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PIGMENT DISPERSION SYNDROME - HOW TO UTILIZE IN VIVO LASER CONFOCAL MICROSCOPY

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ABSTRACT
Purpose: To demonstrate in vivo laser confocal microscopy as an option for precise diagnosis and monitoring of the cornea in pigment dispersion syndrome, including dynamic microstructural observations.
Design: Prospective Ten corneas with clinically visible pigment dispersion syndrome were examined by in vivo laser confocal microscopy (HRTII Rostock corneal module). Several examinations were performed in order to facilitate quantitative and qualitative analysis of the subbasal nerve plexus, endothelial cells and bright granules, presumed to be pigment.
Results: Descriptive analysis was performed by two independents investigators. The most significant findings were hyper-reflective, polymorphic granules on endothelial surface measured 10-25 μm. Granules' size and density increased in higher intraocular pressure patients. A correlation between the clinical characteristic and the degree of polymegathism and plesiomorphism of affected endothelial zones was observed.
Concusion: In vivo laser confocal microscopy demonstrates new perspectives for diagnostics of the pigment dispersion syndrome, including staging. The method has wider applications for monitoring and long term prognosis.

Key words: cornea, pigment dispersion syndrome, in vivo confocal microscopy

INTRODUCTION

In vivo confocal microscopy facilitates optical slicing throughout the living cornea and provides imaging at cellular level in both its physiological and pathological states.(1) This technology has led to a better understanding of the cellular microstructure in health and disease, enabling quantitative and qualitative analysis of the human cornea in vivo. There are number of studies dedicated to corneal nerves, stromal keratocite density and endothelial characteristics of the normal human and ageing cornea. However, in the published literature there are diverse papers describing different pathological observations.

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The main purpose of this pilot study is to describe and measure number of characteristics of the patient with PDS using HRT II in vivo confocal microscopy, Rostock corneal module.

Pigment dispersion syndrome is a relatively rare condition that leads to secondary open angle glaucoma. Pigmentary glaucoma is a disease most common amongst young myopes of male gender. (2)Vertical pigment deposition on the corneal endothelium was identified by Krukenberg in the late 1800s.(3) He considered this to be a congenital anomaly caused by the approximation of the pupillary membrane to the cornea during early embryogenesis.(3) However, it was not until 1940 that Sugar described the first case of pigmentary glaucoma (PG).(4) Discovery which lead to several controversies before our eventual understanding of PG.(5,6) Key event in history was the proposal by Von Hippel in 1901 that pigment obstructed aqueous outflow and had a role in elevating intraocular pressure

(IOP)(7) Source of the pigment was proposed 8 years later by Levinsohn, who demonstrated pigment within the trabecular meshwork (TM) and suggested an origin from the iris.(8) Later, others suggested a causal relationship between pigment deposition and glaucoma, although at that time many opposed this concept.(9,10) In 1949, Sugar and Barbour reported the detailed clinical features of two cases of PG, both were myopic patients with corneal endothelial pigment deposition, iris trans-illumination defects, heavy pigmentation and elevated IOP. (11) By definition pigment dispersion syndrome (PDS): an ocular condition characterized by dispersion of iris pigment throughout the eye. PDS can be associated with ocular hypertension (OH) or glaucoma and is usually bilateral.

The purpose of our study was to describe the structural changes of the cornea in patients with pigment dispersion syndrome and to demonstrate in vivo laser confocal microscopy opportunities for precise diagnosis and long term monitoring.

MATERIALS AND METHODS

Five patients (10 eyes) between the age 35- 60 years 3 female and 2 male with clinical signs of PDS were selected for the purpose of the study. Each eye was examined with slit-lamp biomicroscopy, goniscopy, OCT, fundoscopy and *in vivo* laser confocal microscopy. Microstructural assessment was focused on quantity and quality of subbasal nerve plexus, endothelial cells and morphology of the pigment granules.

Laser scanning in vivo confocal microscopy was performed on all subjects using the HRT II corneal module that uses a 670 nm red wavelength diode laser source. Heidelberg Retina Tomograph II Rostock Corneal Module (RCM); Heidelberg Engineering GmbH, Heidelberg, Germany). A 606 objective water immersion lens with a numerical aperture of 0.9 (Olympus, Tokyo, Japan) and a working distance, relative to the applanating cap (tomo-cap), of 0.0–3.0 mm was used. Corneal in vivo confocal microscopy were performed using standard protocol for HRT II corneal module. After detailed explanation and obtaining informed consent patient's cornea was anaesthetized with one drop of Alcaine 1% (Alcon). A sterile applanation tomo-cup was inserted after application of one drop Cornere gel (Bausch and Lomb) over the front of the lens to facilitate immersion. The examination head was justified and the front plate of the cup was set as zero plane. All subjects were requested to fixate on a distance target aligned to enable examination of the central cornea. The patient`s cornea was gently applanated using the visual control by the camera followed by the examination. The full thickness of the central cornea was scanned using the ''section'' mode. The total duration of in vivo confocal examination was approximately 2 min for each eye.

For each cornea three images were selected from the following levels: basal epithelium, sub basal nerve plexus, anterior stroma, mid stroma, posterior stroma and endothelium. Collected data were analyzed independently by 2 investigators using the same criteria.

RESULTS

The study highlighted changes at three different levels: epithelium, sub-basal plexus and endothelium **(fig. 1).**

At superficial level the most prominent observation was the changing morphology of the basal epithelial cells in correlation to clinical stage of the disease. In advanced cases, especially associated with increased IOP, epithelial mosaic was irregular with presumed oedema at this level. **(fig 1 row A)**

Sub-basal nerve plexus also demonstrated pleomorphic morphology, however with advancement of the pigmentation, the nerves appear to decrease in density and increase in diameter. Also change in morphology was noted as looping and beading. **(fig 1 row B)**

Corneal stroma had less prominent change but generally with advancement of disease we encountered decreased number of keratocytes. **(fig 1 row C)**

A correlation between the clinical characteristic and the degree of polymegathism and pleomorphism of affected endothelial zones was also observed. Quantitative analysis found a mean density of the pleomorphic endothelium to be 699 ± 76 cells/ mm^2. However the periphery endothelium appears to be normal with density 2203 ± 58 cells/ mm^2. This observation was clinically undetectable.

The most significant findings are hyper-echogenic, polymorphic granules on the back side of endothelial cells', measured 20 μm ±15, corresponding to the IOP. The size and density of the granules in patients with high intraocular pressure was significantly enlarged. **(fig 1 row D)**

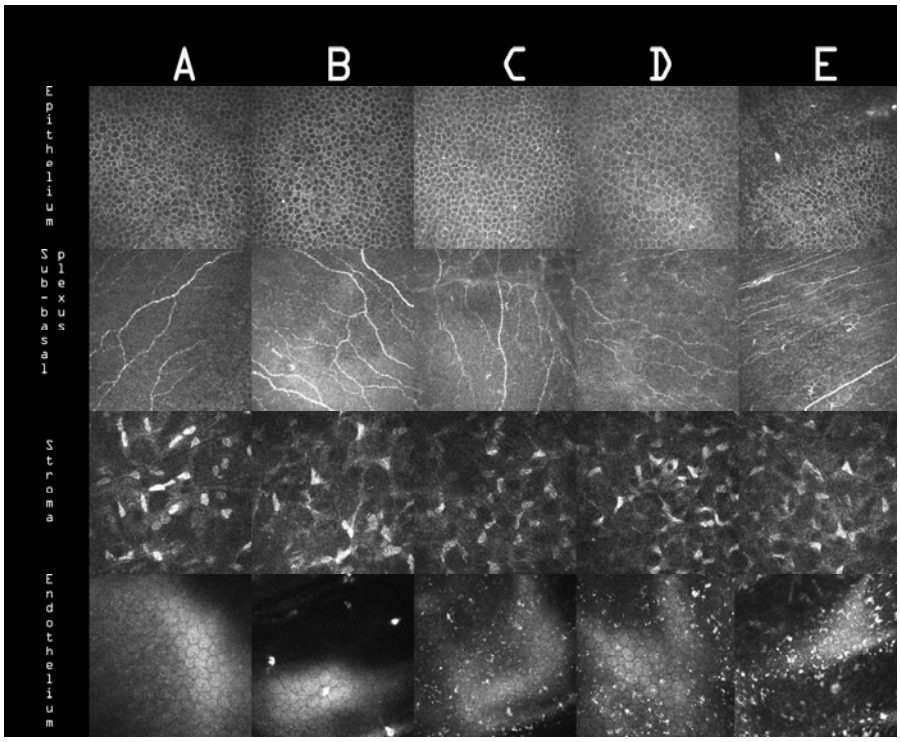

Figure 1. In vivo confocal microscopy microstructural characteristics at different levels of the cornea affected by PDS: epithelium (A), sub-basal nerve plexus (B), stroma (C) and area of pigment granules on the back surface of the endothelium (D). The columns are demonstrating the specified levels for normal cornea and corneae with mild, moderate and advance development of the PDS as well in case with pigmentary glaucoma.

DISCUSSION

In the literature there are limited number of case reports describing PDS using in vivo confocal microscopy, and specifically HRT II Rostock corneal module for morphometric analysis. Our study demonstrated new perspectives for diagnostic the pigment dispersion syndrome, including staging. The observations would have a monitoring and prognostic advantage and differential diagnostic value with conditions associated with clinically similar pigment deposit on the back surface of the cornea over the endothelium. These will include inflammation, post-surgical and post-traumatic pigment dispersion and Fuch's endothelial dystrophy.

In our study we described interesting changes in nerve morphology, which differs from other observations. The most prominent feature was thickening of the nerves in advancement of disease. As the patients had no history of any other ocular or systemic disease, nor prior cataract surgery, we believe that this is related to the syndrome. Whether this is an isolated nonspecific finding or whether thickened nerve plexuses may be more frequent in patients with PDS requires further observations in longer follow up over few years.

In some cases, uveitis can cause pigment epitelitis of the iris with release of pigment, inflammatory cells and debris behind endothelium. After resolution of the inflammation clinical observations might be mistaken for PDS, as other authors had demonstrated.(15) Cataract surgery also can cause features similar to PDS, with iris trans-illumination defect, pigment behind endotelium and increase IOP.(16-22)In our study however, we utilized in vivo confocal microscopy to rule out prior incidents by observing morphology of endothelial cells and characteristics of the granules. We believe that polymegathism and pleomorphism in PDS are localized in the area of Kruckenberg spindle and the rest of endothelium is relatively normal. That could be an important diagnostic characteristic for differentiation of other conditions.

The largest study in the literature by Harold and al. reported 409 patients with PDS, clinically observed over a period of 30 years in population suspected for glaucoma. PDS comprised 4.4% of the entire "glaucoma in suspect" group. An average frequency real pigmentary glaucoma was 13.1 per year among patients with PDS.(23) Regardless this small incidence, PDS is an important often underdiagnosed condition because it affects

young people with potential risk of irreversible blindness. Laser scanning in vivo confocal microscopy may not only detect pigment particles in early stages when impossible to be observed by slit lamp biomicroscopy, but also precisely measure the size and record changes in morphology. Furthermore this technique allows observation at microstructural level of all corneal levels and precise follow up of the dynamic changes in epithelium, sub-basal plexus and endothelium. Therefore, eye specialist may rely not only on precisely diagnose but may utilize prognostic characteristics and utilize those for follow up.

CONCLUSIONS

Laser scanning in vivo confocal microscopy provides a novel method for examining micro-structural alteration in PDS in the cornea, as well as other corneal pathology and might be in use for diagnosis and differentiating number of subclinical disorders. This new in vivo technology may hopefully now be used to screen for abnormalities at cellular level. Laser scanning in vivo confocal microscopy is an instantaneous, noninvasive imaging technique with strong perspective to improve early detection of anterior segment pathology. The study demonstrated ability of in vivo laser confocal microscopy for diagnostics of the pigment dispersion syndrome, including staging. The method has wider applications that are still to be developed and utilised for monitoring and long term prognosis.

REFERENCES

1. Erie JC, McLaren JW, Hodge DO, et al. The effect of age on the corneal subbasal nerve plexus. Cornea 2005;24:705–9.
2. Nuwan Niyadurupola MRCOphth and David C Broadway FRCOphth Pigment dispersion syndrome and pigmentary glaucoma a major review Clinical and Experimental Ophthalmology 2008; 36: 868–882.
3. Krukenberg F. Beiderseitige angeborene melanose der hornhaut. Klin Monatsbl Augenheilkd 1899; 37: 254–8.
4. Sugar HS. Concerning the chamber angle. I. Gonioscopy. Am J Ophthalmol 1940; 23: 853–66.
5. Campbell DG, Schertzer RM. Pathophysiology of pigment dispersion syndrome and pigmentary glaucoma. Curr Opin Ophthalmol 1995; 6: 96–101.
6. Ritch R. A unification hypothesis of pigment dispersion syndrome. Trans Am Ophthalmol Soc 1996; 94: 381–409.
7. Von Hippel E. Zur pathologischen anatomie des glaucoma. Arch Ophthalmol 1901; 52: 498.
8. Levinsohn G. Beitrag zur pathologische anatomie und pathologie des glaukoms. Arch Augenheilkd 1909; 62: 131.
9. Koeppe L. Die rolle des irispigment beim glaukom. Dtsch Ophthalmol Ges 1916; 40: 478.
10. Jess A. Zur frage des pigmentglaukoms. Klin Monatsbl Augenheilkd 1923; 71: 175.
11. Sugar HS, Barbour FA. Pigmentary glaucoma: a rare clinical entity. Am J Ophthalmol 1949; 32: 90–2.
12. Sugar HS. Pigmentary glaucoma: a 25-year review. Am J Ophthalmol 1966; 62: 499–507.
13. Fiebel RM, Perlmutter JC. Anisocoria in the pigmentary dispersion syndrome. Am J Ophthalmol 1990; 110: 657–60.
14. Dua HS, Dick AD, Watson NJ, Forrester JV. A spectrum of clinical signs in anterior uveitis. Eye 1993; 7: 68–73.
15. Ballin N,Weiss DM. Pigment dispersion and intraocular pressure elevation in pseudophakia. Ann Ophthalmol 1982; 14:627–30.
16. Caplan MB, Brown RH, Love LL. Pseudophakic pigmentary glaucoma. Am J Ophthalmol 1988; 105: 320–1.
17. Cykiert RC. Pigmentary glaucoma associated with posterior chamber intraocular lenses. Am J Ophthalmol 1986; 101: 500–1.
18. Huber C. The gray iris syndrome. An iatrogenic form of pigmentary glaucoma. Arch Ophthalmol 1984; 102: 397–8.
19. Samples JR, Van Buskirk EM. Pigmentary glaucoma associated with posterior chamber intraocular lenses. Am J Ophthalmol 1985; 100: 385–8.
20. Smith JP. Pigmentary open-angle glaucoma secondary to posterior chamber intraocular lens implantation and erosion of the iris pigment epithelium. J Am Intraocul Implant Soc 1985; 11:174–6.
21. Woodhams JT, Lester JC. Pigmentary dispersion glaucoma secondary to posterior chamber intra-ocular lenses. Ann Ophthalmol 1984; 16: 852–5.
22. HAROLD G. SCHEIE' AND J. DOUGLAS CAMERON Pigment dispersion syndrome: a clinical study British Journal of Ophthalmology, 1981: 65: 264-269