NEUROPATHIC EYE PAIN

How to diagnose this condition and discuss emerging therapies with patients.

BY JACOB LANG, OD, FAAO

Neuropathic eye pain (NEP) is increasingly recognized as a distinct entity in ocular surface disease, often coexisting with or masquerading as dry eye disease (DED). The Tear Film & Ocular Surface Society Dry Eye Workshop II report highlights that NEP arises from dysfunction in the peripheral and/or central nervous system, leading to disproportionate pain symptoms despite minimal clinical signs.[1] Patients often report burning, stabbing, or electric shock-like pain, along with photophobia, hyperalgesia, and allodynia.[1,2] Pain may be triggered by everyday stimuli, such as wind, light touch, or blinking.[1,2]

DIAGNOSIS

A key feature of NEP is a mismatch between symptoms and clinical signs. A patient with severe pain with minimal corneal staining or tear film dysfunction should raise suspicion (ie, "pain without stain").[1,2] The tetracaine challenge test may help differentiate NEP from classic DED, as topical anesthetic should provide relief for patients with DED but often fails to alleviate or even decrease neuropathic pain.[2] Confocal microscopy may reveal corneal nerve abnormalities (Figure), and corneal esthesiometry can assess sensory dysfunction.[2] Symptom surveys such as the Standardized Patient Evaluation of Eye Dryness, the Ocular Surface Disease Index, and the Dry Eye Questionnaire can be used to quantify pain levels; however, the Ocular Pain Assessment Survey is specifically designed to quantify ocular pain.[1,2]

Clinicians should also heighten their suspicion of NEP when significant clinical improvements are noted without a corresponding improvement in symptoms. In my clinical experience, I have seen patients with NEP have symptoms worsen with improved corneal health. I suspect this might be because of increased nerve function (essentially, increasing the ability for dysfunctional nerves to become even more dysfunctional).

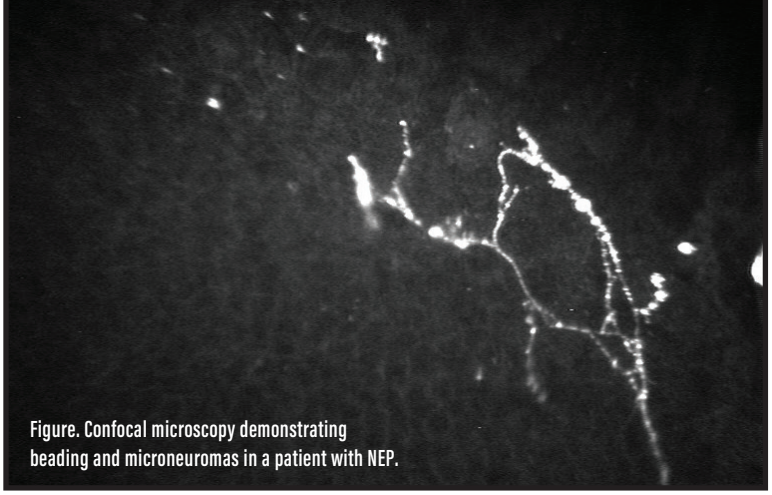

Figure. Confocal microscopy demonstrating beading and microneuromas in a patient with NEP.

EMERGING THERAPIES

Low-dose naltrexone, an opioid receptor antagonist with antiinflammatory and neuroprotective properties, has shown promise in reducing NEP symptoms.[3] Topical agents such as TRPV1 antagonists and autologous serum tears, which aim to restore corneal nerve homeostasis, have also been shown to restore or improve nerve function.[2] A novel G-protein–coupled receptor agonist, OK-101 (Okyo Pharma), is under development for the reduction of inflammation and NEP. A phase 2 clinical trial is underway to evaluate its efficacy in treating patients with neuropathic corneal pain.[4] Systemic options such as gabapentinoids, serotonin-norepinephrine reuptake inhibitors, and botulinum toxin injections, as well as neuromodulation techniques such as transcranial magnetic stimulation, are also under investigation to treat NEP.[2]

OUTLOOK AND PATIENT EDUCATION

Treating NEP is challenging due to its variable response to therapies. Many patients experience frustration after multiple failed treatments, and providers may experience fatigue and skepticism after multiple failed treatments. Moreover, NEP often requires systemic and neuromodulatory approaches, which fall outside traditional ocular surface management.

Setting realistic expectations with patients is critical. Providers should emphasize that NEP is a nerve-based pain condition, rather than one resulting from tear deficiency. Using analogies, such as comparing NEP with phantom limb pain, can help explain the disconnect between symptoms and clinical findings. Encouraging mental health support, such as cognitive behavioral therapy and/or pain management counseling, can also help patients cope with NEP. ■

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