Contact Lens Update
CLINICAL INSIGHTS BASED IN CURRENT RESEARCH

A case of Pain in the Eyes

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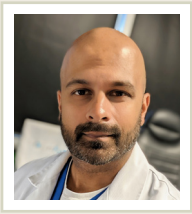

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Background

The presence of confounding and disproportionate symptoms in the dry eye population is a feature of dry eye disease (DED) that can confuse the clinical picture. As detailed in the TFOS DEWS II report, pain and dysesthesia associated with corneal neuropathic pain (CNP), are specific symptoms that fit into a distinct category, lying adjacent to the DED population.[1] The principle clinical feature of CNP is the presence of severe pain symptoms and the absence or minimal presence of obvious biomarkers of ocular surface disease.[2]

Treatment of CNP is nuanced and standard clinical guidelines are not yet established. The understanding that its symptoms are triggered by both peripheral and central neurosensory mechanisms suggests that management of suboptimal tear film homeostasis should be prioritized. Pain also requires parallel consideration in addition to tear film care, which is best achieved in collaborative care with pain specialists, as is exemplified in the following case.

History

A 57-year-old female patient presented to the clinic with a 10-year history of having bilateral uncomplicated LASIK. Her chief complaint was chronic ‘dry eye-like pain’ which was diffuse, foreign body sensation with persistent extreme photosensitivity, exacerbated by screen use. Onset was reported within six months of her post-operative period however, her symptoms increased episodically over the last decade. She was using various OTC ophthalmic lubricants which provided little relief and at present, was using Hylo (1% hyaluronate non-preserved) lubricants (Candorvision, Montreal, QC, Canada) q1-2h OU. She noted pre-operative mild dry eye symptoms, more so while using her daily disposable contact lenses. Her medical systemic history included breast cancer (remission) and generalized anxiety and depression which was not currently being medically treated. She noted that during an active treatment phase of her breast cancer, her symptoms had improved while she was taking Tamoxifen and Naltrexone. Her symptom severity gradually increased after the active treatment phase. She had been prescribed Restasis 0.05% cyclosporine ophthalmic emulsion, (Allergan, Irvine, CA, USA) bid OU the year prior, however found it intolerable and discontinued after 1 month of use.

Entrance testing results showed uncorrected visual acuities OD 20/20 OS 20/20 with corrected 0.37M near VA. Pupils were equal and reactive with no APD noted. EOMS were full and binocularity was unremarkable.

Her validated Dry Eye Questionnaire (DEQ – 5) symptom score was 18/22 and Standardized Patient Evaluation of Eye Dryness (SPEED) score was 25/28. Anterior segments were deep and quiet OU. Corneas showed a superiorly hinged LASIK flap in both the OD and OS. Tear break-up time (TBUT) was 5s and 6s OD and OS respectively. Tear osmolarity was 289 and 300 mOSm/L OD and OS and NaFl staining was negative for corneal and conjunctival epitheliopathy OU. Matrix-metalloproteinase-9 (MMP-9 – InflammaDry, Quidel, San Diego, CA,

USA) was faintly positive in both eyes. Lid margins showed mild non-obvious meibomian gland dysfunction and no blepharitis. Meibomian gland yielding liquid score (MGYLS) was 7 and 8 OD/OS respectively. Schirmer volume without anaesthetic was 8mm OU.

Further problem specific testing which included meibography and tear film interferometry confirmed normal meibomian gland morphology OD and OS with mild truncation, or degree 1, on the Pult 5-point scale, and a stable lipid layer OU.[3] Topical anesthesia was applied to both eyes (0.5% alcaine – Alcon, Fort Worth, TX, USA) to assess the remaining pain state. The patient reported a dampening of foreign body symptoms by 50%, however her photoallodynia symptoms (photosensitivity) were unaltered. A Cochet-Bonnet corneal aesthesiometer was not available.

The absence of consistent clinical findings classically associated with the severity of her symptoms was apparent. Evaporative rate (TBUT: 5s OD, 6s OS) was moderate and osmolarity was below the 308 mOsm/L mark although the inter-eye difference was 9 mOsm/L. The persistence of her neuropathic symptoms after anesthesia confirmed the source of the pain was at least, in part, posterior to the cornea.

Diagnosis

Based on all the available findings, her primary diagnosis was CNP. Like most cases of CNP, there were likely both peripheral and centralized components. Although confocal microscopy was not available to confirm corneal axonopathy, the reported history of photoallodynia, LASIK, as well as anxiety and depression, the clinical picture was consistent with a neurosensory etiology. She was also given a secondary diagnosis of mild evaporative dry eye (EDE) based on reduced TBUT and non-obvious MGD.

Treatment Plan

The treatment plan targeted all potential peripheral sources of sensitization in addition to higher order pain management through collaborative care with a medical pain clinic.

1. **Evaporative Dry Eye – Manage the stress**: The patient was started on warm compresses using a Bruder thermal mask (Bruder, Alpharetta GA, USA) and iDrop MGD (I-MED Pharma, Montreal QC, Canada) to manage her evaporative dry eye The rheological characteristics of iDrop MGD would allow for increased residence time and were compatible with the dynamics of a blink.[4]
2. **Corneal Neuropathic Pain – Manage the pain**: To address her peripheral sensitization, she was prescribed autologous serum eye drops (ASED) 50% qid OU which was obtained at a local compounding pharmacy. Given the patients previous intolerance to Restasis and the active MMP-9 marker of inflammation, ASED was most appropriate. Additionally, ASED has demonstrated efficacy at improving sub-basal nerve plexus morphology in CNP populations, suggesting a possible effect (see Figure 1).[5-7]

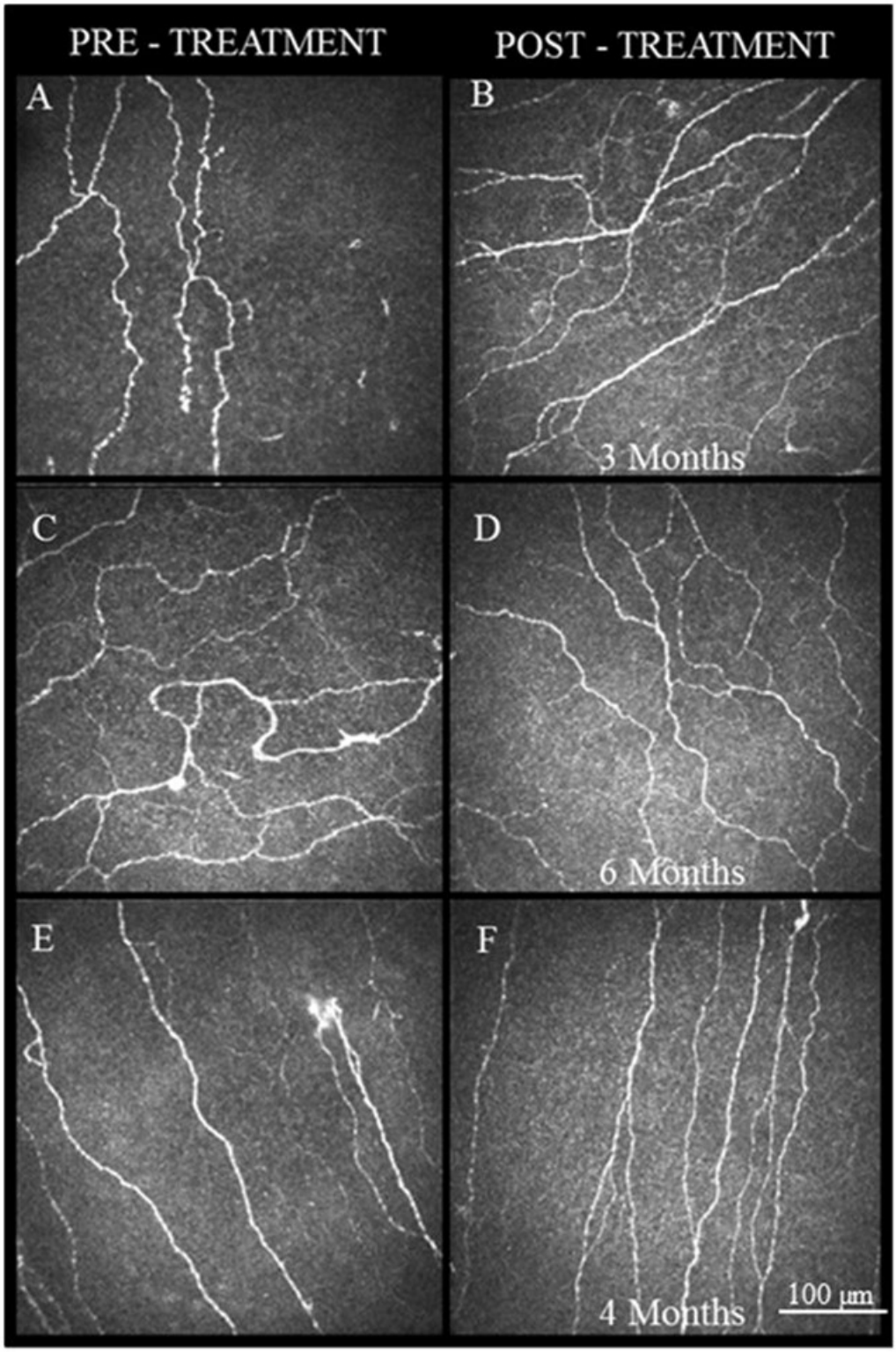

Figure 1. Confocal microscopy at the level of the corneal subbasal nerve plexus demonstrates the improvement in nerve density and morphology following treatment with autologous serum tears. A, C, E. Images at baseline showing increased reflectivity and tortuosity of nerves with presence of beading and neuromas. B, D, F images post-treatment corresponding to same patients as A, C, E.[7]

Her pain management provider had considered Gabapentin (Neurontin, Pfizer, New York, NY, USA), an anticonvulsive oral medicine use to treat neuropathic pain, however based on her history of taking Naltrexone during her breast cancer therapy, her physician agreed to start her on low dose Naltrexone (LDN) starting at 3.0 mg/day which was increased to 4.5mg/day for 30 days.[8] Naltrexone's proposed mechanism of action is temporary opioid receptor blocking, which yields an endogenous endorphin release, and binding to toll-like receptor 4, reducing inflammation of neural tissue.[8]

Follow-up

Her follow-up visit three months later revealed a significant reduction in DEQ-5 to 7/22, and improvement in TBUT globally. Her pain specialist had maintained her LDN at 3.0mg/day and she was to continue ASED 50% bid for the next six-month period. Topical palliative therapy was maintained in addition to her thermal eyelid mask at-home care.

Discussion

Before DEWS II included CNP as a distinct subcategory, there have been limited options available for its treatment, in part due to the low rate of diagnosis, resulting in a lack of widespread research into its medical management. [1]

A multimodal approach using topical anti-inflammatories and ocular surface lubricants has been used as first line therapy with reasonable efficacy in respect to peripheral pain. Off-label therapies that target nerve and epithelial repair include commercially available amniotic tissue as well as human autologous serum eye drops, amniotic fluids, and platelet-rich plasma (PRP) that are sourced through compounding pharmacies.[8, 9] These are typically reserved for more severe forms of DED. However, it is also in these disease states that neuropathic damage occurs in tandem.

Centralized pain is quite difficult to manage as there is a paucity of validated evidence with respect to treatment. Rosenthal has had some success with oral anticonvulsants, tricyclic antidepressants, and serotonin reuptake inhibitors.[10] Gabapentin, typically starting in low doses (100-300mg po qd), is gradually increased to achieve optimal effect. The pain blocking mechanism is through inhibition of the tonic phase of nociception.11 Non-invasive use of transcutaneous supraorbital nerve stimulation has also demonstrated efficacy at reducing pain symptoms by 27% and without associated adverse events, through inhibition of ascending pain signals using neuromodulation.[13]

This case demonstrates the complexity and nuanced nature of both diagnosing and treating CNP. This patient had a positive response to the above therapy, which resulted in a reduction in symptoms by 60% as well as a subjective reported improvement in quality of life, anxiety, and a return to work.

Those affected by CNP are a part of a largely underdiagnosed population with symptoms that can be debilitating and agitating to their mental health.[10] In this author's experience, many of these cases can spiral into depression and anxiety. As primary eye care providers to this population, it is important to recognize the clinical features as well as become familiar with current treatment approaches that are both within our scope and collaborative reach.

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