Transient Corneal Microcysts Associated With Interferon Therapy

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Purpose: To report transient corneal epithelial microcysts associated with interferon therapy.

Methods: Case report.

Results: Transient corneal epithelial microcysts appeared bilaterally with the onset of therapy with pegylated interferon and ribavirin for the treatment of hepatitis C. These microcysts resolved completely after discontinuation of the pegylated interferon with ribavirin therapy.

Conclusions: Pegylated interferon therapy was associated with transient corneal epithelial microcysts in our patient.

Key Words: cornea, microcysts, interferon, intercellular adhesion molecule-1

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Interferons constitute a class of cytokines and have immunomodulating actions. Intercellular adhesion molecule-1 (ICAM-1) is a transmembrane glycoprotein, functioning as an adhesion molecule in a variety of biologic situations.[1] Furthermore, ICAM-1 expression in human corneal epithelial cell culture is thought to play an important role in cell migration.[2] Interferon has been shown to increase expression of ICAM-1 in cultured human corneal epithelial cells.[3] Ribavirin is a synthetic guanosine analogue, which is active against RNA and DNA viruses.[4] Interferon and ribavirin are effective in the systemic treatment of hepatitis C.[4]

Corneal microcysts are often seen in Meesmann and map-dot-fingerprint dystrophies.[5] In addition, microcysts can be seen in conditions involving corneal trauma, infection, and edema.[5] The pathogenesis of microcysts in epithelial dystrophies involves the trapping and abnormal anterior migration of cellular and basement membrane-like debris within the epithelium.[5]

To the best of our knowledge, there is no reported association between interferon administration, ribavirin administration, or hepatitis C with visually observable changes in the corneal epithelium. A MEDLINE search attempting to link interferon, ribavirin, or hepatitis with corneal microcysts failed to document any such reports. We now report a case in which we believe interferon mediated upregulation in ICAM-1 caused increased intercellular adhesion and altered cell migration dynamics, ultimately leading to transient corneal microcysts.

CASE REPORT

Our patient is a 24-year-old woman who presented with a 5-month history of "blurred vision, redness, and pain" OU. She also reported fluctuating vision associated with changing refractions. She was diagnosed with and treated for dry eye syndrome and corneal microcysts by the referring ophthalmologist 4 weeks before presentation. Previous routine optometric care revealed no ocular history. Her medical history was significant for hepatitis C, hypothyroidism, iron deficiency, and depression. Her medications included pegylated interferon and ribavirin (starting 8 months before presentation), venlafaxine, levothyroxine, iron, and ethinyl estradiol/norgestimate. Her ocular medications were artificial tears OU 5 times per day and hypertonic saline ointment (5%) OU QHS. She reported an allergy to penicillin. Her family history was significant for hypertension. She neither drinks nor smokes.

On presentation at the Penn State Milton Hershey Medical Center Cornea Service, she exhibited uncorrected vision of 20/40 OD and 20/200 OS. Pinhole testing revealed 20/20 OD and 20/30 OS. Her anterior examination was significant for meibomian gland dysfunction. Her bulbar conjunctiva was white and quiet OU. Her corneas revealed diffuse microcysts and superficial punctate epitheliopathy OU (Fig. 1). The microcysts appeared throughout the epithelium, from the basal layers to the surface. Her anterior chambers were deep and quiet. Her pupil examination was normal. Her intraocular pressures were normal OU. Schirmer testing with anesthesia demonstrated 11 mm OD and 15 mm OS. The remainder of her ophthalmic examination was within normal limits.

She was treated with eyelid hygiene daily, nonpreserved artificial tears OU every 1 hour while awake and GenTeal Gel OU QHS. One month after presentation to us, she underwent silicone punctal plug insertion of the lower puncta OU, with some symptomatic relief. However, there were no objective changes in the patient's corneal superficial punctate epitheliopathy or microcystic findings, through her third month of follow-up. At no time did she have symptoms or demonstrate signs consistent with corneal erosion.

During her fifth month of follow-up with us, and within 7 weeks of discontinuation of her interferon-ribavirin therapy, the patient returned for her scheduled care. There was no change in her medical status or review of systems. Her other systemic medications were unchanged. Her symptoms had resolved completely at that time, and she therefore self-discontinued her ocular lubrication. Similarly, her corneal microcysts had completely disappeared on examination 7 weeks after discontinuation of her interferon-ribavirin therapy.

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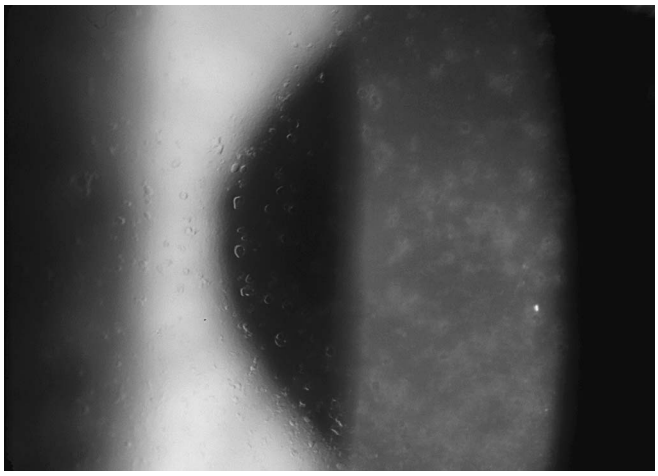

FIGURE 1. Corneal epithelial microcysts.

DISCUSSION

Our patient began with healthy corneas and developed transient microcysts with the start of interferon-ribavirin therapy. These microcysts resolved completely with discontinuation of the interferon-ribavirin therapy. This case appears to demonstrate an association between interferon therapy and corneal microcysts. Interferon is known to be secreted in human tears.[6] We postulate that increased levels of systemic interferon give rise to increased interferon levels in tears. A proposed mechanism to possibly explain these observations could be in the aforementioned interferon-mediated upregulation of corneal epithelial ICAM-1. The resulting increase in intercellular adhesion and altered epithelial cell migration dynamics could, in turn, change the normal epithelial anterior movement process and give rise to the microcysts. Withdrawal of the interferon would then have allowed normalized epithelial anterior migration and adhesion, with the resulting microcyst resolution that the patient demonstrated.

We believe that it was the interferon therapy that was associated with the transient corneal microcysts. The ribavirin is unlikely to be the cause of the microcystic changes. Human respiratory epithelium infected with respiratory syncytial virus, with or without ribavirin exposure, resulted in similar levels of ICAM-1 expression in human epithelial cells.[7] Hence, we cannot hypothesize a mechanism whereby ribavirin could induce microcyst formation. We also believe that the disease course of the hepatitis is unlikely to be the cause of the microcystic findings. One would think that, given the prevalence of hepatitis during modern ophthalmic history, an association between hepatitis and corneal microcysts would have been noticed, even if rare. Confirmation and further study of these observations will be valuable.

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