Experimental myelin intrusion in the nerve head

David G. Cogan and Robert D. Yee

On the assumption that myelin intrusion into the papilla and peripapillary region might occur with traumatic lesions of the optic nerve, a study was made of the clinical and histopathologic changes that might be expected. Nine monkey eyes were subjected to hemostat compression of the nerve close to the globe and studied over variable periods up to 28 days. Myelin was demonstrable ophthalmoscopically, followed by variable and increasing amounts of hemorrhage. The myelin was demonstrable histopathologically only during the first 2 weeks after the manipulation and was then masked by the associated hemorrhage and gliosis. The optic nerve showed expected myelinolytic reactions.

Key words: myelin intrusion, optic nerve papilla, histopathology, demyelination.
Fig. 1. Posterior portion of an eye transected through the nerve head, showing myelin squeezed forward into the prepapillary and peripapillary regions. The patient was an 11-year-old boy whose eye was removed as part of the surgery for an orbital tumor. The eye, which had been clinically normal, developed the myelin intrusion at the time of enucleation.

Fig. 2. Interior of an eye showing the peripapillary corona of what subsequently proved to be myelin. The eye was enucleated on account of glaucoma secondary to partial occlusion of the central retinal vein and hemorrhagic retinopathy. The myelin intrusion apparently occurred at the time of enucleation.

Fig. 3. Fundus of a patient who developed massive hemorrhage in the retina and white material beneath the peripapillary retina from a blunt blow during a football scramble. The eye was immediately blinded, and the photograph was taken the day after the injury. The question posed is whether or not the white material could be myelin and if so how long it would be detectable histologically if such an eye were removed.

Material and methods

Observations were made on five monkeys (nine eyes) with initially normal nerve heads. Under general anesthesia the optic nerves and posterior portions of the eyes were exposed through lateral orbitotomies after appropriate removal of bone. One or two hemostat clamps were then placed on the optic nerve by one of us while the other watched for changes in the nerve head by means of indirect ophthalmoscopy. In some cases a simple squeeze was induced by a single clamp, and in other cases the squeeze was induced by one clamp while a second clamp placed posteriorly prevented myelin from moving backward. The most successful technique consisted in massaging the optic nerve by a gentle and incomplete compression of the nerve close to the globe.
No attempt was made to prevent associated occlusion of the central retinal vessels, since prior experience had shown that myelin intrusion occurred only with compression in the portions of the nerve containing the vessels and, in any case, the clinical condition which we were attempting to replicate would similarly involve the vessels.

Fundus photography and fluoroangiography were performed in selected cases during the manipulation. At the conclusion of the surgery the skin was resutured, and the monkey returned to his cage for periodic observation. The eyes and adjacent optic nerves were removed for histopathologic study at times varying between 15 minutes and 28 days after the surgery. The tissues were fixed in formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin (H & E) for cytology and with Luxol Fast Blue (LFB) for myelin. In order to use LFB properly, it is necessary to understain the section in order to minimize the staining of red blood cells and of collagen, and it is imperative to correlate the staining with the granular appearance of myelin.

Results

An unsuccessful attempt was made to induce myelin intrusion in one eye by blunt injury applied to the cornea of an anesthetized monkey by finger compression and by hammer blows. The procedure simply resulted in increased fluorescein transit into the anterior chamber (and, incidentally, angle recession) but induced no ophthalmoscopically evident abnormality of the nerve head.

On the other hand, massage of the optic nerve with either one or two hemostats resulted in the prompt appearance of white material, presumed to be myelin, in six eyes and in the occurrence of some peripapillary yellow material, presumed to be exudate, after a delay of an hour or more in two eyes. No intruded or exudative material was noted in one eye. That which was presumed to be myelin protruded into the nerve head, peripapillary area, and vitreous. It was most evident beneath the retina about the disc (Fig. 4, A). It usually had a crescentic configuration, and in no case was it more extensive than the size of the disc.

Hemorrhages varying from a few splinter petechiae about the disc to massive hemorrhage into the prepapillary area occurred in all cases but not until 5 to 10 minutes after the manipulation (Fig. 4, B). The hemorrhages usually increased over the course of the subsequent few days.

Segmentation of the blood column occurred transiently in one case. Two eyes showed immediate pallor of the nerve head and prompt narrowing of the retinal arteries with total lack of filling of retinal arteries by fluoroangiography while the choroid showed the normal angiographic flush. Two other eyes with normal appearing vessels showed a delay of 1 to 2 minutes before

Fig. 4. Fundus photographs of monkey eye after compression of the optic nerve. A, At 10 minutes after manipulation. Noteworthy is the crescentic opacity, believed to be myelin, temporal to the disc and two flame-shaped hemorrhages on the margin of the disc. B, At 20 minutes after the manipulation. The hemorrhages and papillary edema have increased. The eye was removed 16 days after the surgery and showed minimal evidence of residual myelin in the eye.
the dye entered the retinal vessels. From these observations it was concluded that some obstruction in circulation probably occurred in all cases but that complete and persistent arterial occlusion occurred only occasionally. Although retinal hemorrhages on or about the disc occurred in all cases, none showed the widespread hemorrhagic retinopathy that is typical of venous occlusion in human beings.

Eight eyes were studied histopathologically. (One animal was disposed of without salvaging the eyes.) The two eyes which were removed within 1 hour after surgery showed myelin in the nerve head and beneath the adjacent retina (Fig. 5). Except for the associated hemorrhage, which was minimal in one case and marked in the other, the myelin had caused no cellular reaction. But one case did show a serofibrinous exudate in addition to the myelin beneath the retina.

The eye removed 2 days after surgery showed a small amount of myelin within the nerve head without appreciable reaction (Fig. 6) and a moderate amount of blood in the peripapillary retina. Clinically this eye had shown only a small amount of myelin intrusion at the time of manipulation and an increasing number of flame-shaped hemorrhages in the hour of observation after surgery.

The eye removed 1 week after surgery showed a combination of absorbing myelin, hemorrhage, fibrinous exudate, and gliosis, with loss of myelin from the anterior portion of the optic nerve and replacement by lipid histiocytes (Fig. 7). Although still identifiable, the myelin was considerably obscured by the associated hemorrhage.
Fig. 6. Small amount of myelin (arrows) in the prelaminar nerve head. The optic nerve had been squeezed 2 days previously. (LFB stain; x60.)

Fig. 7. Nerve head 1 week after manipulation, showing absorbing myelin (single arrow) and obscuration of the myelin by the hemorrhage (double arrow). Myelin is obvious in the subretinal space to the left of the papilla, but it has been largely replaced by lipid macrophages on the right. The nerve substance is severely gliotic and hemorrhagic. Immediately after surgery this eye had shown a corona of myelin intrusion about the papilla. Two days later it had shown extensive papillary hemorrhages as well. (LFB stain; x25.)
Fig. 8. Papilla and optic nerve 25 days after manipulation, showing marked gliosis of nerve head and the compression lesion just behind the globe. There is a sharp junction of demyelinated and myelinated portion of nerve in the lower portion of the photograph. (LFB stain; ×9.)

The other four eyes were removed at 16, 25, 25, and 28 days after surgery. All showed extensive lipid histiocytosis, with complete loss of myelin from the retrobulbar portion of the optic nerve, but an abrupt preservation of myelin posterior to the demyelinated area. The nerve heads showed extensive gliosis, with variable amounts of hemorrhage, fibrovascular proliferation into the vitreous, and degeneration of the inner layers of the retina (Fig. 8). The outer layer of the retina showed infrequent and spotty loss of the photoreceptive layer and local loosening of the pigment epithelium but no significant abnormality in the choroid. Myelin was not definitely identified in any of these cases, although admixture with blood may have obscured whatever myelin was present.

The transitional zone between the demyelinated and myelinated portions of the optic nerves was of incidental interest. This zone extending over an area of about 1 mm. in length was characterized by a granular attenuation of myelin (Fig. 9). Anterior to this, myelin was completely replaced by glial proliferation and lipid histiocytes, whereas posterior to it, myelin appeared to be of normal consistency but contained numerous empty "holes" 20 to 50 μ in diameter. This loculation of myelin is well known in degenerating white matter of the central nervous system and is termed vacuolar degeneration. Within the transi-
Fig. 9. Transitional zone between demyelinated and myelinated portion of nerve of preceding case. (H & E stain; x38.)

Fig. 10. Vacuoles in transitional zone of preceding case, showing occasional content of "myelin balls" (arrows). (H & E stain; x625.)
tional zone vacuoles of a similar dimension were present, but unlike those posterior to it, they often contained balls of amorphous material staining like myelin (Fig. 10). From these observations it would appear that the vacuoles are formed by segregation of the myelin into "balls," which then drop out artefactually to leave empty spaces. Why the myelin should be better retained in the vacuoles of the transitional zone than posterior to it is not apparent but might be due to less complete separation from the walls in this zone. In any case vacuolar degeneration is a stage in myelinolysis of the optic nerve as it is in that of the central nervous system.

Comments and conclusions

Myelin may be forced into the substance of the nerve head and adjacent regions during life, in a manner analogous to what occurs artefactually in routine enucleations. The myelin may be identified histopathologically for as long as a week after the manipulation but becomes progressively obscured by the associated hemorrhage and glial reactions. At 2 weeks the intruded myelin is no longer recognizable.

Whether or not myelin intrusion occurs clinically is questionable and can be proved only by histopathologic observation. The present experiments suggest that the masking effect of the associated hemorrhage and the rapid disappearance of the intruded myelin would require examination of suspected eyes within the first few days after the injury.

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REFERENCE