Cell Component of Proliferative Vitreoretinal Membranes

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Abstract-The ultrastructure of the proliferative vitreoretinal membranes in various eye conditions such as peripheral uveitis, penetrating eye injury, aphakic retinal detachment, and traction retinal detachment were studied in human, and experimental study was performed in 27 pigmented rabbits to investigate the origin of cells participating in healing process of retinal injuries. The experimental rabbits were divided into two groups according to the degree of retinal injury; mild injury and severe injury groups. The retinal injury was made on avascular retina two disc diameters below the optic disc by gentle touch with a 21 gauge needle tip inserted through pars plana of rabbit eyes. The mild injury revealed a faint scratch line on the retinal surface. The severe injury was made in the same way but retinal scratch was so deep that choroidal damage and visible retinal hemorrhage were complicated.

The following conclusions were obtained.

1. The proliferative vitreoretinal membranes of various eye conditions were composed mainly of fibrocyte-like cells and glial cells, and the retinal pigment epithelial cells were not found in the membranes formed without retinal break.

2. In the mild injury group of experimental animal, only the glial proliferation was noted in the case of the mechanical injury confined to the inner layer of the retina, and the retinal pigment epithelial cells were found to proliferate and migrate into the inner layer when the retinal damage extended to the outer retinal layer.

3. In the severe injury group, the proliferation of the choroidal fibroblast was noted.

On the basis of the above findings, it is suggested that the fibrocyte-like cells found at the vitreoretinal membranes in eyes with nonrhegmatogenous retinal detachment or without retinal detachment, are not derived from the retinal pigment epithelial cells.

Key Words: Vitreoretinal membrane, Closed vitrectomy

INTRODUCTION

Proliferative vitreoretinal membranes are encountered in several ocular conditions including ocular inflammation, trauma, surgery, retinal vascular disorder or retinal detachment. They often exert traction on the underlying retina, and vision of the patient may be reduced if these membranes cover or distort macula, or cause traction detachment of the macula.

It will be a prerequisite to know the cellular structure of the membrane and the mechanism of membrane formation to treat or prevent this vision-threatening conditions. Idiopathic epiretinal membranes are said to be made of glial cells by studying autopsy specimens (Roth and Foos 1971 & 1972; Foos 1972, 1974 & 1977; Spitznas and Leuenoberger 1977; Sidd et al. 1982; Bellhorn et al. 1975)

The nature of the proliferative vitreoretinal membrane has not been clarified yet due to the difficulty in obtaining specimens from the living eye. Recent improvement in surgical technic of closed vitrectomy make it easier to take the membrane surgically, and Machemer et al. (1975 & 1978) reported that the proliferative membrane in retinal detachment is chiefly made of retinal pigment epithelial cells.

The cellular components and origins of the proliferative vitreoretinal membrane in various conditions are still controversial. Observing the structural
changes of the retinal and choroid, and clarifying cellular components participating in the formation of proliferative membrane after various degrees of retinal injury, will be of great help to understand the mechanism of the membrane formation.

We studied various proliferative vitreoretinal membranes of human eyes to define their cellular components and observed the ultrastructure of the rabbit retina after insulting various degrees of retinal injury to induce vitreoretinal membrane.

MATERIALS AND METHODS

1. Human Case Study
Surgically obtained proliferative vitreoretinal membranes from 7 patients were examined. All membranes were obtained at the time of pars plana vitrectomy with Ocutome (Cooper Vision). The specimens were immediately fixed in phosphate buffered 3% glutaraldehyde solution for 2 hours. They were then postfixed in 1% osmium tetroxide for 2 hours, dehydrated in graded series of ethanols, and embedded in Epon 812. For histologic observation, 1 micron sections were stained with toluidine blue. Thin sections (600 A) were stained with uranyl acetate and lead citrate, and examined under an electron microscope (Hitachi H-500).

2. Animal Experiment
1) Preparation: 27 non-albino rabbits of 2.0-2.5 kg body weight were used. After dilation of the pupil with 1% atropine and 10% phenylephrine HCl, the animals were anesthetized with intramuscular injection of ketamine (25 mg/kg). The superotemporal sclera was exposed and a 2 mm limbus-parallel incision was made 3 mm from the limbus exposing the underlying choroid.

A 21 gauge needle was inserted through the sclerotomy site into the vitreous to reach the retinal surface and 4-5 gentle scratches were made on the avascular retina 2 disc diameters below the optic disc. The experimental animals were divided into three groups according to the degree of the retinal injury: (1) mild injury group; rabbits with mild pallor or hardly visible scratch line without visible hemorrhage on the retinal surface, (2) severe injury group; rabbits with visible retinal or choroidal injury with hemorrhage, and (3) control group; rabbits with needling into the vitreous without retinal injury. Visible retinal or choroidal hemorrhage in the severe injury group meant that the incision was deep enough to expose the retinal pigment epithelial cell layer and underlying Bruch’s membrane. The eyes which developed operative complications were excluded, and 6 rabbits (10 eyes) in mild injury group and 10 rabbits (17 eyes) in the severe injury group, and 3 rabbits (6 eyes) in control group were observed for 16 weeks after injury.

2) Fundus examination: Eyes were examined with direct and indirect ophthalmoscope at 1, 4 days after surgery, then weekly thereafter for 6 weeks, and then on the 8th, 10th, 12th and 16th weeks. Absorption of retinal hemorrhage, development of the retinal pigmentation, and development of the proliferative membrane were observed and recorded.

3) Histopathologic evaluation: Eyes were enucleated at 8, 12, 16 weeks after surgery. In mild injury group, 2 eyes were enucleated at 8 weeks after surgery. Four eyes at 12th weeks, 3 eyes at 16th weeks, and in severe injury group, 4 eyes, 4 eyes, and 9 eyes respectively, and in control group, 2 eyes at each period. Immediately after enucleation, the eyeball was bisected and 1x1 mm sized specimen containing the injury site was made in the 3% glutaraldehyde solution. The specimens were then prepared by the same method as human case.

Uncertainty regarding the contributing cell types of the proliferative vitreoretinal membrane in the previous literature is thought to be, in part, by im-

Table 1. Diagnostic criteria of various cells

<table>
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<tr>
<th>Cell Type</th>
<th>Criteria</th>
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<tr>
<td>Fibrous astrocyte</td>
<td>large &amp; often fusiform, occurring in cluster or monolayer, interdigitating cytoplasmic process, occasional junctional complex, masses of intermediate-type filament (10 nm) in the cytoplasm</td>
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<tr>
<td>Fibrocyte</td>
<td>fusiform shape, absence of polarity, occasional desmosomal attachment, infrequent intracytoplasmic filaments, numerous cisterna or RER, some SER, prominent Golgi</td>
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<tr>
<td>Macrophage</td>
<td>pleomorphic contents, especially melanin and hemosiderin, absence of surface specialization or polarity</td>
</tr>
<tr>
<td>Retinal pigment</td>
<td>lepithelium-like polarity, well developed</td>
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<tr>
<td>Epithelial cell</td>
<td>underlying basement membrane and free-surface microvilli, juxtaocular complex, single-membrane limited melanosome, intracytoplasmic filament arranged either in a monolayer or in a rosette like or acinar configuration</td>
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precise morphologic criteria for cellular identification, so we used the following diagnostic criteria presented at Table 1 (Kampik et al., 1981).

RESULTS

1. Human Case Study

Case 1. An 11-year-old boy with peripheral uveitis and complicated traction retinal detachment received pars plana vitrectomy, and the traction band was obtained and examined under the electron microscope (Fig. 1, 2).

Transmission electron microscopy (TEM) revealed cells scattered among the collagen fibers. Fibrocytes were predominant, with long and slender cytoplasmic process and rich rough endoplasmic reticulum (RER). There were also many round lymphocytes with many cytoplasmic process. A probable glial cells with intracytoplasmic RER, fine fibrils and electron-dense body with occasional basal lamina were occasionally found.

Case 2. 70 year-old man with peripheral uveitis and complicated traction retinal detachment received pars plana vitrectomy, and surgically obtained traction band were observed with TEM. (Fig. 3, 4)

TEM showed numerous fibrocytes. These spindle-shaped cells contained many RER and occasional electron-dense body in their cytoplasm. A capillary with a single layer of endothelial cells was also seen. Cells with spindle-shaped nucleus was noted occasionally, and was thought to be a glial cell (fibrous astrocyte) due to their densely packed fine intracytoplasmic filaments and patch areas of basement membrane formation.

Case 3. 44 year old patient with idiopathic preretinal membrane received membrane peeling operation by pars plana approach and the peeled membrane was observed with TEM. (Fig. 5, 6)

Electron microscopy revealed numerous long fibrous astrocytes densely packed each other. They had compactly packed fine intracytoplasmic filaments, and showed a tendency to polarization with well developed basement membrane and villous projection at the opposite side. Fibrocytes and macrophages were occasionally encountered at the periphery.

Case 4. 22 year old man with intraocular foreign body and complicated traction retinal detachment received closed vitrectomy, and the traction band was examined with TEM.

Ultrastructurally spindle-shaped fibrocyte were predominant, and fibrous astrocyte-like cells were noted occasionally. Macrophage-like cell containing pigments and with pleomorphic configuration was seen between the fibrocytes. (Fig. 7, 8)

Case 5. 29 year-old man developed aphakic retinal detachment with massive periretinal proliferation after cataract extraction for traumatic cataract. Pars plana vitrectomy was performed, and the proliferative periretinal membrane was examined under the electron microscope.

Ultrastructurally, fibroblasts were predominant, and pleomorphic macrophages were also seen. Uncertain cells with intracytoplasmic granules and occasional intercellular junctional complex, but not other evidence of polarity was observed. (Fig. 9, 10)

Case 6. Pars plana vitrectomy was done on a 10 year-old boy with traction retinal detachment, and the traction band was obtained.

Ultrastructurally numerous fibrocyte-like cell were observed, although detailed examination was difficult due to poor fixation technique.

Case 7. Pars plana vitrectomy was performed on a 51 year-old woman with proliferative diabetic retinopathy, and the surgically obtained proliferative membrane was examined under the electron microscope.

Ultrastructurally, fibrous astrocytes were predominant. These cells had abundant fine intracytoplasmic filaments, well developed basement membrane.

Table 2. Cellular components of human proliferative vitreoretinal membranes

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Vitreoretinal condition</th>
<th>Cell component</th>
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<tr>
<td>1.</td>
<td>Peripheral uveitis with vitreous band</td>
<td>Fibrocyte, Lymphocyte</td>
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<td>2.</td>
<td>Peripheral uveitis with traction retinal detachment</td>
<td>Glial cell?</td>
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<td>3.</td>
<td>Idiopathic preretinal membrane</td>
<td>Fibrocyte, Blood vessel</td>
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<td>4.</td>
<td>Intraocular foreign body with traction retinal detachment</td>
<td>Fibrous astrocyte?</td>
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<td>5.</td>
<td>Aphakic retinal detachment with massive periretinal proliferation</td>
<td>Macrophage</td>
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<td>6.</td>
<td>Traction retinal detachment</td>
<td>Fibrocyte</td>
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<td>7.</td>
<td>Proliferative diabetic retinopathy</td>
<td>Fibrous astrocyte</td>
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<td>Macrophage, Plasma cell</td>
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Fig. 1. Proliferative vitreoretinal membrane from a patient with traction retinal detachment due to peripheral uveitis (Case 1). Fibrocytes with long and slender cytoplasmic processes (arrow) are seen on the left side (x 4,200).

Fig. 2. Other portion of proliferative membrane from Case 1. A probable glial cell with basal lamina (arrow head) and few intracytoplasmic filament (f) is seen (x 14,000).
Fig. 3. Proliferative vitreoretinal membrane from a patient with preipheral uveitis (Case 2). A spindle-shaped fibrocyte is seen with rough endoplasmic reticulum (r)(x 9,800).

Fig. 4. Other portion of proliferative vitreoretinal membrane from Case 2. A probable fibrous astrocyte with masses of fine intracytoplasmic filaments (f) and occasional basal lamina (arrowhead) are seen(x 14,000).
Fig. 5. Idiopathic preretinal membrane developed at macular area (Case 3). Glial cells are densely interspersed. Distinguishing features are presence of masses of fine intracytoplasmic filaments (f) and basal lamina (arrow head) (x 7,000).

Fig. 6. Idiopathic preretinal membrane (Case 3). Fibrocytes with long, fusiform configuration and rough endoplasmic reticulum (r) is seen. The cell shows absence of polarity (x 4,200).
Fig. 7. Proliferative vitreoretinal membrane from a patient with secondary traction retinal detachment due to intraocular foreign body (Case 4). A fibrocyte (A) with fusiform configuration and absence of polarity is seen (x 8,400).

Fig. 8. Other portion of vitreoretinal membrane from Case 4. A probable fibrous astrocyte with dense intracytoplasmic filaments is seen (x 8,400).
Fig. 9. Proliferative vitreoretinal membrane from a patient with massive periretinal proliferation developed after traumatic cataract operation. Many fibrocytes with slender configuration are seen. These cells contain numerous rough endoplasmic reticulum (x 4,200).

Fig. 10. Other portion of proliferative vitreoretinal membrane from Case 5. Atypical cells with junctional activity (circle) are seen. Villous projection (w) is also seen but no basal lamina can be noted (x 16,800).
Fig. 11. Proliferative vitreoretinal membrane due to diabetic retinopathy (Case 7). Fibrous astrocytes with fine intracytoplasmic filaments (f) are interspersed. Basal lamina (arrow head) and occasional junctional activity (circle) are also seen (x 14,000).

Fig. 12. Proliferative vitreoretinal membrane from Case 7. A macrophage with pleomorphic configuration is seen. A plasma cell is noted at the right side (p) (x 4,200).
brane and intercellular junctional complexes. Macrophages containing hemosiderin and melanin pigments were also observed. Occasionally plasma cells were observed with compact RER around their nucleus. (Fig. 11, 12) Above findings were summarized at Table 2.

2. Animal Experiment

(1) Clinical observation

1. Absorption of the retinal hemorrhage in severe injury group: Minimal retinal hemorrhage was absorbed at the day 4, but in most cases the hemorrhage was began to be absorbed at second week, and was completed at 4th week (Fig. 1).

2. Development of the retinal pigmentation: In 10 eyes of mild injury group, only one eye showed retinal pigment deposition from 3rd week after injury. In 17 eyes of severe injury group, 9 eyes showed retinal pigmentation; 4 eyes from the 2nd week, 5 eyes at 3rd week, 7 eyes at 4th week, and 9 eyes at 5th week(Fig. 2).

3. Development of the proliferative membrane: In mild injury group, no visible proliferative membrane could be observed ophthalmoscopically till the enucleation. In severe injury group, visible proliferative membranes were noted in 6 eyes. At 8th week, we could observe definite membrane in 3 eyes and suspicious one in 2 eyes, and at 12th week definite membranes in 3 more eyes and suspicious one in 2 eyes (Table 3).

(2)Histopathologic findings

1. Light microscopic findings

Mild injury group: By the degree of injury, the eyes in this group could be divided into two; the superficial injury group in which the retinal injury was limited to inner layer of the retina, and the deeper injury group in which the retinal injury was extended to outer retina, near the retinal pigment epithelial layer. In superficial injury group, the choriodapillaris, retinal pigment epithelial layer and outer layer of the retina were intact, and only mild alteration in cellular arrangement was noted in the inner layer of the retina. In deeper injury group, localized proliferation and migration of the retinal pigment epithelial cells was observed. Cellular arrangement of the inner and outer retina became irregular, and probable retinal pigment epithelial cells containing pigments could be noted at inner retinal layer and nerve fiber layer. Cells of unknown nature were noted to proliferate into the vitreous cavity through the break of the inner limiting mem-

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± : Minimal or suspicious formation of the membrane
+ : Mild formation of the membrane
++ : Moderate formation of the membrane
∗ : Cataract
Fig. 13. Rabbit retina of mild injury group. Glial cell processes are interdigitated on the vitreal side of retina, with villous projection of cytoplasmic process (arrow) toward the vitreous cavity (x 4,200).

Fig. 14. Rabbit retina of mild injury group. A new growth of glial cell (G) is seen over the surface of intact internal limiting membrane (arrow head) (x 28,000).
Fig. 15. Rabbit retina of mild injury group. Retinal pigment epithelial cells multiplied into several layers over the irregular Bruch's membrane (arrow) (x 4,200).

Fig. 16. Rabbit retina of mild injury group. A probable retinal pigment epithelial cell containing pigments (arrow) is seen in the outer nuclear layer (x 4,200).
Fig. 17. Rabbit retina of mild injury group. Retinal pigment epithelial cell is in the nerve fiber layer (R), surrounded by the processes of glial cells. Another retinal pigment epithelial cell is in the vitreous cavity (arrow)(x 4,200).

Fig. 18. Rabbit retina of severe injury group. Severely damaged retina with irregular surface is largely replaced by the glial cells. Newly formed basal lamina is noted at the vitreal surface (arrow)(x 5,600).
brane.

Severe injury group: The retinal layer was severely deteriorated. In addition to the changes in mild injury group, the choroidal fibroblasts were seen to proliferate into the retinal layer, over the surface of the retina, and burst out into the vitreous cavity.

2. Electron microscopic findings

Mild injury group: In superficial injury group, the processes of the glial cell were interdigitated each other, and projected into the vitreous cavity. No regeneration of the inner limiting membrane could be found. Their cytoplasm contained a lot of RER and SER. In some area, glial cell was proliferated over the intact inner limiting membrane, forming a proliferative membrane.(Fig. 13, 14).

These findings suggest that if the retinal injury was confined to inner layer, only the glial cells proliferate and participate in the repair mechanism, and give rise to the proliferative membrane.

In deeper injury group, in addition to the above findings, irregularity of the Bruch’s membrane and proliferation of the retinal pigment epithelial cells into several layer were also noted (Fig. 15). Also, cells containing pigments were observed in photoreceptor layer and inner nuclear layer surrounded by the processes of the glial cells, and in the vitreous cavity (Fig. 17). These cells seemed to be derived from the retinal pigment epithelial cell, because they had many large, rather sharp, spine shaped pigments and intracytoplasmic RER and SER, sharp, spine shaped pigments and intracytoplasmic RER and SER, being characteristics of the rabbit retinal pigment epithelial cells. Cells in the vitreous cavity had many villous cytoplasmic processes projecting to surrounding vitreous cavity.

Severe injury group: Cellular arrangement of the retinal was severely deteriorated, and glial cells were proliferated over the damaged retinal surface, with newly formed basement membrane along the vitreal surface (Fig. 18). Cells with irregular, elongated nucleus was proliferated from the choroid into the retina, which had intracytoplasmic small, round pigment and electron dense body, long cytoplasmic process (Fig. 19), characteristic of the choroidal fibroblast. These cells proliferated and covered the retinal surface. A few lymphocytes were noted occasionally.

DISCUSSION

Proliferative vitreoretinal membranes occur in a number of conditions, including proliferative diabetic retinopathy, ocular inflammatory conditions, retinal vascular disorders, after blunt or penetrating ocular injury, after vitreous hemorrhage, and associated with rhegmatogenous retinal detachment, and as an idiopathic process in otherwise normal eye.

Until now, no medical treatment is available, and surgical removal of the membrane has great risks. As an effort to search for the pathogenesis of the membrane and method of treatment, the cellular structure of the proliferative membrane was investigated in various way. But, because of the difficulty in obtaining the specimen, the exact cell types contributing proliferative membrane are still uncertain.

Earlier studies about the structure of proliferative membrane were performed with specimens from the autopsy(Roth and Foos 1971 & 1972; Foos 1972,1974 & 1977; Spitznas 1977; Sidd 1982; Rentsch 1977; Kamilik 1980). Roth and Foos (1971 & 1972) and Foos (1972, 1974 & 1977) reported that the major cellular component of idiopathic proliferative membrane was glial cells, and these cells were migrated from the inner layers of retina through a break in the internal limiting membrane.

After development of vitrectomy technique, Many studies were reported about the proliferative membrane associated with rhegmatogenous retinal detachment (van Horn et al. 1977 Machemer et al. 1968, 1975 & 1978; Newsome et al. 1981; Wallow and Miller 1978; Laqua 1975; Raithe et al. 1981; Stern et al. 1982). They demonstrated that retinal pigment epithelial cells were the major component of the membrane, and glial cells participated in part (Newsome 1981). They also demonstrated the proliferation of retinal pigment epithelial cells by tissue culture of the membrane, and proliferation of them from experimental rhegmatogenous retinal detachment in rhesus monkey (Machemer et al. 1975). By these findings one can conclude that retinal pigment epithelial cells proliferate over and under the retina, migrated through a retinal break in case of rhegmatogenous retinal detachment.

In contrast to these reports, none of our specimens showed retinal pigment epithelial cells. The difference can be explained by the fact that all of our cases are nonrhegmatogenous retinal detachment. The result of our experiment supports our clinical observation. Funduscopy of these animal showed pigment clumping in many severe injury group, but only one mild injury group. Light and electron microscopy revealed that, the structural alterations were confined to the inner layer of retinal only in mild injury group leaving the outer retina
intact.

Fooks (1973) and Rentsch (1973) found that, after mild injury to the retina, Mueller cells proliferated initially, followed by proliferation of fibrous astrocyte. These findings coincide with our results. In our superficial mild injury group, proliferated glial cell processes filled the empty space, and the retinal pigment epithelial cells showed occasional local proliferation but no migration into inner layer of the retina. But in our deeper mild injury group, there were proliferation and lateral migration of retinal pigment epithelial cell, and occasional migration into inner layer of the retina, along the tract of injury. These findings suggest that proliferation of retinal pigment epithelial cells could be initiated by various type of injury or stimulation, but the retinal pigment epithelial cell was unable to migrate through the intact healthy retina. But once the sensory retina in front of the retinal pigment epithelial cell layer is damaged, the retinal epithelial cell might migrate through the tract, and seem to be able to proliferate over the retina, and into the vitreous.

Another characteristic finding we could observe in the human specimen is that fibrocyte was noted in nearly all the human specimen. As the retinal tissue is of neural ectodermal origin, fibrocyte can not exist normally. One possible explanation of its origin is that it might migrate from the peripheral blood cell and make a metaplasia and fibrosis. In proliferative membrane after intraocular hemorrhage or inflammation, macrophage or other inflammatory cell might migrate and possibly do metaplasia. But in other traction retinal detachment, intraocular foreign body, diabetic retinopathy or aphakic retinal detachment, one can not explain the origin by the above theory. Another explanation is that the retinal glial cell may transform into fibrocyte (Laqua and Machemer 1975), but this theory is not proved experimentally.

Another possible explanation is that the retinal pigment epithelial cell might transform into fibrocyte-like cell (Newsome et al. 1981). But, as we can see in our experiment, the retinal pigment epithelial cell can not migrate and participate in making proliferative membrane without prior damage in the sensory retina.

It would be reasonable to search for a local factor to explain the similar cellular response of fibrocytic proliferation in various disease, as is seen in our human case. The most reasonable explanation is that these cells are derived from the hyalocyte,
proposed by Kampik et al. (1980). These cells have been described as a type of granular connective tissue cell with phagocytic properties. Bloom and Balaze (1965). Hogan distinguished these cells from macrophages by the scarcity of their lysosomes, but Grabner et al. (1980) found the appearance of macrophage-like cell after culture of hyalocyte. The origin of hyalocyte is still controversial, but they appear to be a cell very similar to macrophage and fibrocyte, and it seems most probable that the fibrocyte-like cells in our specimen were derived from the hyalocytes. This is supported by the findings of Rentsch (1977) that he could observe hyalocyte-like cell participating in the formation of macular pucker although the glial cell was predominant.

In animal experiment, we observed vigorous proliferation of choroidal fibroblast into vitreous cavity containing characteristic uveal pigment, such findings being rarely reported in the literature. Topping (1977) and Cleary et al. (1979 and 1980) after experimental double perforating injury in the rabbits, observed proliferation of fibroblast. They postulated that these are derived from the episcleral tissue. But the scleral wall was intact in our experiment, and the participation of choroidal fibroblast in proliferative membrane formation in perforating injury is most probable.

As a conclusion we propose that proliferative vitreoretinal membranes are formed by various combinations of several basic cells according to the degree of retinal injury. It seems most probable that the proliferative membrane in minimal injury or mild stimulation is formed by glial cells, and in the proliferative membrane in somewhat greater stimulation or injury the hyalocyte is stimulated and participate in the formation. And if a retinal hole exist, the retinal pigment epithelial cell participate in the formation of proliferative membrane, and in case of greater injury where the choroid is exposed into vitreous cavity the choroidal fibroblast participate in the membrane formation.

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요지

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민경훈, 이제홍, 정홍

저자들은 증식성 망막을 구성하는 세포가 어떤 것이며, 어디에서 유래하였는지를 규명하기 위하여 여러 안절환에서 조작된 검체들을 시행한 후 복합적인 증식성 망막을 전자현미경으로 관찰하여 그 세포의 형태와 변화를 관찰하였고 아울러 틈의 망막에 여러 정도의 기체적인 손상을 가하여 회복과정을 체계적으로 연구하여 다음의 결과를 얻었다.

1. 망막 전 증식막은 주로 섭유세포양 세포와 교세포로 이루어져며 망막에 염증이 없는 경우에는 망막세포상피세포가 증식막에서 발견되지 않았다.
2. 틈의 망막의 내층에만 손상을 입힌 경우는 교세포만 수복과정에 참여하며 망막세포상피의 망막내내의 이동은 관찰되지 않았다.
3. 틈의 망막의 완전한 손상을 입었던 경우는 망막세포상피세포의 증식과 망막내내의 이동이 관찰되었다.
4. 틈의 망막의 완전한 손상을 입었던 경우는 망막세포상피세포의 증식과 망막내내의 이동이 관찰되었다.
5. 따라서 염증 유무와 증식막막이 이와의 증식성막에서 관찰되는 섭유세포양세포는 망막세포상피세포 이와의 세포에서 유래하였을 것으로 생각한다.