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Pseudo-strabismus secondary to macular heterotropia: a case report and literature review

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Abstract

Aim: **To present a case of pseudo-strabismus secondary to macular heterotropia, caused by retinopathy of prematurity (ROP). An overview is given of the literature on this subject.**
Methods: **The case of a 9-year-old child born prematurely at 26 weeks' gestation and who had cryotherapy treatment for stage 3 ROP, is reported with reference to her birth history and her ophthalmic, orthoptic and photographic findings.**
Results: **The patient had a pseudo-exotropia resulting from an abnormal shifting of the macula known as macular heterotropia, an abnormal fundus appearance found in ROP, especially in eyes treated with cryotherapy. Macular heterotropia has been reported in conditions such as retinal tear, idiopathic retinal folds, persistent hyaloid vessels, chorioretinal coloboma, chorioretinisis, *Toxocara canis*, vitreous structural anomalies, and very high myopia.**
Conclusions: **Orthoptists should be aware of the features of macular heterotropia and its associations with ROP and pseudo-strabismus.**

Key words: Angle kappa, Cryotherapy, Macular heterotropia, Pseudo-strabismus, Retinopathy of prematurity (ROP)

Introduction

The clinical features of a pseudo-strabismus caused by macular heterotropia are described and the relevant literature is discussed.

Case report

A 9-year-old girl presented to the Eye Department of Birmingham Children's Hospital having recently moved into the area.

Birth history

Following a normal pregnancy, the baby was born prematurely at 26 weeks' gestation by emergency caesarean section due to maternal placental abruption and haemorrhaging. Birth weight was 900 g. The baby spent 3 months in the neonatal unit, receiving oxygen therapy for 2 months and continuous positive airway pressure (CPAP) for 1 month.

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Previous ophthalmic history

At age 3 months (corrected gestational age 38 weeks), the baby was diagnosed with bilateral stage 3 zone II retinopathy of prematurity (ROP) (Fig. 1). Both maculae and discs were found to be healthy and unaffected. She underwent immediate cryogenic treatment to zone III in both eyes, which was considered successful.

The child attended for regular ophthalmic follow-up. At 8 months of age she was found to have dragged optic discs (R>L) and myopia of right eye −1.50 DS, left eye −3.00 DS, but glasses were not prescribed at that point. At the age of 22 months glasses were prescribed for full-time wear (−3.00 DS right and left eye) and compliance with glasses wear was reported as good.

Cover testing revealed fine manifest horizontal jerky nystagmus with a consistent abnormal head posture of face turn to the left, which was noticed from infancy. During 6 years of orthoptic follow-up, the cover test findings were variable and ranged from a variable left esotropia to right exotropia, and the nystagmus and abnormal head posture persisted. The child's co-operation with testing was at times noted as limited.

During the follow-up period visual acuity was repeatedly recorded as both eyes open 6/18, right eye 6/18, left eye 6/60, using age-appropriate tests over subsequent years. No occlusion therapy was prescribed. The local Visiting Teacher Service provided educational support.

Previous medical history

The child had a minor heart condition that required no medical intervention. She was described as chesty and clumsy, but was otherwise fit and well. She had normal neuro-motor development, but minor reading difficulties at school.

Orthoptic and ophthalmic examination

The child attended the Eye Department in the Birmingham Children's Hospital aged nearly 9 years. Corrected visual acuity was both eyes open 0.24 logMAR (6/10), N5 for near using Bailey Lovie logMAR and Maclure tests. Monocular visual acuities were right eye 0.44 (6/15) and left eye 0.86 (6/38). The child was noticed to turn her head to the left during right visual acuity testing.

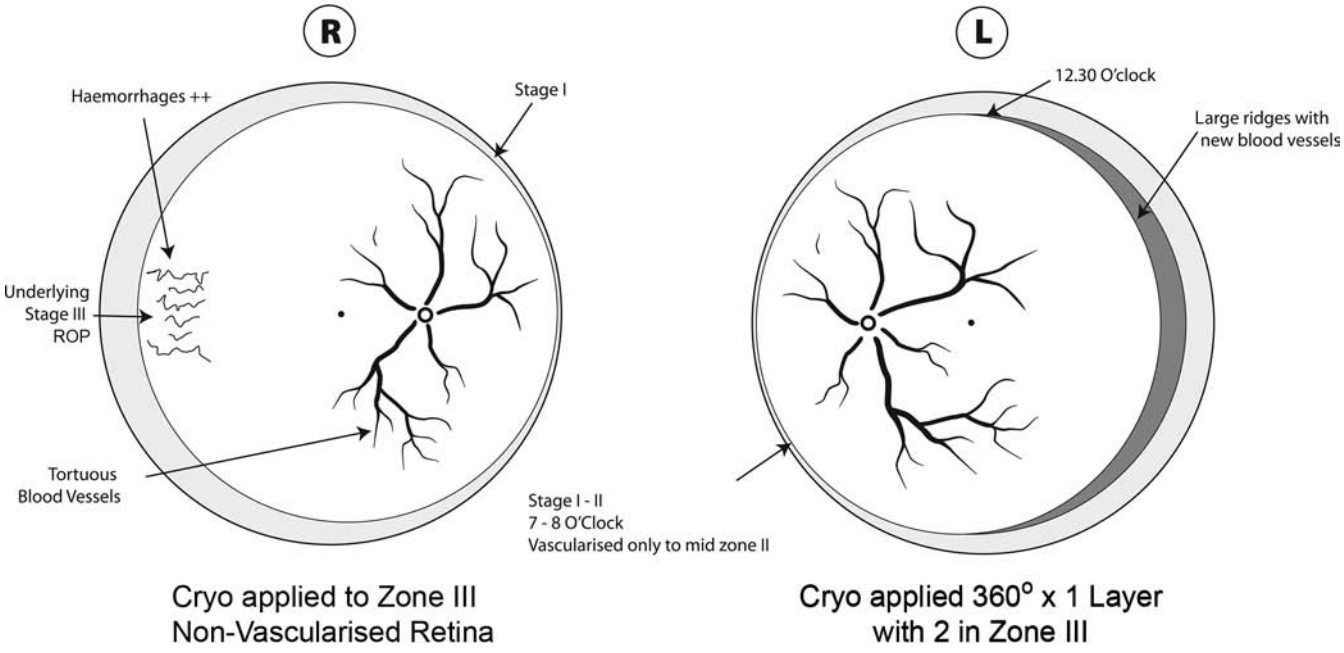

Fig. 1. Drawing to show the stage 3, zone II retinopathy of prematurity at age 3 months detailed in the child's neonatal notes.

There was no abnormal head posture noted during binocular visual acuity assessment or on observation. The glasses prescription obtained from a community optician was right eye plano/-0.50×45, left eye $+1.00/-3.50 \times 5$.

On observation, by corneal reflections, there appeared to be a moderate right exotropia, with the right reflection being displaced nasally by approximately 25 dioptres base-in by prism reflection test (Fig. 2). The family reported that the right eye was noticed to 'turn' constantly and was noticed by the child's peers.

Cover testing revealed orthophoria to a light and accommodative target for near and distance. Fine manifest horizontal jerky nystagmus was noted, which increased on lateral gaze; ocular movements otherwise appeared full. No binocular functions were demonstrable.

Anterior segment assessment was unremarkable, with normal intraocular pressures. Dilated fundus examination revealed a dragged right macula, dislocated away from the optic disc towards the temporal peripheral retina. The left macula was normal.

Discussion

Pseudo-strabismus is a common orthoptic problem, most frequently pseudo-esotropia associated with wide epicanthic folds during infancy. A less prevalent but well-documented cause of pseudo-strabismus is displacement of the macula, known as macular heterotropia or macular ectopia, first described in 1898 by Bernhard.[1]

Normally, the macula is situated 3–4 mm from the temporal edge of the optic disc; any change less than 0.75 mm (half a disc diameter) can be considered physiological. Any greater variation in these findings is termed macular heterotropia. In 90% of macular heterotropia cases the macula is displaced temporally,[2] but it can also be displaced upwards, downwards or nasally.[3]

Macular heterotropia occurs where there are changes in growth rate in different areas of the retina, probably post-natally.[4] In the early stages of embryological development the growth rate in the macular region is high, but decreases by the third month to lag behind the rate of differentiation in surrounding retina, until the seventh month of gestation where a further marked acceleration is seen in the development of macular cells. When a child is born prematurely this growth cycle is interrupted, and abnormal variations in growth rate of either the retina or macula can result in shifting of the macula from its usual location,[5] as shown in Fig. 3.

Alternatively, the macula is mechanically dragged by retinal traction on the inner layer of optic cup before complete coaptation of inner and outer retinal layers at the posterior pole.[4] The optic disc takes on an 'octopus' shape and the condition can be unilateral or bilateral.[6] It is usually a congenital anomaly, though some authors suggest it can be acquired secondary to retinal trauma.[7]

Macular heterotropia is not a barrier to binocular functions. Prognosis for visual acuity is good and may be achieved using an abnormal head posture to utilise an eccentric fixation point, as was noticed in this child during right eye visual acuity testing. In this case, the eye with macular heterotropia achieved the better

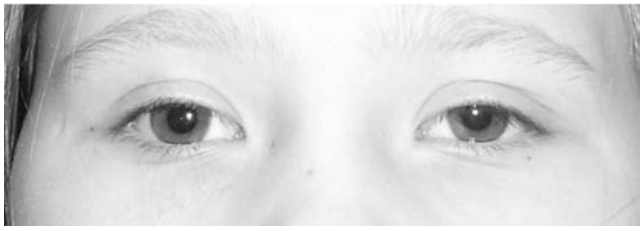

Fig. 2. The apparent right exotropia and nasally displaced right corneal reflection.

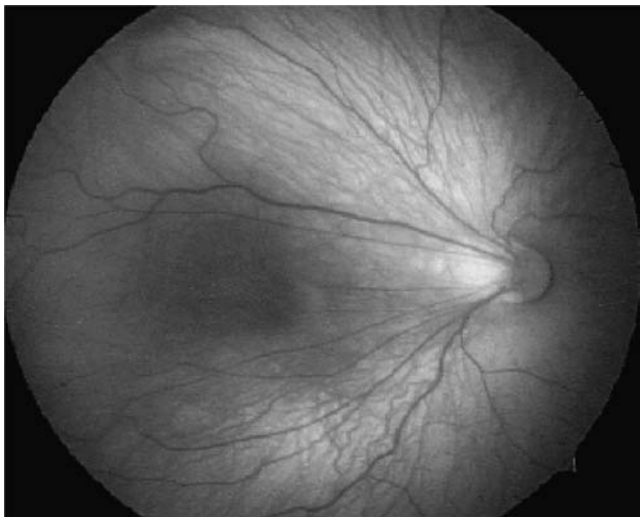

Fig. 3. Example of a fundus examination showing the dragged right optic disc and macular heterotropia.

monocular vision. The reduction in left eye visual acuity was attributed to anisometropic amblyopia. It is not known why occlusion treatment was not given to this child.

The shifting of the macula causes an abnormally large angle kappa. Angle kappa is the angle between the pupillary axis and visual axis, which is caused by a failure of the visual axis (the line of sight connecting the fovea to fixation target) and optical axis (an imaginary line connecting the centres of the cornea and lens) to coincide.[8] Usually the optical axis is positioned slightly nasally and inferiorly to the pupil, and normal corneal reflections are nasal to the centre of the pupil. This patient's temporal macular shift resulted in an abnormally large positive angle kappa, and a nasally displaced corneal reflection, thus giving the illusion of an exotropia.

It is well documented that premature babies both with and without ROP have a higher incidence of orthoptic problems, including strabismus, myopia, and refractive errors, compared with a normal population.[9–11] ROP, historically known as retrolental fibroplasia, is the most common cause of macular heterotropia[12] and the incidence in this patient group is reported as between 7.5% and 20%.[13–15]

Recent studies suggest that laser photocoagulation for threshold ROP (defined as that requiring intervention, with a median onset at 36–37 weeks' gestation) results in better anatomical, visual and refractive outcomes than cryotherapy.[16–19] Bianchi *et al*.[20] retrospectively studied 33 premature babies with acute ROP, of whom 20 patients underwent cryotherapy and 13 had spontaneous regression of their ROP. Macular heterotropia was not observed in any of the spontaneously regressed ROP group. The frequency of macular heterotropia in the eyes treated with cryotherapy was 2.7%, and is thought to be associated specifically with stage 2–3 ROP, as in this case. Sahni *et al.*[13] cited the incidence of macular heterotropia following cryotherapy as 20%, compared with 7% in laser-treated eyes.

Macular heterotropia can occur in conditions other than ROP. Wilkinson[21] described a case of pseudo-exotropia in a patient with a retinal tear. Brown and Haining[22] documented a similar pseudo-esotropia with idiopathic retinal folds, whilst Bergin[23] cited a case of macular heterotropia due to persistent hyaloid vessels. Other authors suggest associations with chorioretinal coloboma, chorioretinisis, *Toxocara canis* and vitreous structural anomalies.[4,24–26] Damms *et al*.[27] reported cases of pseudo-esotropia where the macula was dislocated in the direction of the optic disc in children with very high myopia (between −17 DS and −20 DS) without any other retinal abnormalities.

Management options for the pseudo-strabismus include surgery to improve cosmesis, despite contraindications such as loss of binocular single vision and inducing diplopia.[22,27] Fresnel prisms can be used to relieve post-operative diplopia. Prisms may be placed over the apparently 'fixing eye' to give the pseudo-strabismic eye an 'orthotropic' appearance. However, the prism may reduce visual acuity.[25]

Treatment for macular heterotropia is generally not advocated, the emphasis being treatment and control of retinal damage and correction of refractive error rather than aesthetic defects.[20]

Conclusion

Orthoptists should be aware of the features of macular heterotropia and associations with pseudo-strabismus, especially in cases of ROP. Orthoptists should take into account the anatomical fundus structure if cover test and orthoptic findings are inconsistent.

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References

1. Bernhard P. Ein Fall von abnormer Lage der Macula lutea und partiellem Colobom der Chorioidea. *Arch Augenheilkd* 1898; **37:** 51–57.
2. Scheiman M, Gallaway M, McKewicz L. Heterotropia of the macula (ectopic macula): an unusual presentation. *Am J Optom Physiol Opt* 1986; **63:** 567–570.
3. Silverman WA, Flynn JT. *Retinopathy of Prematurity: Current Controversies*, p. 243. Boston, MA: Blackwell Scientific, 1985.
4. Acers TE. Hypertelorism, heterotropia of maculas and pseudo-exotropia. *Am J Ophthalmol* 1965; **59:** 494–495.
5. Horwich H, Linfesty JW. Pseudostrabismus caused by heterotropia of the macula; report of a case and review of the literature. *AMA Arch Ophthalmol* 1956; **56:** 194–206.
6. Mintz-Hittner HA, Kretzer FL. Postnatal retinal vascularization in former preterm infants with retinopathy of prematurity. *Ophthalmology* 1994; **101:** 548–558.
7. Stein R. Heterotropie der Makula infogle narbiger Verziehung der Netzhaut nach Ignipunktur einer Netzhautblosung. *Klin Monatsbl Augenheilkd* 1931; **86:** 188–195,
8. Rowe F. *Clinical Orthoptics*, 2nd edition. Oxford: Blackwell Science, 2004.
9. Bullock H, Butcher JM, Burrows C, Hordern K, Smith L, Clegg S. Incidence and nature of orthoptic problems found in children previously screened for retinopathy of prematurity: an argument for orthoptic follow-up? *Br Ir Orthopt J* 2007; **4:** 54–57.
10. Schalij-Delfos NE, de Graaf MEL, Treffers WF, Engel J, Cats BP. Long term follow up of premature infants: detection of strabismus, amblyopia, and refractive errors. *Br J Ophthalmol* 2000; **84:** 963–967.
11. O'Connor AR, Stephenson TJ, Johnson A, Tobin MJ, Ratib S, Fielder AR. Strabismus in children of birth weight less than 1701 g. *Arch Ophthalmol* 2002; **120:** 767–773.

12. D'Esposito M, Caccia Perugini G. Aspetti ottico-fisiologici e clinici delle ectopie maculari. *Ann Ottal Clin Ocul* 1968; **94:** 725.
13. Sahni J, Subhedar NV, Clark D. Treated threshold stage 3 versus spontaneously regressed subthreshold stage 3 retinopathy of prematurity: a study of motility, refractive, and anatomical outcomes at 6 months and 36 months. *Br J Ophthalmol* 2005; **89:** 154–159.
14. Orozco-Gomez LP, Moguel-Ancheita S, Ruiz-Morfin I, Lambarry-Arroyo A. Evolution of threshold retinopathy after argon laser treatment under indirect ophthalmoscopy. *Cir Cir* 2006; **74:** 73–78.
15. Dogra MR, Narang S, Biswas C, Gupta A, Narang A. Threshold retinopathy of prematurity: ocular changes and sequelae following cryotherapy. *Ind J Ophthalmol* 2001; **49:** 97–101.
16. Connolly BP, McNamara JA, Sharma S, *et al*. A comparison of laser photocoagulation with trans-scleral cryotherapy in the treatment of threshold retinopathy of prematurity. *Ophthalmology* 1998; **105:** 1628–1631.
17. Laws F, Laws D, Clark D. Cryotherapy and laser treatment for acute retinopathy of prematurity: refractive outcomes, a longitudinal study. *Br J Ophthalmol* 1997; **81:** 12–15.
18. Pearce IA, Pennie FC, Gannon LM, *et al*. Three year visual outcome for stage 3 retinopathy of prematurity: cryotherapy versus laser. *Br J Ophthalmol* 1998; **82:** 1254–1259.
19. Ng EY, Connolly BP, McNamara JA, *et al*. A comparison of laser photocoagulation with cryotherapy for threshold retinopathy of prematurity at 10 years. Part 1. Visual function and structural outcome. *Ophthalmology* 2002; **109:** 831–833.
20. Bianchi PE, Guagliano R, Salati R, Traselli GP, Trimarchi F. Esotropia and pseudoexotropia in acute ROP sequelae: clinical features and suggestions for treatment. *Eur J Ophthalmol* 1996; **6:** 446–450.
21. Wilkinson C. An interesting case of pseudostrabismus. *Br Orthopt J* 1980; **37:** 101.
22. Brown J, Haining W. The problems of pseudo-strabismus. *Br Orthopt J* 1998; **45:** 86.
23. Bergin DJ. Nasal heterotropia of the macula with persistent hyaloid vessel. *J Paediatr Ophthalmol Strabismus* 1978; **15:** 373–375.
24. Alfieri MC, Magli A, Chiosi E, De Crecchio G. The Annete von Droste-Hulshoff syndrome. Pseudostrabismus due to macular ectopia in retinopathy of prematurity. *Ophthalmic Paediatr Genet* 1988; **9:** 13–16.
25. Foster RS, Metz HS, Jampolsky A. Strabismus and pseudostrabismus with retrolental fibroplasia. *Am J Ophthalmol* 1975; **79:** 985–989.
26. Hoole J, Nelson O, Davey K. *Toxocara* as a cause of pseudohypertropia occurring with actual hypodeviation of the same eye. *Br Orthopt J* 1997; **54:** 63–66.
27. Damms T, Damms C, Schulz E, Haase W. Pseudo-esotropia caused by nasal dislocation of the macula in patients with high infantile myopia. *Ophthalmologe* 1994; **91:** 77–80.