Original Research Article

Specular microscopic study of cornea in infectious and non-infectious uveitis in rural population of south India

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Abstract

Background: Intermediate uveitis is a form of uveitis localized to the vitreous and peripheral retina. Primary sites of inflammation include the vitreous of which other such entities as pars planitis, posterior cyclitis, and hyalitis are encompassed. Intermediate uveitis may either be an isolated eye disease. Involvement of the corneal endothelium during uveitis has not been extensively studied even though it might participate in or constitute a target of ocular inflammation. Formation of keratic precipitates (KP) is a characteristic finding in several forms of uveitis.

Aim: The aim of this prospective study was to examine the vicinity of keratic precipitates in infectious and non-infectious uveitis by specular microscopy.

Materials and methods: Patients with infectious and non-infectious uveitis in any activity level and presence of keratic precipitates were enrolled. A noncontact specular microscope was used to capture endothelial images in the vicinity of keratic precipitates. The automated morphometric analysis was done for cell size, cell density and cells coefficient of variation. Statistical comparisons were made between the infectious and non-infectious groups.

Results: Totally 50 patients were enrolled in this study, 30 (64%) eyes presented infectious uveitis, 20 (36%) non-infectious uveitis and 1 (3%) eye were excluded due to the impossibility to obtain a specular image. The mean cell density estimated was 2,628 ± 204 cells/mm^2 in the infectious group and 2,622 ± 357 cells/mm^2 in the non-infectious group. The mean cellular area in the infectious and non-infectious group was respectively 385 ± 31 µm^2 and 390 ± 60 µm^2. The coefficient of variation (%) of the cellular area in the vicinity of keratic precipitates was 26.36 ±3.44 in infectious and 27.69 ±

4.61 in the non-infectious group. The differences between the groups were not statistically significant (P<0.005 / Mann-Whitney test) for the three morphologic variables.

Conclusion: The clinical applicability of specular microscopy in patients with uveitis can be a useful tool to evaluate the corneal endothelium in the presence of keratic precipitates, however, the handicap of the specular image formation might not be discarded in some cases. The differences found were not clinically meaningful between the infectious and non-infectious groups, however the uveitis in various degrees of intraocular inflammation

Key words

Corneal topography, Endothelium, Corneal, Uveitis, Microscopy, Methods, Precipitation.

Introduction

Uveitis occurs when the middle layer of the eyeball gets inflamed (red and swollen). This layer, called the uvea, has many blood vessels that nourish the eye. Uveitis can damage vital eye tissue, leading to permanent vision loss. There are 3 types of uveitis [1]. They are based on which part of the uvea is affected. Swelling of the uvea near the front of the eye is called anterior uveitis. It starts suddenly and symptoms can last up to 8 weeks. Some forms of anterior uveitis are ongoing, while others go away but keep coming back. Swelling of the uvea in the middle of the eye is called intermediate uveitis. Symptoms can last for a few weeks to many years [2]. This form can go through cycles of getting better, then get worse. Swelling of the uvea toward the back of the eye is called posterior uveitis. Symptoms can develop gradually and last for many years anterior uveitis, no associated condition or syndrome is found in approximately one-half of cases. However, anterior uveitis is often one of the syndromes associated with HLA-B27. Presence of this type of HLA allele has a relative risk of evolving this disease by approximately 15%.The most common form of uveitis is acute anterior uveitis (AAU). It is most commonly associated with HLA-B27, which has important features: HLA-B27 AAU can be associated with ocular inflammation alone or in association with systemic disease. HLA-B27 AAU has characteristic clinical features including male preponderance, unilateral alternating acute onset, a non-granulomatous appearance, and frequent recurrences whereas HLA-B27 negative AAU has an equivalent male to female onset, bilateral chronic course, and more frequent granulomatous appearance [3].

Formation of keratic precipitates (KP) is a characteristic finding in several forms of intraocular inflammation. Typically KP is created by the small aggregates of inflammatory cells accumulated on the corneal endothelial surface. Clinical aspects of these KP can provide useful information on etiology and degree of inflammatory activity. The KP is said to be granulomatous when they are large, and they might be secondary to etiology such as sarcoidosis, tuberculosis or toxoplasmosis. Other precipitates are called non-granulomatous when they are small, for example in HLA-B27 associated anterior uveitis and Behçet's syndrome [4]. Although recently KP was analyzed using in vivo confocal microscopy; the technique requires a coupling gel to reduce light scattering at the corneal epithelium and it is not readily performed in all clinics as well as the number of machines in use remains limited. The noncontact specular microscopes are better tolerated by patients and are preferred by physicians, they do not require corneal contact, are quicker and easier to use, and currently equipped with auto-focus and built-in image analysis software. In a specular microscopy, an image of the corneal endothelium is obtained after light refraction at the anterior corneal surface [5].

Materials and methods

This was a prospective study of 50 patients with mean age of 40.5 (±14.2) years that were examined at the Uveitis department of the Ophthalmology Department at Meenakshi Medical College and Research Institute, Kanchipuram. Informed consent was obtained from all subjects for their participation in the study. Patients with previous ocular surgery, trauma, contact lens use history, corneal dystrophy, corneal edema, high intraocular pressure and any other anterior segment disorders affecting the corneal endothelium were excluded from the study. Only patients with infectious and non-infectious uveitis in any activity level and presence of KP were enrolled. The clinical ocular diagnosis was made by two different uveitis specialists using standard departmental protocol. This included a thorough history, including an extensive review of systems, ophthalmic examination, and pertinent laboratory investigations. On initial examination data concerning age, gender, ocular symptoms, medications, previous surgery and systemic diseases were recorded. Every patient underwent a complete anterior and posterior segment examination. On slit lamp examination the presence of KP was noted and any number, size, nature, pigmentation and their position on the endothelium were included.

Results

Totally 50 patients were enrolled in this study, 30 (64%) eyes presented infectious uveitis, 20 (36%) non-infectious uveitis and 1 (3%) eye were excluded due to the impossibility to obtain a specular image. The mean cell density estimated was 2,628 ± 204 cells/mm^2 in the infectious group and 2,622 ± 357 cells/mm^2 in the non-infectious group. The mean cellular area in the infectious and non-infectious group was respectively 385 ± 31 µm^2 and 390 ± 60 µm^2. The coefficient of variation (%) of the cellular area in the vicinity of the KP was 26.36 ± 3.44 in infectious and 27.69 ± 4.61 in the non-infectious group. All these differences were not statistically significant ($p<0.005$ / Mann-Whitney test) for the three morphologic variables.

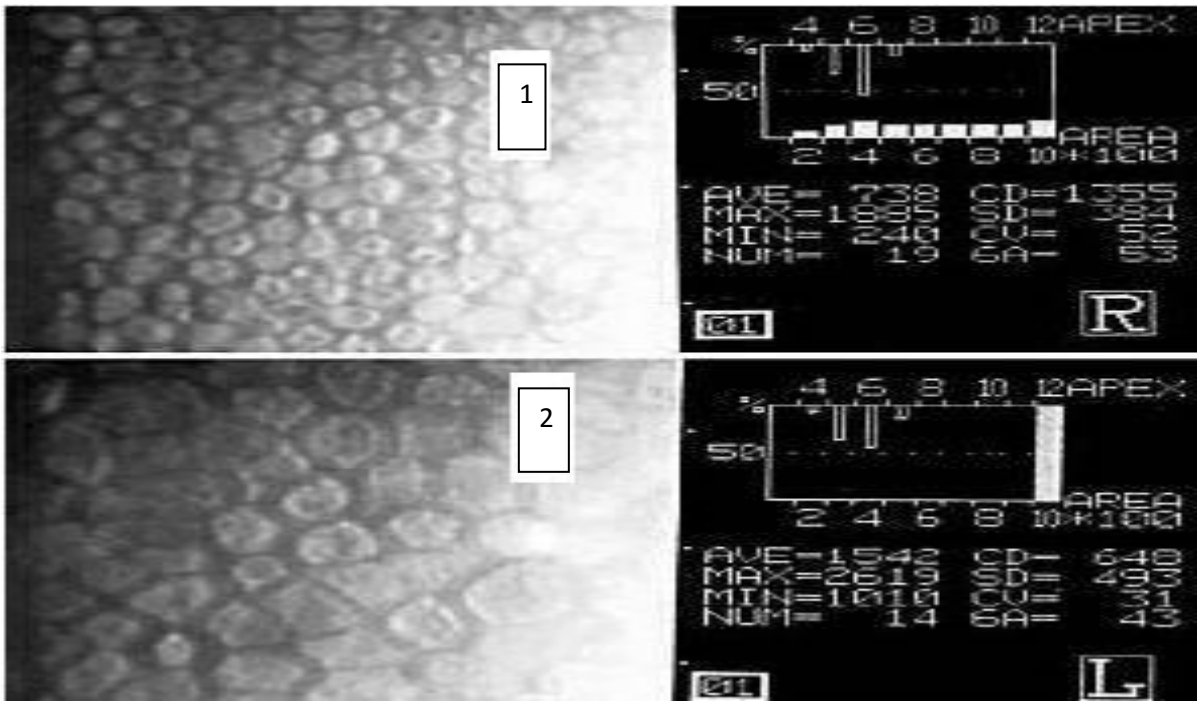

Photo – 1: shows the corneal infected uveitis and **Photo – 2:** shows the corneal uninfected uveitis indicates the keratic precipitates corresponding to the dark halo surrounding the central white deposit with indistinct cellular margins. The white-boxed region demarcates the vicinity area

used for generating the morphologic variables which are indicated for the ellipse. The single KP in Posner-Schlossman syndrome appeared globular occupying more than 15±20 cells diameters on specular microscopy and was actually a conglomeration of three individual KP. The individual KP was morphologically similar to those of large fresh KP and the three KP were connected by one or more elongated pseudopodia. Although the margin of the conglomerate was well demarcated from the surrounding endothelium, the transition between the individual KP was less distinct.

Discussion

Morphological changes of endothelium associated with cell loss occur in many conditions including corneal dystrophies, keratoconus, congenital glaucoma, blunt ocular trauma, cataract extraction, and penetrating keratoplasty. Endothelial abnormalities had been observed in cases of anterior and posterior uveitis. Brooks, et al. studied the endothelial abnormalities in various corneal disorders and also in uveitis with specular microscopy. To our knowledge, this is the first study to elucidate the different specular microscopic features of KP in different types of uveitis and the distinct morphological changes occurring with are a solution of uveitis [6]. Specular microscopy is indicated in several specific conditions and has become widespread to evaluate situations in which the cornea is suspected of having an endothelial abnormality and in which the accuracy of the estimated cell count from slit-lamp biomicroscopy is thought to be less than satisfactory [7]. These situations include but are not limited to eye banking, preoperative evaluation, and corneal disease follow-up. In uveitis, the role of the corneal endothelium has not been widely studied, and little is known about the mechanisms of KP formulation, probably because the endothelium is hard to access, making investigation difficult. When the human corneal endothelium is damaged, healing is a process of cellular enlargement and spreading to create a continuous layer of cells on the inner surface of the cornea [8]. The degree of endothelium cell loss from disease, for instance, can be documented with specular microscopy as an increase in individual cell surface area and a decrease in the endothelial cell density for the cornea. Endothelial abnormalities had been observed in cases of anterior and posterior uveitis [9]. Some authors studied these abnormalities in various corneal disorders and also in uveitis with specular microscopy. It is a well-established fact that endothelial abnormalities occur in uveitis Some authors studied the vicinity of fresh KP and there was significant statistical difference in endothelium mean cell size and density compared with normal endothelium of the opposite eye, besides the mean endothelial cell size decreased with a corresponding increase in cell density on resolution of uveitis; the absolute values did not return to normal. According to a recent study review for FDA clinical trials, the ideal specular microscopy study would be performed by one examiner at one clinical site with one specular microscope model. One examiner should analyze all the specular micro-graphs, which would give uniformity in the subjective decision of identifying cells. Furthermore, Specular Microscopy Reading Center repeatability is best achieved by one examiner [10]. The estimated cell density can have a ± 2% to ± 5% variability. All these recommendations were followed in the present study and are crucial to standardization and minimization of variables. In a specular microscopy, an image of the corneal endothelium is obtained after light refraction at the anterior corneal surface. Endothelial cell density can be estimated by counting the number of cells within a certain area, in the present study such estimation was possible in KP vicinity, only one eye was excluded the analysis because the endothelium image was impossible, probably the specular reflex at corneal central area was not regular and smooth-surfaced because KP was very distributed along this area, making impossible the cell identification [11]. The image quality is directly related to the identification of cell borders, which is determined by the number of cells visible in the field. Each examiner may have a different subjective ability to identify an

individual cell. Other authors found that image quality evaluation of 688 images by 2 examiners was identical only 64% of the time. In our study the quality of the image was considered good, each patient had three images from affected eye and they were analyzed separately, however for statistical analysis the mean from endothelial density and the cellular area was considered. The endothelial cell density analysis can be performed by comparison method, frame method (fixed or variable), corner method and center to center method [12]. Regardless of the method, the accuracy depends on the quality of endothelial cell image to identify individual cells. The present study used the center-to-center method which is a common technique incorporated into specular microscopes. In our study, fresh KP appeared as glistening, dense white deposits and with the clinical remission of uveitis, these deposits appeared less dense and were also smaller in size [13]. A dark halo was noted around the shrinking central white deposit and, eventually, in some instances, a dark shadow or defect, corresponding to the original KP, remained as a sequel. The dark shadow or halo observed with the resolution probably indicates degranulation of the precipitate. The solitary KP observed in Posner-Schlossman syndrome by slit lamp examination was actually a conglomeration of two or three large KP connected by slender pseudopodia which were well demarcated from the normal endothelium [14]. This has not been described before to our knowledge with specular microscopy. Sometimes the distribution of the new KP was limited to one quadrant of the cornea on slit lamp examination; on specular microscopy they were seen scattered throughout the endothelium and with their solution they were seen to disappear without any sequel. Walter, et al. explained that the brand position surrounding the inflammatory cells caused the stellate appearance of the KP in cytomegalovirus retinitis and demonstrated the cell pattern of the KP by electron microscopy. Probably the conglomeration of KP observed in Posner-Schlossman syndrome was due to the fibrin deposition around individual KP [13, 14].

Conclusion

In conclusion, we have described the distinct specular microscopic appearances of KP in different types of uveitis and the changing morphology of the KP with treatment. Significant changes were observed in endothelium in the vicinity of KP inactive uveitis, which returned to near normal values on the resolution. These blebs probably indicate endothelial stress and with chronic, recurrent, inflammation corneal decompensation may occur. In our series, in spite of recurrent inflammation and the presence of numerous large and small blebs on the endothelium, none of the patients had corneal decompensation. It could be explained that probably some corneas could withstand the stress better in spite of these blebs.

References

1. Academy of Ophthalmology. Ophthalmic procedures assessment. Corneal endothelial photography. Ophthalmology, 1991; 98: 1464-8.
2. AMV, Grant G, Gillies WE. The use of specular microscopy to investigate unusual findings in the corneal endothelium and its adjacent structures. Aust NZ Ophthalmol., 1988; 16: 235-43.
3. Brooks AMV, Grant G, Gillies WE. Differentiation and assessment of corneal endothelial changes associated with diseases of the anterior segment of the eye. Aust NZ J Ophthalmol., 1987; 15: 65-70.
4. Hartman C, Konitz W. Automated morphometric endothelial analysis combined with video specular microscopy. Cornea, 1985; 3: 155-67.
5. Hartmann C, Konitz W. Automated morphometric endothelial analysis combined with video specular microscopy. Cornea, 1984; 3: 155-67.
6. Inomata H, Smelser GK. Fine structural alterations of corneal endothelium during experimental uveitis. Inves Ophthalmol Vis Sci., 1970; 4: 272-85.
7. Lester JM, McFarland JL, Bursell SE, et

al. Automated morphometric analysis of corneal endothelial cells. Inves Ophthalmol Vis Sci., 1981; 20: 407-10.

8. Olsen T. Changes in the corneal endothelium after acute anterior uveitis as American seen with the specular microscope. Acta Ophthalmol., 1980; 58: 250-6.
9. Olsen T. Transient changes in the specular appearance of the corneal endothelium and in corneal thickness during anterior uveitis. Acta Ophthalmol., 1981; 59: 100-9.
10. Price NC, Cheng H. Contact, and non-contact specular microscopy. Br J Ophthalmol., 1981; 65: 568-74.
11. Sherrard ES, Buckley RJ. The relief mode. Arch Ophthalmol., 1982; 100: 296-300.
12. Stevenson R, Kirkness CM. A comparison of contact and non-contact specular microscopy in quantifying corneal morphology. Invest Ophthalmol Vis Sci., 1994; 35(s): 1598.
13. Sugar A. Clinical specular microscopy. Surv Ophthalmol., 1979; 24: 21-32.
14. Walter KA, Coulter VL. Corneal endothelial deposits in patients with cytomegalovirus retinitis. Am J Ophthalmol., 1996; 121: 391-6.