Localising patterns of optic nerve hypoplasia—retina to occipital lobe

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SUMMARY  Six cases are presented which provide clinical evidence that optic nerve hypoplasia can occur as a result of a lesion at any site in the developing visual system. The mechanisms of hypoplasia are discussed in the light of recent understanding of optic nerve development.

Optic nerve hypoplasia (ONH) results from damage at any site in the developing visual pathway.

The development of the anterior visual pathways is intimately linked with that of the globes, which begin as evaginations from the neural ridges, first seen as small pits at the 2-6 mm stage. By 4 mm the evaginations have grown rapidly, containing the hollow optic vesicles, which are connected to the developing prosencephalon by optic stalks.1 The wall of the vesicle, which ultimately forms among other structures the retina, including the ganglion cells, is neuroectodermal and is several layers thick by this stage.

At the 5 mm stage the optic vesicles become invaginated, forming the optic cups. During this process an inferiorly located groove remains open, forming the embryonic or fetal fissure, containing paraxial mesoderm.1 Fusion of this fissure begins at 10 mm and is completed by the 17 mm stage.

The first optic nerve elements are seen at the 13–14 mm stage in the form of dendriform fibrils emerging from the retinal ganglion cells proceeding towards the primitive epithelial papilla, the forerunner of the neuroectodermal optic disc.1

The fibres fill the optic stalk as they travel towards the future chiasm. By 22–30 mm the chiasm is formed, and the entire stalk is filled by fibres, cutting off the open communication between the optic vesicle and forebrain.

Decussating fibres appear first (22 mm), with the uncrossed fibres not appearing until much later at the 59 mm stage.2 The optic tract is formed by 48 mm.

Mesodermal elements give rise to the vascular and sepal system of the optic nerve and its dural sheath.

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isolated ONH a primary ganglion cell failure, occurring before the 17 mm stage (seven weeks gestation) has been implicated. This failure is most dramatically seen in optic nerve aplasia, which is believed to occur very early in the first trimester of development.

Whether primarily or secondarily involved, retinal and CNS ganglion cell failure may result from events occurring very early in gestational life, producing diverse CNS defects and ONH. Some congenitally anomalous discs represent lesser degrees of severity of ONH, and events up to and including the perinatal period may result in ONH. Margalith et al. described ONH coexisting with optic nerve atrophy in cases where defect-producing insults are assumed to have acted before or after visual pathway maturation.

The localisation of the defect is less clear than its timing. Scheie and Adler's frequently quoted paper implicates a primary mesodermal or ganglion cell failure. Others have argued for a primary CNS locus of insult. The absence of ganglion cells in the presence of normal outer retinal layers on histopathological examinations has led to the acceptance of primary retinal ganglion cell failure as being a causative event in ONH, especially in isolated unilateral cases. The amacrine and horizontal cells which arise from the same line are normal in these cases. Causes of the primary failure may be impaired induction of differentiation, unexplained and possibly genetic, though nearly all cases described are thought to be sporadic. Noxious and other environmental influences have been implicated. In optic nerve aplasia there may be a complete failure of ganglion cells to send axons.

Mesodermal failure in optic nerve aplasia is made unlikely owing to the presence of other normal mesodermal derivatives.

In the setting of an enormous normal axonal loss any abnormal influences would enhance such a loss either directly or by interfering with their trajectory to central synapses. Such an influence at any site could result in a hypoplastic nerve. Environmental influences may be important in this sensitive stage of ganglion cell development. One may speculate that such influences could alter the intrauterine environment sufficiently, at the critical point in time and location, to result in ONH and CNS defects.

Developmental abnormalities in the CNS may result in secondary retrograde optic nerve axon degeneration either directly or transsynaptically. Retrograde degeneration of optic nerve axons is not a new concept. Encephaloclastic processes which result in major defects, such as porencephaly, hydranencephaly, and anencephaly, have been associated with ONH. Hoyt et al. linked ONH with cerebral abnormalities, and many published cases implicate the CNS at various levels. ONH may also develop in association with early onset cerebellar tumours.

Central lesions may act via several mechanisms. A chiasmal or third ventricular lesion could obstruct outgrowing axons or deflect them, preventing them from securing central connections, which are necessary for their survival. This would result in an axonal degeneration and may be accompanied by a midline CNS defect and an endocrinopathy. Similar axonal effects may be seen in more posterior lesions. Hemispheric abnormalities could produce a retrograde axonal degeneration transsynaptically. A developing CNS could also stretch the ganglion cell axons, resulting in their secondary degeneration. Thus ONH could result from a multitude of influences acting early in embryonic life and at several points along the visual pathway.

In this paper we shall present six cases which provide clinical evidence that ONH occurs as a result of lesions at several sites in the visual pathway from the retina to the occipital lobe.

Case reports

CASE 1
This 4-year-old boy, who was deaf, presented with a right sided squint. It was not possible to measure his acuity, but he fixed well with the left eye. The right eye had a larger macular coloboma than the left, with evidence of sector hypoplasia in the part of each optic disc.

Fig. 1 Case 1. Left eye showing a nerve fibre layer defect related to a temporal segment of hypoplasia in the optic disc.
CASE 2
This 6-month old boy presented with a squint and was found to have a relative afferent pupil defect in the right eye associated with a profoundly hypoplastic optic disc (Fig. 2). The left eye was unequivocally normal on examination. The visual evoked response (VER) and electroretinogram (ERG) were normal on the left.

Fig. 2  Case 2. The right eye has a profoundly hypoplastic optic disc, while the left is normal.

Fig. 3  Case 3. A: The left optic disc has a hypoplastic upper half associated, B: with a total inferior altitudinal field defect. C: The right eye was normal.

disc corresponding to the papillomacular bundle (Fig. 1).
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CASE 3
This 16-year-old girl presented because of non-specific headache. The visual acuity was 20/15 in each eye. Visual field examination revealed an absolute inferior altitudinal defect in the left eye (Fig. 3A) and there was a left relative afferent pupil defect. The left optic disc showed a markedly hypoplastic upper half with a marked retinal nerve fibre layer defect superiorly (Fig 3B). The right eye was normal (Fig 3C). A CT scan was normal.

CASE 4
This 17-year-old girl had had a fine rotary and horizontal nystagmus from early life. The visual acuity was 20/25 in the right eye and 20/100 in the left eye. She had normal colour vision in both eyes and normal pupil reflexes. There was a bitemporal visual field loss, with normal visual thresholds along the vertical meridian (Fig. 4A). Bilateral optic nerve hypoplasia in particular affecting the nasal and temporal segments of both optic discs, with relative preservation of the superior and inferior nerve fibre layer, was found on fundus examination (Fig 4B). Neuro-radiological investigations were all normal.

CASE 5
This 20-year-old Korean girl had had unsteady eyes from early childhood. She was found to have an
acuity of 20/30 in the right eye and 20/100 in the left eye with an asymmetrical nystagmus with a see-saw component, with the left eye having a more or less vertical nystagmus with some rotary component, while the right had a purely horizontal nystagmus (Fig. 5). A bitemporal hemianopia was noted. There was bilateral optic nerve hypoplasia, in particular affecting the nasal and temporal segments of the optic disc. Pneumoencephalography demonstrated an absent septum pellucidum.

CASE 6
This 20-year-old girl was found to have a left homonymous hemianopia when she was examined for the investigation of headaches. Both optic discs were found to be small and the left showed a relative loss of disc substance and the associated nerve fibre layer in the nasal and temporal segments. The right optic disc was diffusely small (Fig. 6A). A CT scan (Fig. 6B) revealed a porencephalic cyst in the right occipital pole.

Discussion

Our cases provide clear evidence that there is no one site for the lesion responsible for ONH. The large congenital macular colobomas in case 1 have commensurate deficiencies in retinal ganglion cell axons in hypoplasia of a segment of the optic nerve, which demonstrates a primary ocular embryological insult causing ONH.

A well demarcated unilateral altitudinal field defect and the relative afferent pupil defect, with the other eye being normal (case 2), implicate the distal end of the optic nerve or the retina. The purely unilateral case 3 implies a site anterior to the optic nerve chiasmal junction.

Bitemporal hemianopic field defects in cases 4 and 5 are associated with chiasmal lesions, and see-saw nystagmus, as seen in case 5, is usually associated with suprasellar lesions with bitemporal hemianopia.

Neurological investigations in case 4 were unrewarding, whereas in case 5 an absent septum...
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Fig. 6B

Fig. 6  Case 6. A: Incidental finding of a left homonymous hemianopia led to a porencephalic cyst of the right occipital lobe. B: Both optic discs are hypoplastic, the left (associated with the temporal hemianopia) showing a relative loss of disc substance and associated peripapillary nerve fibre layer nasally and temporally.

Professor Philip Aitken, of Burlington, Vermont, kindly allowed us to publish case 3.

References


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