Retinal neoplasia and dysplasia. II

Retinal neoplasia and dysplasia. II. Retinoblastoma occurring with persistence and hyperplasia of the primary vitreous

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The occurrence of retinoblastoma in an eye with persistent hyperplastic primary vitreous (PHPV) is reported. These are both rare lesions. The absence of previous reports of their association has led to the clinical impression that the occurrence of PHPV in a microphthalmic eye precludes the presence of retinoblastoma. The coexistence of these lesions in the present case may represent a coincidence. Their occurrence in the same eye is felt to be noteworthy, nonetheless, because of its clinical implications and the possibility of a common underlying etiology.

Key words: retinoblastoma, persistent hyperplastic vitreous, retinal dysplasia, metastatic cancer

Retinoblastoma, the most common ocular tumor of children, is estimated to occur in 1 in 15,000 to 34,000 births. The incidence of persistent hyperplastic primary vitreous (PHPV) has not, to our knowledge, been established, but its occurrence is rare. Retinal dysplasia, a principal characteristic of PHPV, was found in 22 of 1,065 (2.1 percent) eyes examined in a recent study. Therefore, the coexistence of these two presumably unrelated lesions must be extremely infrequent and, to our knowledge, has heretofore not been reported. A recent study of an
Fig. 1. Low-power view of the mass filling the vitreous cavity, with tumor spreading along the surface of the vitreous. (Hematoxylin and eosin; ×4.)

experimentally induced ocular tumor by feline leukemia virus resulted in the development of retinal dysplasia as well, and further increases our curiosity regarding the relationship of the retinal lesions in the present case.

Clinical summary

At birth, a white boy was noted to have right microphthalmus and a small tumor of the scalp located slightly in front of the anterior fontanelle. The left eye was reported to be normal, but there is no report of a detailed fundus examination having been done. The scalp lesion grew and was excised at 5 months of age. Microscopically, it was consistent with but not absolutely characteristic of metastatic neuroblastoma. Four doses of x ray were given to the scalp lesion, and the child was transferred to Children's Hospital, Los Angeles, Calif., where pathologists, and consultants from the Armed Forces Institute of Pathology, reviewed the original slides of the scalp tumor and concurred with the diagnosis of metastatic neuroblastoma. In December, 1967, at 10 months of age, an exploratory laparotomy failed to reveal tumor. During the ensuing 8 months, the right eye remained unchanged, the scalp tumor grew, and a lesion clinically resembling retinoblastoma appeared in the left eye. A second biopsy of the scalp lesion was submitted to the Estelle Doheny Eye Foundation, where because of the retinal tumor in the left eye, a diagnosis of probable metastatic retinoblastoma to the scalp from the right eye was made. Therefore, at 18 months of age, the right eye was enucleated.

At this time, the right eye was small, its anterior chamber shallow, and the pupil non-reactive. There were annular central posterior synechiae. A cataractous lens prevented view of the posterior segment.

Following enucleation, the patient was treated with Cytoxan, 5 mg/kg body weight per day, every 2 weeks for 10 weeks. Following this, 300 Kr. of x radiation were given to the total brain and 4,800 r. were directed at the skull. Four months later, a swelling of the right mandible was noted, and cobalt-60 in a total dosage of 4,351 r. was administered to the right skull, the pterygoid, and the right mandible during the ensuing 30 days. Bone marrow studies were negative. A month later, the child was discharged on Cytoxan therapy. Two months later he died.
Fig 2. Representative field of the retinoblastoma showing undifferentiated cells as well as Flexner-Wintersteiner rosettes. (Hematoxylin and eosin; ×250.)

at approximately 3 years of age. An autopsy was not done.

Results

**Gross description.** The specimen is a right eyeball measuring 19 mm. vertically, 19 mm. horizontally, and 18 mm. anteroposteriorly. The pupil showed a white reflex. The cornea measured 9 mm. horizontally and 9 mm. vertically. The optic nerve was 7 mm. in length and 2 mm. in diameter exclusive of its sheath. The globe did not transilluminate.

The specimen was opened horizontally, with the larger calotte taken inferiorly. A large white mass was seen filling the vitreous cavity. An area of calcification was noted. The retina could not be discerned. The optic nerve head was not visible. The lens appeared to be grossly enlarged and in its normal position.

**Microscopic description.** A whitish tumor filled the vitreous cavity (Fig. 1) and seeded along the surface of the choroid, focally invading that layer. Microscopically the tumor was characteristic of retinoblastoma, showing rosettes, necrosis, and calcification (Fig. 2). Tumor invaded the optic nerve anterior to the lamina cribrosa. Cross sections of the optic nerve revealed cells within the pia-arachnoid tissue suspected of being neoplastic extensions, presumably from a choroidal tumor adjacent to the optic disc. Foci of neoplasm were seen on the anterior iris surface, and there were dense peripheral anterior synechiae occluding the anterior chamber angle recess. Catarrhous lens fragments revealed the capsule to be wrinkled and ruptured anteriorly and posteriorly. Abortive lens fibers and liquefaction necrosis were seen within the lens cortex.

In addition to the pathological conditions characteristic of retinoblastoma, there were changes typical of PHPV (Fig. 3, A and B). The glial tissue suggestive of
Fig. 3. A, Area of changes typical of PHPV. (Hematoxylin and eosin; ×35.) B, Higher-power view of area in A, showing dysplastic retina, gliosis, and mesodermal tissue suggestive of PHPV. (Hematoxylin and eosin; ×120.)
hyperplastic primary vitreous invaded the lens through ruptures in the capsule anteriorly and posteriorly, filled the lentinal and circumlental space, and presented the gross configuration of an enlarged lens. The mesodermal tissue filling the circumlental space attached to the ciliary processes which appeared to have been pulled with the retinal elements along the posterior surface of the iris and ciliary body centrally toward the lentinal space. Dysplastic retinal rosettes were seen in some sections, particularly behind the ciliary body. In some sections the remnant of the hyaloid artery could be seen centrally and anteriorly in the area of PHPV behind the lens. Sections of this artery were also seen posteriorly between layers of detached retina adjacent to the nerve head.

Discussion

Retinoblastoma and PHPV have long been clinically regarded as unrelated and even “mutually exclusive” lesions. Retinoblastoma characteristically occurs in normal-sized eyes without other developmental defects and probably begins in the last part of embryonic life. Conversely, PHPV in the absence of glaucoma is found in a microphthalmic eye and, because of its main pathologic features (i.e., persistence of portions of the tunica vasculosa lentis, including both interstitial connective tissue and vascular components, and retinal dysplasia) probably begins early in development when the secondary vitreous normally forms and the primary vitreous concomitantly regresses.

At the time of enucleation of the right eye, our belief was that if there was microphthalmus without atrophy, retinoblastoma would be unlikely. However, if atrophy was present, the most likely diagnosis would be bilateral retinoblastoma, atrophy of the right eye secondary to retinoblastoma, and metastasis to the scalp. Because of the coexistence of pathological conditions in the right eye and scalp tumor at birth, with the later development of retinal neoplasm in the left eye, it seems most likely that the scalp metastasis was from the right eye.

Although most cases of PHPV and retinal dysplasia are of unknown etiology, a number of viruses and other toxic agents have been demonstrated to be capable of causing these changes. The evolution of the term “retinal dysplasia,” our present concept of its changes, and its relation to PHPV are discussed in a recent review. The recent finding that an oncogenic virus can induce both malignant change and retinal dysplasia leads us to wonder whether or not the presence of retinoblastoma and PHPV in this case is merely a rare coincidence or represents PHPV induced by an unusually early onset of retinoblastoma, or whether both lesions were possibly viral induced.

REFERENCES