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Diagnosis and Treatment of Uveal Effusion Syndrome: a Case Series and Literature Review

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Key words: uveal effusion syndrome; idiopathic; classification; sclerectomy

Objective To explore the diagnosis, classification, and management of uveal effusion syndrome (UES).

Methods The clinical data of 10 patients diagnosed with UES in our hospital between 1990-2010 were extracted from hospital records and analyzed, including ophthalmologic examination, ophthalmologic ultrasonography, ultrasound biomicroscopy (UBM), fundus fluorescence angiography (FFA), indocyanine green (ICG) angiography, surgical procedures, and outcomes.

Results The fundus examination of all impacted eyes showed bullous retinal detachment shifting with head position, confirmed by ultrasonography revealing retinal and choroidal detachment. UBM showed annular peripheral ciliochoroidal detachment in all cases. FFA was performed in 5 patients and revealed leopard spots without leakage from choroid into subretinal space. ICG angiography was performed in 3 patients and demonstrated diffused granular marked hyperfluorescence in the choroidal fluorescence in the very early phase, which increased with time and persisted until the late phase. Four eyes of 2 patients underwent full-thickness sclerectomies and 1 eye of 1 patient underwent subcleral sclerectomy, all of whom achieved reattachment of the retina without recurrence during 1-year follow-up.

Conclusions Comprehensive preoperative evaluation, including ophthalmologic ultrasonography, computed tomography, and magnetic resonance imaging, is crucial for accurate classification of UES and selection of proper management strategy. Surgical treatment can achieve optimal clinical outcomes for type 1 and type 2 UES.

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UVEAL effusion syndrome (UES) is a rare ocular disease, characterized by fluid accumulation within suprachoroidal space and serous retinal detachment (RD), and is combined with hyperpresbyopia or nanophthalmos in some cases.¹ It has a protracted and relapse-remitting course, and ultimately results in significantly reduced visual acuity. Since the first case of USE reported by Schepens and Brockhurst in 1963,² knowledge regarding its epidemiology, pathogenesis, classification, treatment, and prognosis has been markedly expanded. The present article summarizes the clinical courses of 10 patients (14 eyes involved) diagnosed with UES at Peking Union Medical College Hospital from 1990 to 2010, and discusses the key points in the diagnosis and treatment of this disease with a literature review.

PATIENTS AND METHODS

Patients and data collection

This retrospective case series included outpatients and inpatients who were diagnosed with UES from October, 1990 to March, 2010 in ophthalmology department of our hospital and with more than 6-month follow-up. Demographic and clinical data including ophthalmologic examination, ophthalmologic ultrasonography, ultrasound biomicroscopy (UBM), fundus fluorescence angiography (FFA), indocyanine green (ICG) angiography, surgical treatment, and outcomes, were extracted from the patients' hospital records.

Diagnostic criteria

The diagnosis of UES is based on the following criteria proposed by Uyama et al.³ (1) detection of RD in the lower periphery by fundus examination, without retinal break; (2) presence of subretinal fluid shifting with head position; (3) no leakage from choroid membrane into subretinal space revealed by FFA; (4) RD accompanied by peripheral flat or annular ciliochoroidal detachment; (5) detectable ora serrate without the compression of sclera; (6) exclusion of other causes of ciliochoroidal detachment, including decreased intraocular tension, intraocular tumor, rhegmatogenous retinal detachment, and intraocular inflammation.

Surgical procedures

For cases diagnosed in early stage, scleral buckle combined with subretinal fluid drainage and cryotherapy was used. Then the preferred procedure was changed to vortex vein decompression, during which scleral flaps measuring 3 mm × 4 mm were prepared near the vortex vein, 14 mm behind inferonasal and inferotemporal corneal limbus, to expose choroid.

From 2005, half-thickness lamellar sclerectomy with sclera measuring 5 mm × 7 mm excised at the equators of the 4 quadrants, and full-thickness sclerectomy with sclera measuring 1 mm × 1.5 mm excised from 2-4 quadrants of the sclerectomy, have been frequently chosen for surgical treatment. In some cases, triamcinolone (0.1 mL/4 mg) was injected into intravitreal space during operation.

Over the latest 2 years, subscleral sclerectomy has been adopted. This surgical procedure includes preparation of two-third-thickness scleral flaps measuring 4 mm × 5 mm at the equators of inferonasal and inferotemporal quadrants, excision of the remaining thickness of sclera in pieces of 3 mm × 4 mm under the scleral flaps, and exposure of choroid.

RESULTS

Characteristics of the included patients

From October, 1990 to March, 2010, 10 patients (14 eyes) were diagnosed with UES and treated at our hospital, including 9 males (13 eyes) and 1 female (1 eye). The patients were mostly young or middle-aged, with an average age of 42.5 years (range, 33-61 years). Among the 14 affected eyes, 9 (64%) were right eyes, and 5 (36%) were left eyes. Four patients had involvement of both eyes.

All the patients presented with decline in visual acuity and 4 (40%) reported curtain or shadow in visual field. The duration of symptoms varied from 3 months to 8 years, and the symptoms were often significantly aggravated during a period of 20 days to 3 months before the first visit at clinics. The visual acuity of 11 affected eyes ranged from hand motion to 20/400, and that of the other 3 affected eyes was relatively preserved (20/200-20/40). The intraocular pressure in all the cases was within the normal range. Dilation of episcleral veins was reported in 10 eyes of 7 patients. Fundus examination of all the affected eyes revealed bullous retinal detachment shifting with the change of the head position, with 1/4 or more of the entire retina involved (Fig 1).

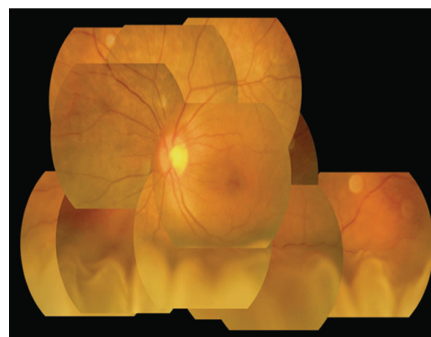


Figure 1. Fundus photograph of the left eye of a patient with uveal effusion syndrome (UES) shows retinal and choroidal detachment.

Ultrasonography, UBM, FFA, ICG angiography, and pathologic evaluation

Ophthalmologic ultrasonography revealed retinal and choroidal detachment in all the 14 eyes (Fig. 2A). In 8 patients, the eyewall thickening was observed in the affected eyes and the contralateral eyes. Small eyeballs were also revealed in 4 eyes of 2 patients, with the diameter of the eyeballs being 15/13mm and 14/14mm, respectively. UBM of the affected and the contralateral eyes revealed annular peripheral ciliochoroidal detachment (Fig. 2B). FFA was preformed in 5 patients, revealing leopard spot pattern of hyperfluorescence without leakage of fluorescence (Fig. 2C). ICG angiography was performed on the affected and the contralateral eyes in 3 patients, demonstrating diffused granular hyperfluorescence in the choroidal fluorescence in very early phase (10-17s after ICG injection), which increased over time and persisted until the late phase (Fig. 2D).

During the operations, the thickening of the sclera by 2-3 mm was documented in most cases. Biopsy and pathologic evaluation was performed for 2 eyes from one patient and revealed fibroplastic proliferation and hyaline degeneration of lamellar sclera and episclera (Fig. 3).

Surgical treatment and outcome

Surgical treatment was provided to all the patients. One eye in 1 patient underwent scleral buckle, and the condition of choroidal and retinal detachment persisted after operation. Two patients (2 eyes) received vortex vein decompression and still had mild RD after the operation. Among 5 eyes of 3 patients which underwent full-thickness sclerectomy, 4 eyes of 2 patients had complete reattachment of retina (Fig 4), in which relapse occurred in 1 eye after 2 years. One eye in 1 patient still had moderate RD after the operation, which lasted for 3 months. For 4 eyes of 2 patients which underwent lamellar scleral resection, all still had moderate RD. Second surgery of full-thickness sclerectomies were performed in all the 4 eyes, with intravitreal triamcinolone (IVTA) injection in 2 eyes of 1 patient. Reattachment of retina was achieved in the 2 eyes with IVTA injection, and significant improvement in the other case without IVTA injection was also observed. For 2 eyes of 2 patients which underwent subscleral sclerectomy, one had reattachment of retina without recurrence in 1-year follow-up, while the other eye still had moderate RD lasting for 3 months.

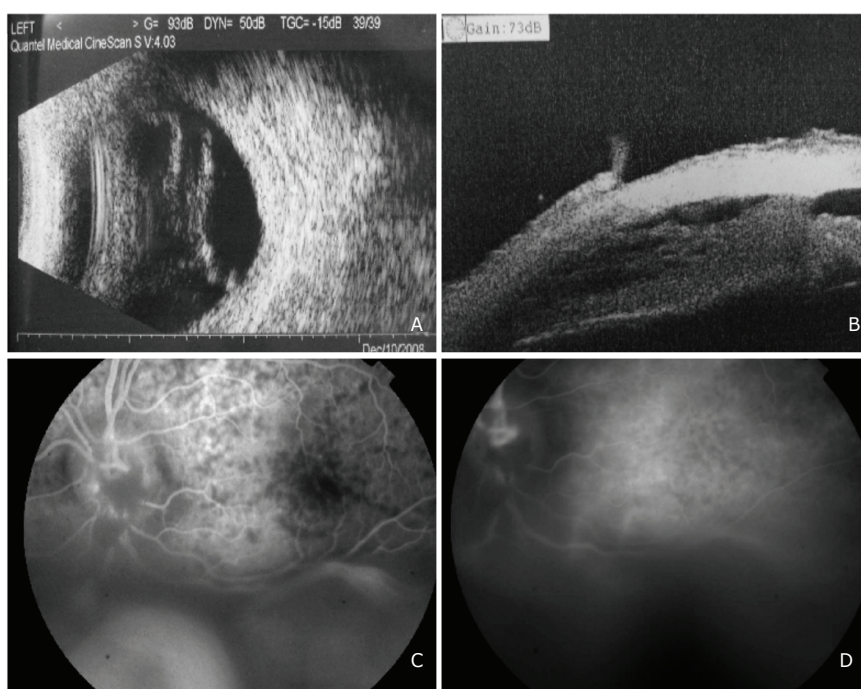


Figure 2. Preoperative evaluation of 3 patients with UES.

- A. Ophthalmologic ultrasonography reveals retinal and choroidal detachment and thickening of the eyewall.
- B. Ultrasound biomicroscopy shows liquid accumulation under the ciliary body and the thickening of sclera.
- C. Fundus fluorescence angiography shows hyperfluorescence with leopard spot pattern at the posterior pole, without leakage.
- D. Indocyanine green angiography demonstrates diffused granular hyperfluorescence in the choroid fluorescence in very early phase.

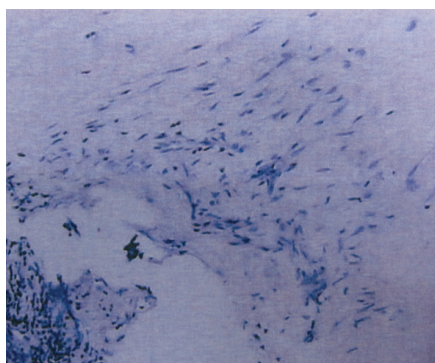


Figure 3. Histologic specimen of sclera excised during operation, showing excessive fibrous tissues in sclera and hyaline degeneration. HE $\times 60$

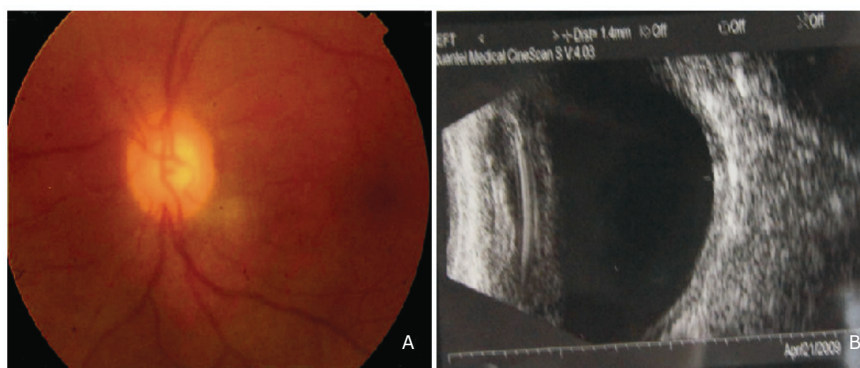


Figure 4. Follow-up evaluation of a UES patient in the fourth month after full-thickness sclerectomy.
A. Fundus photography shows complete reattachment of retina and choroid.
B. Ophthalmologic ultrasonography confirms retina and choroid reattachment, and the remaining thickened eyewall.

DISCUSSION

Only individual cases or case series of UES have been reported in literatures so far, without large clinical studies. UES shows no obvious genetic predisposition, and its risk factors remain unclear. In our case series, the majority of the patients were middle-aged men, with bilateral eyes affected, consistent with the finding of previous reports.¹⁻⁶ The clinical course of UES was typically prolonged, rarely accompanied with systemic diseases.^{4,5} In ophthalmologic examination, subretinal fluid shifting with head position was observed in all cases and dilated veins on the surface of sclera in some cases, with normal intraocular pressure. Additional evaluation allows for detection of further demonstrations, for instance, ultrasonography can show the thickening of eyewall and FFA can demonstrate the characteristic leopard spot pattern of the retinal pigment epithelium (RPE).^{7,8}

UES was previously classified into 2 types: one type was those accompanied by hyperopia or nanophthalmos, and the other type was idiopathic ones. The new classification proposed by Uyama et al³, which is more practical for clinical application and has been adopted in our hospital,

consists of 3 categories: type 1 and type 2 both have scleral dysfunction, with type 1 accompanied by microphthalmia and type 2 having normal eyeball; type 3 has normal eyeball with none documentable scleral dysfunction.³ The percentages of these 3 types in different case series varied.^{3,6} Among the cases in our study, scleral thickening was observed in 80% of the 10 patients, with small eyeballs seen in 4 eyes of 2 patients. For accurate preoperative classification of the disease, computed tomography (CT) and magnetic resonance imaging (MRI) can be used to further evaluate the presence of scleral thickening and measure the thickness of sclera,^{1,3,9} which unfortunately have not been performed on our patients. Biopsy during operation and subsequent pathologic evaluation are also helpful for demonstrating scleral dysfunction as shown in this report.

The pathogenesis of UES has long been the focus of relevant researches. So far, two possible mechanisms have been proposed to cause the fluid accumulation in supra-choroidal space. One is reduced scleral permeability. Trelstad et al¹⁰ discovered scleral thickening in UES patients with nanophthalmos, and disarrangement of collagen fiber bundles of variable sizes. Alcian blue staining and electron microscopy revealed the deposition of glycosa-

minoglycan (GAG) in the stroma of collagen fiber bundles, resulting in reduced scleral permeability. Jackson et al⁸ found irregular arrangement of collagen fiber bundles of sclera in all UES cases, but the sediments among the collagen fiber bundles were more prominent in nanophthalmos cases. Irregular collagen fiber bundles and abnormal deposition of GAG in scleral stroma increase the resistance of transscleral fluid outflow. The other theory involves compression of vortex vein by thickened sclera, leading to congestion of choroidal vein. This hypothesis is based on the observation from clinical studies reporting increased pressure of choroidal vein in some cases, indicated by dilation of episcleral veins and/or hyperemia of Schlemm's canal.^{11, 12} In Rhesus Macacus models, however, clinical or histological change of choroidal or retinal detachment did not occur after blocking all the vortex veins,^{11, 13} suggesting that venous obstruction might merely be a secondary change after scleral swelling resulting from protein leakage. One research reported that in UES patients, the protein level in subretinal fluid, which contains mainly albumin, was as high as 200 g/L, 5 times of that in serum.¹⁴ But there was also one study showing that in idiopathic UES patients without reduced eyeball size and detectable scleral thickness, anatomic abnormality of vortex veins and the reduced caliber of the veins could be found.¹⁵ In some cases, vortex veins were even absent in some quadrants.¹⁵

In the present study, ICG angiography of 3 patients demonstrated diffused granular hyperfluorescence in the choroidal fluorescence during very early phase, which persisted and increased during the late phase. This finding indicates high vascular permeability of choroidal vessels, and the accumulation of large amount of fluid in choroidal stroma caused by thickened sclera. ICG angiography also confirmed involvement of bilateral eyes in all the 3 patients, partly consistent with published case series where bilateral involvement occurred in 65% of patients.¹⁶ In the early stage of the disease, fluid accumulates in choroid, especially in suprachoroidal space, when annular peripheral ciliochoroidal detachment can be observed but patients are usually asymptomatic. As the disease progresses, the accumulation of choroidal fluid gives rise to metabolic disorder of RPE, in which the pumping function of RPE is impaired, and the trans-RPE fluid flow becomes difficult. With the constant accumulation of subretinal fluid (instead of the leakage from choroid to suprachoroidal space), serous RD occurs. In this stage, the ocular symptoms gradually appear, involving unilateral or bilateral eyes. It is sclera dysfunction that triggers the whole process of UES.^{1, 7, 8}

Improved understanding on the pathogenesis of UES

provides theoretical basis for the selection of proper surgical treatment. During 1980s, Brockhurst¹² recommended the resection of surrounding scleral wall to decompress the vortex vein. This operation is generally difficult, as excessive bleeding occurs commonly. Later, Gass⁷ achieved better result by using full-thickness sclerectomies for the first time, without vortex vein decompression. Johnson et al¹⁷ conducted full-thickness sclerectomies on 20 patients with idiopathic UES. In that report, after one or two sclerectomies, subretinal and ciliochoroidal fluid completely resolved within 6 months in 95% of the cases, with the retinal reattachment taking place within an average of 2.4 months. During a 41-month follow-up, 25% of the cases experienced relapse, but all recovered either naturally or after a second operation. The visual acuity was improved or stabilized in 90% of the affected eyes. Uyama et al³ conducted subscleral sclerectomy on 19 eyes of 16 patients, in which a small piece of choroid was excised subsclerally to expose choroid. The principle of this procedure was similar with that of trabeculectomy, in which an alternative pathway for the outflow of intraocular fluid is constructed. Among a total of 17 eyes with type 1 or type 2 UES, 16 (94%) completely recovered after the operation, without any complications.³ This operation gradually gains popularity for its simplicity, operability, and satisfactory outcome. Suzuki et al⁹ conducted subscleral sclerectomy on a 16-year-old patient with nanophthalmos using mitomycin C (0.2 mg/mL), which mitigated the postoperative scarring effect with satisfactory result. The surgical outcome for type 3 UES was not satisfactory, perhaps because scleral dysfunction was not the main cause of subretinal fluid accumulation in that type.

Other less invasive treatments have been studied, including systemic application of glucocorticoid, non-steroid anti-inflammatory drugs, and laser photocoagulation, which all achieved little effect.¹ Some studies suggested that prostaglandin analogs might increase the outflow *via* uvea and sclera by improving the scleral permeability, thus might reducing fluid accumulation in UES patients.¹⁸ However, this conception has not been clinically proved.

Postoperative ICG angiography may reveal long-term and slight abnormality of choroid. Retinal detachment and ciliochoroidal detachment may recur in some cases, but is usually responsive to the second operation.^{1, 3, 7, 9, 17} During the second operation, the adherence of Tenon's capsule and sclera resulting from the first operation should be carefully cleaned. The scarred sclera should also be resected to ensure that choroid is adequately exposed and the fluid in suprachoroidal space can readily flow out to restore the normal retina position.

Without operation, the natural process of UES usually results in a progressive RD of variable degree, a protracted course, and gradual decline in visual acuity. In a previous case series including 20 cases without surgical intervention, 9 (45%) experienced spontaneous reattachment of retina and choroid within a period from 3 months to 8 years after diagnosis, while the remaining 11 cases (55%) had persistent RD until the end of that study.¹⁷

In summary, this case series of Chinese patients with UES share similar epidemiological and clinical characteristics with previous reports, suggesting a weak influence of ethnical difference on this disease. As shown in the present study and other ones, comprehensive preoperative evaluations, including ophthalmologic ultrasonography, CT, and MRI, are of significant value for the classification of UES. Researches on the pathogenesis of UES have played a crucial role in selecting practical and effective operation methods. For type 1 and type 2 UES patients, surgical treatment can achieve good clinical outcome.

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