

Case Report

Unsuspected periventricular leukomalacia in children with strabismus: a case series

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ABSTRACT.

Purpose: We report a case series of seven patients who presented with strabismus and no apparent known neurological deficit.

Methods: A retrospective review of notes was performed on all patients presenting at the Royal Liverpool Children's Hospital (Alder Hey) with strabismus, in whom subsequent investigation revealed the presence of periventricular leukomalacia (PVL).

Results: All seven patients presented with esotropia. One patient also had dissociated vertical deviation. A history of premature birth was elicited in six cases; however, one patient had been born at 42 weeks. Apparently uncomplicated routine surgery produced unexpectedly poor results.

Conclusions: Patients with undiagnosed PVL may present to the ophthalmologist with strabismus and no other apparent neurological abnormality. Where it is suspected that the patient may have suffered a significant hypoxic-ischaemic event, the ophthalmologist should have a low threshold for investigating with magnetic resonance imaging, particularly if the patient shows unexpected outcomes following appropriate treatment. Patients and parents should be counselled on possible suboptimal results prior to the offer of surgical correction of strabismus.

Key words: strabismus – periventricular leukomalacia – undiagnosed – MRI – surgical outcomes

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Introduction

Periventricular leukomalacia (PVL) is commonly the result of ischaemic events in the brain of a premature visual system, resulting in characteristic radiological findings on magnetic resonance imaging (MRI). The exact pathogenesis is still not entirely under-

stood, but it is thought that a hypoxic-ischaemic insult to immature (premyelinated) white matter may be an important causative factor (Kinney et al. 2005). Some children with PVL have no history of premature birth or perinatal problems; in these children PVL may be the result of antenatal factors. Viral and immunological aeti-

ologies have been postulated (Gibson et al. 2006).

Children with this condition may have delayed visual maturation, poor visual acuity, visual field anomalies, ocular motility disorders and other systemic associations, such as cerebral palsy and mental handicap (Jacobson et al. 1996). Consequently, the patient may present to the ophthalmologist with a wide spectrum of complaints.

Diagnosis of PVL usually antedates the presentation of strabismus and amblyopia. Here we discuss ocular motility dysfunction and/or amblyopia as the presenting feature in a series of patients without a prior diagnosis of PVL.

We report a case series of seven patients who presented with strabismus and no apparent known neurological deficit. Subsequently, the patients were discovered to have subtle neurological deficits and to show features of PVL on radiology.

Materials and Methods

A retrospective review of notes was performed on all patients presenting to the Royal Liverpool Children's Hospital (Alder Hey) with strabismus, and in whom subsequent investigation revealed the presence of PVL. Patients were identified from a strabismus database, covering an 8-year period. Those patients with known neurological pathology prior to presentation at our department were excluded. Case

notes were examined for medical history, type of strabismus, refraction, amblyopia, treatment, reasons for requesting imaging studies and surgical outcomes.

Results

Seven patients had strabismus and undiagnosed PVL prior to commencement of treatment were identified. All seven presented with esotropia and one also had dissociated vertical deviation (Table 1). A history of premature birth was elicited in six cases, although one patient had been born at 42 weeks (but the mother had suffered an epileptic seizure during pregnancy). Six patients had been admitted to the special care baby unit (SCBU) and had an average stay of 28.7 days (range 9–56 days). Case 2 had been transferred from another hospital; it is not entirely clear from the notes how long she had spent in the SCBU before her transfer, but we do know that her entire stay was at least 29 days. None of these children had a history or diagnosis suggestive of PVL at referral to our unit.

The size of the esotropia prior to surgery was variable, with an average of 29.3 prism dioptres (PD) (range 16–45 PD). MRI scans were ordered on these patients for the following reasons. Case 1 had a history of premature birth and showed reduced

vision despite correction of the refractive error and excellent compliance with occlusion therapy for amblyopia (Table 2). Cases 2, 3 and 4 had significant obstetric histories and associated ocular and neurological findings, such as latent nystagmus (Table 1). Cases 5 and 6 had both suffered premature birth and spent significant periods in the SCBU (14 and 29 days, respectively). They also showed significant variation in the size of strabismus at different times. Case 7 had also been born prematurely and had undergone three operations for coarctation of the aorta, necessitating cardiac bypass.

All seven patients were reported to have varying degrees of PVL on radiological examination. Radiological features on T2 weighted scans included high-signal lesions in the periventricular white matter, together with ventricular enlargement (Fig. 1). Fluid attenuation inversion recovery (FLAIR) sequences also demonstrated loss of periventricular white matter and compensatory focal ventricular enlargement (Fig. 2), particularly in the anterior and posterior horn regions (Baker et al. 1988). The FLAIR sequence shows periventricular changes more clearly as a result of the contrast between low-signal cerebrospinal fluid in the ventricles and high-signal gliosis.

Examination of the patients by a neurologist showed normal gross

function in all of them. However, subtle neurological deficits like poor concentration, learning difficulties, impaired fine motor skills and speech impairment were discovered in six patients (Table 1). These had not been previously apparent and may have become more obvious at school age. The one patient (case 5) in whom no neurological deficit had so far been found, had definite PVL (Fig. 1).

Apparently uncomplicated routine surgery produced unexpected results. Five of the seven patients were operated upon. Three patients had a satisfactory immediate postoperative result, with the esotropia reduced to ≤ 10 PD (Table 1), but two of these began to relapse later. A further two patients had unexpected results: one patient had consecutive exotropia, and one had persisting large esotropia.

Discussion

Periventricular leukomalacia lesions were first described by Banker & Larroche (1962), who considered them to result from hypoxic-ischaemic injury to the brain prior to 34 weeks gestation. The lesions represent a non-specific finding on imaging: they reflect a loss of white matter in a relatively classical distribution, resulting from a number of possible insults to an immature developing brain. Although PVL is commonly reported in

Table 1. Summary of patients' clinical histories.

Case	Birth at week	Obstetric history	SCBU days	Age at presentation	Other ocular features	Neurological features	Strabismus	Size	Immediate post-surgical result in PD
1	32	Nil	9	7 months	Amblyopia (OD)	Poor concentration	Esotropia	20	Exotropia 5 PD to esotropia 10 PD
2	Premature	Maternal heroin abuse	> 29	8 months	Latent nystagmus	Dyspraxia	Esotropia	40	Exotropia 4–10 PD
3	42	Epileptic seizure	0	22 months	Nil	Short attention span	ACS, then esotropia	16	Exotropia 25 PD
4	32	Premature rupture of membranes	35	6 years	Latent nystagmus	Mild learning difficulties	Esotropia and DVD	35	No surgery
5	32	Nil	14	21 months	Nil	Nil	ACS	45	Esotropia 20 to + 25 PD
6	29	Nil	29	3 years	Nil	Slight learning difficulties	Esotropia	35	Exotropia 2 PD
7	32	Nil	56	5 years	Bilateral disc pallor	Poor concentration Speech delay	Esotropia	20	No surgery

SCBU = special care baby unit; OD = right eye; OS = left eye; PD = prism dioptres; ACS = alternating convergent strabismus ; DVD = dissociated vertical deviation.

Table 2. Refractive errors and amblyopia treatment in patients with undiagnosed periventricular leukomalacia.

Case	Refraction						Earliest recorded visual acuity (Snellen)		Last recorded visual acuity (Snellen)		Treatment
	OD			OS			OD	OS	OD	OS	
	Sph	Cyl	Axis	Sph	Cyl	Axis					
1	+ 0.50	0	0	+ 0.50	0	0	6/18	6/12	6/18	6/18	Spectacles and occlusion therapy
2	+ 1.75	0	0	+ 1.50	0	0	6/12	6/60	6/9	6/9	Spectacles and occlusion therapy
3	0	0	0	0	0	0	6/6	6/7.5	6/6	6/7.5	Nil
4	+ 2.5	+ 0.5	90	+ 2.50	0	0	6/24	6/24	6/9	6/9	Spectacles
5	+ 1.75	+ 1.25	40	+ 1.00	+ 1.50	140	6/24	6/18	6/6	6/6	Spectacles
6	+ 0.75	0	0	+ 0.75	+ 0.25	90	6/7.5	6/9	6/7.5	6/7.5	Spectacles and occlusion therapy (poor)
7	+ 1.25	0.00	00	+ 1.75	0	0	2/30	6/12	6/60	6/12	Spectacles and occlusion therapy

OD = right eye; OS = left eye; Sph = spherical value; Cyl = cylindrical value.

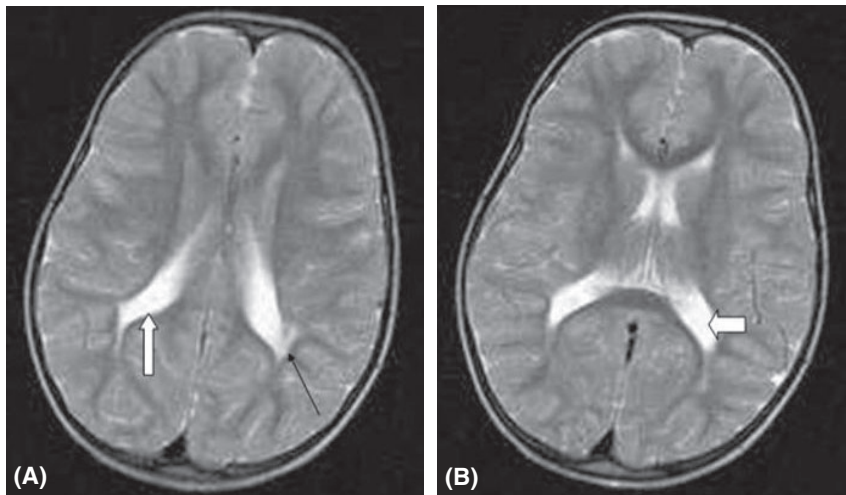


Fig. 1. (A, B) MRI T2 weighted axial images from case 5, showing areas of periventricular high-signal changes (black arrow) and associated ventricular enlargement (white arrows).

children born prematurely, it can also occur in full-term pregnancies, as demonstrated in one of our cases (case 3). This may have been due to a period of brain hypoxia (secondary to a maternal grand mal seizure). Lou (1988) has argued that stresses in the birth process causing fluctuations in arterial pressure can result in cerebral hypoperfusion, to which arterial watershed zones in the periventricular areas are particularly susceptible. Other reported obstetric risk factors include maternal urinary tract infections, neonatal acidosis at birth, meconium-stained amniotic fluid and premature rupture of membranes (Verma et al. 1997; Spinillo et al. 1998). Recently, however, there has

been a growth in evidence for the supposition that perinatal infections and exposure to neurotropic viruses such as group B herpes viruses (varicella zoster, human herpes viruses 6 and 7) are associated with an increased incidence of preterm delivery and cerebral palsy (Perlman et al. 1996; Kinney et al. 2005).

These lesions are associated with a variety of clinical manifestations ranging from cerebral palsy and quadriplegia to less severe neurological deficits. Ocular associations may include delayed visual maturation, visual field defects, crowding, nystagmus and strabismus, as well as other anomalies involving the visual system (Eken et al. 1995; Jacobson et al.

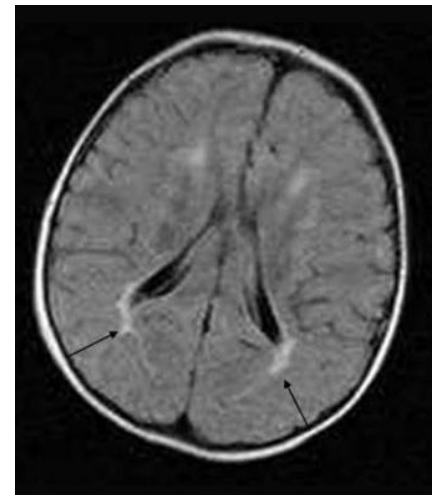


Fig. 2. MRI axial FLAIR (fluid attenuation inversion recovery) image from case 3. Bilateral high-signal white matter change is shown around the atria of the lateral ventricles (black arrows). White matter thinning in this area with compensatory mild focal ventricular enlargement can be seen.

2002). However, PVL is usually diagnosed before presentation with strabismus. In our case series there had been no previous diagnoses of PVL prior to our investigation with MRI.

Hiles et al. (1975) showed satisfactory alignment following strabismus surgery in brain-damaged children. They reported surgical results in cerebral palsy as satisfactory in 77% of esotropia surgeries and 86% of exotropia surgeries. However, as is the case with many neurological conditions, the outcomes of surgical intervention depend on the extent and evolution of

the neurological injury. Holman & Merritt (1986) reported poorer results for esotropia surgery in patients who had concomitant neurological conditions (55.2% satisfactory outcome), compared with controls with only esotropia (83.3% satisfactory outcome). However, the first group of patients differed in their neurological aetiologies and the extent of their lesions is not entirely clear.

Periventricular leukomalacia patients tend to show more variability, with spontaneous conversion between esotropia and exotropia, and hence the results and best timing of surgery are less well understood (Jacobson & Dutton 2000).

Our cases were apparently 'normal', without any neurological problems. Careful review of the patients' and mothers' medical histories led us to investigate with neuroimaging, thereby revealing hidden pathology. In all seven cases white matter lesions (PVL) were identified on MRI scans. All the children received a detailed report for educational purposes and strategies were implemented to help with their education.

In our case series the patients did not respond to surgery as well as had been expected. Cases 1 and 2 initially had a good result from surgery. However, case 1 had a variable strabismus of -5 PD to +10 PD and developed a right exotropia of 20-30 PD approximately 2 years later. Case 2 also developed a left exotropia and dissociated vertical deviation 4 years later. The other two cases had unsatisfactory surgical outcomes. Only one of the five patients (case 6) had a satisfactory outcome. The remaining two cases have not yet undergone any surgical intervention.

Conclusions

Patients with undiagnosed PVL may present to the ophthalmologist with strabismus and no other apparent neurological abnormality. A careful

history needs to be taken, not only looking for prematurity of birth, but also any possible events that may have caused a hypoxic-ischaemic insult to the immature visual system. The ophthalmologist should have a low threshold for investigating with an MRI scan if it is suspected that such an insult may have occurred and the index of suspicion should be increased if unexpected outcomes are noted following appropriate treatment with good compliance.

Surgery in this group of patients may have unexpected results. Therefore, patients and parents should be counselled about possible suboptimal results prior to the offer of surgical correction of strabismus. Neurological assessment may lead to the identification of neurological deficits that will impact significantly on the subject's education.

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