Peer-Reviewed Literature:

The Treatment of Thygeson's Superficial Punctate Keratitis

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Thygeson's superficial punctate keratitis is a rare, noninfectious, and potentially chronic form of keratitis that is a poorly understood clinical entity. Traditionally, topical corticosteroids have been the standard treatment. Because the long-term use of steroids is undesirable, however, the efficacy of alternate therapies has recently been investigated. This article evaluates the evidence supporting the use of topical cyclosporin A and PRK as treatment modalities for Thygeson's superficial punctate keratitis. The following articles were reviewed:

1. *Thygeson P. Superficial punctate keratitis.* J Am Med Assoc. *1950;144:1544-1594.*
2. *Nagra PK, Rapuano CJ, Cohen EJ, Laibson PR. Thygeson's superficial punctate keratitis: ten years' experience.* Ophthalmology. *2004;111:34-37.*
3. *Reinhard T, Roggendorf M, Fengler I, Sundmacher R. PCR for varicella zoster virus genome negative in corneal epithelial cells of patients with Thygeson's superficial punctate keratitis.* Eye. *2004;18:304-305.*
4. *Connell PP, O'Reilly J, Coughlan S, et al. The role of common ocular viral pathogens in Thygeson's superficial punctate keratitis.* Br J Ophthalmol. *2007. Available at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?CMD=search&DB=pubmed. Accessed May 14, 2007.*
5. *Reinhard T, Sundmacher R. Topical cyclosporin A in Thygeson's superficial punctate keratitis.* Graefes Arch Clin Exp Ophthalmol. *1999;237:109-112.*
6. *Fite SW, Chodosh J. Photorefractive keratectomy for myopia in the setting of Thygeson's superficial punctate keratitis.* Cornea. *2001;20:425-426.*
7. *Goldstein MH, Feistmann JA, Bhatti MT. PRK-PTK as a treatment for a patient with Thygeson's superficial punctate keratopathy.* CLAO J. *2002;28:172-173.*
8. *Seo KY, Lee JB, Jun RM, Kim EK. Recurrence of Thygeson's superficial punctate keratitis after photorefractive keratectomy.* Cornea. *2002;21:736-737.*
9. *Netto MV, Chalita MR, Krueger RR. Thygeson's superficial punctate keratitis recurrence after laser in situ keratomileusis.* Am J Ophthalmol. *2004;138:507-508.*
10. *Jabbur NS, O'Brien TP. Recurrence of keratitis after excimer laser keratectomy.* J Cataract Refract Surg. *2003;29:198-201.*

INTRODUCTION

In 1950, Phillip Thygeson gave the first report of a unique punctate keratitis that now bears his name.[1] He characterized the disease as having five key features, including (1) a chronic, bilateral punctate inflammation, (2) a long duration with sporadic remissions and exacerbations, (3) healing without significant scarring, (4) the absence of a clinical response to antibiotics, and (5) a striking symptomatic reaction to topical corticosteroids.

The most common symptoms of Thygeson's superficial punctate keratitis include photophobia, blurred vision,

and irritation.[2] Slit-lamp examination demonstrates intraepithelial, elevated, round, star- or oval-shaped, grey-white lesions, located mainly centrally, that stain fluorescein. The conjunctiva is usually not injected. There is no corneal edema or stromal infiltrates, but corneal sensation may be slightly decreased. The vast majority of cases (96%) are bilateral. The pathology typically runs a chronic, recurrent course, with attacks lasting 1 to 2 months followed by 4- to 6-week periods of remission. The median duration of active keratitis is 3.5 years with a range of 2 to 30 (or more) years. Most patients retain excellent visual acuity.

PATHOGENESIS

The etiology of Thygeson's superficial punctate keratitis is unknown. Many different theories have been proposed with the most popular suggesting either an infectious or autoimmune pathophysiology. The contention of an underlying viral pathogenesis has been largely disproven by recent studies using sensitive tools for viral detection. In one such study, epithelial cells from punctate epithelial lesions in nine patients with Thygeson's superficial punctate keratitis all tested negative for varicella zoster virus.[3] More recently, Connell et al[4] analyzed epithelial samples in eight patients with active Thygeson's superficial punctate keratitis. They tested for herpes simplex virus 1 and 2, varicella zoster virus, and adenovirus. No evidence of viral infection was documented in any case. The lack of a demonstrable infectious agent in Thygeson's superficial punctate keratitis provides further support for the competing autoimmune theory of the condition. The autoimmune theory was originally proposed based on documented associations with certain human leukocyte antigens (especially human leukocyte antigen DR3) as well as the consistently observed clinical response to topical steroids.[1]

TREATMENT

The initial treatment for Thygeson's superficial punctate keratitis consists of the use of artificial tears for lubrication. If patients do not experience relief, low-potency topical steroids such as fluoromethalone usually provide an adequate clinical response. Clinicians have placed therapeutic bandage contact lenses in certain cases, normally in an effort to avoid the long-term complications from topical steroids in patients with chronic disease. More recent steroid-sparing treatment modalities include the use of topical cyclosporin A 2% as well as PRK. Unfortunately, the evidence supporting these treatments is wanting.

Currently, there is one randomized controlled study that evaluated the efficacy of cyclosporin A in Thygeson's superficial punctate keratitis. Reinhard and Sundmacher[5] investigated 2% topical cyclosporin A in 52 eyes of 28 patients (40 adults and 12 children) at a dose of three drops daily for 1 month, followed by a 5-month tapering such that each patient was off all drops at 6 months. The investigators found that 72% of the adults responded with complete suppression of epithelial opacities during treatment, with 40% remaining in remission while off the cyclosporin A drops, at a median follow-up of 17 months. The children apparently demonstrated a lower response rate, with 40% responding completely during the administration of cyclosporin A. The difference between subject groups may be related to compliance, because cyclosporin A drops are known to be quite irritating.

The evidence for the use of PRK as a therapeutic modality for Thygeson's superficial punctate keratitis is scant. In 2001, Fite and Chodosh[6] reported the first case of PRK to treat active the condition. They found that, at 17 months post-PRK, lesions were only present peripheral to the ablated zone. The investigators proposed that PRK may decrease the risk of recurrent Thygeson's superficial punctate keratitis by reducing the inflammatory signals present in the anterior stroma. Goldstein et al[7] reported a similar case. They described an 8-month remission after treating active Thygeson's superficial punctate keratitis with PRK. Conversely, there is one reported case of recurrent Thygeson's superficial punctate keratitis after PRK.[8]

In contrast, LASIK may increase the risk of recurrent Thygeson's superficial punctate keratitis. In two case reports, the condition returned within treated zones after LASIK[9,10] just as it did after LASEK.[8] All of the aforementioned case reports' evidence suggests that anterior stromal ablation may be effective in treating Thygeson's superficial punctate keratitis, but there is insufficient evidence to recommend therapy routinely.

THE BOTTOM LINE

Thygeson's superficial punctate keratitis is a rare and potentially chronic epithelial keratitis, and its pathogenesis is poorly understood. Although topical steroids remain the mainstay of treatment, cyclosporin A can be considered as an alternative treatment, particularly in patients with a chronic keratitis and those for whom the use of corticosteroids is undesirable. Further studies are needed to clarify the role PRK may have in the management of this condition. ■

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