Extensive persistent pupillary membranes in teens

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Abstract: We reported a 17-year-old young male with unilateral extensive hyperplastic persistent papillary membranes, present since birth, with poor visual acuity. The membranes were excised surgically; visual acuity improved. Extensive persistent papillary membrane can be removed safely by surgical methods if they are large enough to obscure the papillary axis and affect visual acuity.


Keywords: Pupillary membrane

Introduction

In 1986, Cibis and associates reported a distinct variety of neurocristopathy different from Rieger’s anomaly and persist papillary membranes, called congenital papillary-iris-lens membranes (1). The has been hypothesized that this condition is unilateral and represents ectopic iris on the lens with abnormal iris stroma and the anterior chamber angle from aberrant induction, migration, and regression of neural crest cells (2). The prevalence of persistent papillary membranes (PPM) is roughly 4% to 5% now. Severity varies considerably; most consist of fine, diaphanous that have no impact on vision. Most PPMs which belong to a congenital anomaly require no treatment because they usually undergo considerable atrophy during the first year of life and only rare cause visual impairment. The remnants of pupillary membrane are common clinical finding in about 95% of healthy neonates and 20% of adults. Besides, they are more common in premature babies (3). However, the PPMs are usually nonpathogenic physical signs of normal intrauterine development. Moreover, the histopathologic examinations of PMMs revealed an increased number of fibrocytes and collagen in the iris stroma. The increased amounts of collagen in the stroma are thought to resultant in delayed or lack of atrophy of the membrane during normal development (4). They presented the remnants of anterior tonica vasculosa lentis and their regression begins from the 6 month of gestation which leads to complete disappearance at 8 month.

When present after birth, they still continue to regress in the first year of life. Sometimes extensive persistence of the papillary membrane is rare and it may not regress unfortunately. However, the papillary membrane are dense and cover the visual axis, the management of patients with PPMs remained controversial, and a case-dependent decision of balancing the risk of surgery of against amblyopia needs to be made (5). The PPMs are non-pigmented strands of obliterated vessels and may attach secondarily to the lens or cornea at times. As the pupil becomes smaller, the vision should decrease (6). Therefore, the patients with occluded pupils from extensive PPM may complain about blurred vision. Although most PPMs do not usually affect visual acuity, the large hyperplastic membranes which are dense to obscure the pupillary axis and should result in amblyopia in children or a decrease in vision in adult may require removal (7). Therefore, even only smaller percentage some form of intervention is required. Pharmacological therapy, and laser treatment may need to evaluate at first. If failed, surgery had been employed to clear the visual axis and optimize visual development (8).

In this article, we reported the case of a 17-year-old young male who had received surgery treatment for extensive persistent papillary membranes in right eye that causing poor vision since childhood.

Case Report

A 17-year-old young boy complained of photophobia, poor visual acuity in his right eye since childhood. He searched for medical help from our hospital (Fooyin University Hospital) for the significant visual loss and cosmetic problems last year (in 2016). On examination, the best-corrected visual
acuity under normal illumination was 0.1 (6/60) in right eye and 0.5 (6/12) in left eye. Refraction was -2.25 – 1.50 x 75 in his left eye (OS), however, proper refraction could not be performed because of poor fundus reflex in the right eye (OD) due to dense PPM. His visual acuity of left eye could reach to 1.0 (6/6) by spectacle and only remained 0.1 (6/60) on right eye unfortunately. The patient told to us that amblyopia (OD) was diagnosed by other ophthalmologists since childhood and he did not receive any therapy. Now, his only symptom was mild glare from lights at night, which he described as stable and tolerable from tolerable for many years. Slit-lamp biomicroscopy revealed dense pupillary membrane obscuring the visual axis and a few small pinholes on the membrane (OD) (Fig.1). A cover-uncover test was normal. The normal anterior segment and posterior fundus was found in the left eye, however, retinoscopy was difficult to evaluate the red reflex accurately because of the dense PPM in right eye. We tried to pharmacologic dilation of the pupil of left eye, but we all failed. Furthermore, the gonioscopy revealed a closed anterior chamber angle in 270 degrees but the intraocular pressure was normal (15mmHg). Moreover, ultrasound biomicroscopy confirmed the vascular lesion was restricted to the anterior lens capsule without posterior extension (Fig.2), and there were no clear structure anomalies of the anterior segment. According to his statements, no any past ocular, medical, family or traumatic history mentioned.

Because of the too dense pupillary membrane of left eye, surgery was arranged after 2 weeks of OPD visiting. The pupil was dilated with atropine 1% to stretch the dense pupillary membrane as soon as possible. With the surgeon (Dr. Horng) at the superior site, clear incision of 4.0 mm was made at the 12 o’clock position. Sodium hyaluronate (ophthalmic visosurgical device; OVD) 1% was injected into the anterior chamber and behind the pupillary membrane to separate the membrane from the lens carefully. Additional OVD was injected beneath the iris strands after the central adhesion were lysed. After all possible adhesion between the pupillary membrane and the normal iris was cut by intraocular lens scissors (Vannas scissors) in tracamerally, the isolated and floating pupillary membrane was removed completely with a forcep, and the corneal incision was closed with a 10 Nylon suture.

Post-operative medications included topical prednisolone acetate 1% drops 4 times daily, ciprofloxacin eye drop each time 2 hours until going to bed, cyclopentolate drops daily and neomycin/polymyxin B/dexamethasone ophthalmic ointment at night tapered over 3-4 weeks. Postoperative examinations were performed 1 day, 1 week, 2 week and 1 month following surgery, including assessment of visual acuity, pupil size, symmetry, and reactivity; anterior chamber depth; and intraocular pressure when possible. One month later, no significant inflammation, iridodialysis, fibrin deposition, synechiae or other complications expect a few little small patches of iris atrophy present. We had successfully clearance of the visual axis and the mild round pupil was found. Two month operatively, the refractive error could finally show - 1.75 - 0.50 x 5 by autofractor. The best corrected visual acuity had only improved 0.4 (6/15) because of the persistence of amblopia since childhood.

**Fig. 1:** Slit-lamp biomicroscopy revealing dense and large pupillary membrane cross the central portion of pupil (Green line: land mark of length measurement ). A very small pinhole in the central membrane.

**Fig. 2:** B-scan ultrasonography of right eye reveal a flat retina and no abnormal findings in the vitreous cavity.

**Discussions**

The pupillary membrane is formed by buds from the annular vessel of the iris that grow centrally to
form the anterior vascular tunic of the lens. During embryonic development, the iris initially forms as a solid sheet of mesodermal tissue known as pupillary membrane. It is composed of vessels and mesenchyme and lies ventral to the lens. On the dorsal part of the lens, the hyaloid vessels form a network around the posterior lens capsule. These vessels extend anteriorly to anastomose with the network of vessels in the pupillary membrane. The pupillary membrane vessels are derived mainly from the anterior ciliary arteries. Centrally the pupillary membrane is almost acellular except for three or four tiers of small blood vessel arcades (9,10). By the seventh gestational month, the central portion of the pupillary membrane has opened. At 8 1/2 months, involution is usually complete so that only the first arcade remains as the lesser circle of the iris. However, the severity and associated finding vary. Very small percent that consists of diffuse, dense membranes that cause deprivational amblyopia (11,12).

When an extensive PPM is present at birth, considerable atrophy of the membrane is to be expected during the first year. If remnants remain after the first year, they will probably be present to some extent thereafter. They typically regress within the first weeks after birth and the probability of regression may depend on the composition of membrane. They may also be large and dense enough to affect vision, necessitating intervention. In older children, monitoring for the development of amblyopia can usually be achieved in the clinic (13,14). However, owing to the congenital nature of the anomaly, patients with PPMs are usually preverbal on presentation. Therefore, the decision to operate hinges on identification of those patients with PPMs substantial enough to potentially compromise visual development (15). Kraus et al. reported that required surgery was found to have some characteristics: impaired red reflex, obscured view of the fundus through the lesion, and decreased visual acuity as measured by SSVEP (16). The decision to operate is based on the density of the membranes, due to the concern of deprivation development with delayed treatment. In the opthalmic literature, authors recommended surgical treatment of this condition before amblyopia develops (17).

Most cases are unilateral and sporadic, however, familial and infectious agents (e.g. Toxoplasma gondii, rubella) were also reported (18,19,20). Some authors suggested that it may be an autosomal dominant inherited trait. However, Sari et al. reported that PPMs could have been caused by a recessive gene in 3 siblings from white family. The causes of PPMs and postponement of its involution are not known. Although there are reported cases of autosomal dominant inheritance, most cases are sporadic. Inflammation or metabolic factors preventing the closure of blood vessels, thus precluding resorption, are not proven (3,21,22). The remnants of the pupillary membrane as white strands are seen clinically in 17% to 32% cases, but persistent functional vessels are found in only 0.3% (17). It is found that unilateral PPMs might be more likely than bilateral ones to produce amblyopia, but a trial of conservative therapy may nevertheless be appropriate before surgical intervention (23). Moreover, PPMs may be seen in isolated, or in association with other abnormalities, for example, aniridia, anterior segment abnormalities (goniodysgenesis and aniridia), microcornea, megalocornea, posterior keratoconus, cornea plana, cataract, anterior capsular opacity, strabismus, uveitis, posterior segment anomalies (congenital retinal detachment, retinal folds and hypoplasia of the macula or optic nerve head), Tetralogy of Follot, Zellweger syndrome, Donnai-Barrow syndrome, and Floppy Iris syndrome (24,40). However, PPMs have not been associated with systemic disorders in the past literature.

Persistent papillary membranes are most often seen are fine networks of strands and have no clinical significance. However, the most complication of the PPMs is ambylophia which could impact the human vision. Moreover, a few cases may show some trouble problems. For example, the type of pupil-iris-lens membrane could progress toward pupillary occlusion, papillary obstruction with secondary iris bombe and even angle-closure glaucoma. Furthermore, spontaneous hyphema secondary to a vascularized fragment of persistent papillary membrane has ever been reported (25,45).

When a nonverbal child has a dense membrane, it is often difficult to assess whether this membrane is causing amblyopia (26). There are three methods in treating the PPM including medical, laser lysis and surgery now. However, the choice of surgery or laser depends on the age of the patient and the characteristics of the membrane (27). Lee et al suggested that medical treatment solely was instituted until 1 year of age. Surgery was chosen when there was no improvement or some deterioration of visual acuity with medical treatment (23). Moreover, a decision to operate was made when mydriatic drops failed to obtain a clear central papillary aperture and the vision decreased. Laser lysis is not suitable for younger children and for fibrotic, thick, or tough pupillary membrane (6). As for surgery, Lambert et al. suggested that the membrane should be excised and enlarged the pupil with irs sphieotomies as larger as possible (28). Kumar et al and colleague reported that surgical intervention has been attempted
in those rare instances in which visual acuity has been compromised, the results have proved unsatisfactory (29). The major PMMs are fine strands that regress within the first weeks of life. Some may be amlyogenic, the decision to excise them depends on an assessment of their likely effect on visual development. Similar to congenital cataract, the amblyopic risk of a PMMs could be lead to irreversible vision loss. As the pupil becomes smaller, the vision is limited by the effects of diffraction and decreased retinal illumination. Even Kolin et al. suggest that all hyperplastic PMMs in children do not cause amblyopia and may not require any intervention (30). However, most of the researchers favor the created hole in dense PMMs. For example, Miller and Judish reported that a pupil of at least 1.5 mm is required for optimum vision (6). Furthermore, Viswanathan et al. demonstrated that the pinhead-sized fenestration in the membrane was inadequate in size and eccentric in location, justifying surgical intervention. After the holes were open, the refraction may be found easily. Most of the PMMs showed anisometropia, especially anisometropic hyperopia (15). It is interesting that Kolin et al. reported that bilateral PMMs is less amblyopic than unilateral PMMs and even patching the good eye in a patient with unilateral membrane could resolve the amblyopia without resorting to surgery (30). Reynolds et al. suggested that in newborns, it is especially important to assess whether the membrane involves the visual axis because the decision to operate needs to be made in the first 6 months when acuity is developing and judgment can be difficult (31). Many older patients received surgery but the result is not satisfactory. For example, Gupta et al and his colleagues took into consideration that adequate clearing of the pupillary axis was achieved with improvement of vision in simulated sunlight (32). However, there is not much improvement in the visual acuity because of the existence of visual deprivation amblyopia in older patients.

Medical therapy is the first choice in treating PMMs. Kim et al reported that even PMMs could lead to satisfying visual results with conservative treatment (25). Visual acuity decreases with decreased retinal illumination. Diffraction substantially decreases visual acuity when the pupil diameter is less than 1.5 mm. The smallest useful pinhole size was said to be 1.5 mm. If adequate dilation is not obtained, amblyopia remains a threat. Refraction as the pupil enlarges is important to permit correction of astigmatism, which should be suspected because of membrane-lens contact. Leo and Kurt reported that small PMMs can be managed conservatively. A regimen of mydriatics, refractive correction and patching for amblyopia has been employed successfully in some cases (13,17). Yu and his co-workers suggested that congenital PMMs requires surgical intervention when progressive occlusion of pupil occurs or when there is threat of angle closure glaucoma (26). Most PMMs are asymptomatic and require no treatment or only medical treatment with a mydriatic agent. Pupillary dilation may be useful in some patients to provide a better optical dilation. Mydriatic drops to maximize the papillary opening, close monitoring of the fixation pattern, and occlusion therapy as indicated until the minimum undilated pupillary dimension is 1.5 mm should insure normal visual development. Amblyopia treatment by occlusion was applied when needed according to the age of the patients after surgery (33).

In the ophthalmic literature, authors recommend surgical treatment of this condition before amblyopia develops. Surgical excision and laser lysis of a membrane have been advocated, and the choice depends on the patient’s age and the characteristics of the PMMs (the size and thickness of membrane, and involved area if cross the pupil) (34). For example, laser membranectomy is technically difficult in young children and may not be effective in patients with thick, fibrotic membranes. Hence, laser lysis is obviously not a procedure that can be done for younger children in most facilities. Moreover, membranes present at birth are often more fibrotic, thicker, and tougher, and the laser may not be an option with such membranes. However, in older children and adults either of the two options can chosen (35). Gupta et al. even believed that Nd: YAG laser sectioning of the membranes has definite advantage over surgery and should be preferred (32). We thought that the choice may take into account the complexity of the issues and the greater variability of congenital PMMs. Wallace et al. even reported that management could be conservative even in cases of dense bilateral PMMs. Factors favoring conservative management could include visualization of red reflex and fundus with dilation (36). A trial of refractive correction and amblyopia therapy is recommended before deciding on surgery on surgery for this condition (36). Reynolds et al. even reported that care must b taken to avoid the use the strong cycloplegic agents in hyperopic infants unless optical correction is con-currently used (31). If an adequate opening is not obtained, amblyopia remains a threat. Refractive defect and amblyopia should be treated immediately if the pupil opening is adequate. After the initial correction, these patients should be treated with optical correction and partial occlusion at least for a periods of 3-6 months (patching the involved eye for a few hours each day). However, Lee
et al. found that patients could be treated with mydriatics and occlusion therapy for approximately 11 months with good compliance and outcome (23). As to the time, no effect of age was found in children 3 to 7 years of age treated for amblyopia. Recently, a newer report showed that amblyopia could be treated beyond 7 years of age. Recently, most of the ophthalmologists take into consideration that if PPMs are appropriate managed, the visual prognosis can be relatively. Besides, surgery must be considered within the first few weeks if the pupil does not respond to mydriasis. However, we suggested that aggressive treatment for patients with PPMs is necessary because of un-detectable outcome.

Laser lysis (non-surgical technique) is another method used to manage the extensive PPMs. Most of the cases were performed by using an Nd: YAG laser (photodisruption) which may disrupt superior quadrants of the adhesion between the strands of the membrane and the collarette of normal iris (32, 35, 37). Hence the membrane is displaced downward, clearing the visual axis (38). Pigment dispersal, microhemorrhage, recurrent hyphema, uveitis, and increased intraocular pressure are the major complications after laser (29). Our patient had Medusa-like PPMs, with numerous adhesions, so it was difficult and risky to disrupt all adhesion in the superior quadrants with a laser. Tsai and his co-workers suggested that laser method should prevent damage to the lens and corneal endothelium (38). Furthermore, surgeons can manage every part of the membrane easily. This helps to completely remove the PPMs. It is interesting that some ophthalmologists used the Nd: Argon laser (photocoagulation) other than Nd: YAG laser (39). For instance, Ahmad et al. used the Nd: YAG laser to cut the dense PPMs because the patients may feel pain and the procedure should cause pigment dispersion and bleeding (17, 23). Todd et al. found that Nd: YAG laser treats the non-vascularized PPMs occluding the visual axis as well as for recurrent spontaneous hyphema associated with anomalous iris vessels, iris nevi, vascular tufts of the iris and abnormal anterior chamber angle vessels. Therefore, they suggested the usage of Nd: YAG laser is advantage and another choice (41). Vega et al. also suggested that they treated PPMs by Nd: YAG laser membraneotomy successfully. These patients were older, i.e., teenagers to adults, and were treated for either cosmetic reasons or to improve visual function in bright light (The final vision may reach 20/20 – 20/40) (42).

The main goal is to construct a papillary opening in these cases to prevent deprivation amblyopia. Surgical management of the papillary membrane was indicated to create an optimum papillary aperture, recognize and correct the existing refractive error and anisometropia, performed a detailed examination of the eyes and begin to receive occlusion therapy at least 6 months (43). The advantage of surgical intervention is reserved for large, dense PPMs that obscure the papillary axis. Therapy of PPMs involves cutting the membrane in the anterior chamber with Vannas scissors via a wound. Besides, the membrane could also be removed by iris spatula, vitrectomy probe (cutting port), peeling instruments, suction cutters and vitreous scissors (12, 38, 44). However, some PPMs are numerous, elastic and slippery and it is technically difficult to cut and remove. Furthermore, some of the surgeries should be combined with pupioplasty, and peripheral iridectomy to prevent from glaucoma. Besides, it is important not to cut the normal iris when dragging and cutting the membrane for avoiding the formation iridodialysis (38). Under a tilted microscope and the suggested surgical position, the PPMs and the normal iris can be clearly differentiated; otherwise, there is a risk for iridectomy. A patch of iris atrophy is a common but harmless postoperative complication; however, traumatic cataract can be induced if the lens is accidentally damaged. Oltra et al. proposed that we must avoid crossing the pupil (decreased the incidence the traumatic cataract) and potentially damaging the lens capsule, several paracenteses may be necessary. It may not be possible completely remove the membrane from the angle, although we have not found that this causes any complications or later recurrences (47). Further enlargement of the pupil with sphincterotomies was not needed here; however, we should enlarge the pupil sufficiently to prevent papillary block glaucoma and the membranes recurrence (43). Tsai et al. suggested that we had better make corneal wound in each quadrant (38). Hence, we could manage every part of the membrane easily. This helps to completely remove the PPMs. It is important not to cut the normal iris when dragging and cutting the membrane strands. It is also important to avoid causing iridodialysis. Besides, we also must pay attention to the problems of infection, inflammation, and damaging the corneal endothelium when dragging. However, surgery can be performed safely in fibrotic, thick, and extensive papillary membranes by experienced ophthalmologists. Besides, surgical management is fraught with risk of anesthesia, intra-operative bleeding and infection.

According to the past literature, most amblyopic patients with the PPMs showed unilateral deprivation; however, bilateral anisometropic amblyopia was relatively rare.

After removing the PPMs, bilateral refractive
amblyopia can develop in children with large amount and most cases of un-correct hypermetropia, astigmatism, or both in each eye. Therefore, Wallace et al and his workers revealed that treatment consists of prescribing the appropriate refractive correction with the possible addition of occlusion or pharmacologic penalization. Thus, Lee et al. reported that it seems that most cases with PPMs are not significant enough to have complaints and so might go undetected. Our patient was beyond the age of visual development, therefore, the outcome is not good. Indeed the surgery for removing PPMs is not warranted even if significant amblyopia exists. However, surgical intervention was considered because of the patient’s significant visual loss in bright light and sunlight and the troublesome cosmetic problems. Besides, Lee et al reported that surgical intervention would accelerate the effects of the occlusion therapy, and this led to some mild improvement in vision. Furthermore, Pandey and Kumur all claimed that in older children and adults with hyperplastic PPMs, treatment is not warranted if significant amblyopia exists. However, intervention may be considered if there is not much visual impairment under normal illumination but a significant visual loss in bright light. According to the previous research, poor visual outcome after therapy is initial poor fixation pattern, unilateral PPMs and late discovery.

We reported a 17-year-old young male with PMMs in right eye when he was born. He received complete removal of the dense papillary membrane without any complication last year. Because of delayed time for treating, only spectacle correction was for the patient, however, the occlusion therapy was un-necessary. His best corrected visual acuity only mild reached 6/15. Early detection and treatment regimen design was important in this experience.

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