

Neuropathic Corneal Pain in Dry Eye Disease

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Abstract

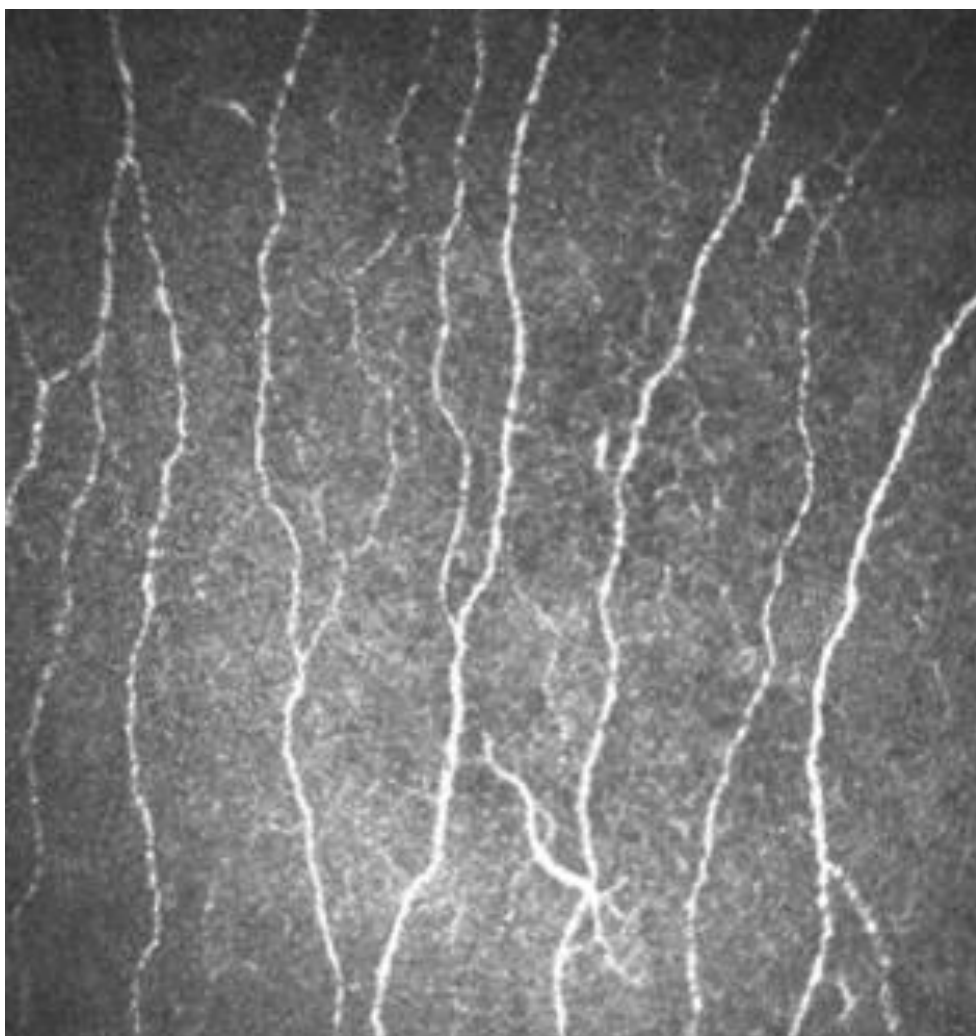
Case report of a 27 year old female with presumed neuropathic corneal pain following LASIK. Relevant background as well as evaluation and management options for this condition will be reviewed.

Introduction

Dry eye disease is both a multifactorial condition and a complicated entity. It has been established that corneal nerve dysfunction plays a fairly central role, and that neurosensory abnormalities are in part responsible for the dichotomy that is often found between signs and symptoms of dry eye. In addition, it is a chronic and progressive condition that can share many of the same features as chronic neuropathic pain. As corneal nerve axons are damaged, nociceptors may be up-regulated and become hypersensitive to what otherwise would be non-painful stimuli. In addition, this increased neuronal excitability (hyperalgesia) persists even when the tissue is apparently healed and the initially damaging stimulus has been removed. Thus, patients with neuropathic corneal pain tend to experience non-specific pain sensations (such as light sensitivity, burning, aching, and eye pressure) with no to minimal signs found on dry eye testing and slit lamp examination.

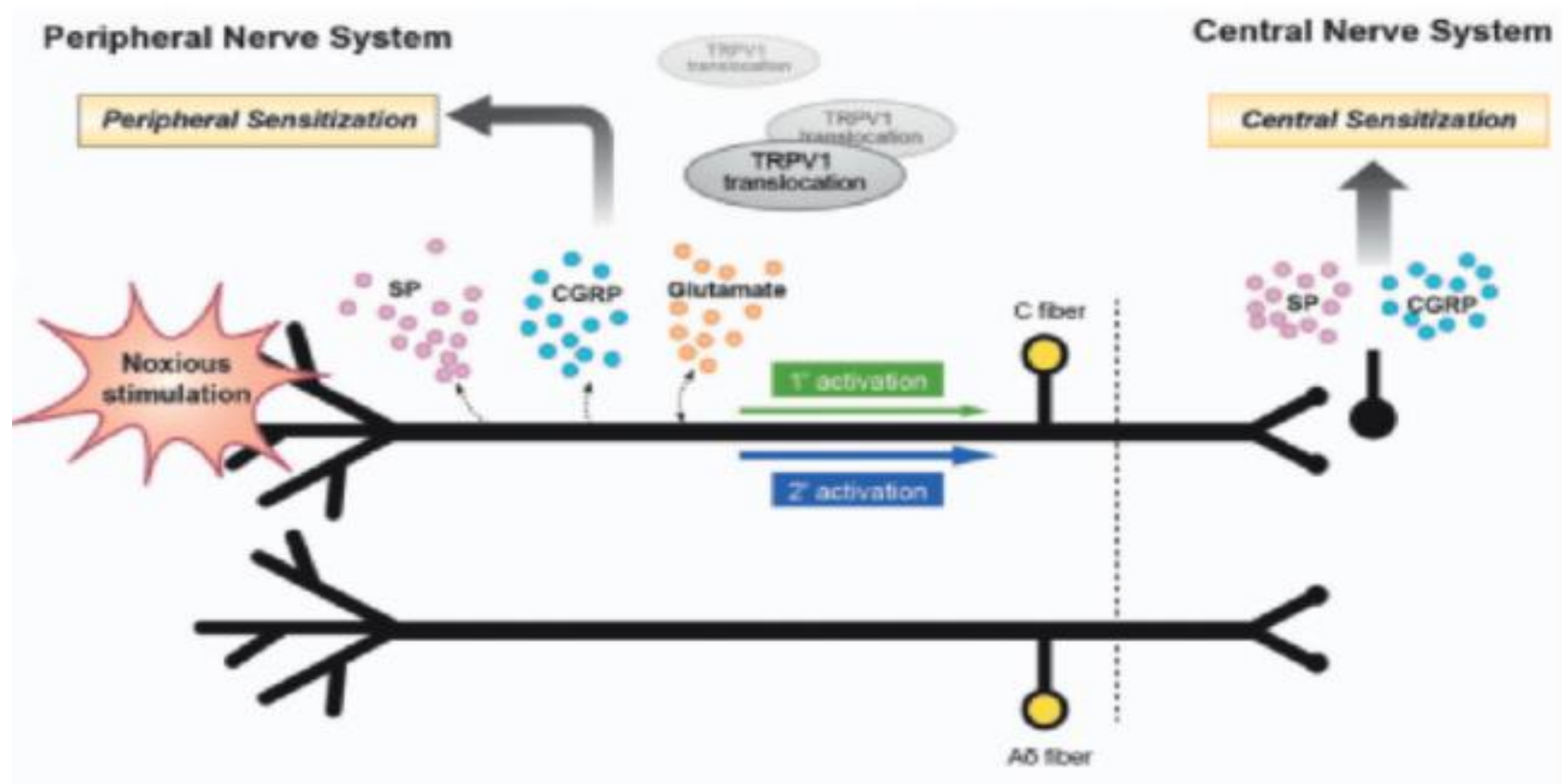
Neuropathic Pain

Definition: “Pain initiated or caused by a primary lesion or dysfunction of the nervous system.” As the most richly innervated system in the body, it is no surprise that it can also occur in the cornea. It may have either a peripheral (local damage) or systemic origin.



Pathophysiology

Tissue damage and/or chronic inflammation of the ocular surface can result in peripheral corneal axonal injury and stimulate additional release of inflammatory mediators (the vicious cycle). This has the potential to result in increased sensitivity of peripheral nerves and intensify peripheral pain signals. Eventually, this can result in central sensitization as well, with central neurons producing heightened pain awareness as well. If this occurs, the hallmark of central sensitization is pain disconnected from ongoing peripheral signs.



Case Description

A 27 year old female presented to our clinic for a dry eye evaluation concerned with an intense and debilitating burning sensation she was feeling in both eyes.

- Ocular history:** Cataract surgery as an infant for congenital cataracts, mild optic atrophy, and monovision LASIK in March of 2021.
- Medical history:** heritable mitochondrial disorder associated with hearing loss, optic atrophy, and congenital cataracts
- Systemic medications:** none
- Current and previous (ineffective) dry eye treatments:**
 - LipiFlow, Xiidra, Eysuvis, gentel tears at night, Refresh Mega-Three artificial tears, warm compresses, hypochlorous acid lid scrubs, lid seal mask, and omega-3 supplements.
- Initial examination:** minimal to no dry eye signs found on corneal topography, tear film analysis, meibography, InflammDry, meibomian gland expression evaluation, sodium fluorescein staining, and lissamine green staining
- Plan:** autologous serum four times per day and cryopreserved amniotic membranes
- Most recent update (after 4 months of serum tears):** still no dry eye signs, but the patient reports slightly increased eye comfort for the first time in 3 months.

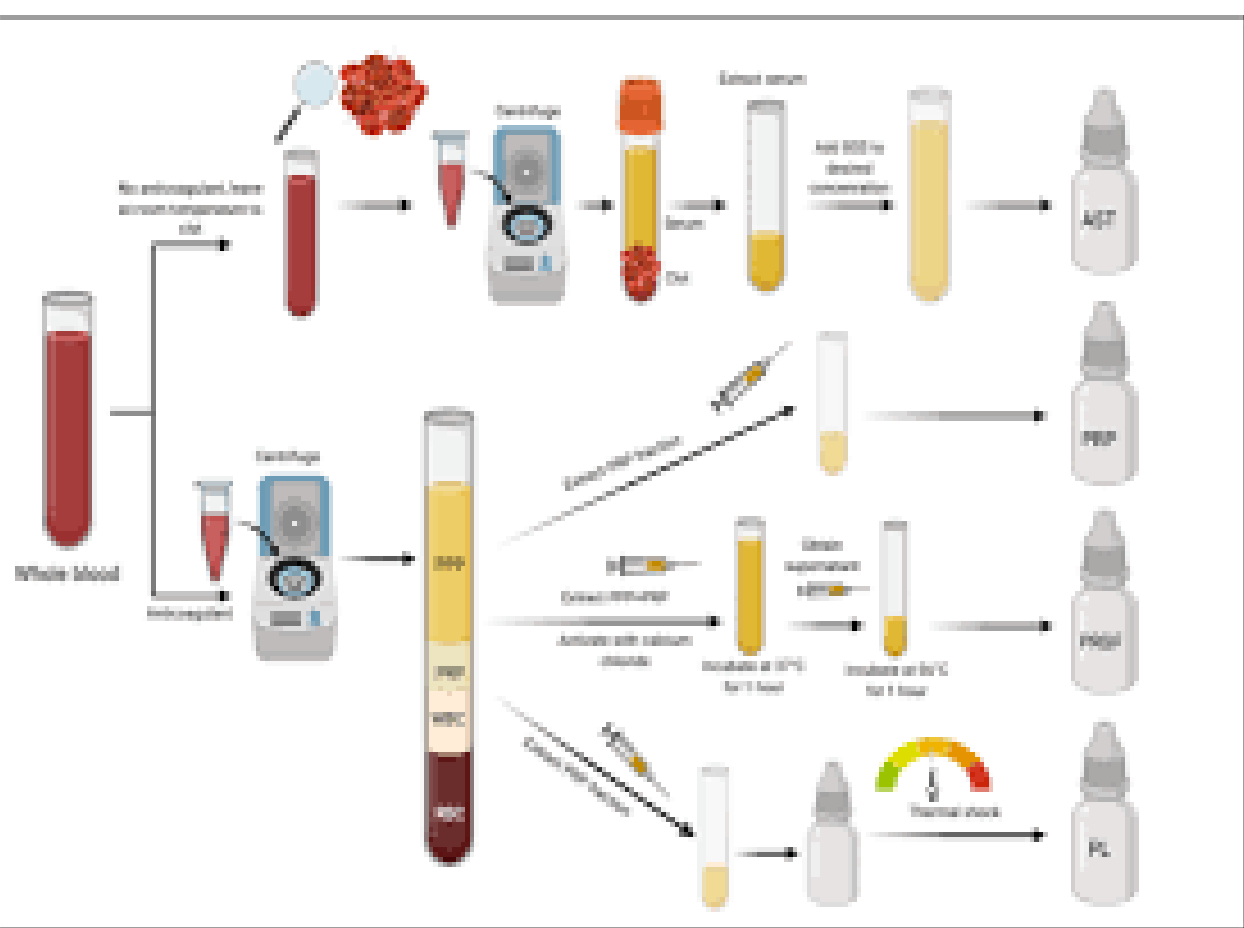
Proparacaine Challenge Test

Purpose: to distinguish between central and peripheral neuropathic pain
Principle: topical proparacaine will abolish peripheral pain, but will have no effect on pain from central sensitization.



Recommended Therapies

- Neuro-Regenerative:** heal nerves
 - Autologous serum tears
 - Cryopreserved amniotic membranes
 - NGF? (Oxervate)
- Anti-Inflammatory:** reduce damage
 - Steroids
 - Immunomodulators
- Manage co-morbidities**
 - Thermal pulsation, lid scrubs, moisture chamber goggles, IPL, TTO, BCL, sclerals, etc.
- Manage central sensitization**
 - Systemic medication required
 - TCAs, carbamazepine, low dose naltrexone, tramadol, gabapentin, SNRIs, sodium channel blockers, etc.
- Lifestyle changes**
 - Cardio exercise (can decrease inflammation and increase neurotrophic factors in the CNS)
 - Omega-3 supplementation
 - Trial gluten free diet
 - Meditation and mindfulness
- Alternative medicine**
 - Transcranial magnetic stimulation (TMS)
 - Acupuncture



Conclusions

A mismatch between signs and symptoms is frequent when dealing with dry eye disease, complicated by the neurosensory abnormalities that are at play in the cornea. Patients with severe symptoms but no signs have many things in common with patients with chronic neuropathic pain. While nerve damage is a prerequisite for this condition and true diagnosis is made by impression cytology or in vivo confocal microscopy, it is not uncommonly found in ocular surface disease, after herpetic infections, or post-refractive surgery.

Treatment typically is complex, often multi-step, and frequently refractory. As corneal nerve dysfunction and damage is contributing to the condition (in conjunction with likely psychosomatic components), neuro-regenerative therapies such as autologous serum tears and cryopreserved amniotic membranes are a good choice to both rehabilitate the corneal nerves and bring symptomatic relief to the patient. In addition, systemic and/or alternative medicine may need to be considered in extreme cases, particularly those in which central sensitization is present.

Limitations

It is difficult to quantify the extent of corneal nerve regeneration without being able to objectively measure it with something like confocal microscopy. In this case, we have nothing to go on besides subjective improvement, which is notoriously unreliable in the setting of dry eye disease. In addition, improvement in these cases is slow, and can be over the course of a few years; we have only been managing this patient for a few months.

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References available upon request.