

EXTENDED REPORT

Outcomes in persistent hyperplastic primary vitreous

A Hunt, N Rowe, A Lam, F Martin

Br J Ophthalmol 2005;**89**:859–863. doi: 10.1136/bjo.2004.053595

See end of article for authors' affiliations

Correspondence to: Dr Adrian Robert Hunt, Sydney Eye Hospital, 8 Macquarie Street, Sydney, Australia 2000; hunt_adrian@bigpond.com

Accepted for publication 5 October 2004

Aims: To report outcomes in cases of persistent hyperplastic primary vitreous (PHPV) and examine factors predictive of visual acuity in patients selected for surgery.**Methods:** Retrospective case series of 55 eyes in 50 patients presenting between 1990 and 2001 at the Children's Hospital, Westmead. 33 eyes underwent surgery aimed at visual rehabilitation.**Results:** In surgical patients, median age at surgery was 77 days, and median age at final follow up was 28 months. Six (18%) achieved a visual acuity at final follow up of 6/60 or better and eight (24%) achieved acuity of less than 6/60 to counting finger vision inclusive. Those undergoing surgery before 77 days were approximately 13 times more likely to obtain a visual acuity of counting fingers or better than those operated later ($p=0.01$). Neither posterior segment PHPV nor post-surgical glaucoma was a significant predictor of outcome in this selected group.**Conclusion:** Early surgery aimed at rehabilitation markedly improves the likelihood of useful visual outcome in selected eyes with PHPV.

Persistent hyperplastic primary vitreous (PHPV) causes considerable visual morbidity in affected eyes. Previous surgical series have documented variable visual and anatomical outcomes even with highly selected cases.^{1–13} Poor visual outcomes temper the decision to pursue surgery and ongoing visual rehabilitation.

We report on a series of 55 eyes diagnosed with PHPV managed surgically and conservatively over a 10 year period at the Children's Hospital at Westmead, Sydney. Data were analysed to determine factors predictive of visual outcome in eyes receiving surgical intervention aimed at visual rehabilitation.

PATIENTS AND METHODS

The medical records of patients with PHPV diagnosed by consultant paediatric ophthalmologists between January 1990 and March 2001 were reviewed retrospectively. The ethics committee of the Children's Hospital, Westmead, approved the research protocol. Departmental and hospital records were screened for potential PHPV, including cases coded as congenital cataract, microphthalmia, and congenital vitreous disorders. The inclusion criteria for this study involved documentation of typical anterior and/or posterior segment features of PHPV.^{1–3 12–15} These included microphthalmia,¹⁶ cataract, retrolental plaque, shallow anterior chamber, elongated ciliary processes, persistent hyaloid artery, retinal dysplasia, and retinal detachment. Diagnosis was made based on a combination of clinical, examination under general anaesthesia, and ultrasound findings. The difficult distinction between bilateral PHPV and Norrie disease was not defined by molecular genetic analysis.¹⁷ Preoperative ancillary tests including B-scan ultrasound with Doppler, computed tomography (CT), magnetic resonance imaging (MRI), and visual evoked potentials (VEP) were performed as directed by the treating ophthalmologist. Four surgeons performed or supervised all procedures.

In this study PHPV was categorised as anterior if a retrolental opacity, elongated ciliary processes, or cataract was present on clinical examination. PHPV was categorised as posterior when one or more of the following features was associated with an elevated vitreous membrane or stalk from the optic nerve: a retinal fold or retinal dysplasia, retinal detachment, or optic nerve hypoplasia.

Surgical interventions aimed at visual rehabilitation included lensectomy with or without anterior or total vitrectomy, and trabeculectomy. Cases with isolated anterior involvement or glaucoma were routinely selected for early surgery. Cases with minimal posterior involvement were selected upon the treating surgeon's discretion. Occlusion therapy combined with aphakic correction (contact lens, or spectacle if bilateral) followed surgery.

Visual acuity was assessed with age appropriate tests including Kays picture tests, Teller cards, Sheridan-Gardner, and Snellen tests.¹⁸ Age at surgery was calculated in days, and cases categorised into early and late surgery groups using the median value.

For patients receiving surgical intervention aimed at visual rehabilitation, final visual acuity was categorised into "useful" (counting finger vision or better) and "poor" (worse than counting fingers). Associations between clinical factors (age at surgery, sex, presence of posterior PHPV, and late glaucoma) and visual outcome were examined using 2×2 tables and logistic regression modelling. Statistical analyses were performed using SPSS, and significance defined as $p<0.05$.

RESULTS

Fifty five eyes of 50 patients were included in the study, with 31 (62%) males and 19 (38%) females. Five (10%) of the patients were diagnosed with bilateral PHPV and were assigned a single case number; 25 right eyes (45%) and 30 left eyes (55%) were included. Median age at diagnosis was 44 days. Three quarters were diagnosed within 90 days. PHPV was an isolated abnormality in most of the patients (76%). Twelve patients had systemic abnormalities, seven of which were neurological and one case of Walker-Warburg syndrome (table 1). Fifteen eyes (27%) had anterior segment involvement only. Thirty three (60%) eyes had combined involvement. Seven (13%) had purely posterior involvement, including hyaloid remnants (two eyes) with disc atrophy (one eye), large retrolental/central vitreous masses (five eyes) with vitreous haemorrhage (one eye), and retinal detachment (three eyes). Five (71%) of the

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; PFV, persistent fetal vasculature; PHPV, persistent hyperplastic primary vitreous; VEP, visual evoked potentials

Table 1 Additional diagnoses in 12 patients

Case No	Condition
18	Bilateral deafness, behavioural abnormalities
21	Ipsilateral retinopathy of prematurity
23	Ipsilateral facial asymmetry
24	Tracheomalacia, polymicrogyria with seizures
28	Walker-Warburg syndrome, hydrocephaly, polycythaemia
30	Patent ductus arteriosus
32	Microcephaly
38	Developmental delay, syndactyly, ear/nose abnormalities
41	Microcephaly
45	Ipsilateral hemifacial dysmorphism
48	Ipsilateral hypoplasia of right optic nerve, chiasm, carotid artery and cerebrum
50	Bilateral deafness

eyes with pure posterior PHPV had neurological abnormalities listed in table 1.

Early surgical intervention aimed at visual rehabilitation

Thirty three (60%) eyes underwent early surgery directed at visual rehabilitation (table 2). Median age at diagnosis was 40 days. Median age at surgery was 77 days, and one quarter underwent surgery in the first month of life. Median age at final follow up was 28 months.

Signs of incipient or actual angle closure glaucoma complicated the clinical course in seven (23%) eyes of this group. Two eyes in one patient underwent initial trabeculectomy because of congenital glaucoma with cloudy corneas. Subsequent visualisation of the extent of bilateral disease in this patient combined with significant co-morbidities led the clinician to pursue a more conservative approach. Five eyes were complicated by glaucoma after lensectomy. Late trabeculectomy was performed on two eyes (final VA: 1/24, NLP), medical management undertaken in two eyes (1/60, NLP), and photocoagulation performed in one eye (NLP). Strabismus was documented in 22 (67%) patients and six of these underwent eye muscle surgery. Retinal detachment was documented in three (9%) eyes and phthisis documented in another four (12%) eyes in this group.

Subsequent interventions in this group included pupilloplasty in two eyes, YAG laser capsulotomy (one eye), surgical capsulotomy (one eye), and secondary intraocular lens implantation (two eyes). Two eyes were enucleated and three eyes had socket moulding for fitting of prostheses.

Visual acuity data were available for 31 eyes (94%) in this group at final follow up. Six (18%) achieved a visual acuity at final follow up of 6/60 or better. Eight (24%) achieved acuity of less than 6/60 to counting finger vision inclusive. Seven (21%) had hand movement to light perception vision inclusive, and 11 (33%) had no light perception or had undergone enucleation.

Cases 21, 24, and 28 were excluded from statistical analysis, as visual outcome may have been affected by ocular or neurological conditions in addition to PHPV. There was no significant correlation between "useful" vision (defined as counting fingers at 1 metre or better acuity) at final follow up, and sex, eye, location of PHPV, or post-surgical glaucoma in regression analyses. After adjustment for post-surgical glaucoma and posterior segment PHPV, surgery before 77 days of age was found to strongly predict "useful" vision (OR 13.0, $p = 0.01$).

Conservative management

Twenty two eyes were managed without early surgical intervention aimed at visual rehabilitation (table 3).

Median age at diagnosis was 55 days. Median age at final follow up was 13 months.

Retinal detachment was documented in six (28%) eyes in this group. Angle closure glaucoma was documented in one eye. Strabismus was documented in six (28%) patients in this group. Strabismus surgery was performed in one patient in this group. Moulding for prosthesis fitting was performed on three eyes. Probing was performed for nasolacrimal duct obstruction for one patient.

Final visual acuity was available for 20 of these patients. One (4%) achieved a visual acuity at final follow up of 6/48 or better. One (4%) achieved acuity of 6/60 to counting finger vision inclusive. Six (28%) had hand movement to light perception vision inclusive. Ten (45%) had no light perception and one had undergone enucleation as a primary procedure.

DISCUSSION

Persistent hyperplastic primary vitreous was first described by Reese in 1955 in his Jackson Memorial Lecture.¹⁴ Representing a form of persistent fetal vasculature (PFV), Goldberg has suggested the terminology change to better reflect the pathology.¹⁸ The exact aetiology remains unknown. Characteristically PHPV presents as unilateral leucocoria with variably severe microcornea or microphthalmia.¹³ PHPV is usually found in otherwise healthy full term infants, however, it has been described in association with systemic and, in particular, neurological abnormalities.¹⁹ Severity can range from pupillary strands or an isolated Mittendorf dot, to more severe forms with retrolenticular membranes, retinal dysplasia, or detachment.^{13 15 18 20 21}

PHPV management is based on the extent of anterior and posterior segment involvement. Posterior PHPV has been associated with a poor visual outcome in previous studies.¹⁻¹³ Including all patients in our study, the absence of posterior involvement predicted counting finger or better vision but this failed to reach statistical significance (OR 1.6, $p = 0.44$). For patients receiving visual rehabilitation surgery, presence of posterior segment involvement was found not to be associated with visual acuity at final follow up ($p = 0.46$). This failure to achieve statistical significance may be due to small patient numbers, short follow up time, and/or a selection for surgery of patients with only minimal posterior segment disease.

Pollard stated that age at presentation is a major predictor of visual outcome.³ Karr and Scott found surgical patients achieving 20/200 or better acuity presented at a mean age of 2.4 months, whereas those that achieved 20/300 or worse presented at a mean age of 4.3 months.⁵ Our study showed surgery before 77 days was associated with useful vision (OR 13, $p = 0.01$). This provides a useful prognostic factor in case selection that concurs with previous anecdotal reports. Comparing results with Karr and Scott's series, eyes achieving 6/60 or better in our study had mean age at surgery of 41 days (1.3 months), excluding one patient operated at age 15 months who achieved 6/48. Mean age at surgery for patients achieving worse than 6/60 was 121 days (4.0 months).

Other factors examined in the statistical analysis (sex, laterality, and late glaucoma) were found not to be significantly associated with visual outcomes, although a possible trend for poor final acuity in males was found after multivariate adjustment (odds ratio 0.08, $p = 0.09$). However, the limited size of our series means all calculated associations are unstable to small changes in frequencies in any category of predictor or outcome factor. These low frequencies are also reflected in the large confidence intervals obtained for significant associations. The authors also recognise other factors such as compliance with occlusion

Table 2 Surgical rehabilitation patient data

Case No	Sex	Eye	Age at diagnosis (months)	Best preoperative visual acuity	PHPV type	Indications for surgery	Surgery	Age at surgery (months)	Sequelae and clinical course	Age at final follow up (months)	Visual acuity at final follow up
1	M	RE	2	Vague LP	A	C RP	L/V	4		30	F&F
2	F	LE	2	Vague LP	A/P	C RP	L/V	3		14	Vague LP
3	M	RE	3	Poorly F&F	A/P	C	L	9	Indrawing of ciliary processes, LXT small Post-PHPV noted	8	Poorly fixes
4	M	RE	1	Vague LP	A/P	C G	L	13	postoperatively, RET	16	NLP
5	M	LE	0	NA	A	C RP	L/V	0	Glaucoma, trab, RD	42	3/18 Kays
6	F	RE	0	Poorly F&F	A	C RP	L/V	1	RXT variable, CL	43	1/60 SGSL
7	F	RE	0	NA	A/P	C RP	L/V	1	compliance poor Pupil closure,	12	6/570Teller
8	M	LE	1	NA	A/P	C RP	L/V	1	pupilloplasty, RET RD, CL compliance poor	116	LP
9	M	RE	14	Poorly F&F	A/P	C RP	L/V	15	CL compliance poor, secondary IOL	25	6/48 Teller
10	F	LE	2	NA	A/P	C	L	2	RET	107	6/48 Snellen
11	F	RE	10	Poorly F&F	A/P	C RP	L/V	10	Pupil closure, pupilloplasty, RET	42	LP
12	M	LE	2	No F&F	A/P	C RP	L/V	2	Phthisis	23	Prosthesis
13	M	LE	4	No F&F	A/P	C RP AC	L/V	4	Glaucoma, phthisis	22	NLP
14	M	LE	1	Poorly F&F	A/P	C	L	2	LET small	32	6/36 Teller
15	M	RE	0	Poorly F&F	A	C RP	L/V	2	RXT	1	F&F
16	F	LE	4	6/480 Teller	A/P	C RP	L/V	5	LET, squint surgery	95	3/36 Snellen
17	F	LE	2	NA	A	C	L	2	LXT, CL compliance poor, secondary IOL	54	3/36 Kays
18	M	LE	0	Poorly F&F	A	C RP	L/V	4	LXT, enucleation	20	NLP
19	M	RE	1	NA	A	C RP	L/V	1	YAG laser capsulotomy	22	6/36 Teller
20	F	LE	7	Poorly F&F	A/P	C	L	6	LET, CL compliance poor	123	LP
21	M	LE	2	NA	A/P	C	L	6	LET, squint surgery, threshold ROP, cryotherapy, glaucoma	17	1.5/60 Teller
22	F	LE	4	NA	A/P	C RP	L/V	4	LET variable	1	NA
23	M	RE	1	NA	A/P	C RP AC	L/V	1	Glaucoma, photocoagulation	28	NLP
24	M	RE	0	NA	A	C	L	1	RET, squint surgery, capsulotomy	13	NLP
25	M	LE	0	6/240 Teller	A/P	C	L	10	RET, RD	44	NLP
26	F	RE	3	NA	A	C RP	L/V	5	RHT/XT, squint surgery	104	NA
27	M	LE	0	NA	A/P	C	L	1	Dead (PUO) at age 14 months	8	6/120 Teller
28R	F	RE	0	NA	A/P	G	Trab.	NA	Presented with glaucoma	8	NLP
28L	F	LE	0	NA	A/P	G	Trab.	NA	Presented with glaucoma	8	NLP
29L	F	LE	1	Poorly F&F	A/P	C RP	L/V	1	AET, squint surgery	52	1/18 SGSL
29R	F	RE	1	Poorly F&F	A/P	C RP	L/V	1	AET, squint surgery, glaucoma, trab age 4	52	1/24 SGSL
30R	F	RE	2	NA	A/P	C RP	L/V	4	RD, phthisis, enucleation	80	NLP
31L	F	LE	1	LP	A	C	L	2		63	3/24 SGSL

LP, light perception; NLP, no light perception; F&F, fixing and following; A, anterior PHPV; P, posterior; C, cataract; RP, retrolental plaque; G, glaucoma; AC, shallow anterior chamber; Trab, trabeculectomy; L, lensectomy; V, vitrectomy; RET, right esotropia; LET, left esotropia; RXT, right exotropia; RHT, right hypertropia; AET, alternating esotropia; RD, retinal detachment; ROP, retinopathy of prematurity; CL, contact lens; secondary IOL, secondary intraocular lens; SGSL, Sheridan-Gardner single letters.

and correction of refractive errors may influence outcome, but precise measurement of all potential confounders was limited by the retrospective nature of the study. Caution must be exercised in interpreting results given treatment groups (early versus late surgery) were not randomly allocated.

The difficult task of managing anisometropic amblyopia in neonatal aphakia is cited as a major factor contributing to poor visual outcome.²² Anteby *et al* concluded that intraocular lens implantation may be a favourable and beneficial option for the management of children with unilateral PHPV in their series of 89 children.²³ Thirty of the 61 eyes in that study underwent cataract extraction/vitrectomy with intraocular lens implantation. High intraocular pressure and glaucomatous changes were observed less commonly with

pseudophakia (8%) compared to aphakia (23%), and the incidence of NLP was 10% and 43% respectively. Our predominantly aphakic experience has been similar with a 23% incidence of glaucoma, and final VA of NLP in 32%. The two secondary pseudophakic cases in our series were not complicated by glaucoma and achieved 3/36 Kays and 6/48 Teller VA.

Surgical intervention has previously been recommended for globe preservation in PHPV complicated by progressive retinal detachment, angle closure glaucoma, and recurrent intraocular haemorrhage.^{1-4 14 15 24} In the surgical group eight eyes were complicated by glaucoma or retinal detachment, and seven of these had no light perception at final follow up. Four eyes underwent trabeculectomy with three having no

Table 3 Conservative management patient data

Case	Sex	Eye	Age at diagnosis (months)	Visual acuity at presentation	PHPV type	Contraindications to early surgery	Miscellaneous	Age final follow up (months)	Visual acuity at final follow up
30L	F	LE	2	NLP	A/P	SA SP	Corneal diameter 7 mm, patent hyaloid artery	80	NLP
31R	F	RE	1	LP	A	G SA SP	Glaucoma at presentation, phthisis, prosthesis	63	NLP
32L	M	LE	2	LP	P	SP	Large retrolental mass, rsmicrocephaly	2	LP
32R	M	RE	2	Vague LP	P	SP	RD, microcephaly	2	Vague LP
33	F	LE	0	NLP	A/P	SA SP	Microphthalmos, prosthesis	95	NLP
34	F	RE	2	Vague LP	A/P	SP	Patent hyaloid artery to disc	2	Vague LP
35	M	RE	0	NLP	A/P	SA SP	Shallow anterior chamber, AP 14 mm	1	NLP
36	M	RE	0	NLP	A	SA	Shallow anterior chamber, late lensectomy for glaucoma	17	NA
37	F	LE	5	Poorly F&F	A/P	SP	Patent hyaloid artery to disc, nystagmus	47	3/60
38	F	RE	0	NA	A/P	SA SP	Ectopia lentis, retinal dysplasia, L-ptosis and duct blockage requiring probing.	22	NLP
39	M	RE	0	NA	A/P	SA SP	Corneal diameter 8 mm, AP rs14 mm	11	NLP
40	M	LE	4	NA	A/P	SA SP	Corneal diameter 8 mm, AP rs13 mm	3	NLP
41	M	LE	1	LP	P	SP	Hyaloid artery, hypoplastic disc, roving nystagmus, microcephaly	9	LP
42	M	LE	0	NA	P	SP	Progressive phthisis, enucleation	37	NLP
43	M	LE	3	Good F&F	P	MP	Hyaloid artery only, developmental delay	11	6/18
44	M	LE	3	NA	A	SA	Shallow anterior chamber with pupil bound down	3	NLP
45	F	RE	NA	NA	A	SA	Prosthesis	13	NLP
46	M	LE	0	Poorly F&F	A/P	SA SP	Retrolental mass, AP 12 mm and left ptosis, roving nystagmus	56	LP
47	M	LE	8	NA	A	SP	Retrolental mass	8	NA
48	M	RE	1	Roving	P	SP	Vitreous haemorrhage, RD	14	NLP
49	M	LE	4	NA	P	SP	Hyaloid artery and retrolental mass,	9	NLP
50	M	RE	2	Poorly F&F	A/P	SA	Shallow anterior chamber, strabismus surgery	59	NLP

LP, light perception; NLP, no light perception; F&F, fixing and following; A, anterior PHPV; P, posterior; MP, minimal posterior PHPV; SP, severe posterior PHPV not amenable to surgery; SA, severe anterior PHPV not amenable to surgery; G, glaucoma; RD, retinal detachment; AP, globe anteroposterior diameter; MRI, magnetic resonance imaging.

light perception at final follow up; none of these eyes went on to develop phthisis or required enucleation.

Mild PHPV can run a relatively benign natural course without surgery.^{1,25} Two patients in our series with an isolated hyaloid artery the only manifestation of PHPV achieved ~6/18 (Teller) at age 11 months and 3/60 (Sheridan-Gardner) at 4 years with conservative management. Surgery may be avoided if the visual axis is clear, anatomical anomalies are not progressive, and the anterior chamber angle is not compromised.^{1,26}

Optimal timing of surgery aimed at visual rehabilitation is presumably governed by the early critical periods of visual development.^{27,28} The study findings support the value of early diagnosis and early intervention to maximise visual potential in selected patients.

ACKNOWLEDGEMENTS

We are grateful to the orthoptic staff at the Children's Hospital, Westmead, and also Professor Frank Billson, Dr Jeremy Smith, and Dr Michael Giblin, for their contribution to this article through patient care and management.

Authors' affiliations

A Hunt, N Rowe, F Martin, Department of Ophthalmology, The University of Sydney, New South Wales, Australia

A Lam, Department of Radiology, The Children's Hospital, Westmead, Sydney, Australia

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