Spectrum of optic nerve hypoplasia

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SUMMARY Optic nerve hypoplasia is a non-progressive condition characterised by subnormal vision and a subnormal number of optic nerve axons. It may be unilateral or bilateral, isolated or combined with other defects. Analysis of fundus photographs from a series of 7 patients with a stationary abnormality of different degrees showed that the functional defects could be closely correlated with defects in the retinal nerve fibre layer. Our observations show that the condition has a wide range of both functional and anatomical defects and that a subnormal diameter of the optic disc is not a requisite for the diagnosis. Presumably, there is also a wide variety of causes, not only a primary failure of development of retinal ganglion cells. We suggest that optic nerve hypoplasia can be viewed as a non-specific manifestation of damage to the visual system, sustained any time before its full development.

Hypoplasia of the optic nerve is a congenital condition that occurs in both man and domestic animals. More than 100 cases have been recorded (for recent reviews see Awan, 1976; François and de Rouck, 1976). Optic nerve hypoplasia may be coupled with other malformations but is often isolated; it may be unilateral or bilateral. A cardinal sign of severe hypoplasia is a subnormal diameter of the optic nerve head. The hypoplastic optic disc is commonly surrounded by a yellowish ring of approximately normal disc diameter; sometimes there is also an inner, pigmented ring. An additional but inconstant sign is a small diameter of the optic canal (Merin *et al.*, 1971). The most important functional corollaries are amblyopia with strabismus or nystagmus (Edwards and Layden, 1970; Walton and Robb, 1970). There are rare cases on record where only the peripheral visual field suffers and acuity approaches normal (Gardner and Irvine, 1972). An afferent pupillary defect is common and signifies a subnormal number of afferent retinal channels. Deficiency of retinal ganglion cells and optic nerve axons has also been documented histologically (Whinery and Blodi, 1963).

In addition to cases with the classical picture of optic nerve hypoplasia we have seen a number of patients with much less obvious abnormalities of apparently congenital origin. All had photographically documented defects in the retinal nerve fibre layer corresponding to their functional defects. In

some cases optic disc diameters were within normal limits. Our observations indicate that optic nerve hypoplasia may show considerable variation in severity, with a spectrum ranging from severe to a minimal deficiency of optic nerve axons. Our findings are detailed below.

Methods

Fundus photographs were obtained with the Carl Zeiss fundus camera and Kodachrome 25 ASA film. The diapositives were copied on Kodak Plus-X black-and-white film, using 'red-free' light (Kodak Wratten filter No. 40). Black-and-white prints were then produced, using unsharp masking for additional enhancement of nerve fibre bundle contrast (Frisén and Hoyt, 1973).

Final magnification was $\times 20$ (including nominal camera magnification).

Case reports

Case 1, a schoolboy of 14, was referred in connection with an investigation for small stature. He was -2 standard deviations in weight for his age, and -3 standard deviations in height. No systemic or endocrinological abnormalities were disclosed. His parents were also of small stature.

He stated that he had always had a convergent squint and poor vision on the right. Treatment for amblyopia had been tried at the age of 1 but was of no avail. He had therefore been admitted to his county hospital for further investigation. The file

Right eye

Left eye

Fig. 1 Case 1. Severe optic nerve hypoplasia on the right; left eye normal. Note the small size of the right optic disc, and the apparent absence of nerve fibre opacity and striations. All vessels are clearly exposed. Vision was questionable perception

was not available for review, but a diagnosis of unilateral amblyopia of presumably congenital origin was made.

Neuro-ophthalmological abnormalities at the age of 14 were restricted to the right eye, which converged 15°. The motility was not impaired. There was a prominent afferent pupillary defect on the right commensurate with the vision; questionable perception. The right eye bulb appeared identical to the fellow eye except for the small size of the optic disc and the apparent absence of a retinal nerve fibre layer (Fig. 1). Left eye acuity was 6/5 unaided, and isopters to Goldmann targets II and I4 were normal in size and shape. There was nothing to suggest septo-optic dysplasia or basal encephalocoele. A diagnosis of pronounced hypoplasia of the right optic nerve and disc was made.

Case 2 was seen in consultation at the age of 11 because of periodic diffuse headaches. Paediatric and neurological examinations disclosed nothing abnormal.

The patient denied eye symptoms. Visual acuity was approximately 6/7.5 (−1.0 cyl. 90°). Visual field examinations disclosed severely contracted visual fields, much more so in perimetry than in confrontation tests, suggesting an important functional component. There were no discernible focal visual field defects. The optic discs were somewhat pale and surrounded by double rings. The retinal nerve fibre layer seemed very thin in all sectors (Fig. 2). The neuro-ophthalmological examination was otherwise unremarkable. Optic canal diameters were

within normal limits. The diagnosis of bilateral optic nerve hypoplasia was supported by lack of change during two years of follow-up.

Fig. 2 Case 2, bilateral optic nerve hypoplasia. Both eyes were equally affected; only right eye is shown here. The optic disc is somewhat small and pale. There is an incomplete double ring sign (a pigmented ring separates the true disc border from the yellowish peripapillary area). Note the apparent absence of nerve fibre opacity and striations, and the exposure of retinal vessels. There was concentric contraction of the visual field, and subnormal visual acuity (6/7.5)

The headaches were attributable to difficulties in school.

Case 3, a 23-year-old schoolteacher, was referred in connection with an investigation for amenorrhea following one year's use of contraceptive pills. Nothing abnormal was disclosed in the general and endocrinological examinations.

She stated that myopia on the left had been diagnosed 5 years earlier. She had no other known eye problem. Visual acuity was 6/4 in both eyes, without correction on the right, -2.0 sph. on the left. Perimetry revealed a nasal contraction in the left eye visual field (Fig. 3). There was no discernible afferent pupillary defect. The left optic disc was

Fig. 3 *Case 3. Contraction of the nasal periphery of the left visual field due to left optic nerve hypoplasia*

poorly defined but appeared smaller than the right.

The arcuate bundles, which serve the nasal visual field, appeared thinner on the left. There was no disc pallor (Fig. 4). There were no other abnormalities. A diagnosis of unilateral optic nerve and disc hypoplasia appeared warranted.

Case 4, a 28-year-old shop assistant, was referred because of suspicion of a cerebral tumour. She had suffered severe frontal headaches during the last 3 months and had noticed occasional photopsias on the left during that time. She had recently had 3 Jacksonian seizures on the left, with transient hemiparesis and dysaesthesia. A left-sided visual field defect had been noted during the general examination.

The neuro-ophthalmological examination disclosed a temporal visual field depression and contraction in the left eye; there was no abnormality on the right (Fig. 5). Acuity was 6/6 in both eyes unaided; cycloplegic refraction was +1.0 sph. on the right, +0.5 sph. on the left. There was no clear-cut afferent pupillary defect. Colour vision was normal (Ishihara test). There was no disc pallor. The retinal nerve fibre layer appeared overall thinner on the left, particularly on the nasal side, corresponding to the field defect (Fig. 6). There were no other abnormalities. A diagnosis of coincidental hypoplasia of the left optic nerve and disc was made.

No cerebral tumour was disclosed during the subsequent investigation. Electroencephalograms and ultrasound encephalograms were normal. Arterial hypertension was present. The headaches

Right eye

Left eye

Fig. 4 *Case 3. Left optic nerve hypoplasia. Note relative thinning of the arcuate bundles and lower height of the optic disc in the left eye, predicting a nasal visual field defect (cf. Fig. 3). Visual acuity was 6/4 OS*

Fig. 5 Case 4. Contraction and depression of the left visual field due to left optic nerve hypoplasia

and the seizures did not recur after antihypertensive medication.

Cases 5 and 6 were uniovular twin brothers, in whom unilateral impairment of vision was noted at a routine examination at the age of 4. They were otherwise in excellent health. Case 5 was right-handed and had poor vision on the left; his brother was his mirror image in these respects.

Both had an unaided acuity of 10/15 (HOTV test) in the better eye, and 10/100 in the fellow eye. Cycloplegic refraction was about +1 D in the better eye, and -1 D in the other. Vision in the poor eye improved to 10/35 on correction. There was no further improvement with a pinhole. None had a clear-cut afferent pupillary defect.

Both patients had optic discs of approximately

normal size, with distinct double rings. The eye with the poorer vision had a relatively thinner retinal nerve fibre layer than the fellow eye (Fig. 7), suggesting the presence of a concentric visual field depression. Formal testing of the visual fields was not possible; informal tests gave normal results.

There was no change at follow-up 1 year later.

Minor, unilateral optic nerve and disc hypoplasia was diagnosed in both cases, on the left in Case 5, on the right in his brother.

Case 7. This woman was born with a spastic hemiparesis on the right. Although retarded in mental development and additionally handicapped by a seizure disorder, she grew up to become a capable farmer's wife and a mother of 2 children. Because of intractable seizures she was subjected to

Right eye

Left eye

Fig. 6. Case 4. Left optic nerve hypoplasia. The optic discs are approximately equal in size but the retinal nerve fibre layer is much thinner on the left, particularly on the nasal side, predicting a predominantly temporal visual field defect (cf. Fig. 5). Visual acuity was 6/6 OS

Fig. 7 Cases 5 (above) and 6 (below). Unilateral optic nerve hypoplasia in uniovular twins. Optic discs are small but within normal limits. The retinal nerve fibre layer appears overall thinner in the eye with subnormal acuity (the left eye in Case 5, the right in Case 6)

a left hemispherectomy at the age of 30. Left-sided hydranencephaly was diagnosed at that time. She was known to have a complete hemianopsia to the right since childhood. The right eye was amblyopic. At the last examination, at the age of 40, she presented exotropia on the right. Visual acuity was 6/30 (-2.5 sph. -1.5 cyl. 90°) on the right, 6/6 (-4.5 sph.) on the left. There was no afferent pupillary defect. She had a complete homonymous hemianopsia to the right, respecting the vertical meridian.

Fundus examination disclosed rather small optic discs on both sides (Fig. 8). There was no pallor. Because of an apparent lack of retinal nerve fibres in the nasal and papillomacular sectors, the arcuate bundles (which serve the functioning temporal hemiretina) were very conspicuous. The left optic disc was more oval in shape. Retinal nerve fibres were present round all its circumference, but the arcuate bundles were much thinner than on the right. A diagnosis of homonymous hemioptic hypoplasia

Right eye **Left eye**
 Fig. 8 Case 7. Homonymous hemioptic hypoplasia. The optic discs are quite small. Nasal and papillomacular sectors of the retinal nerve fibre layer appear to be missing in the right eye, enhancing the contrast of the arcuate bundles. In the left eye, the arcuate bundles are much thinner. These abnormalities correspond to a complete homonymous hemianopia to the right

was made. It was most likely due to a suprageniculate lesion on the left.

Discussion

The first case fulfils classical criteria of severe optic nerve hypoplasia. In view of the apparently complete absence of a retinal nerve fibre layer in the affected right eye it might be argued that aplasia is a more appropriate designation. However, it has previously been suggested that the term aplasia should be reserved for cases lacking also a retinal vascular supply (Kreibitz, 1959; François and Hruby, 1970; Little *et al.*, 1976). The second case was less severely affected, although the condition was bilateral. The retinal nerve fibre layer was exceedingly thin, in keeping with the uniformly depressed and contracted visual fields, and the subnormal visual acuity. Case 2 also exhibited the peripapillary double ring sign, with an incomplete pigment ring adjacent to the true disc border, and an outer yellowish ring. The abnormality seen in these 2 cases is easily recognised provided the examiner is not misled by the double ring feature (Edwards and Layden, 1970; Walton and Robb, 1970). Nevertheless, Case 1 had been subjected to amblyopia treatment.

Cases 3 and 4 present less striking abnormalities but qualify for a diagnosis of unilateral optic nerve hypoplasia in that they had minor unilateral abnormalities of the optic disc and the retinal nerve

fibre layer corresponding to their minor, stationary visual handicap. These degrees of optic nerve hypoplasia are more difficult to identify. Their detection requires a high index of suspicion in addition to fundus photographs of good quality (Seeley and Smith, 1972). Juxtaposition of bilateral fundus photographs showed a thin peripapillary retinal nerve fibre layer corresponding to areas of impaired function in the affected eye, with foreshortening of the optic disc, and incomplete double rings. An additional important sign that suggests a congenital condition was lack of optic disc pallor. None of these cases had a clinically clear-cut afferent pupillary defect, suggesting that the mass of optic nerve fibres serving the central visual field was fairly normal. The acuity results also point to a normal or nearly normal density of macular afferent channels (*cf.* Frisén and Frisén, 1976).

Cases 5 and 6 represent the smallest degree of optic nerve hypoplasia that we have been able to document with available techniques. The fundus abnormalities are so subtle that it is possible that they might have been missed altogether. What led to closer investigation was the fact that Cases 5 and 6 are uniovular twins and perfect mirror images with regard to laterality of visual impairment, handedness, and distribution of hair whorls. The subsequent investigation disproved a complete situs inversus in either twin.

As indicated above, smaller than classical

Right eye

Left eye

Fig. 9 Unmasked fundus photographs of clinically normal, emmetropic eyes, illustrating the normal range of disc size. Note the inverse relationship between marginal blur and disc diameter

degrees of optic nerve hypoplasia are difficult to detect in cases lacking a normal fellow eye for comparison. *Bilateral*, low-degree hypoplasia is exceedingly difficult to diagnose from the appearance of the disc because of the difficulties of defining optic nerve and disc parameters *in vivo*. The size of the disc image in fundus photographs is influenced by the anatomical dimensions of the eye and optical aberrations. The magnitudes of these factors are generally not known for individual eyes, but it has recently been claimed that their effect is relatively small (Bengtsson, 1976). Emmetropic eyes may show the smallest variation in this regard: even so, we have observed that the horizontal diameters of well-focused disc images in colour diapositives from normal emmetropic eyes range between at least 7 and 12 mm at 5 $\times$ nominal magnification in the Carl Zeiss fundus camera. Franceschetti and Bock (1950), using a contact lens and a measuring microscope, also found an extensive range of normal disc diameters (1.23 to 1.99 mm). It is worthy of note that the optic discs of the majority of our cases fall within the normal range of disc sizes. Paradoxically, hypoplasia may thus occur in optic discs of normal size.

Evaluation of the retinal nerve fibre layer offers an alternative approach to the problem of recognising minor optic nerve hypoplasia. This approach is also more direct, as the neuroanatomical hallmark of hypoplasia is a smaller than normal number of optic nerve axons. It is unfortunate that many cases of optic nerve hypoplasia show a uniformly thin

nerve fibre layer within affected areas, as this particular type of defect is much more difficult to define unambiguously than are focal defects (Hoyt *et al.*, 1973). Distinctive signs occur only in severely affected eyes. Such signs include absence of nerve fibre layer opacity and striations, exposure of small retinal vessels normally hidden in the nerve fibre layer, and the appearance of broad, bright reflexes along major retinal vessels. The latter sign may reflect loss of perivascular nerve fibre bundles that normally prevent vascular indentations of the posterior vitreous or the internal limiting membrane. Smaller degrees of diffuse thinning of the nerve fibre layer are most easily recognised by scrutiny of the optic disc border. In normal eyes, there is an inverse relationship between the size of the optic disc and the degree of blurring of its border (Figs. 9a and b). Whenever the diameter of the disc is small, there is a small circumference of the scleral opening, and axons from the retinal ganglion cells become crowded at the disc margin. Small normal optic discs are sometimes difficult to differentiate from early papilloedema (Hoyt and Knight, 1973). Conversely, large discs are relatively much better defined with regard to their borders, and really large specimens may give the impression of partial optic atrophy. These features of normal optic discs appear to be conserved in cases of minor optic nerve hypoplasia, suggesting that the disc may accommodate to the actual mass of nerve fibres during embryological development. Such accommodation is also suggested by the double ring sign. This may be viewed as a

reflection of secondary filling-in of a relatively too large scleral opening. The pigment ring may represent fragmentation of the pigment layer associated with centripetal movement of the scleral anlage, while the pale ring may reflect lack of such movement of the choriocapillaris.

However, some cases of optic nerve hypoplasia show much less blur of the disc border than expected from the size of the disc. Pallor may be an additional feature of these cases (e.g., Case 2). It may be that these features reflect damage occurring at such a late date during development of the eye that secondary filling-in processes are incomplete or even lacking. The fundus picture then resembles ordinary, acquired optic atrophy, where dissociation between disc size and marginal blur is a characteristic feature.

This observation raises the important question of precisely what differentiates optic nerve hypoplasia from ordinary optic atrophy. The term hypoplasia is commonly used to indicate a primary failure of development, in this instance a primary failure of development of retinal ganglion cells. Following Scheie and Adler (1941), most contributors appear to subscribe to this hypothesis. Although it may apply to some cases of bilateral abnormality, for example, in connection with toxic or infectious conditions (McKinna, 1966; Cagianut and Theiler, 1976; Hittner *et al.*, 1976), this hypothesis is difficult to accept in cases with a more circumscribed, unilateral abnormality. In this context it is worthy of note that patients with congenital, unilateral damage to the suprageniculate visual pathway show a highly similar form of fundus abnormality (Case 7, Fig. 8), so-called homonymous hemioptic hypoplasia (Hoyt *et al.*, 1972; Manor and Korczyn, 1976). In these cases the fundus abnormality must be viewed as a consequence of descending, trans-synaptic optic atrophy. The same may apply in the septo-optic dysplasia syndrome (*cf.* Davis and Shock, 1975). It may be that most cases of optic nerve hypoplasia should be regarded as no more than ordinary but non-progressive optic atrophy acquired any time before full development of the eye and the visual pathway. Conceivably, similar pictures could be produced even by perinatal damage.

What, then, indicates that damage occurred before complete development? The double ring peripapillary sign may be helpful, but is often absent. Its occasional occurrence in clinically normal eyes diminishes its diagnostic value. An inferior conus may be significant (Manor and Korczyn, 1976). Radiological determinations of optic canal dimensions are of little help (Walton and Robb, 1970). B-scan ultrasound measurements of the diameter of the orbital optic nerve may be more informative

(Boynton *et al.*, 1975). At present it appears that optic nerve hypoplasia can be diagnosed with reasonable certainty only in cases showing accommodation of the disc to the remaining mass of nerve fibres and by exclusion of progressive conditions. The size of the disc itself may be misleading, at least in cases with minor hypoplasia.

On the basis of our observations and the above discussion we consider optic nerve hypoplasia to indicate non-specifically that the eye or the visual pathway has sustained irreversible axonal damage at some time before full development of the eye. The precise nature and location of the primary injury is unknown in most cases. The spectrum of optic nerve hypoplasia appears to be very wide also with respect to the extent of damage. It should be stressed that there are many minor variants. Their recognition may save much agony.

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