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Multiple Ocular Anomalies Associated With Maternal LSD Ingestion

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• Severe ocular malformations, including microphthalmos, intraocular cartilage, cataract, persistent hyperplastic primary vitreous, and retinal dysplasia, occurred in a premature baby girl. The mother had ingested LSD during the first trimester of pregnancy. To our knowledge, this is the third case reported of ocular teratogenesis associated with maternal LSD ingestion. Further cases must be documented to establish an actual cause and effect relationship between the drug and the induced malformations.

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Abnormalities in the development and the invagination of the primary optic vesicle have been associated with a variety of physical, chemical, and hereditary factors.[1] Microphthalmos and uveal coloboma, as well as other ocular malformations, have been reported in two infants born to women who had ingested LSD during the first trimester of prenatal development.[2,3] We present an additional case of severe bilateral microphthalmos in a premature infant exposed to LSD, cocaine, and heroin, with similar ocular developmental anomalies. The present case is somewhat unusual because of the additional finding of intraocular cartilage.

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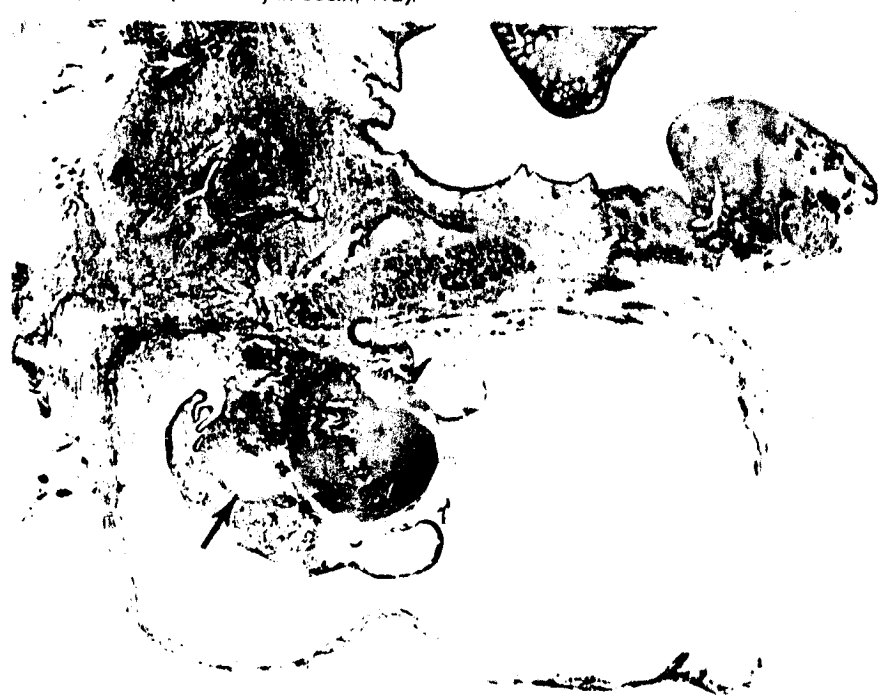
Fig 1.—*Infant weighing 1,850 gm demonstrates poorly developed ocular adnexa and cryptophthalmus.*

Fig 2.—Cystic right eye with attached eyelids (L) and maldeveloped cornea (C) beneath bulbar conjunctiva. Lens is cataractous (*). Retrolental mass with island of cartilage (arrow) is seen (hematoxylin-eosin, ×2).



REPORT OF A CASE

After a 32-week gestation, a 16-year-old mother was delivered of a female infant. The mother had a history of sporadic use of LSD and other drugs, including cocaine and heroin, during the first trimester of pregnancy. The pregnancy was complicated by episodic fevers that were treated briefly with tetracycline during the fourth month. There was no history of congenital anomalies in the family. At birth, the baby had bradycardia and no spontaneous respirations, and died after one hour, despite attempts at resuscitation. Chromosomal study showed a normal karyotype.

AUTOPSY FINDINGS

The infant weighed 1,850 gm and her crown-heel length was 47 cm. Both orbits appeared small (Fig 1). The foramen ovale was widely patent and the aorta was narrowed proximal to a widely patent ductus arteriosus. The remaining great vessels of the mediastinum and the major branches of the aorta were normal. The left lung was hypoplastic and the right lung was of normal size. Most of the upper intestinal tract lay in the left side of the thoracic cavity through a defect in the left side of the diaphragm. The vertebrae were grossly unremarkable and no limb abnormalities were noted. Results of the neuropathologic examination were normal.

OCULAR PATHOLOGY

The specimen removed from the right orbit consisted of a soft, bluish, cystic structure covered by lid and orbital tissue. No cornea or anterior chamber could be identified grossly. A small spherical lens was present, and the cystic globe contained clear fluid.

Microscopically, the right eye was very poorly developed (Fig 2). The eyelids and conjunctivas were normal. Disorganized extraocular muscle was present. Beneath the bulbar conjunctiva, no cornea was observed, although irregular collagenous tissue was seen. There was no anterior chamber. Rudimentary fragments of ciliary body, pigment epithelium, and ciliary muscle were present anteriorly. The spherophakic lens demonstrated cataractous degenerative changes, including the posterior migration of lens epithelium, bladder cell formation, liquefaction of lens fibers, and areas of capsular rupture. Behind the lens, there was a mass of fibrovascular tissue containing a large plaque of cartilage (Fig 3 and 4). Dysplastic retina was drawn up in folds behind the retrolental mass. No retinal pigment epithelium or choroid was present. The outer layer of the cystic globe resembled poorly developed retina with poorly developed choroid, and minimal external collagenous tissue (Fig 5). No optic nerve was noted.

The left eye measured 11 × 11 × 10.5 mm. A vertical section was cut for microscopic examination (Fig 6). The conjunctiva was normal. Dense connective tissue covered the anterior surface of the cornea. An island of corneal epithelium was present, but no Bowman's membrane was seen. Vascularized stroma and immature endothelial cells without Descemet's membrane were identified. Within the precorneal tissue, there was a plaque of cartilage (Fig 7). A rudimentary iris with pigment epithelium and ciliary muscle was present. The lens was larger than the lens of the fellow eye, with similar cataractous changes. A retrolental mass consistent with persistent hyperplastic primary vitreous (PHPV) was present. The retina was well developed, except at the periphery where it was adherent to the PHPV and showed dysplastic changes (Fig 8). The choroid was thin and the sclera was normal. The optic nerve was hypoplastic (Fig 9).

The ocular diagnosis included severe microphthalmos of the right eye with retinal dysplasia, PHPV, retrolental intraocular cartilage, and a severely abnormal anterior segment.

Fig 3.—Behind lens, surrounding cartilage with retrolental fibrous plaque, is dysplastic retina (hematoxylin-eosin, original magnification ×60).

Fig 4.—Retrolental cartilage shown in higher magnification (hematoxylin-eosin, original magnification ×100).

Fig 5.—Outer wall of cystic globe consists of poorly developed neuroretina, rudimentary choroid, and no retinal pigment epithelium. In some areas, minimal fibrous tissue compatible with sclera was found external to this tissue (hematoxylin-eosin, original magnification ×250).

Fig 6.—Microphthalmic left eye with retrolental fibrous plaque (arrow) (hematoxylin-eosin, original magnification ×2).

The left eye had less severe microphthalmos, retinal dysplasia, PHPV, and precorneal hyaline cartilage.

COMMENT

Although limb malformations have

Fig 7.—Plaque of hyaline cartilage is noted on precorneal tissue of left eye (hematoxylin-eosin, original magnification ×45).

Fig 8.—Retrolental mass in left eye is composed of fibrovascular tissue tightly adherent to posterior capsule of lens (L) consistent with persistent hyperplastic primary vitreous. Areas of retinal dysplasia are present as well (arrow) (hematoxylin-eosin, original magnification ×100).

Fig 9.—Optic nerve in left eye is hypoplastic (hematoxylin-eosin, original magnification ×80).

most commonly been associated with maternal LSD ingestion,[1] CNS and ocular defects also have been described.[2-4] The infant described by Bogdanoff et al[2] had unilateral microphthalmos, cataract, and severe retinoschisis, and Apple and Bennett's patient[3] demonstrated unilateral microphthalmos, corneal vascularization, coloboma of iris, and early cataractous changes. The present infant represents an additional example of abnormalities of ocular development associated with documented maternal exposure to LSD during the first trimester, and suggests a similar teratogenic event leading to the ocular malformations. Neither cocaine nor heroin is known to have an established teratogenic ocular effect.[5]

The presence of intraocular cartilage within the retrolental mass is somewhat unusual. Intraocular cartilage is well described in association with uveal and ciliary body colobomas in trisomy 13-15 syndrome,[6] medulloepitheliomas,[7,8] and rarely in eyes with PHPV.[9,10] Trisomy 13-15 syndrome has been reported in association with LSD use,[11] but a normal karyotype and the lack of typical associated defects[12] make its occurrence in the present case unlikely.

The actual role of maternal LSD ingestion as the cause of the ocular malformations reported here and previously is difficult to delineate, and a truly causal relationship cannot be inferred.[13] The similarities in the infants, however, may suggest a common teratogenic event.

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