SCIENTIFIC REPORT

Clinical evaluation of cornea pseudoguttata

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Br J Ophthalmol 2007;91:22–25. doi: 10.1136/bjo.2006.102624

Aim: To report on cornea pseudoguttata which occurred in 44 eyes from 40 patients.

Methods: In 3521 consecutive patients seen at a local eye clinic, eyes were examined with a slit-lamp biomicroscope in specular illumination. When guttate appearance was found, specular microscopy was performed.

Results: Cornea pseudoguttata was found in 44 eyes of 40 patients (1.1%). All patients had some form of anterior-segment ocular diseases, including keratitis (corneal infiltration) with contact lens wear ($n=16$), epidemic keratoconjunctivitis ($n=8$), corneal epithelial defect ($n=6$), superficial punctate keratitis ($n=4$), corneal foreign body ($n=3$), keratitis of unknown causes ($n=3$), corneal ulcer ($n=2$), herpetic keratitis ($n=1$), and iritis ($n=1$). Six eyes were lost to follow-up, but in the remaining 38 eyes, cornea pseudoguttata completely resolved as the primary anterior-segment diseases subsided. Specular microscopy, measured after resolution of cornea pseudoguttata, showed that corneal endothelial cell density was not different between the affected and contralateral healthy eyes.

Conclusion: Cornea pseudoguttata is commonly found in cases with corneal infiltration and inflammation. These results indicate that cornea pseudoguttata is reversible in its nature and resolves completely without any damage to the corneal endothelial cells.

Cornea pseudoguttata represents transient corneal endothelial changes that are caused by anterior-segment diseases such as iritis and keratitis.^{1–3} Unlike primary cornea guttata, which is usually associated with corneal endothelial dystrophy and consists of focal thickening of Descemet's membrane, cornea pseudoguttata is characterised by reversible corneal endothelial cell oedema.¹ In 1981, Krachmer *et al*¹ reported three cases of cornea pseudoguttata that were seen during a short-term episode of iritis and corneal inflammation. Zantos and Holden² described the rapid appearance and gradual disappearance of guttate endothelial changes in a patient who experienced an acute red-eye symptom associated with continuous wear of contact lenses.² Several other reports described clinical findings of cornea pseudoguttata.^{4–5} To the best of our knowledge, however, there have been no other reports of cornea pseudoguttata in the literature, and thus its clinical characteristics are not known in detail, including long-term clinical consequences, incidence and influences on corneal endothelial cell morphology. In this article, we report on 44 eyes with cornea pseudoguttata that were found in 3521 consecutive cases at the Nakashima Eye Center, Fukuoka, Japan.

SUBJECTS AND METHODS

Of the 3521 consecutive patients (mean age 47.8 (standard deviation (SD)) 20.3 years) who were seen at the Nakashima Eye Clinic between March and October 2003, 1252 (35.6%) were men and 2269 (64.4%) were women. All patients were examined using the slit-lamp biomicroscope in specular

illumination. Eyes with corneal opacity, which hindered observation of the corneal back surface, were excluded from the study. When dark lesions of the endothelium in specular reflection resembling cornea guttata were recognised, specular microscopy (SP-6000, Konan, Hyogo, Japan) was performed. The presence of true cornea guttata was excluded by serial examinations, observation of the contralateral eye or heredity.

The severity of cornea pseudoguttata was classified into three grades (fig 1): grade 1, several dark spots; grade 2, many dark spots that are not in contact with each other; and grade 3, numerous dark spots that are in contact with each other.

RESULTS

Among the 3521 patients examined, cornea pseudoguttata was found in 44 eyes of 40 patients (1.1%), mean age 41.1 (SD 19.2, range 12–85) years. The 40 patients included 18 (45%) men and 22 (55%) women. All patients had some form of anterior-segment ocular disease, including keratitis (corneal infiltration) with contact lens wear ($n=16$), epidemic keratoconjunctivitis ($n=8$), corneal epithelial defect ($n=6$), superficial punctate keratitis ($n=4$), corneal foreign body ($n=3$), keratitis of unknown causes ($n=3$), corneal ulcer ($n=2$), herpetic keratitis ($n=1$) and iritis ($n=1$). The average (SD) log minimum angle of resolution visual acuity was -0.105 (0.074) in grade 1 ($n=12$), -0.02 (0.133) in grade 2 ($n=21$) and 0.123 (0.311) in grade 3 ($n=11$). Among the 44 eyes, six eyes were lost to follow-up. In the remaining 38 eyes, endothelial abnormalities completely resolved as the primary anterior-segment diseases subsided.

In 10 patients with unilateral cornea pseudoguttata, specular microscopy was measured after cornea pseudoguttata disappeared. The mean (SD) corneal endothelial cell count was 2903 (194) and 2986 (205)/mm² in the affected and contralateral healthy eyes, respectively. We found no significant difference between eyes ($p=0.525$; paired-sample *t* tests).

Case 1

A 50-year-old woman came to our clinic with ocular pain and conjunctival injection in her left eye during contact lens wear. Visual acuity was 20/20 OS. A diffuse anterior stromal infiltrate was present. The endothelium showed a diffuse, confluent guttate appearance when viewed in specular illumination (fig 2). During the next few days, corneal infiltrate and conjunctival injection resolved, and cornea pseudoguttata disappeared. Serial specular microscopy showed the time course of changes in cornea pseudoguttata, including its complete remission within a few days (fig 3).

Case 2

A 46-year-old man was seen at our clinic with a foreign body in his left cornea. Slit-lamp examination showed an iron foreign body surrounded by infiltration in the corneal stroma (fig 4). The endothelium in the area of the foreign body showed the appearance of cornea pseudoguttata among the normal endothelial mosaic pattern (fig 5). Visual acuity was 20/20 OS. The iron foreign body was removed. The stromal infiltration and epithelial lesion cleared within 2 weeks. The cornea

Figure 1 Cornea pseudoguttata classified into three grades. (A) Grade 1, several dark spots. (B) Grade 2, many dark spots that are not in contact with each other. (C) Grade 3, numerous dark spots that are in contact with each other.

pseudoguttata disappeared and the endothelium appeared normal in specular illumination.

Case 3

A 12-year-old girl developed epidemic keratoconjunctivitis and was seen at our clinic. The first examination showed a slight corneal subepithelial infiltration in her left eye, but cornea pseudoguttata was not found using the biomicroscope and specular microscopy (fig 6A). After 1 week, corneal stromal oedema was exacerbated and the endothelium appeared to have confluent cornea pseudoguttata (fig 6B). The keratoconjunctivitis gradually resolved during the next week, and cornea pseudoguttata was completely resolved, with the remission of keratoconjunctivitis (fig 6C). The corneal endothelial cell count was 3468/mm² before the onset of cornea pseudoguttata and 3450/mm² after pseudoguttata disappeared.

Figure 2 Cornea pseudoguttata in a patient with keratitis, seen in specular reflection.

DISCUSSION

We found cornea pseudoguttata in 1.1% of patients who were seen at Nagashima Eye Center, Fukuoka, Japan. During the study period, there was a small outbreak of epidemic keratoconjunctivitis, which might have increased the incidence of pseudoguttata in our study population. If eight eyes with epidemic keratoconjunctivitis are excluded, the incidence is 0.9%. Krachmer *et al*¹ reported three cases of cornea pseudoguttata, and described that cornea pseudoguttata was frequently observed in patients in their practice. The actual incidence of pseudoguttata, however, was not reported in their article. This is the first report of the incidence of cornea pseudoguttata in a clinic population. It should be noted that our study patients were not the general population but were patients who visited a local eye clinic. The incidence of cornea pseudoguttata in the general population must be much lower than in our study, because this condition seems to be associated with anterior-segment ocular disorders such as keratitis and corneal infiltration. We did not calculate the incidence of cornea pseudoguttata in patients with corneal inflammation or infiltration. Obviously, not all patients with keratitis develop cornea pseudoguttata. This will be the topic of future studies.

The true cornea guttata is usually seen in middle to older age patients and its incidence is higher in women than in men.⁶ In our study, there was no sex-related difference in the incidence of cornea pseudoguttata. On the contrary, the ratio of female patients with cornea pseudoguttata (55%) was lower than that of the study population (64.4%). As for the age of patients, 70% of patients with pseudoguttata were aged <40 years. This trend is totally different from that observed in cases of true cornea guttata. This was because keratitis (corneal infiltration) with contact lens wear was the leading cause of cornea pseudoguttata in our patients. Thus, our study indicates that the epidemiology and pathophysiology of cornea pseudoguttata are completely different from those of true cornea guttata.

Changes in the appearance of the corneal endothelial mosaic are reported to be observed within minutes after insertion of contact lenses in unadapted patients.⁷⁻⁹ These changes are called transient endothelial blebs, which consist of increased separation between cells and circumscribed black zones obscuring or displacing the mosaic. The endothelial blebs can be differentiated from pseudoguttata in that endothelial blebs

Figure 3 (A) Specular microscopy shows diffuse, confluent guttata appearance. (B) Next day, pseudoguttata decreased moderately. (C) Pseudoguttata resolved completely 4 days later.

reach a maximum at 10–50 min after contact lens insertion in the unadapted eye and disappear soon thereafter.^{7–9}

Krachmer *et al*¹ experimentally created cornea pseudoguttata in animals.¹ They induced anterior uveitis in the eyes of adult albino rabbits by injecting bovine serum albumin into the anterior chamber or superficial cautery of the localised area of the cornea. Iritis and corneal inflammation resulted in the transient appearance of dark spots, which interrupted the normal endothelial mosaic seen in specular reflection. Scanning and transmission electron microscopy of the cornea showed transient endothelial cell oedema. Clinically and histopathologically, the lesion resolved completely as inflammation subsided. As the lesions bear no histopathological relationship with cornea guttata (focal thickening of Descemet's membrane), Krachmer *et al*¹ suggested the term “cornea pseudoguttata” rather than “transient cornea guttata”.

Our study is the first report of specular microscopy in patients with cornea pseudoguttata. In every patient, the presence of dark spots was confirmed by specular microscopy, which was performed when a pseudoguttata appearance was found on biomicroscopic examination. In 10 patients with unilateral cornea pseudoguttata, specular microscopy was carried out after cornea pseudoguttata disappeared. It was found that corneal endothelial cell density did not differ between the affected and unaffected healthy eyes. In one patient, specular

microscopy was performed before and after the episode of cornea pseudoguttata, and the corneal endothelial cell count after remission of cornea pseudoguttata was similar to that before the onset of pseudoguttata. These results indicate that corneal endothelial cells are not adversely affected by the episode.

In conclusion, we have reported on 44 eyes of 40 patients with cornea pseudoguttata. Cornea pseudoguttata is not necessarily an extremely rare condition, but can be commonly found in patients with corneal infiltration and inflammation. Our clinical observation and specular microscopy measurements show that cornea pseudoguttata is reversible in nature and does not induce permanent damage to corneal endothelial cells.

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Funding: This study was supported in part by a grants-in-aid for scientific research from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Competing interests: None.

Figure 4 Corneal foreign body and surrounding stroma infiltrate.

Figure 5 Cornea pseudoguttata in a patient with corneal foreign body.

Figure 6 Specular microscopy in a patient with epidemic keratoconjunctivitis. (A) On day 1, there was no cornea pseudoguttata. (B) After 1 week, corneal stromal oedema was exacerbated and the endothelium seemed to have confluent cornea pseudoguttata. (C) During the next week, cornea pseudoguttata was completely resolved with the remission of keratoconjunctivitis.

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Accepted 2 September 2006

Published Online First 13 September 2006

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