Pathological Changes of the Anterior Lens Capsule

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Received 9 March 2021; Accepted 27 April 2021; Published 4 May 2021

Academic Editor: Edward Manche

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The anterior lens capsule (ALC), as the thickest basement membrane in the body, encapsulates the crystalline lens and acts as a barrier and separates the lens from infectious viruses and bacteria together with the posterior capsule and pericapsular membrane. The ALC is an acellular, soft, smooth, transparent basement membrane secreted by lens epithelial cells (LECs). The ALC with the accompanying monolayer subcapsular epithelium represents the most important metabolic element of the crystalline lens. Recently, the biomechanical properties and biomedical engineering perspectives of the ALC were reviewed by us [1]. Also, here, we provide a brief review of the pathological changes of the ALC in several eye disorders, which were never mentioned previously.

1. Introduction

The anterior lens capsule (ALC), as the thickest basement membrane in the body, encapsulates the crystalline lens and acts as a barrier and separates the lens from infectious viruses and bacteria together with the posterior capsule and pericapsular membrane. The ALC is an acellular, soft, smooth, transparent basement membrane secreted by lens epithelial cells (LECs). The ALC with the accompanying monolayer subcapsular epithelium represents the most important metabolic element of the crystalline lens. Recently, the biomechanical properties and biomedical engineering perspectives of the ALC were reviewed by us [1]. Also, here, we provide a brief review of the pathological changes of the ALC in several eye disorders, which were never mentioned previously.

2. Pathological Changes

2.1. Cataract. Cataract is most simply defined as opacification of the crystalline lens inside the eye, which is the commonest cause of vision loss worldwide [2, 3]. Under normal physiological conditions, the ALC with the lens epithelium represents a major site of ion transport and fluid transport, which plays a vital role in maintaining lens homeostasis and transparency by providing the driving force for the ionic gradients and the fluid circulation [4, 5]. Therefore, any factor disturbing the transport processes, components or biomechanical characteristics of the ALC, and morphology or biochemistry of the lens epithelium will lead to water accumulation in the lens and the subsequent unbalance of lens homeostasis, thus resulting in cataract formation [6]. Using AFM, Choi et al. [7] found that the cataract group showed significantly lower surface roughness in the anterior side of the ALC and higher surface roughness in their posterior side than the noncataract control group. They also found lower Young's modulus in the cataract group compared to the control group, regardless of the ALC side. Compared to nuclear cataracts, intumescent white cataracts do not have a significant difference in ALC thickness but differ in ultrastructure morphology, including extrusions at the basement membrane epithelial border, lamellation, rarefication, and filaments in the basement membrane [8].

In eyes with mature cataracts, poor fundus red reflex and poor visibility of the capsule makes surgery more
2.3. Climatic Droplet Keratopathy. Climatic droplet keratopathy (CDK) is a corneal degeneration disease and characterized by a band-shaped pattern of subepithelial opacities and golden-yellow spherules [20, 21]. There is a strong association between changes of the ALC and presence of CDK. The capsule changes are usually confined to the central pupillary area, which includes a white opalescence, an elevation in front of the contour of the rest of the lens to form a plateau, and a “bag” or herniation of the lens capsule through the pupil. These ALC changes might be caused by excessive ultraviolet light exposure, which is also the main cause of CDK [22].

2.4. Exfoliation Syndrome. Exfoliation syndrome (XFS) or pseudoexfoliation syndrome is an age-related disease in which abnormal fibrillar extracellular material is produced and accumulates in many ocular tissues, mainly the ALC and the pupillary margin. The typical distribution of ALC deposits consists of three zones: a granular, often layered, peripheral zone; a central disc, and a clear area between them. Several studies confirmed fibrils accumulation above or in the basement membrane of the ALC in XFS eyes [23–28], and another unknown, electron-dense, microgranular, unbound material was also observed by transmission electron microscopy beneath the lens epithelium in XFS patients [29]. By immunofluorescence and electron microscopic immunogold techniques, heparan sulfate and chondroitin sulfate proteoglycans, laminin, entactin/nidogen, fibronectin, and amyloid P protein were shown to be an integral constituent of XFS material [30]. The ALC thickness was reported to vary greatly measured by light microscopy, and there was no statistical difference between XFS lenses and controls [31], while with high-resolution anterior segment optical coherence tomography, the ALC was found to be thicker in XFS patients than normal people [32]. The ALC ultrastructural abnormalities (diffuse intracellular and extracellular edema, transparent vacuoles, apoptotic cells, and destroyed epithelial cells) were also found to be more extended and more frequently observed in XFS patients than cataract controls [33]. XFS can be unilateral or bilateral, but exfoliation material can also be found in the unaffected eyes of patients with clinically unilateral XFS [34, 35]. If capsule staining (i.e., trypan blue) is needed, lower concentration and/or exposure is recommended because the ALC has more affinity to trypan blue in XFS patients [36].

2.5. True Exfoliation Syndrome. True exfoliation syndrome (TEX) is a rare disorder in which characteristic lamellar separation of the ALC occurs. The pathogenesis of TEX is not clear; although intense infrared radiation is thought to be the main causative factor, most cases are idiopathic. Histologically, a thickened delaminated structure, perpendicular fibrils and vesicular degeneration in the capsule, and degenerative lens epithelium have been documented [37]. Recently, double delamination and pigment deposition on the detached membrane are reported to be new findings in TEX patients [38].

2.6. Alport Syndrome. Alport syndrome is a rare disorder of the basement membrane characterized clinically by progressive hereditary nephritis, sensorineural hearing loss, and ocular abnormalities. Genetically, Alport syndrome is due to mutations involving the coding for type IV collagen resulting in a defective synthesis of type IV collagen [39]. Clinically, the typical ocular manifestations of Alport syndrome are a flecked retinopathy and bilateral anterior lenticonus, which is resulted from the conical protrusion of the lens anteriorly through the thinnest and weakest part of the capsule [39]. Several electron microscopic studies have demonstrated the marked thinning and vertical desiccation of ALC in Alport syndrome [40–43]. Spontaneous rupture of the ALC was also reported, which is suggestive of defective capsular strength [44, 45]. By using the lens capsule of wild-type and Alport syndrome mice as a model, the osmotic swelling experiments from the work of Gyoneva et al. [46] revealed direction-dependent changes. They found Alport lenses strained significantly more than wild-type lenses in
the anterior-posterior direction, which is consistent with clinical data: Alport patients develop conical protrusions on the anterior and posterior lenticular poles.

2.7. Silicone Oil Tamponade. Silicone oil is an intraocular tamponade after vitrectomy surgery, which is used for the treatment of complicated retinal detachment [47]. However, intravitreal silicone oil can lead to several complications including cataract, glaucoma, band keratopathy, oil emulsification [48, 49], and ALC changes.

In Citirik et al.’s study, by electron microscopy, silicone oil was detected on the posterior surface of the ALC in 50% cases and surface irregularities, pits, and depressions were present in the posterior surface of the ALC in all the ten silicone oil tamponade cases [50]. Ultrastructural effects of silicone oil on the ALC of the clear crystalline lens of myopic eyes were also studied [51]. Light microscopic examination showed relatively more flat cells with irregular outline of LECs with wide intercellular spaces, deeply stained nuclei, and multiple intracytoplasmic vacuoles. Collagenous surfaces filled with multiple pits, depressions, and abnormal deposits were found under scanning electron microscopy, while transmission electron microscopy revealed LECs with apoptotic changes, cytoplasmic vacuoles, and filopodia-like protrusions between LECs and the capsule [51]. In the ALC of rabbit eyes with silicone oil tamponade, many vacuoles amid matrix accumulation were present on the posterior surface, suggesting the deposition of emulsified silicone oil droplets [52], which is similar to the histopathological findings of human eyes [53].

Clinically, rigidity of the ALC is frequently encountered during cataract surgery in silicone-oil-filled eyes [54], which increases the mechanical difficulties of anterior capsulorrhexis. The anterior subcapsular tissue plaque resulted from silicone oil tamponade may be responsible for the increased mechanical resistance of the ALC [55].

The different pathological changes of the ALC in different diseases are summarized in Table 1.

3. Conclusions

The ALC, as structural support for the lens within the eye, plays an important role on normal lens growth and metabolism. However, the biomechanical properties of the ALC may change in several ocular diseases, including cataract, aniridia, climatic droplet keratopathy, exfoliation syndrome, true exfoliation syndrome, Alport syndrome, and silicone oil tamponade. These pathological changes vary from biomechanical alterations (surface roughness, Young’s modulus, elasticity, stiffness, rigidity, fragility, etc.) to ultrastructural abnormalities (increase or decrease in thickness, abnormal material accumulation, lamellar separation, vesicular degeneration, ALC dehiscence, surface irregularities, cytoplasmic vacuoles, etc.) in different ocular diseases. If cataract surgery is scheduled for these eyes, the surgery procedure, especially the capsulorrhexis, would be challenging. Therefore, attention should be raised when performing cataract surgery for these patients.

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare to have no potential conflicts of interest.
Acknowledgments

This work was supported by a grant from the National Natural Science Foundation of China (grant no. 81800825), Tianjin Clinical Key Discipline Project (grant no. TJLCZDXKKQ023), and Open Project of Tianjin Key Laboratory of Retinal Functions and Diseases (grant no. 2020tjswmq003). The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

References

[1] D. Huang, C. Xu, R. Guo, J. Ji, and W. Liu, "Anterior lens capsule: biomechanical properties and biomedical engineering perspectives," Acta Ophthalmologica, 2020.

[2] J. Thompson and N. Lakhani, "Cataracts," Primary Care: Clinics in Office Practice, vol. 42, no. 3, pp. 409–423, 2015.

[3] P. Asbell, I. Dualan, J. Mindel, D. Brocks, M. Ahmad, and E. H. Sage, "Age-related cataract," The Lancet, vol. 365, no. 9459, pp. 599–609, 2005.

[4] J. Fischbarg, F. P. J. Diecke, K. Kuang et al., "Transport of fluid by lens epithelium," American Journal of Physiology-Cell Physiology, vol. 276, no. 3, pp. C548–C557, 1999.

[5] J. F. Hejtmancik, S. A. Riazuddin, R. McGreal, W. Liu, A. Cvekl, and A. Shiels, "Lens biology and biochemistry," Progress in Molecular Biology and Translational Science, vol. 134, pp. 169–201, 2015.

[6] Q. Yan, J. I. Clark, T. N. Wight, and E. H. Sage, "Alterations in the lens capsule contribute to cataractogenesis in SPARC-null mice," Journal of Cell Science, vol. 115, no. 13, pp. 2747–2756, 2002.

[7] S. Choi, H.-J. Lee, Y. Cheong et al., "AFM study for morphological characteristics and biomechanical properties of human cataract anterior lens capsules," Scanning, vol. 34, no. 4, pp. 247–256, 2012.

[8] M. Hawlina, S. Stunf, and A. Hvala, "Ultrastructure of anterior lens capsule of intumescent white cataract," Acta Ophthalmologica, vol. 89, no. 4, pp. e367–e370, 2011.

[9] C. Simsek and O. Gokmen, "The effects of vital dyes on mechanical properties of the human anterior lens capsule," Indian Journal of Ophthalmology, vol. 68, no. 1, pp. 66–70, 2020.

[10] C. Haritoglou, S. Maueell, R. G. Schumann et al., "Increase in lens capsule stiffness caused by vital dyes," Journal of Cataract and Refractive Surgery, vol. 39, no. 11, pp. 1749–1752, 2013.

[11] G. Wollensak and E. Spoerl, "Influence of indocyanine green staining on the biomechanical properties of porcine anterior lens capsule," Current Eye Research, vol. 29, no. 6, pp. 413–417, 2004.

[12] G. Wollensak, E. Spoerl, and D.-T. Pham, "Biomechanical changes in the anterior lens capsule after trypan blue staining," Journal of Cataract and Refractive Surgery, vol. 30, no. 7, pp. 1526–1530, 2004.

[13] B. H. Dick, S. E. Alivyeva, and F. Hengerer, "Effect of trypan blue on the elasticity of the human anterior lens capsule," Journal of Cataract and Refractive Surgery, vol. 34, no. 8, pp. 1367–1373, 2008.

[14] C. Simsek, S. Oto, G. Yilmaz, D. D. Altinors, A. Akman, and S. G. Gungor, "Comparison of the mechanical properties of the anterior lens capsule in senile cataract, senile cataract with trypan blue application, and pseudoexfoliation syndrome," Journal of Cataract and Refractive Surgery, vol. 43, no. 8, pp. 1054–1061, 2017.

[15] R. Jaber, L. Werner, S. Fuller et al., "Comparison of capsulorhexis resistance to tearing with and without trypan blue dye using a mechanized tensile strength model," Journal of Cataract and Refractive Surgery, vol. 38, no. 3, pp. 507–512, 2012.

[16] I. Ivanov, A. Shuper, M. Shohat, M. Snir, and R. Weitz, "Aniridia: recent achievements in paediatric practice," European Journal of Pediatrics, vol. 154, no. 10, pp. 795–800, 1995.

[17] H. Lee, R. Khan, and M. O’Keefe, "Aniridia: current pathology and management," Acta Ophthalmologica, vol. 86, no. 7, pp. 708–715, 2008.

[18] S. Schneider, R. H. Osher, S. E. Burk, T. B. Lutz, and R. Montione, "Thinning of the anterior capsule associated with congenital aniridia," Journal of Cataract and Refractive Surgery, vol. 29, no. 3, pp. 523–525, 2003.

[19] Z. Q. Hou, Y. S. Hao, W. Wang, Z. Z. Ma, Y. F. Zhong, and S. J. Song, "Clinical pathological study of the anterior lens capsule abnormalities in familial congenital aniridia with cataract," Beijing Da Xue Xue Bao Yi Xue Ban, vol. 37, no. 5, pp. 494–497, 2005.

[20] C. S. Matta, K. F. Tabbara, J. A. Cameron, A. A. Hidayat, and A. A. al-Rajhi, "Climatic droplet keratopathy with corneal amyloidosis," Ophthalmology, vol. 98, no. 2, pp. 192–195, 1991.

[21] R. H. Gray, G. J. Johnson, and A. Freedman, "Climatic droplet keratopathy," Survey of Ophthalmology, vol. 36, no. 4, pp. 241–253, 1992.

[22] G. Johnson, D. Minassian, and S. Franken, "Alterations of the anterior lens capsule associated with climatic keratopathy," British Journal of Ophthalmology, vol. 73, no. 3, pp. 229–234, 1989.

[23] K. N. Sorkou, M. E. Manthou, S. Meditskou, N. Ziakas, and I. T. Tsinopoulos, "Transmission electron microscopy of exfoliation syndrome," Current Eye Research, vol. 44, no. 8, pp. 882–886, 2019.

[24] T. T. Kivelä, "Histopathology of exfoliation syndrome," Journal of Glaucoma, vol. 27, no. 1, pp. S38–S43, 2018.

[25] J. C. Morrison and W. R. Green, "Light microscopy of the exfoliation syndrome," Acquired Ophthalmological, vol. 66, no. 184, pp. 5–27, 1988.

[26] Z. Sheity, P. M. Palmiero, C. Tello, J. M. Liebmann, and R. Ritch, "Noncontact in vivo confocal laser scanning microscopy of exfoliation syndrome," Transactions of the American Ophthalmological Society, vol. 106, pp. 46–55, 2008.

[27] R. Ritch, "Ocular findings in exfoliation syndrome," Journal of Glaucoma, vol. 27, no. 1, pp. S67–S71, 2018.

[28] J. H. Seland, "The ultrastructural changes in the exfoliation syndrome," Acta Ophthalmologica, vol. 66, no. 184, pp. 28–34, 1988.

[29] K. N. Sorkou, M.-E. Manthou, K. T. Tsououis, P. Baziokitos, and I. T. Tsinopoulos, "Transmission electron microscopy study of undescribed material at the anterior lens capsule in exfoliation syndrome," Graefe’s Archive for Clinical and Experimental Ophthalmology, vol. 256, no. 9, pp. 1631–1637, 2018.

[30] U. Schlötzer-Schrehardt, S. Dörfler, and G. O. H. Naumann, "Immunohistochemical localization of basement membrane components in pseudoexfoliation material of the lens capsule," Current Eye Research, vol. 11, no. 4, pp. 343–355, 1992.
[31] J. Ruotsalainen and A. Tarkkanen, “Capsule thickness of cataractous lenses with and without exfoliation syndrome,” *Acta Ophthalmologica*, vol. 65, no. 4, pp. 444–449, 1987.

[32] M. Batur, E. Seven, S. Tekin, and T. Yasar, “Anterior lens capsule and Iris thicknesses in pseudoexfoliation syndrome,” *Current Eye Research*, vol. 42, no. 11, pp. 1445–1449, 2017.

[33] K. Sorkou, M. E. Manzhou, N. Ziakas, K. T. Tsaeuiss, and I. T. Tsinopoulo, “Severe abnormalities of lens epithelial cells in exfoliation syndrome: a transmission electron microscopy study of patients with age-related cataract,” *Medicina (Kaunas)*, vol. 55, no. 6, p. 235, 2019.

[34] Z. Sbeity, P.-M. Palmiero, C. Tello, J. M. Liebmann, and P. Parekh, W. R. Green, W. J. Stark, and E. K. Akpek, “Mechanical response of wild-type and Alport murine lens ultrastructural confirmation of Alport syndrome in the lens crystalline lens of the human eye,” *European Journal of Ophthalmology*, vol. 28, no. 5, pp. 566–572, 2018.

[35] Y. Ohnishi, “Deposition of silicone oil droplets in the residual anterior lens capsule after vitrectomy and lensectomy in cataracts after prolonged exposure to anterior capsulotomy technique and histopathology of the anterior lens capsule,” *European Journal of Ophthalmology*, vol. 34, no. 12, pp. 2020–2023, 2008.

[36] K. G. Riedel, V.-P. Gabel, L. Neubauer, A. Kampik, and O.-E. Lund, “Intravitreal silicone oil injection: complications and treatment of 415 consecutive patients,” *Graefe’s Archive for Clinical and Experimental Ophthalmology*, vol. 228, no. 1, pp. 19–23, 1990.

[37] M. Citirik, M. F. Sargon, S. Has, and S. Bilgin, “Alterations of the anterior lens capsule in vitrectomized eyes with silicone oil tamponade,” *Retinal Medicine*, vol. 118, no. 7, pp. 895–897, 2000.

[38] F. H. J. K. Koch, A. Cusumano, P. Seifert, M. Mougharbel, and A. Nafady, “Ultrastructural effects of silicone oil on the clear crystalline lens of the human eye,” *European Journal of Ophthalmology*, vol. 34, no. 12, pp. 2020–2023, 2008.

[39] A. J. Augustin, “Ultrastructure of the anterior lens capsule after vitrectomy and lensectomy in cataracts after prolonged exposure to anterior capsulotomy technique and histopathology of the anterior lens capsule after vitrectomy and lensectomy in rabbits,” *British Journal of Ophthalmology*, vol. 88, no. 5, pp. 703–707, 2004.

[40] S. Saika, T. Miyamoto, T. Tanaka, Y. Ohnishi, A. Ooshima, and W. Kimura, “Histopathology of anterior lens capsules in vitrectomized eyes with tamponade by silicone oil,” *Journal of Cataract and Refractive Surgery*, vol. 28, no. 2, pp. 376–378, 2002.

[41] C.-W. Yung, A. Oliver, J. M. Bonnin, and H. Gao, “Modified anterior capsulotomy technique and histopathology of the anterior capsule in cataracts after prolonged exposure to intravitreal silicone oil,” *Journal of Cataract and Refractive Surgery*, vol. 34, no. 12, pp. 2020–2023, 2008.

[42] F. H. J. Koch, A. Casasuso, P. Seifert, M. Mougharbel, and A. J. Augustin, “Ultrastructure of the anterior lens capsule after vitrectomy with silicone oil injection. correlation of clinical and morphological features,” *Documenta Ophthalmologica*, vol. 91, no. 3, pp. 233–242, 1995.