://doi.org/10.1038/s41433-020-0971-4.

49. Wu W, Dawson DG, Sugar A, et al. Cataract surgery in patients with nanophthalmos: results and complications. J Cataract Refract Surg. 2004. https://doi.org/10.1016/j.jcrs.2003.07.009.

50. Areiter E, Neale M, Johnson SM. Spectrum of angle closure, uveal effusion syndrome, and nanophthalmos. J Curr Glaucoma Pract. 2016. https://doi.org/10.5005/jp-journals-10008-1211.

51. Rajendrababu S, Babu N, Sinha S, et al. A randomized controlled trial comparing outcomes of cataract surgery in nanophthalmos with and without prophylactic sclerostomy. Am J Ophthalmol. 2017;183:125–33.

52. Chang JSM, Ng JCM, Chan VKC, Law AKP. Cataract surgery with a new fluidics control phacoemulsification system in nanophthalmic eyes. Case Rep Ophthalmol. 2016. https://doi.org/10.1159/000452158.

53. Vijaya L, Rewri P, George R, Balekudaru S. Cataract surgery in eyes with nanophthalmos and relative anterior microphthalmos. Am J Ophthalmol. 2012. https://doi.org/10.1016/j.ajo.2012.07.010.

54. Faucher A, Hasanee K, Rootman DS. Phacoemulsification and intraocular lens implantation in nanophthalmic eyes: report of a medium-size series. J Cataract Refract Surg. 2002. https://doi.org/10.1016/S0886-3350(01)01161-0.

55. Anguita R, Marquez J, Roth J, Salinas A, Moya R. The spectrum of uveal effusion syndrome, medical therapy, and surgical treatment. Pan Am J Ophthalmol. 2021;3(1):4. https://doi.org/10.4103/pajo.pajo_64_20.

56. Park JH, Lee EK. Medical therapy for bilateral uveal effusion syndrome in nanophthalmos. Can J Ophthalmol. 2017;52(6):e199–201. https://doi.org/10.1016/j.jcjo.2017.04.017.

57. Pautler SE, Browning DJ. Isolated posterior uveal effusion: expanding the spectrum of the uveal effusion syndrome. Clin Ophthalmol. 2014. https://doi.org/10.2147/OPTH.S75448.

58. Andrijević Derk B, Benčić G, Ćorluka V, Zorić Geber M, Vatavuk Z. Medical therapy for uveal effusion syndrome. Eye. 2014;28(8):1028–31. https://doi.org/10.1038/eye.2014.126.

59. McGhee CNJ, Dean S, Danesh-Meyer H. Locally administered ocular corticosteroids benefits and risks. Drug Saf. 2002. https://doi.org/10.2165/00002018-200225010-00004.

60. Fledelius HC, Fuchs HJ, Jensen PK, Scherfig E. Uveal effusion and ultrasonic imaging: a clinical series. Acta Ophthalmol Scand. 2002. https://doi.org/10.1034/j.1600-0420.2002.800216.x.

61. Tong B, Wang C, Qi X. Unusual rapid resolution of postsclerectomy exudative retinal detachment with topical NSAIDs therapy in a case of nanophthalmos. J Int Med Res. 2020. https://doi.org/10.1177/0300060519847376.

62. Wang JW, Woodward DF, Stamer WD. Differential effects of prostaglandin E2-sensitive receptors on contractility of human ocular cells that regulate conventional outflow. Investig Ophthalmol Vis Sci. 2013. https://doi.org/10.1167/iovs.13-12363.

63. Alm A, Nilsson SFE. Uveoscleral outflow—a review. Exp Eye Res. 2009. https://doi.org/10.1016/j.exer.2008.12.012.

64. Nilsson SFE, Drecoll E, Lütjen-Drecoll E, et al. The prostanoid EP2 receptor agonist butaprost increases uveoscleral outflow in the cynomolgus monkey. Investig Ophthalmol Vis Sci. 2006. https://doi.org/10.1167/iovs.05-1627.

65. Daniel Stamer W, Piwnica D, Jolas T, et al. Cellular basis for bimatoprost effects on human conventional outflow. Investig Ophthalmol Vis Sci. 2010. https://doi.org/10.1167/iovs.09-4955.

66. Weinreb RN. Enhancement of scleral macromolecular permeability with prostaglandins. Trans Am Ophthalmol Soc. 2001;99:319–43.

67. Farzam K, Abdullah M. Acetazolamide. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532282/

68. Moldow B, Sander B, Larsen M, Lund-Andersen H. Effects of acetazolamide on passive and active transport of fluorescein across the normal BRB. Investig Ophthalmol Vis Sci. 1999;40(8):1770–5.

69. Kwon SJ, Park DH, Shin JP. Bilateral transient myopia, angle-closure glaucoma, and choroidal detachment induced by methazolamide. Jpn J Ophthalmol. 2012. https://doi.org/10.1007/s10384-012-0159-y.

70. Vishwakarma P, Raman GV, Sathyan P. Mefenamic acid-induced bilateral transient myopia, secondary angle closure glaucoma and choroidal detachment. Indian J Ophthalmol. 2009. https://doi.org/10.4103/0301-4738.55066.

71. Guo J, Cao X, Li X. Partial thickness sclerectomy and intravitreal anti-VEGF therapy for intractable uveal effusion syndrome. Int Ophthalmol. 2019. https://doi.org/10.1007/s10792-018-0992-1.

72. Song L, Dong F, Yi C. Rapid resolution of severe exudation in uveal effusion syndrome with anti-vascular endothelial growth factor alone in a case of bilateral nanophthalmos: a case report. J Med Case Rep. 2021. https://doi.org/10.1186/s13256-021-03101-z.

73. Craig JE, Ong TJ, Louis DL, Wells JM. Mechanism of topiramate-induced acute-onset myopia and angle closure glaucoma. Am J Ophthalmol. 2004. https://doi.org/10.1016/S0002-9394(03)00774-8.

74. Roh YR, Woo SJ, Park KH. Acute-onset bilateral myopia and ciliochoroidal effusion induced by hydrochlorothiazide. Korean J Ophthalmol. 2011. https://doi.org/10.3341/kjo.2011.25.3.214.

75. Lee GC, Tam CP, Danesh-Meyer HV, Myers JS, Katz LJ. Bilateral angle closure glaucoma induced by sulphonamide-derived medications. Clin Exp Ophthalmol. 2007. https://doi.org/10.1111/j.1442-9071.2006.01365.x.

76. Malagola R, Giannotti R, Pattavina L, Arrico L. Acute cilio-choroidal effusion due to acetazolamide: unusual posterior involvement (OCT

aspects). Eye (Basingstoke). 2013. https://doi.org/10.1038/eye.2013.41.

77. Malagola R, Arrico L, Giannotti R, Pattavina L. Acetazolamide-induced cilio-choroidal effusion after cataract surgery: unusual posterior involvement. Drug Des Devel Ther. 2013. https://doi.org/10.2147/DDDT.S38324.

78. Musetti D, Nicolò M, Bagnis A, Cutolo CA, Traverso CE. Bilateral choroidal detachment and myopic shift after acetazolamide intake for laser capsulotomy. Eur J Ophthalmol. 2022. https://doi.org/10.1177/1120672120974284.

79. Lee W, Chang JH, Roh KH, Chung JK, Ohn YH. Anorexiant-induced transient myopia after myopic laser in situ keratomileusis. J Cataract Refract Surg. 2007. https://doi.org/10.1016/j.jcrs.2006.10.072.

80. Kong M, Kim JH, Kim SJ, Kang SW. Full-thickness sclerotomy for uveal effusion syndrome. Korean J Ophthalmol. 2013. https://doi.org/10.3341/kjo.2013.27.4.294.

81. Ozgonul C, Dedania VS, Cohen SR, Besirli CG. Scleral surgery for uveal effusion. Retina. 2017. https://doi.org/10.1097/IAE.0000000000001521.

82. Khatri A, Singh S, Joshi K, Kharel M. Quadrantic vortex vein decompression with subretinal fluid drainage for manangement of Nanophthalmic choroidal effusions—a review of literature and case series. BMC Ophthalmol. 2019. https://doi.org/10.1186/s12886-019-1213-z.

83. Konrád A, Penčák M, Veith M, Studený P. Uveal effusion syndrome. Case report. Ceska a Slovenska Oftalmologie. 2021;77(4).