Ultrastructure of the hyaloid vasculature in primates

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The histology and ultrastructure of the hyaloid vascular system was studied in 16 monkeys, ages 85 days in utero to 3 years old. The well-developed hyaloid artery is identifiable ultrastructurally as an arteriole consisting of a nonfenestrated intima, a multilayered smooth muscular media, a connective tissue adventitia, and a perivascular sheath. By the fourth week after birth, the vessel walls appear hyalinized and acellular; the lumen is occluded by a thrombus. The time of the complete disappearance of the hyaloid artery varied considerably in individual monkeys; remnants of the hyaloid artery were often present on the disc (Bergmeister’s papilla) in adult life. The vasa hyaloidea propria and tunica vasculosa lentis are small branches of the hyaloid artery which fill the primary vitreous. Ultrastructurally, they are Type A-1a capillaries having a nonfenestrated endothelium, incomplete pericyte layer, and basement membranes surrounding each. Fluorescein angiography of several newborn monkeys revealed nonleakage of dye from the hyaloid artery and its branches, thus correlating with the presence of endothelial tight junctions.

Key words: Hyaloid artery, embryonic intraocular vasculature, tunica vasculosa lentis, primates, ultrastructure of primary vitreous vessels.

The embryonic hyaloid vascular system is important for the growth and matura-

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of the human primary vitreous, the elongated perivascular sheath of the hyaloid artery, has not been described in an animal model. We have found such a well-developed sheath in the monkey, which represents an anterior extension of the epipapillary sheath of Bergmeister. This sheath, which is described in detail in a later study,11 is analogous to that seen in man and is not well developed in rodents.

**Methods**

The eyes of 16 monkeys (Macaca speciosa, M. irus, and M. cynomolgus), ranging in age from 85 days in utero to 3 years postnatally, were enucleated immediately after sacrifice of the animal. The eyes were fixed in 4 percent glutaraldehyde-0.1M phosphate buffer solution.

The globes were examined with a dissecting microscope, looking specifically for remnants of the hyaloid artery. When the artery was found extending from the optic disc, a small segment
Fig. 2. Electron micrograph of the wall of the hyaloid artery, showing the lumen (L), intimal endothelial cell (E), media (M), adventitia (A) containing a large fibroblast (F). S, Compressed perivascular sheath. The arrows indicate junction of the vessel and its sheath with the secondary vitreous. Note basement membrane at this junction. (Uranyl acetate and lead citrate; original magnification, x17,000.)

of artery together with the optic disc was dissected away from the rest of the eye (Fig. 1). This specimen was processed for electron microscopy by washing in phosphate buffer, postfixing in osmium tetroxide, dehydrating, clearing, and embedding in epoxy resin. Sections 1 μ thick, stained with Mallory blue, were studied by light microscopy; thin sections stained with uranyl acetate and lead citrate were examined with the electron microscope.

Results

In all eyes included in this series, ages 85 days in utero to 3 years, the hyaloid artery was identified—either as a well-developed, patent vessel or as an occluded remnant. Seen at the height of development, the hyaloid artery emerges from a vascular bulb in the optic nerve and extends through the vitreous toward the lens (Fig. 1). Surrounding the artery is a glial sheath (Fig. 2). The wall of the hyaloid artery is composed of three layers: the intimal, medial, and adventitial layers (Fig. 2). The intima is composed of the layer of endothelium and its basement membrane. The endothelial cells are non-fenestrated and maintain tight junctions at the point of contact with each other (Fig. 3). Fluorescein angiography confirmed this tight bonding in that no dye leakage occurred. The nuclei of the endothelial cells are elongated; mitochondria and ribosomes are prominent throughout the cytoplasm (Fig. 3).

The media of the hyaloid artery contains several layers of typical smooth muscle cells with their basement membranes (Figs. 2 and 4). Characteristic dense bodies which are helpful in the recognition of the smooth muscle are seen adjacent to the cell membranes in Fig. 4. The smooth muscle cells are thin and elongated...
with fibrillar cytoplasm, spindle-shaped nuclei, and cytoplasmic organelles distributed predominantly at the longitudinal poles of the nucleus (Figs. 2 and 4). Interspersed between muscle cells are their enveloping basement membranes (Fig. 4) and occasional collagenous bundles. At the origin of the hyaloid artery at the optic disc, the muscular media is less prominent.

The subendothelial space and the adventitia are largely composed of collagen (Figs. 2 and 3). The collagen fibrils at the outermost aspect of the arterial adventitia merge with primary vitreous fibrils which occupy the space between the artery and its perivascular sheath (Fig. 2).

By the first month after birth, as the hyaloid artery is undergoing active involution, the lumen of the hyaloid artery narrows and becomes occluded by debris derived from erythrocytes, leukocytes, platelets, and fibrin (Figs. 5 and 6). The wall of the artery appears hyalinized and acellular (Figs. 5 and 6). Just prior to its complete disappearance, the hyaloid artery remnant is visualized as a small protrusion of fibrotic tissue on the surface of the disc (Fig. 7).

The vasa hyaloidea propria are small, capillary branches extending from the main trunk of the hyaloid artery throughout the vitreous (Figs. 8 and 9). Ultrastructurally, the walls of these capillaries (as well as those of the tunica vasculosa lentis) consist of (1) a complete layer of nonfenestrated endothelium with intervening tight junctions encircled by a basement membrane and (2) an incomplete layer of pericytes surrounded by another basement membrane (Fig. 9).

Discussion

In man, the main hyaloid artery, a branch of the primitive dorsal ophthalmic artery, enters the optic cup via the open embryonic fissure at the fourth week of
Fig. 5. Light micrograph showing the occluded lumen and the surrounding hyalinized wall (W) of the hyaloid artery; 3 weeks postnatally. The glial sheath (demarcated by arrows) is lined on inner and outer surfaces by a coiled basement membrane. (Mallory blue; x300.)

Fig. 6. A 3-week-old monkey. Electron micrograph of the hyaloid artery wall (HA) with erythrocytes, leukocytes, platelets, fibrin, and debris occluding the lumen (L). (Uranyl acetate and lead citrate; original magnification, x15,000.)

This vessel grows anteriorly to branch at the posterior lens surface, forming the tunica vasculosa lentis. These vessels, in turn, course around the equator of the lens to anastomose with vessels of the pupillary membrane. Additionally, small capillary branches, the vasa hyaloidea propria, bud from the hyaloid artery and fill the vitreous, anastomosing with the tunica vasculosa lentis and with each other. Thus, an intricate vascular network is created which nourishes the eye during gestation. 1-11 This vessel grows anteriorly to branch at the posterior lens surface, forming the tunica vasculosa lentis. These vessels, in turn, course around the equator of the lens to anastomose with vessels of the pupillary membrane. Additionally, small capillary branches, the vasa hyaloidea propria, bud from the hyaloid artery and fill the vitreous, anastomosing with the tunica vasculosa lentis and with each other. Thus, an intricate vascular network is created which nourishes the eye during gestation and disappears normally during perinatal life in man. In monkeys, we have noted that this vascular system largely regresses during the first month of life (which is slightly later than in man), although remnants may be found in the adult. The stimulus for this regression is unknown.

The structure of the hyaloid vascular system has been studied in rodents by scanning electron microscopy, 11 transmission electron microscopy, 9, 12-14 and India ink preparation. 14 Jack 12-14 has examined the ultrastructure of the hyaloid vascular system of rabbits in both development and regression. In our examination of the vascular system in monkeys, we found a structure very similar to that described by Jack in rabbits.
Fig. 7. A 3-year-old monkey. Light micrograph of the occluded and hyalinized remnant of the hyaloid artery (A), and perivascular sheath (arrows) forming Bergmeister's papilla on the optic nerve head. (Mallory blue; x220.)

Fig. 8. Electron micrograph of vasa hyaloidea propria, showing the complete endothelial layer (E), incomplete pericyte investment (P), and their associated basement membranes. (Uranyl acetate and lead citrate; original magnification, x5,000.)
Fig. 9. Electron micrograph of vasa hyaloidea propria from the same animal as in Fig. 8. Note the tight junction between the two endothelial cells. P, Pericyte. (Uranyl acetate and lead citrate; original magnification, x25,000.)

The hyaloid "artery" is more correctly classified as an arteriole, according to the criteria delineated by Rhodin. The hyaloid "artery" is structured as follows. (1) The intima consists of flattened endothelial cells connected by tight junctions; underlying these cells is a basement membrane. (2) The media reveals concentric layers of smooth muscle with basement membranes around each fiber. Dense bodies, also noted by Jack, are seen on the inner surface of the plasma membrane of the muscle cells. Rhodin stated that the dense "bars" are assumed to contain contractile proteins. (3) The adventitia contains scattered fibroblasts and collagen. Unlike Jack's description in rabbits, we find a well-developed glial sheath surrounding the hyaloid artery, which is similar to that found clinically in man. The perivascular sheath and its relation to the forming vitreous and Cloquet's canal will be described in a subsequent paper.

At the time of birth in monkeys, a well-developed intraocular vascular system, including hyaloid artery, tunica vasculosa lentis, vasa hyaloidea propria, and pupillary membrane, is present. The regression of the hyaloid vascular system begins shortly thereafter. The artery remains patent until approximately the third week after birth. At that time, the lumen becomes narrowed and then occluded by a thrombus (Figs. 6 and 7). The vessel gradually becomes attenuated, beginning at the middle of the artery and then extending toward the lens and disc. Remnants of the distal termination of the artery on the lens form Mittendorf's dot, a small opacity located inferonasal to the posterior pole. The occluded remnant of the hyaloid artery persisting at the disc, the so-called persistent Bergmeister's papilla, is by definition composed of the persisting vessel remnant as well as the vessel's glial sheath. Bergmeister's papilla was present...
in all monkeys studied during the first month of life. This occluded remnant was observed in the oldest monkey in this series, who was 3 years old (Fig. 7), demonstrating that this remnant may persist into adult life.

The branches of the hyaloid trunk (the vasa hyaloidea propria and tunica vasculosa lentis) in monkeys have Type A-1-alpha structure of capillaries. This type is characterized by a continuous basement membrane underlying an endothelium without fenestration, with incomplete pericyte investment. This same structural appearance has been noted in hyaloid and retinal capillaries in rodents. The fact that the endothelial cells maintain tight junctions at the point of contact with each other explains the resistance to fluorescein dye leakage. This finding has been substantiated clinically in a human patient with persistence of the tunica vasculosa lentis in which dye leakage from the aborizing retrolental vessels was minimal.

REFERENCES