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Vascular Changes in Pseudoexfoliation of the Lens Capsule and Capsular Glaucoma

A Fluorescein Angiographic and Electron Microscopic Study

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Summary. Ten eyes of eight patients with pseudoexfoliation of the lens capsule were first studied by iris fluorescein angiography. Later, iris specimens were obtained at surgery and vessels that were newly formed or showed abnormally rich extravasation of fluorescein were studied electronmicroscopically.

The proliferated vessels had an abnormal basement membrane which was thin or absent, and there was abnormal extracellular material around the vessels. The endothelium was thin and in some cases fenestrae were observed. The electron-microscopic changes agreed with the rich extravasation of fluorescein from the capillaries seen in angiography.

The results show clearly that there are pronounced vascular changes in the anterior part of the eye in pseudoexfoliation. The way in which these changes affect the collection of pseudoexfoliation material in the eye requires further study.

Introduction

John Lindberg described the grayish flecks at the pupillary border in 1918. Later, the disease was named pseudoexfoliation of the lens capsule. Since then, the disease and its relationship to glaucoma has been widely studied and the clinical picture is well known. In biomicroscopy the exfoliation material is found on the anterior surface of the lens, on the zonules, on the anterior hyaloid membrane, on the ciliary body on the posterior and anterior iris surfaces, on the pupillary margin and in the trabecular area.

Neovascularisation and fluorescein leakage from the vessels in the iris are also an essential part of this syndrome. These changes were discovered by the author in iris angiography in 1969. Further, iris angiography has shown that the radial vessels in these eyes are often fewer than usual and that the caliber of the new formed vessels frequently varies as they form clusters on the surface of the iris. The circulation is sluggish in angiography and the newly formed vessels fluoresce longer than the others. Extravasation of fluorescein, found in the late phase of angiography, is also prominent.

The reason for the increased fluorescein permeability is not known. The aim of this study was to examine the electron microscopic changes in vessels which had shown at angiography increased permeability for fluorescein or were newly formed. In earlier works by Ashton *et al.* (1965) and Ringvold (1969) who studied the vessels in pseudoexfoliation electronmicroscopically, no distinction was made between the normal and abnormal iris vessels. The authors described abnormal extracellular material around the vessels, and noted that the basement membrane was thin or absent.

Material and Methods

The material comprised eight patients and 10 eyes. In six eyes the tension was normal. Four eyes had capsular glaucoma, but the tension was controlled by therapy. The iris specimens were obtained at cataract operations where iridectomy was performed at 12 o'clock. Iris angiography was done by the method described by the author (1969). Most of the patients were followed angiographically for one to two years preoperatively. Thus, the newly formed vessels showing fluorescing leakage were accurately recorded.

All the specimens were prepared for EM by fixing them in 3 per cent glutaraldehyde for three hours at $+4°$C. Postfixing was done with OsO_4 for one hour. The tissue blocks were dehydrated in an alcohol series and embedded in eponaraldite. The specimens were stained with lead citrate or with both lead citrate and uranyl acetate. All the prepations were made so that vessels seen in angiography could be detected again in microscopy.

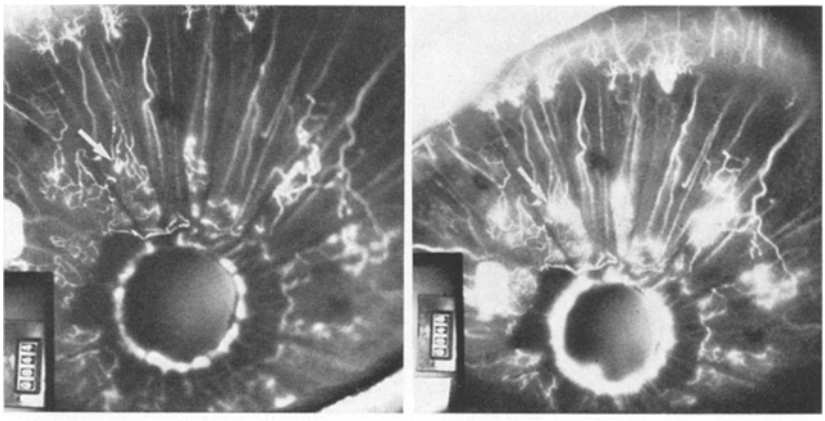
The control material comprised specimens obtained from enucleated eyes and cataract operations on eyes without pseudoexfoliation.

Results

As mentioned, only vessels that in fluorescein angiography showed abnormal leakage or were newly formed (Fig. 1) were studied electronmicroscopically in serial sections to obtain information about the pathological changes.

In EM, the vessels regularly showed an abnormally thin basement membrane or it was lacking completely. Around the vessels there was plenty of abnormal extracellular material (Fig. 2). The cells were bound to each other by zonulae occludentes, and marginal flaps were sometimes seen. Pericytes were noticed outside the basement membrane, but these did not form a continuous layer around the vessels. Some capillaries had a very thin endothelial wall and in a few places the endothelium was extremely thin (Fig. 3). The cytoplasma of the endothelial cells was rich in cell organelles and vesicles (Fig. 4). All these changes were seen regularly in eyes with pseudoexfoliation, and the difference from specimens from the material of normal eyes was clear.

In three of 10 eyes a few capillaries had fenestrated endothelium (Fig. 5). Where fenestrae appeared, there was abundant extracellular material around the vessel. The patients with rich neovascularisation



a b

Fig. 1a and b. Neovascularisation and fluorescein leakage in the iris in capsular glaucoma. Later, iridectomy was performed at a cataract operation and the vessels shown by the arrow had fenestrated endothelium (*EM*, Fig. 5)

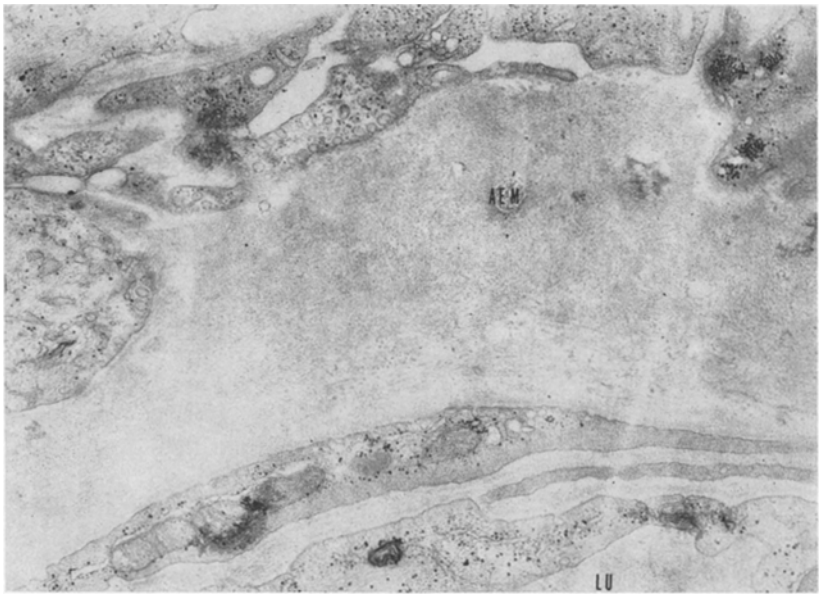


Fig. 2. Abnormal extracellular material (*AEM*) outside the vessels wall. × 20000

and extremely rich fluorescein leakage in the late phase of the angiography showed most fenestrae. (Fig. 1. The same neoformed fenestrated vessels seen in angiography.)

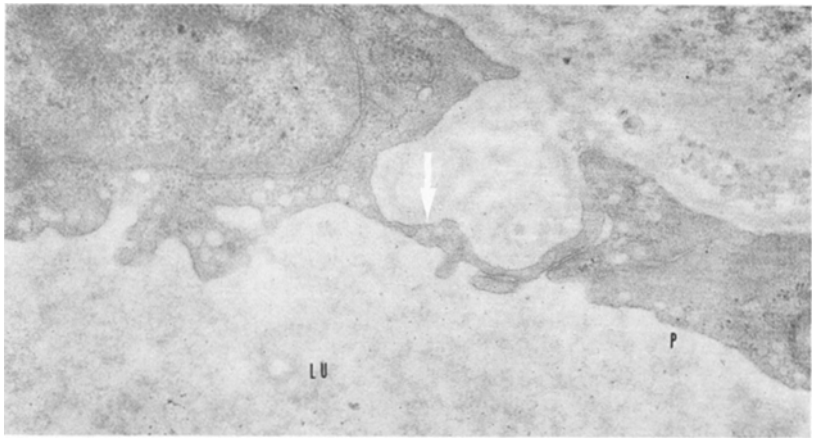


Fig. 3. Thin place in the endothelium (arrow). Pinocytosis (*P*). Lumen (*LU*). × 24000

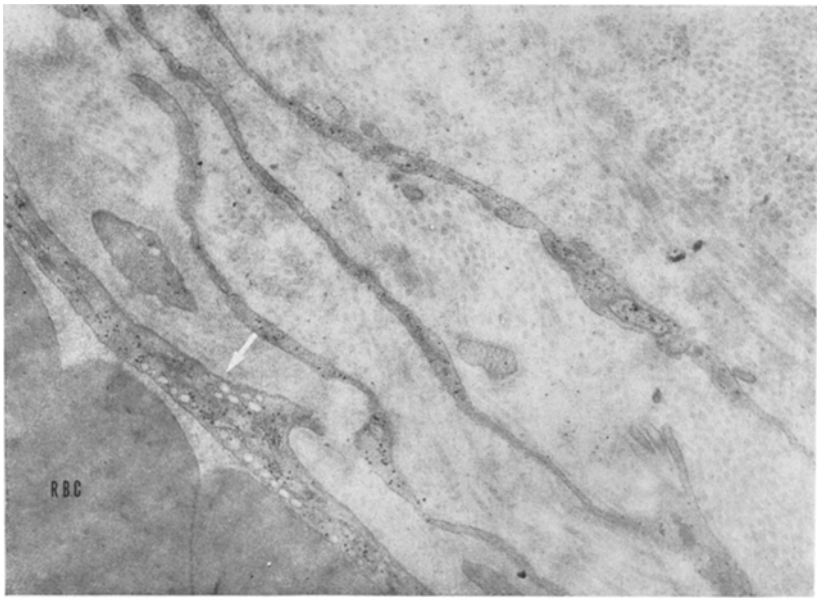


Fig. 4. Endothelial cell contains many vesicles and some organelles (arrow). Red blood cell (*RBC*). × 20000

Discussion

A most interesting and a new feature of pseudoexfoliation and capsular glaucoma was the presence of fenestrae in capillaries in patients

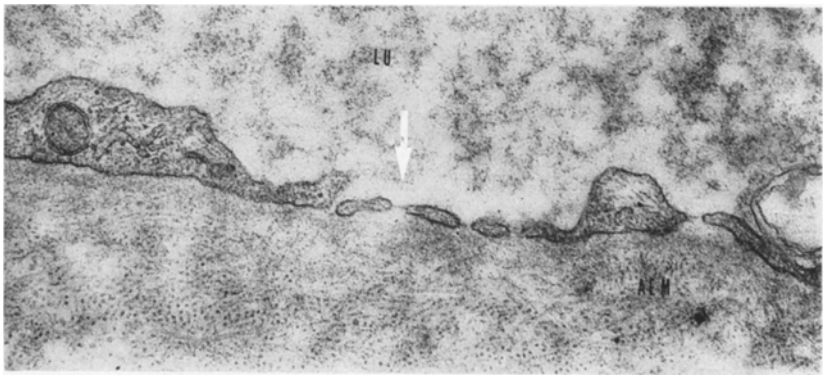


Fig. 5. Fenestrated endothelium (arrow) in *EM* in the vessels shown by the arrow in Fig. 1. × 50000

who had advanced neovascularisation and fluorescein leakage in angiography. The results agree with the studies of Okamura and Rohen (1971) who showed fenestrated capillaries in diabetic rubeosis. The basement membrane in these vessels was also thin. In my experience, diabetics have in fluorescein angiography rich extravasation of the dye in the same way as pseudoexfoliation eyes. One difference is that in diabetes the neovascularisation is often in the pupillary region, but in pseudoexfoliation in the ciliary region. The reason for this phenomenon is unexplained. Another difference is that in pseudoexfoliation in unilateral cases the vascular changes are also unilateral, as shown by A. Vannas (1969). Aqueous flare is also common in these diseased eyes which in advanced cases show abnormal capillary permeability.

Fenestrated capillaries are normally present only in the ciliary body in the eye, and Bill (1965) has shown that a considerable amount of protein is discharged from the ciliary process vessels into the interstitial tissue of the processes. Only traces of this protein appear in the aqueous humour in a healthy eye and it seems reasonable to suppose that the thick external limiting membrane of the ciliary processes is the main filtration barrier to protein there. In the iris there are no further filtration barriers and the protein must be released into the aqueous from the pathological fenestrated capillaries. Although fenestrae could not be seen in all the cases, it can be assumed that the blood aqueous barrier was disturbed in all the eyes because increased extravasation was seen in angiography, and electron microscopy showed a changed basement membrane and abnormal extracellular material in accordance with Ashton (1965) and Ringvold (1969).

Both the present results and the author's fluorescing angiographic studies (1969) show clearly that there are marked vascular changes in pseudoexfoliation syndrome. So far, the changes have been noted only in the iris vessels, but according to Laatikainen (1971) the conjunctival vessels also show abnormalities in angiography. The available information does not confirm whether vascular changes or pseudoexfoliation material appear first. Yet it is apparent that the changes in the blood aqueous barrier influence the development of abnormal protein in the anterior chamber.

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