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Late vitreous hemorrhage in patients with regressed retinopathy of prematurity

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Abstract

Purpose—To describe the characteristics of eyes with late vitreous hemorrhage in children with a history of regressed retinopathy of prematurity (ROP).

Methods—The medical records of consecutive patients with regressed ROP presenting to our institution with late vitreous hemorrhage between 1995 and 2006 were reviewed.

Results—Thirteen patients (14 eyes) were identified. All patients had stage 3 or higher ROP. Prior treatments included cryotherapy in three eyes, laser ablation in eight eyes, and laser followed by vitrectomy for retinal detachment in two eyes. Three eyes had had no prior ocular surgery. Age at late vitreous hemorrhage ranged from 10.8 months to 15 years (mean, 8.4 years). At the time of late vitreous hemorrhage, no eyes had active neovascularization, three eyes had a history of trauma, and three eyes had concurrent retinal detachment; eight eyes were observed (57%) and six (43%) were treated with vitrectomy.

Conclusions—Late vitreous hemorrhage can occur in patients with regressed ROP years after the vascularly active phase of the disease. It likely results from abnormal vitreoretinal traction on otherwise normal retinal vessels or from a normal amount of traction on residual cicatricial tissue. Vitreous hemorrhage may occur in the absence of trauma, retinal tears, retinal detachment, or active neovascularization. With appropriate management, most patients maintained their baseline vision.

In a previous report¹ one of the authors (GBH) described the clinical features of vitreous hemorrhage in 168 children seen at our institution over eight consecutive years. Although children with active retinopathy of prematurity (ROP) were excluded from that series, we found that the most common underlying diagnosis in children with spontaneous vitreous hemorrhage was regressed ROP. The purpose of this report was to describe the clinical features of this subgroup of children in more detail and to identify the pathophysiology of vitreous hemorrhage in these patients. Three additional children with vitreous hemorrhage and regressed ROP seen at our institution since the prior publication were added to the study.

Methods

The Institutional Review Board of the Emory University School of Medicine approved this study. Eligible patients were identified by a computerized search of the Emory Eye Center database for patients age 18 years and under with the International Classification of Diseases-9 diagnostic code “vitreous hemorrhage.” The subgroup of these patients, who also had a history of ROP, was isolated, and the charts were reviewed to subselect patients with

clearly regressed ROP at the time of vitreous hemorrhage. A retrospective chart review was then performed. Regressed ROP was defined as ROP that had either undergone spontaneous involution or had involuted and become stable after treatment. Patients were excluded if active neovascular ROP could not be definitively ruled out as the etiology of their vitreous hemorrhage. Hence patients under 10 months of age were excluded. Clinical features of the remaining patients were entered into a spreadsheet. The following clinical information was retrieved: gestational age, birth weight, highest stage of ROP, refractive history, history of surgical treatment prior to and following vitreous hemorrhage, visual acuity prior to and at the time of vitreous hemorrhage as well as at the final follow-up examination, and etiology of the vitreous hemorrhage. Not all information was available for every patient. Since this was a retrospective study, the patients were not assessed under a systematic protocol. In all patients a dilated fundus examination was performed in an attempt to determine the etiology of the vitreous hemorrhage. If the hemorrhage was mild and the view of the fundus adequate to identify a retinal detachment or retinal tear, and none were found, then the patient was observed. If the vitreous hemorrhage was dense, then B-scan ultrasonography was performed to identify a retinal detachment or tear. If neither was identified, then the patient was observed for a limited time to allow for spontaneous resolution of the hemorrhage. If a retinal tear or detachment was identified on examination or ultrasound, or if the vitreous hemorrhage failed to clear with time, appropriate surgical intervention was undertaken. An examination under anesthesia with ultrasound was performed if the office-based examination was inadequate to rule out treatable pathology.

Results

Sixteen patients (18 eyes) were identified with ROP and vitreous hemorrhage. Of these, 3 patients (4 eyes) were excluded because active ROP could not be definitively ruled out, leaving 13 patients (14 eyes) for analysis. The clinical features are detailed in Table 1 and summarized below.

Mean age at presentation was 8.4 years; median age was 8.6 years (range, 10.8 months to 15 years). Age at presentation equaled the age at onset of vitreous hemorrhage except for Patients 2, 4, 8, and 9, in whom the hemorrhages were found incidentally, but after prior documentation of clear media following the regression of active ROP. Patients were followed at our institution for a mean of 12.1 months after vitreous hemorrhage (range, 1.4 months to 4.3 years).

The mean gestational age and birth weights of the patients were 25.3 (range, 23 to 27) weeks and 705.8 (range, 450 to 950) grams, respectively. All other salient clinical features are shown in Table 1. Although most patients presented with visual complaints (pain, blurred vision, new onset floaters, or parental observation of reduced visual function), there were four patients (five eyes) in whom the vitreous hemorrhage was found incidentally. These patients did not complain of a change in vision for a variety of reasons. One patient with a mild vitreous hemorrhage was deaf and mute, with a history of difficult assessment of visual acuity. The second patient had peripheral vitreous opacities in both eyes that were not visually significant. The third patient was under 1 year of age and had a clear visual axis. The last patient was found to have diffuse white vitreous haze suggestive of old hemorrhage, with 20/100 vision. This patient's last documented visual acuity was 20/60 at an outside institution 5 years earlier, with concern for amblyopia noted retrospectively.

All patients had a history of documented stage 3 or higher ROP. Most patients had received prior treatment in infancy for acute ROP, but two patients (three eyes) had never received any prior treatment other than observation. Treatments for acute ROP in infancy included

cryotherapy (three eyes), laser ablation alone (seven eyes), and laser ablation followed by vitrectomy (one eye).

Seven eyes presented with dense, diffuse vitreous hemorrhage with no view of the retina. All of these eyes were evaluated by B-scan ultrasonography. Two eyes had mild vitreous hemorrhage with diffuse haze. Two eyes had peripheral localized patches of vitreous hemorrhage not involving the macula. Three eyes were incidentally found to have evidence of old vitreous hemorrhage. Diffuse white vitreous opacity with vitreous veils was found in one eye and white peripheral opacities not involving the macula were found in both eyes of a second patient.

There were several other posterior segment findings associated with vitreous hemorrhage in our patients. Two eyes (14%) had acute rhegmatogenous retinal detachments. One eye had a chronic stage 5 retinal detachment. Five eyes had posterior vitreous detachments and/or vitreoretinal traction. Two of these were documented findings at the time of vitrectomy. Three were documented interpretations of ultrasonography at the time of diagnosis with vitreous hemorrhage. On subsequent review of these ultrasounds by the authors, the findings of posterior vitreous detachment (two eyes) and vitreoretinal traction (one eye) were considered equivocal. Figure 1 illustrates the ultrasonographic findings typical of these three patients. In the remaining six eyes there were no retinal tears, detachments, or other visible manifestations of vitreoretinal traction. Four of these five eyes (three patients) were not evaluated by examination under anesthesia or ultrasound, because the hemorrhages were found incidentally and were mild, and the office examination effectively ruled out treatable pathology; thus it is possible that vitreoretinal traction was present in these eyes but was undetected.

A history of trauma was elicited in three patients. One patient (Patient 11) noted loss of vision immediately after hitting his head on the floor and was found to have vitreous hemorrhage and vitreoretinal traction on ultrasound. In this case the vitreous hemorrhage cleared but recurred twice (once spontaneously and once after another minor trauma) before finally clearing completely without treatment. Two other patients, whose vitreous hemorrhages were found incidentally, had a history of chronic self-abusive behavior ("head banging" and "eye poking," in Patients 9 and 7, respectively).

High myopia (>8 D) was documented in eight eyes, mild myopia or emmetropia in three eyes, and in three eyes the refractive error was not determined.

Surgical treatment was undertaken in six eyes, and eight eyes were observed. Of the eyes that were observed, all returned to their baseline visual acuity. Of the six patients who were treated with surgery, two had documented return of vision to baseline after surgery and two were thought to have returned to baseline, but vision could not be documented because of the patients' developmental status. After vitrectomy, the visual axis was clear and the retina was flat in all six eyes. Only two patients (Patients 2 and 5) had documented loss of vision after surgical management of late vitreous hemorrhage. Patient 2 underwent pars plana vitrectomy to clear vitreous hemorrhage and relieve vitreoretinal traction associated with a partial posterior vitreous detachment. This patient's documented baseline visual acuity was 20/60. At his final follow-up evaluation at our institution, which took place only 2.5 months after the onset of his vitreous hemorrhage, his visual acuity was 20/200. Patient 5 had a documented baseline visual acuity of 20/80. He presented to our institution after being treated surgically at an outside institution for a rhegmatogenous retinal detachment, which was subsequently complicated by proliferative vitreoretinopathy. Ultimately this patient required multiple surgeries resulting in a final visual acuity of 20/400.

Discussion

All of the patients described here experienced vitreous hemorrhage from months to years after complete involution of the acute phase of ROP. In contrast to work by Huthcheson et al,² who found vitreous hemorrhage in active high-risk ROP to be a poor prognostic sign, we found that the majority of patients with regressed ROP and late vitreous hemorrhage maintained baseline vision. None of the patients in this series had neovascularization or signs of active proliferative disease. We propose two mechanisms causing late vitreous hemorrhage in these patients with regressed ROP. First, abnormal vitreoretinal traction may disrupt otherwise normal retinal vessels, and second, vitreous traction may disturb residual cicatricial tissue at the vitreoretinal interface.

Abnormal vitreoretinal traction is well described in eyes with regressed ROP. These tractional forces are known to cause avulsion of retinal vessels,³ retinal tears,⁴ and retinal detachments in children⁵⁻⁷ and adults⁸⁻¹⁰ with regressed ROP. Some reports of patients with rhegmatogenous retinal detachment also describe vitreous hemorrhage in a few patients as an incidental finding.^{9,10} In cases where retinal vessels become avulsed or the retina tears, vitreous hemorrhage is a logical outcome. High myopia in many of these patients may also be a predisposing factor.

A second mechanism for late vitreous hemorrhage is traction on abnormal residual cicatricial tissue in eyes with regressed ROP. Vascular perfusion has been described in the cicatricial tissue of eyes with regressed ROP,¹¹ and some mild perfusion of this regressed neovascularization likely persists indefinitely. Bleeding from this tissue may occur spontaneously through vitreous traction generated by normal daily activities or as a result of minor trauma. The second mechanism offers an explanation for vitreous hemorrhage in cases where no retinal tear or detachment was identified. In our series only two patients (14%) had acute rhegmatogenous retinal detachment or retinal tear and one patient (7%) had chronic stage 5 ROP. The other 11 patients (79%) had no retinal break and did not develop detachments.

Two eyes in this series had posterior vitreous detachment according to the interpretation of ultrasonography at the time of diagnosis, and one eye was found to have a partial posterior vitreous detachment at the time of vitrectomy. It is uncertain, however, whether a true separation of the posterior vitreous cortex was actually present in these eyes. Eyes with regressed ROP can have extensive vitreous liquefaction with areas of fibrillar vitreous condensation.¹² The posterior vitreous cortex is known to be tightly adherent to the retinal surface in this age group, and true posterior vitreous detachment is probably rare in children with regressed ROP.¹³ The combination of extensive vitreous liquefaction in some areas and membranelike fibrillar condensation in other areas may give an ultrasound appearance that mimics posterior vitreous detachment. These pathologic changes in the vitreous may also contribute to abnormal tractional forces on the retina and tractional forces on any regressed neovascular tissue that may be present. Splitting of the posterior vitreous cortex and lamellar separation of part of the vitreous, with some cortical vitreous remaining adherent to the retina, has been reported in diabetic eyes with vitreous hemorrhage.¹⁴ In these cases, vitreous hemorrhage results from tractional forces that are transmitted to the retinal surface by the persistently attached lamella of cortical vitreous. Eyes with regressed ROP that have large areas of vitreous liquefaction and attached lamellae of posterior cortical vitreous may develop vitreous hemorrhage by the same mechanism.

Based on our experience, we recommend that any child with a history of regressed neovascularization associated with ROP who notices a change in vision or complains of eye pain be promptly evaluated, since these symptoms may herald vitreous hemorrhage.

Although pain is not generally a symptom of vitreous hemorrhage, some children lack the cognitive ability to verbalize that they have experienced a change in vision and may simply complain of eye pain instead. Such complaints should be taken seriously. Careful examination with ultrasonography is warranted to rule out associated retinal detachment or tears that will generally require surgical intervention. Patients who present with vitreous hemorrhage in the absence of retinal detachment or tears and are past the age for developing amblyopia may safely be observed.

There are several limitations to our study. The study was conducted at a tertiary care hospital whose population may not be representative of the community. In addition, in many cases the retrospective nature of the study imposed limitations on our ability to obtain information about the patients' baseline visual acuity and presence or absence of preexisting retinal traction and precluded a uniform method of assessing best corrected visual acuity and refractive error. Furthermore, because some of the patients were referred for second opinions or surgical management, follow-up with these patients was limited because the patients returned to their primary ophthalmologist for continued care. Finally, short follow-up intervals and small sample size, precluding statistical analysis, are additional limitations.

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FIG 1.

B-scan ultrasound of right eye of Patient 3. Mild vitreous opacity is present, with a membrane-like formation (arrow) of medium reflectivity at the 4 o'clock equator. At the time it was performed, this scan was interpreted as showing partial posterior vitreous detachment. An alternate interpretation would be that blood has layered on an interface of membrane-like fibrillar condensation of the vitreous adjacent to an area of vitreous liquefaction and that the vitreous cortex remains attached.

Table 1

Patient characteristics

Patient	Eye	Age*	Presenting feature	History	Associated findings	SEQ	Treatment for late VH	VA baseline	Presenting VA	VA at final visit	F/U#
1	OD	13	Blurred vision	Untreated ROP; incompletely vascularized retina	RRD; complex with PVR	-9.88	PPV, PPL, SB, SO, EL	Unknown	20/60	20/60	27.1
2	OS	10.8	Incidental finding [†]	Cryotherapy for ROP	Partial PVD and vitreoretinal traction	-14.38	PPV	20/60	20/100	20/200	2.5
3	OD	10.7	New onset floater	Cryotherapy for threshold ROP	Partial PVD by B-scan	Plano	Observation	20/20	20/25	20/30	18.5
4	OS	0.9	Incidental finding [†]	PRP for stage 3 ROP	None [‡]	ND	Observation	Unknown	F & F	CSM	1.4
5	OS	15	Sudden drop in vision	PRP for ROP	RRD	-8.88	PPV, PPL, SB, SO, EL MP [§]	20/80	LP	20/400	3.7
6	OS	1.9	Hyphema	PRP for zone 1 ROP; PPV PPL for stage 5 ROP	Chronic stage 5 RD	ND	Observation	No F & F	No F & F	No F & F	8.3
7	OS	2.4	Parents note vision change	PRP for threshold ROP; monocular due to RD OD	None [§] ; h/o eye poking behavior	-15.25	PPV	F & F	LP	CSUM	51.3
8	OD	8.2	Incidental finding [†]	Untreated mild stage 3 ROP	None [‡]	-0.75	Observation	20/30	20/20	20/20	13.9
8	OS	8.7	Incidental finding [†]	Untreated mild stage 3 ROP	None [‡]	-0.50	Observation	20/20	20/25	20/20	8.6
9	OD	2.4	Incidental finding [†]	PRP for threshold ROP	None [‡] ; h/o "head banging" behavior	ND	Observation	Unknown	Unknown	F & F	1.4
10	OD	8.1	Blurred vision	PRP for threshold ROP	None [§]	-12.25	PPV, MP	20/60	LP	20/50	2.3
11	OD	8.5	Blurred vision, floaters after head trauma [#]	PRP for threshold ROP; monocular due to RD OS	Partial PVD; no tears	-9.50	Observation	20/50	HM**	20/40	25.8
12	OD	13.8	Sudden drop in vision	Cryotherapy for ROP, Stage 4A RD	Regressed tuft of NV with vitreous traction	-19.50	PPV, EL, MS	CSM	? F & F	F & F	0.5
13	OS	12.5	"Pain" in left eye	PRP for threshold ROP	Probably vitreoretinal traction on B-scan	-19.00	Observation	20/50	HM	20/60	3.5

OD: right eye; OS: left eye; VH: vitreous hemorrhage; SEQ: spectral equivalent; VA: visual acuity; ROP: retinopathy of prematurity; RRD: rhegmatogenous retinal detachment; ND: not documented; PVR: proliferative vitreoretinopathy; PPV: pars plana vitrectomy; PPL: pars plana lensectomy; SB: scleral buckle; SO: silicone oil placement; EL: endolaser; MP: membrane peeling; PRP: panretinal photocoagulation; LP: light perception; HM: hand motion; F & F: fix and follow; CSM: central, steady maintain; CSUM: central, steady, unmaintained.

* Age at presentation equals age at onset of vitreous hemorrhage except for Patients 2, 4, 8, and 9, in whom the hemorrhages were found incidentally.

[†] Incidental finding of vitreous opacity after prior documentation of clear media.

[‡] Etiology of VH undetermined; examination under anesthesia and B-scan were not performed.

This patient had two recurrent VHs after the initial VH. One recurrence was associated with minor head trauma; one recurrence was spontaneous. All VHs cleared spontaneously.

** HM was the worst presenting VA (patient had three episodes of VH).

§ Etiology of VH undetermined; examination under anesthesia and B-scan were performed.

¶ Multiple surgeries required.

|| Length of follow-up after late VH in months.