ORIGINAL ARTICLE

Clinical Profile and Corneal Complications of Staphylococcal Blepharitis at the Philippine General Hospital

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ABSTRACT

Objectives. Staphylococcal blepharitis is a common ocular condition that can cause significant visual morbidities due to corneal complications. This study described the clinical profile of patients with staphylococcal blepharitis seen in a tertiary referral eye center, and determined the frequency and the type of corneal complications, the possible reasons for the delay in diagnosis, and the management prior to the consult.

Methods. This study was a single-center, five-year retrospective case series design. The charts of all patients from January 2016 to December 2021 with the diagnosis of staphylococcal blepharitis seen at the External Disease and Cornea Clinic of the Philippine General Hospital that have fulfilled the inclusion and exclusion criteria were included. The data extracted were age, sex, chief complaint, laterality, time of onset of symptoms to consult, previous consults, lid and lid margin findings, conjunctival and corneal findings, pre- and post-treatment uncorrected distance visual acuity, duration of follow-up, and treatments received.

Results. Fifty-five (55) charts out of 107 charts with a diagnosis of staphylococcal blepharitis were included. Eighty percent (80%) or 44 patients had bilateral disease. Ninety-nine (99) eyes of 55 patients were analyzed. The median age of the study population was 19 years. Sixty-seven percent (67%) were female, and 33% were male. The mean duration of follow-up at the External Disease and Cornea Clinic was 10.8 ± 14.61 months. Corneal opacity, eye redness, and blurring of vision comprised 70% of the reasons for consult. The mean time from the onset of symptoms to consult was 18.36 ± 25.69 months. Sixty-seven percent (67%) had prior consults elsewhere and 45% came in with a different diagnosis. Seventy-eight (78) eyes had fibrin or crust on the lashes. Fifty percent (50%) of the eyes had concomitant conjunctivitis, while 30% had meibomitis. Fifty-eight percent (58%) of patients had corneal complications. Seventy-two percent (72%) of eyes had bilateral involvement. The median age of patients with corneal complications subgroup was 13 years. The most common corneal complications noted were neovascularization, phlyctenulosis, pannus formation, and marginal infiltrates or ulcers. Twenty-two percent (22%) of all study eyes had visually disabling corneal complications like corneal ulcer, descemetocele, corneal perforation, and corneal scar. Ninety percent (90%) of the patients received standard medical treatment and three patients underwent penetrating keratoplasty. The mean uncorrected distance visual acuity at initial consult of eyes with corneal complication was 20/55 (LogMAR 0.43 ± 0.51) and 20/35 (LogMAR 0.25 ± 0.40) after treatment (p = 0.032).

Conclusion. Staphylococcal blepharitis was most prevalent among young female patients, and it affected both eyes. Almost all patients manifested the typical lid margin lesions. Nearly 60% of the patients presented with corneal complications and 22% had corneal lesions that were potentially blinding. Close to 50% had delay in treatment due to misdiagnosis.

Keywords: blepharitis, staphylococcus, cornea, blindness

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INTRODUCTION

Nearly 80% of the blind people in the world live in developing countries; thus, blindness continues to be one of the major public health concerns in developing countries like the Philippines.[1] Based on the data of the World Health Organization (WHO), corneal blindness remains a major cause of vision loss and blindness after cataract and glaucoma. In the Third Philippine National Survey on Blindness, corneal blindness was sixth among the top ten main causes of bilateral blindness accounting to 3.5%.[2] The economic burden due to corneal blindness has not yet been extensively studied, but it is highly related to reductions in vision-related quality of life, which can limit daily activities and productivity among affected individuals.[3]

Many of the causes of corneal blindness are preventable and treatable. In a study in India, they noted that 95% of corneal blindness in their population was avoidable. These avoidable causes included keratitis from both infectious and non-infectious causes, bullous keratopathy, and ocular trauma.[3] A common cause of preventable corneal blindness is staphylococcal blepharitis which can lead to corneal complications. It was the fourth most common diagnosis among new consultations in 2021 at the External Disease and Cornea Clinic of the Department of Ophthalmology and Visual Sciences at the Philippine General Hospital (PGH).

Staphylococcus aureus is a major pathogen of the eye that can infect the tear duct (dacryocystitis), eyelid (blepharitis), conjunctiva (conjunctivitis), cornea (keratitis), and vitreous chamber (endophthalmitis).[4] It is the most common cause of infectious blepharitis and is usually seen in adolescent and young adults. In acute cases, staphylococcal blepharitis causes lid ulceration and crusting; however, in subacute and chronic cases, it can cause lid changes such as madarosis, tylosis, poliosis, and trichiasis and will affect other parts of the eye such as the conjunctiva and cornea. The conjunctival changes will present as papillary-follicular conjunctivitis. The corneal changes may present as inferior pannus formation, marginal infiltrates and ulceration, phlyctenulosis, corneal vascularization, and corneal thinning and perforation leading to visually-disabling corneal scars and even blindness due to secondary glaucoma. These corneal changes are the major causes of visual morbidity from staphylococcal blepharitis. However, with prompt diagnosis coupled with early and appropriate treatment, this visual morbidity is totally preventable. Patient education about the chronicity of the condition and good compliance to treatment are likewise essential.[5-7]

Despite being a treatable condition, we have observed a steady increase in the number of these cases with corneal complications in our clinic at PGH. Aside from the fact that there is no local published data regarding this condition, we aimed to describe the clinical profile of patients with staphylococcal blepharitis and to determine the frequency and the type of corneal complications. Moreover, we also wanted to identify the reasons for the delay in diagnosis and the management prior to their consult at PGH. By doing so, we can raise awareness among ophthalmologists of this potentially blinding but treatable disease.

MATERIALS AND METHODS

The study was a single-center, five-year retrospective case series encompassing the charts of patients from January 2016 to December 2021 of the External Disease and Cornea Clinic of PGH. All of the available charts were reviewed and were included in the study if the patient was clinically diagnosed with staphylococcal blepharitis by an external disease and cornea consultant seen by face-to-face consultation or by virtual consultation. The charts were excluded if the patient had any concomitant corneal, neuro-ophthalmic, glaucomatous, or retinal pathology unrelated to staphylococcal blepharitis or if the chart had more than 50% incomplete data.

Staphylococcal blepharitis was clinically diagnosed based on the presence of ocular surface symptoms accompanied by the presence of lid margin erythema, skin ulceration at the base of lashes or lid margin, fibrin formation or collarette, and crusting with or without conjunctival or corneal changes. The clinical data collected from the charts included age in years, sex, laterality, history of present illness (chief complaint or reason for referral, time from the onset of symptoms to consult at PGH, treatments prior to present consult, and reasons for delay in diagnosis and management), uncorrected distance visual acuity in LogMAR on first and last consult, lid margin findings (collarettes, fibrin, crust, erythema, telangiectasia, ulceration, tylosis, madarosis, poliosis, trichiasis), lid findings (hordeolum, chalazion, meibomitis, abscess), conjunctival findings (redness, discharge, follicles, papillae), corneal findings (pannus, marginal ulcer, marginal infiltrates, phlycten, punctate keratitis, central corneal ulcer, neovascularization, lipid keratopathy, descemetocele, corneal perforation), and other associated eye findings. For bilateral cases, both sides/eyes were included. Uncorrected distance visual acuity was included instead of the best corrected visual acuity because corneal complications may be accompanied by changes in corneal curvature and corneal epithelial integrity, and treatment may result in improvement of the ocular surface. These secondary effects were better measured with the uncorrected distance visual acuity. Moreover, accurate best corrected visual acuity would be impossible to measure in eyes with a compromised corneal surface.

The data on prescribed medical treatment, supportive therapy, non-surgical (bandage contact lens, tissue glue) and surgical procedures (conjunctival flap, amniotic membrane graft, corneal patch graft, penetrating keratoplasty), and treatment outcomes were likewise collected.

The data were extracted by the investigators from the patient charts, and all the information were manually entered into an electronic spreadsheet file. The subsequent data

processing and analysis were carried out using the statistical software Stata 13 (StataCorp, Texas, USA).

The patient's identity was not included in the electronic spreadsheet and was replaced by a patient sequence number to ensure privacy and confidentiality. A master list of the patients' names with corresponding sequence number was kept in a separate password-protected electronic spreadsheet.

The investigators adhered to the principles of transparency, legitimate purpose, and proportionality in the collection, retention, and processing of personal information (Data Privacy Act of 2012). The privacy and confidentiality of each subject were upheld. The study was a minimal risk study which was conducted in full compliance with principles of the 7th iteration of the Declaration of Helsinki, Good Clinical Practice of the WHO, Philippine Health Research Ethics Board, and the ethical standards of University of the Philippines Manila (UP Manila). The protocol was submitted for ethical evaluation to the UP Manila Research Ethics Board and was conducted only upon approval (UPMREB 2022-0078-01).

Total sampling for the retrospective medical review of patients who met the inclusion and exclusion criteria was used in this study. Descriptive statistics were used such as mean, median, standard deviation, and range for describing the age of participants in years, duration of follow-up in months, visual acuity in LogMAR; while frequency and percentage were used for the categorical data variables such as sex, chief complaint, clinical findings, and other factors that may affect visual outcome. T-tests were performed to determine the difference between the initial and final visual acuity. The level of significance for all sets of analysis was decided at a p-value less than 0.05 using one-tailed comparisons.

RESULTS

Fifty-five (55) charts out of 107 charts with a diagnosis of staphylococcal blepharitis were included in this study after fulfilling the inclusion and exclusion criteria. Eighty percent (80%) or 44 patients had bilateral disease and only 11 (20%) patients had unilateral affectation. Total of 99 eyes of 55 patients were analyzed. The mean age of the study population was 27 (26.97 ± 22.51) years with median age of 19 years. Figure 1 shows the clustering of patients in the first two decades of life. Sixty-seven percent (67%) of the patients were female, and 33% were male. The mean duration of follow-up at the External Disease and Cornea Clinic was 10.8 ± 14.61 months.

The top three most common reasons for consult or referral to the clinic were whitish corneal opacity (25%), eye redness (23%), and blurring of vision (22%) comprising 70% of the consults. Other reasons for consult were eye discharge, itchiness and pain, foreign body sensation, and lid swelling.

The average time from onset of symptoms to consult at PGH was at 18.36 ± 25.69 months. Sixty-seven percent

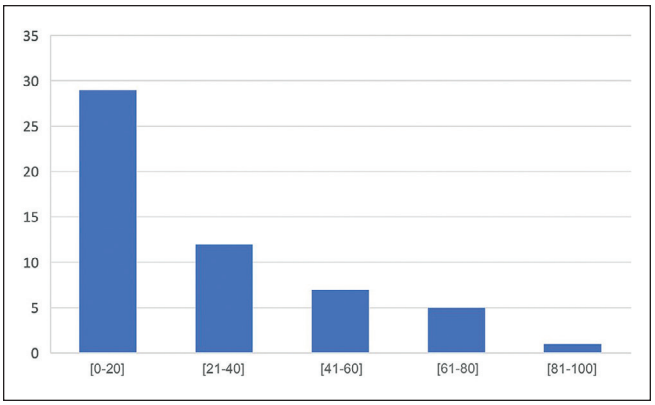

Figure 1. The frequency of patients by age at 20-year intervals (N=55).

Table 1. Frequency of Lid Margin Findings in Eyes with Staphylococcal Blepharitis

Lid Margin Findings	Number of eyes N=99 (%)
Fibrin/crusts/collarettes	78 (79%)
Lid margin erythema/telangiectasia	27 (27%)
Lid margin ulceration	6 (6%)
Madarosis	3 (3%)
Tylosis	11 (11%)
Trichiasis	5 (5%)
Poliosis	0 (0%)
Distichiasis	4 (4%)

Table 2. Frequency of Corneal Complications in Eyes with Staphylococcal Blepharitis

Corneal Complications	Number of eyes N=55 (%)
Pannus formation	17 (31%)
Marginal ulcer/infiltrates	11 (20%)
Phlycten	18 (33%)
Punctate keratitis	8 (15%)
Central corneal ulcer	6 (11%)
Neovascularization	22 (40%)
Lipid keratopathy	1 (2%)
Descemetocele	3 (5%)
Corneal perforation	2 (4%)
Corneal scar/haze	10 (18%)

(67%) of patients had prior consult and treatment with other ophthalmologists. Forty-five percent (45%) had a different diagnosis and 47% had different treatments before being seen in our clinic. Thirty-three percent (33%) of patients had no previous consult with an ophthalmologist.

Table 1 shows the frequency of lid margin findings in eyes with staphylococcal blepharitis. Fibrin, crust, or collarettes around the lashes were most commonly found and were seen in 78 of the 99 eyes included (Figure 2A). This was followed by lid margin erythema at 27 eyes (Figure 2B). These two findings were the most typical signs of acute staphylo-

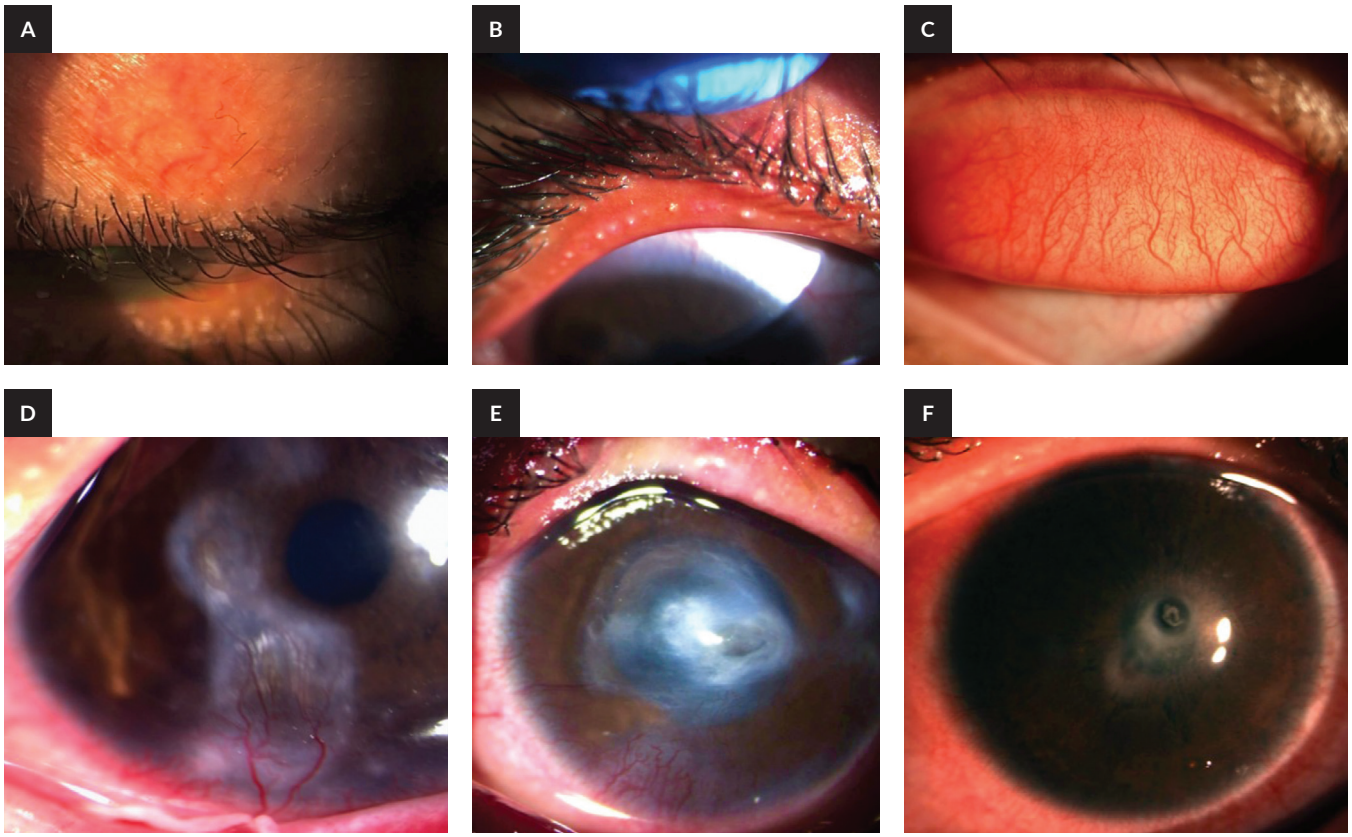

Figure 2. Representative clinical photos of staphylococcal blepharitis and its corneal complications. **(A)** Fibrin crust at the base of the eyelashes; **(B)** Lid margin erythema and telangiectasia with meibomitis; **(C)** Papillary reaction on the upper palpebral conjunctiva; **(D)** Corneal neovascularization with lipid keratopathy; **(E)** Corneal scarring with inferior pannus; **(F)** Ruptured central corneal descemetocele.

coccal blepharitis. The chronic signs like tylosis, madarosis, and trichiasis were less frequently seen. The concomitant findings like meibomitis were seen in 30% (Figure 2B), while 7% came in with hordeolum or chalazion.

The most common conjunctival findings were redness and papillae, which were present in almost half of the study eyes at 49 and 46, respectively (Figure 2C). In other words, close to 50% of the eyes had conjunctivitis. Other less common conjunctival findings were discharge (11 eyes) and follicles (12 eyes).

Fifty-eight percent (32 out of 55) of patients presented with corneal complications. Seventy-two percent (23 patients) had bilateral corneal findings and 28% (9 patients) had unilateral involvement. The mean age of this subgroup with corneal complications was 17.84 years with a median age of 13 years, which was younger than that of the whole study population with a similar female-to-male sex ratio. A total of 55 eyes were analyzed for this subgroup while considering that each eye may have multiple corneal lesions. Table 2 shows the frequency of corneal complications in eyes with staphylococcal blepharitis. Neovascularization (new blood vessel formation going beyond the peripheral cornea) was the most common finding seen in 22 eyes (Figure 2D), followed by phlycten which was seen in 18 eyes. Pannus (peripheral corneal blood vessels) formation was seen in 17 eyes (Figure 2E), while marginal infiltrates or ulcers were noted in 11 eyes. Eight eyes had punctate keratitis, but 6 eyes had frank corneal ulceration which was a severe corneal complication that would cause visual morbidity. Other severe corneal complications that were potentially blinding include descemetocele in 3 eyes and corneal perforation in 2 eyes (Figure 2F). Other visually disabling corneal lesions noted were corneal scars in 10 eyes and lipid keratopathy in 1 eye (Figures 2D and 2E). A total of 22 eyes had visually disabling complications. This number also comprised 22% of all eyes in this study or approximately 1 out of 5 eyes would become visually impaired due to a corneal complication from staphylococcal blepharitis.

Ninety percent (90%) of the patients received standard treatment consisting of daily lid hygiene and lid margin scrub with combination antibiotic-steroid eye ointment at least once daily. Those with conjunctivitis were given combination antibiotic-steroid eye drops, and those with corneal ulcers were given pure antibiotic eye drops initially. Three eyes had to undergo penetrating keratoplasty, while one eye had a glue patch as treatment for corneal perforation.

Table 3. Uncorrected Distance Visual Acuity at Baseline and at last Follow-up

	Initial consult (Mean ± SD)	Last consult (Mean ± SD)	*p*-value
Uncorrected distance visual acuity (with corneal complications)	0.43 ± 0.51	0.25 ± 0.40	0.032
Uncorrected distance visual acuity (all patients)	0.39 ± 0.54	0.25 ± 0.44	0.046

Fifty-three (53) eyes were included in the analysis of visual acuity at baseline and at last follow-up as shown in Table 3. Two eyes which had visual acuity measurements with no LogMAR equivalent were excluded. Of the 53 eyes, the average visual acuity at initial consult of this subgroup was 20/55 (LogMAR 0.43) which was worse than the average visual acuity at initial consult of the whole study population at 20/50 (LogMAR 0.39). The visual acuity of eight or 15% of the eyes at initial consult was 20/200 or worse. The average visual acuity post-treatment, taken at the last consult, was at 20/35 (LogMAR 0.25) which was comparable to the post-treatment visual acuity of the whole study set at 20/36 (LogMAR 0.25). Post-treatment, only 4 or 7.5% of the subgroup eyes had a visual acuity of less than 20/200. The improvement in visual acuity after treatment was statistically significant with a p-value of 0.032.

DISCUSSION

Staphylococcus aureus remains to be the most common cause of ocular and periocular infections. Nearly 35% of the general public and 50-66% of healthcare workers become colonized with the organisms.[8,9] *Staphylococcus aureus* isolates obtained from eye infections has been noted to match those found in the patient's periocular surface.[10] Lipase from *Staphylococcus aureus* breaks down meibomian gland secretion into free fatty acids, cholesterols, and other lipids that accumulate on its orifices contributing to duct blockages and inflammation of the lids and lid margin through recruitment of neutrophils and other inflammatory components to the gland.[11] In this series, staphylococcal blepharitis mostly presented among young females in the second decade of life. The authors believe that this is due to the hormonal changes occurring in this reproductive age group that affect lipid metabolism of the meibomian glands, hence, predisposing them to colonization and infection of *Staphylococcus aureus*.[12] This may also explain why bilateral disease predominates and the presence of meibomitis or inflammation of the meibomian gland in 30% of these patients.

The presence of fibrin, crusts, or collarettes and lid margin erythema were the most common lid margin findings and these are consistent with published literature.[4,5] These findings suggest the colonization of the lid margin with *Staphylococcus aureus* and the formation of biofilm on the lid margin. The formation of biofilm subsequently overcomes the host defense capability by producing large amounts of toxins, which activate the caspase-1 pathway that results in the production of IL-1β, a potent inducer of inflammation.[13] This inflammatory cascade manifests as conjunctival responses, of which vascular reactions presenting as conjunctival redness and papillae were the most common findings in this study.

The inflammatory cascade subsequently spills over the lid margin into the tear film. Staphylococcal toxins pool on the inferior tear meniscus and chronically expose the inferior peripheral cornea to this cytokine-rich fluid. An immunologic reaction then ensues on the peripheral cornea presenting as marginal ulceration and infiltration, phlyctenulosis, and neovascularization. With prolonged conjunctival and corneal inflammation, pannus forms. Moreover, corneal thinning with subsequent descemetocele and perforation can also occur. Once inflammation subsides, corneal scarring with or without lipid keratopathy eventually forms.[14] For this study, 58% of the patients showed corneal complications. The most common corneal findings were corneal neovascularization, pannus formation, and phlyctenulosis which were all signs of immunologic response to a smoldering inflammation. Although around 22% had corneal lesions that are potentially blinding, severe visually disabling findings such as central corneal ulcer, descemetocele, and corneal perforation rarely occurred. Nevertheless, three patients had to undergo corneal transplantation. In a system where donor corneal tissues are not widely available, corneal complication that may necessitate corneal grafting has to be prevented as much as possible.

The average time from onset of symptoms to consult was 18 months. The large standard deviation of 25.69 months was attributed to some patients only seeking consult after 5-10 years from the onset of symptoms or they were previously treated unsuccessfully for a long time somewhere else. The latter is supported by the finding that nearly 50% of the patients had a different diagnosis hence, different management from the previous ophthalmologists. Most misdiagnosis might have arisen from missing the subtle eye lid findings of early staphylococcal blepharitis. It is common knowledge that *Staphylococcus* is a normal skin flora and cannot be eradicated entirely. Long-term treatment is necessary in order to prevent frequent recurrences that may lead to corneal complications. Based on the author's experience, a frequent reason for treatment failure even in cases that were diagnosed correctly is the lack of long-term treatment to prevent recurrences. Once diagnosed correctly and managed appropriately, treatment success is high with statistically significant improvement in visual acuity as shown by the study results.

A limitation of this study was that it was conducted in a tertiary referral national university hospital, thus the results were not generalizable to the population in the community setting. It is a fact that tertiary referral hospitals usually get cases with more serious disease. In addition, there is an inherent limitation to retrospective studies

where confounding variables are not addressed, and the data collected is limited to what is available in the charts during the conduct of the research.

CONCLUSION

This study showed that staphylococcal blepharitis seen at the Philippine General Hospital was most prevalent among young female patients, and it affected both eyes. Almost all patients manifested the typical lid margin lesions that are classic findings of this disease. Nearly 60% of the patients presented with corneal complications, and 22% had corneal lesions that are potentially blinding. Close to 50% had delay in treatment due to misdiagnosis. Timely diagnosis and appropriate treatment of staphylococcal blepharitis are essential to prevent corneal complications and preserve vision.

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Statement of Authorship

All authors contributed in the conceptualization of work, acquisition and analysis of data, drafting and revising of manuscript, and final approval of the version to be published.

Author Disclosure

All authors declared no conflicts of interest.

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