Aplasia of the Optic Nerve

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True aplasia, congenital absence of both the neuronal and the vascular elements, is a very rare anomaly affecting the optic nerve. In the past, problems of differentiation between aplasia and hypoplasia of the optic nerve have led to confusion in the literature which is reflected by numerous cases of actual hypoplasia having been published as cases of aplasia of the optic nerve.

In those cases of true aplasia previously reported, most have occurred in association with severe malformation of the central nervous system such as anencephaly, hydranencephaly, hydrocephaly and with cyclopia. This paper presents a case of true aplasia of the optic nerve in an otherwise healthy and normal child.

CASE REPORT

Our patient was the product of an uncomplicated full-term pregnancy and an uncomplicated delivery, weighing six pounds and 11 ounces at birth. Her two older siblings as well as her mother and father have normal ophthalmoscopic examinations. There is no family history of birth defects or consanguinity.

At birth, the child was found to be normal in every respect with the exception of a small left eye (Fig. 1). She was first evaluated by us at six weeks of age, again at ten weeks of age, and again at the age of five months. The general physical examination revealed an alert Caucasian female who appeared normal in development for her age, and who was in the ninety-seventh percentile for height and weight on the Boston Children's Growth Chart for infant girls.

At the age of ten weeks, she was noted to have good fixation and following movements of the right eye, but absent fixation of the left eye and an accompanying left esotropia. A startle response to bright light was present in the right eye but absent in the left eye. Normal ductions were present in each eye and no nystagmus was noted. Corneal sensation was normal in both eyes. A slight anisocoria was present, the right pupil measuring three mm and the left pupil measuring four mm. A flat one mm pigmented area was present at one o'clock on the iris of the left eye. There was no heterochromia, and the right pupil responded normally to direct light with an accompanying consensual response of the left pupil. However, the left pupil did not respond to direct light stimulation nor did the right pupil react consensually.

Under anesthesia with halothane, the anterior segment and fundus of the right eye were entirely normal (Fig. 2a). Corneal diameters in the horizontal plane measurement 11 mm in the right eye, and nine mm in the left eye. Intraocular pressures (Schlitz) were 12.2 mm Hg, right eye and 14.6 mm Hg, left eye. Except for the microcornea, the anterior segment of the left eye

Fig. 1. Note smaller left eye, slightly eccentric and larger left pupil.
was normal, and the lens was clear and in normal position. Refraction utilizing one percent cyclopentolate (Cyclogyl) was: right eye, +0.50 sph and left eye, −1.00 −1.50 x 30°.

In the left eye, aplasia of the optic nerve was seen — no optic disc or retinal vessels could be identified. In the region normally occupied by the disc, a deep gray pit-like structure was present which was round and about one-third the size of a normal disc and which was surrounded by a lightly pigmented annular zone (Fig. 2b). On its nasal aspect, and in contact with the pit, was a round, one disc diameter coloboma. A second coloboma was present inferior and nasal to the pit and was about the same size as the pit. A third coloboma, again the size of the pit, was present near the equator in the inferonasal quadrant near the six o'clock meridian. The fundus was lightly pigmented, and prominent choroidal vasculature was visible everywhere except within the colobomas. A foveal reflex could not be discerned. Peripheral retina, pars plana and ciliary processes appeared normal with scleral depression. Axial length measurements were done with a Smith-Kline Ekoline-20 A-scan ultrasonography unit utilizing a stand-off well. The right eye measured 17 mm and the left, 15 mm.

Fluorescein angiography using 0.4 cc of a 10 percent solution (4 mg/kg), revealed no retinal vasculature within the limits of the pit or the posterior pole. A faint choroidal flush appeared, which momentarily rendered the larger choroidal vessels less distinct (Fig. 3).

At the age of eighteen weeks, an ERG was done utilizing sedation with meperidine HC1 (Demerol), promethazine HC1 (Phenergan) and chlorpromazine (Thorazine). The response of the dark adapted right eye to a white light was normal. The left eye gave a reduced but definitely reproducible response which contained both A and B waves, though the B wave amplitude was one-half that of the normal eye.

DISCUSSION

Through a review of the literature, as well as the observations made in the present case, differentiation of true aplasia of the optic nerve from hypoplasia of the optic nerve is made here on the basis of clinical and histopathological findings summarized in Table I.

In the normal development of the optic nerve, mesoderm enters the fetal fissure at
### TABLE I
DIFFERENTIATION OF TRUE APLASIA FROM HYPOPLASIA

<table>
<thead>
<tr>
<th>Aplasia</th>
<th>Hypoplasia</th>
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</thead>
<tbody>
<tr>
<td>Vision</td>
<td>Blind (NLP)</td>
</tr>
<tr>
<td>Disc Appearance</td>
<td>Absent</td>
</tr>
<tr>
<td>Vasculature</td>
<td>Central and branch vessels are absent</td>
</tr>
<tr>
<td>Pupillomotor</td>
<td>Afferent pupil defect</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Ganglion cells and nerve fiber layer absent</td>
</tr>
</tbody>
</table>

the 4.5 mm stage and formation of the hyaloid artery is completed by the 10 mm stage when communication with the annular vessel is established. Scheie and Adler have suggested that the defect in aplasia is failure of the hyaloid system to enter the fetal fissure, thus allowing premature closure of the fissure, with subsequent failure to continue normal development of the nerve fiber and ganglion cell layers. Aside from the concept of premature closure of the fissure, we suggest that subsequent loss of the retinal ganglion cells and nerve fibers in aplasia may be due to failure in retinal vascularization with subsequent atrophy of these elements, much as these layers in the adult retina atrophy following central artery occlusion.

In the case of hypoplasia, it is assumed that the hyaloid system develops normally and that the primary defect is in the development of the ganglion cell layer. Normally, the hyaloid system is completed by the 10 mm stage and the retinal ganglion cell layer differentiated by the 17 mm stage. This would suggest that the defect in hypoplasia occurs in the 10 to 17 mm stage, whereas that in aplasia occurs at the 5 to 10 mm stage.

There are alternatives that could be used in explaining the defects responsible for aplasia of the optic nerve. In the present case, the clinical appearance suggests to us that there was no development of the hyaloid vascular system. We feel that this lends support to the concept that the defect in aplasia is primary failure of the development of the mesodermal elements within the fetal fissure.

The presence of a clinically normal lens in our patient is not incompatible with the idea that there was a primary failure in the development of the hyaloid vessels. The tunical vasculosa lentiis, by its nature, is a highly anastomotic network of vessels joining the annular vessel and the hyaloid system; we believe that the lens can develop normally within a vascular tunic supplied solely by the annular vessel.

Based on the foregoing criteria as set forth in Table I, the observations made in the present case, and by reference to the two review papers by Scheie and Adler and by Renelt, we have classified the available literature on aplasia of the optic nerve in Table II. In each case, the pertinent review article is cited, along with the essential features of the case which, in our opinion, renders it a case of either true aplasia or one of hypoplasia. There are 28 cases cited, including the present report. Of these, six meet the criteria of true aplasia. They are the cases reported by von Graefe in 1854, Retze in 1896, Meissner in 1911, Krauss in 1920, Renelt in 1971, and that reported by the present authors.

Of those cases which were in actuality hypoplasia, the earliest are those reported by Newman in 1864. This was a description of two blind sisters. Both patients had normal pupillary responses to light. One of the sisters had nystagmus, which made examination of the fundus difficult. The other was described as having an irregularly star shaped patch of dark nonvascular appearance occupying the place of the disc. Although no retinal vessels or optic disc were described, we believe, because of the presence of normal pupillary responses, that both of these cases represent hypoplasia or some abnormality other than aplasia of the optic nerve.
The cases reported as aplasia by Briere, Magnus, Everbusch, Beard, Duane, Hawley, Schwarz, Cords, Velhagen, Ridley, and Krauss in 1913 have been reviewed by Scheie and Adler and classified as Hypoplasia. Three cases reported by Smith, two reported by Kytita, and those reported by Kreibig and Sommerville have been reviewed by Renelt and classified as hypoplasia.

In 1940, Young reported as aplasia the case of a child with an esotropic, congenitally blind left eye. The fellow eye was blind due to "metastatic uveitis." Examination of the left eye revealed a retinal detachment temporally and a single small retinal vessel with remnants of the hyaloid system present nasally. Although this patient came to autopsy, the left eye was not examined. We believe this to be a case of hypoplasia or some other abnormality because of the presence of retinal and hyaloid vascular elements.

A seven-year-old child examined by Bernoulli in 1949 had absence of a recognizable optic disc in the left eye and it was reported as a case of aplasia. However, normal retinal vessels were present; and, although the vision was only light perception, normal pupillary light responses were present. We have classified this case as one of hypoplasia. The earliest report of true aplasia of the optic nerve was written in 1854 when von Graefe described the case of a ten-year-old boy who had a totally blind, esotropic left eye. The optic disc, central vessels and retinal vessels were absent. These features (absent disc and absent vessels with total blindness) are common to all six cases which have been classified here as true aplasia. In contrast, patients with hypoplasia have a small, but present optic disc and retinal vasculature. These eyes are not blind, but most frequently have poor vision. Walton and Robb reported a series of 17 eyes with hypoplasia in which 14 had less than 20/400 vision. On the other hand, better vision does occur in hypoplasia, and Gardner and Irvine have reported vision as good as 20/20 following occlusion therapy in patients with hypoplasia. The concept that eyes with aplasia of the optic nerve should be totally blind is best
supported by the work of Meissner, who in 1911 described in detail the histologic findings from an infant who died from pneumonia. The child was born with cleft lip and palate and conorneal leukomas. No optic discs or retinal vessels were visible in either eye. The retinas were found to be dysplastic in areas, and there was a complete absence of the nerve fiber and ganglion cell layers.14

On the other hand, Ewald has described the histopathology in cases of hypoplasia, and has shown that the retinal vasculature is normal, while the ganglion cell layer and the nerve fiber layer may be absent or hypoplastic.15 One might conjecture that in hypoplasia, the degree of vision loss and the presence of an afferent pupillary defect would correlate directly with the degree of hypoplasia of the nerve fibers and ganglion cells, total absence of these structures being associated with blindness as is the case in aplasia of the optic nerve. Walton and Robb reported that 80 percent of their cases of hypoplasia had abnormal pupillary light responses.12 We would expect that all patients with aplasia would have afferent pupillary defects.

SUMMARY

A case of unilateral true aplasia of the optic nerve in an otherwise normal and healthy child is presented. Twenty-eight previously reported cases of aplasia have been reviewed and classified according to criteria which we have presented. Only six of these cases, including the present case, represent true aplasia, manifested by total blindness and complete absence of the optic disc and retinal vessels.

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REFERENCES