Experimental retinal vascular occlusion II

A clinico-pathologic correlative study of simultaneous occlusion of central retinal vein and artery

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Abstract

After experimentally occluding the central retinal vein and artery simultaneously at their point of entry into the optic nerve, acute retinal necrosis occurred, but not hemorrhagic retinopathy. In the retinal vasculature, stagnation of blood flow and thrombosis with subsequent recanalization was noted. The necrosis was extensive in the inner retinal layers but focal in the outer retinal layers. The internal limiting membrane was detached and disrupted in every case. Following the post-edematous stage, numerous micro and macroretalinal cysts appeared. The peripheral retina showed much less ischemic changes. A clinico-pathologic correlation was made.

Introduction

The pathogenesis and management of central retinal vein occlusion remain controversial (1-17). Hayreh (9, 10), based on his experimental studies in rhesus monkeys, found that occlusion of the central retinal vein alone, at its site of exit from the optic nerve, produced an ophthalmoscopic appearance of venous stasis retinopathy but when central retinal artery and vein were diathermized simultaneously at their point of entry into the optic nerve, it resulted in the production of typical hemorrhagic retinopathy described classically with central retinal vein occlusion. Thus that study indicated that central retinal vein occlusion is of two types – non-ischemic and ischemic types respectively. This has since been amply confirmed by a number of clinical studies (12, 13, 16–23) (and had been suggested by a few earlier clinical studies (1, 24, 25).

Since fluorescein fundus angiography was not available in 1963 when the above mentioned experimental studies by Hayreh (9, 10) were conducted, the retinal circulation in vivo could not be evaluated in those eyes. Also no detailed histopathological and electron microscopic studies were conducted in that group. We wished to investigate the role of arterial ischemia in the pathogenesis of hemorrhagic retinopathy (i.e., ischemic type of central retinal vein occlusion) in greater detail, using modern techniques; we therefore produced, in healthy rhesus monkeys, various degrees of retinal ischemia, simultaneously with central retinal vein occlusion (14, 15). The retinal ischemia was produced either by clamping the central retinal artery, at the point of its entry into the optic nerve,

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for 2–2½, or 6–7½ hours (to produce transient ischemia of different grades), or by permanently cauterizing the artery at that site. The ophthalmoscopic and fluorescein angiographic findings of these studies are described in detail elsewhere (14, 15). This paper deals with detailed histopathological and horseradish peroxidase studies of eyes where the central retinal artery and vein were cauterized simultaneously; so far no such studies are available in the literature.

It could be argued by some that clinically simultaneous occlusion of the central retinal artery and vein is not seen, and that this experimental model does not represent a clinical condition. In the Ocular Vascular Clinic at Iowa City, we have occasionally seen a patient with such a condition, and as such it is of interest to learn about the histopathological changes in this condition.

Materials and methods

This study was conducted in nine eyes of five healthy rhesus monkeys. Through a lateral orbitotomy incision, the central retinal artery and vein were cauterized and cut simultaneously at the point of entry into the nerve. The method is described in detail elsewhere (14). During the surgical procedure, extreme care was taken to prevent any damage to the short posterior ciliary arteries and other ocular vessels. The fundus of each animal was examined by ophthalmoscopy, color fundus photography, and fluorescein angiography before and after surgery, and serially thereafter until enucleation. Detailed clinical findings of these eyes were published elsewhere (14, 15). Following the clinical studies, the eyes were enucleated for morphologic examination between nine days and eight months after retinal vascular occlusion (Table 1). Thirty minutes before enucleation, five of the animals received an intravenous injection of horseradish peroxidase at a dose level of 200 mg/kg of body weight. The tissues obtained were promptly fixed after enucleation and processed for the localization of horseradish peroxidase (26). The tissues were postfixed in Dalton’s chrome osmium solution, dehydrated in graded alcohol, and embedded in epoxy resin. Serial 1–2 micron sections of the retina and choroid from the macula, posterior pole, and periphery were evaluated by light microscopy after being stained with toluidine blue.

Results

Pathologic changes of the retina varied with the time after occlusion of the blood vessels and showed regional variations.

(A) Retinal vascular changes

Ophthalmoscopically (14, 15), the retinal arteries appeared normal or mildly attenuated immediately after the experimental occlusion and did not fill with dye on fluorescein angiography. Four to five days later the main retinal vessels started to fill slowly, presumably being fed by collaterals from the posterior ciliary artery circulation at the optic nerve head. After 8 to 12 days there was a progressive capillary obliteration at the posterior pole. One month after the occlusion, sheathing of the retinal arteries was clinically observed in about half of the eyes. The retinal veins were engorged soon after the occlusion but looked normal after the first week, and narrowed after one month, and two of the eyes showed perivenous sheathing after five months.