Retinal neoplasia and dysplasia.

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

A. Ray Irvine, Daniel M. Albert, and Delia N. Sang

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 de-
velopment of retinal dysplasia as well,2 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 character-
istic 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 consult-
ants 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

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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. Cataractous 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 lental 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 lental 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