How to Heal When You Can't Feel – Neurotrophic Keratitis Update

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Course Description

This one-hour course will review the etiology and pathophysiology of neurotrophic keratitis. The presentation will review common symptoms, signs, differentials and management options for neurotrophic keratitis. Emphasis will be made on in-office diagnostic testing and the latest management strategies. Case examples will be presented to enhance the learning experience.

Learning Objectives

1. Review the etiology and pathophysiology of neurotrophic keratitis
2. Learn diagnostic testing for neurotrophic keratitis including how to measure corneal sensitivity
3. Understand management options based on disease severity
4. Understand when to intervene with different therapies including co-management
5. Review potential complications of neurotrophic keratitis

Outline

1. Neurotrophic keratitis (NK) definition
    a. Degenerative disease
    b. Corneal sensitivity reduction
    c. Spontaneous epithelium breakdown
    d. Impaired corneal healing
    e. Development of corneal ulceration, melting, and perforation
2. Etiology of NK
    a. Herpetic eye disease (zoster and simplex) diabetes, ophthalmic procedures, neurosurgical procedures, dry eye disease, ocular surface injury / inflammation, topical drug toxicity (such as BAK), topical anesthetic abuse, stroke, systemic medications, chemical and physical burns, contact lens abuse, topical drug toxicity, irradiation to eye or adnexa
    b. Ocular surgery
        i. Both laser in situ keratomileusis (LASIK) and photorefractive keratectomy (PRK) have been linked to NK
        ii. Incidence of transient nerve damage significantly higher in LASIK than in PRK.
        iii. Corneal transplantation surgery may cause corneal denervation
            1. Penetrating keratoplasty (PK)
            2. Deep anterior lamellar keratoplasty (DALK)
        iv. Reduction of corneal sensation was also observed following collagen crosslinking in keratoconus.

3. Pathophysiology of NK
    a. Cornea histological alterations
        i. Thinning/disruption of the epithelial layer
        ii. Cytoplasmic swelling of epithelial cells
        iii. Loss of microvilli
        iv. Disorganization of Bowman's membrane
        v. Stromal melting/scarring
        vi. Corneal neovascularization.
4. Trigeminal nerve and NK
    a. Gives corneal sensation
    b. Supplies trophic factors
    c. Plays key role to maintain the anatomical integrity and function of the ocular surface
    d. Impairment of corneal trigeminal innervation causes morphological and metabolic epithelial disturbances and leads to development of recurrent or persistent epithelial defects.
    e. Common mechanism of trigeminal damage in several causes of NK
        i. Herpetic keratitis, diabetes, and ophthalmic and neurosurgical procedures
    f. Conjunctival changes
        i. Reduction in goblet cell density
        ii. Cell-surface microplicae
5. Diagnosis of NK
    a. Clinical ocular and systemic history
    b. Complete eye examination
    c. Assessment of corneal sensitivity
        i. Cotton swab
        ii. Corneal aesthesiometer
            1. Cochet-Bonnet contact aesthesiometer
            2. CRCERT-Belmonte non-contact aesthesiometer)
        iii. Dental floss
        iv. Noted that eye drops should be applied after testing corneal sensitivity
    d. Corneal staining
        i. Sodium fluorescein, lissamine green or rose Bengal
    e. Schirmer test
    f. Corneal scrapings and cultures if need to rule out bacterial, viral, fungal or parasitic infections. These may be associated with reduced corneal sensitivity
    g. Diagnosis may be challenging since patients do not commonly complain of ocular surface symptoms since corneal sensory innervation is impaired in NK
    h. In vivo confocal microscopy
    i. Mackie classification - classified according to severity of corneal damage
        i. Stage I - epithelial alterations
            1. Hyperplasia and/or irregularity of the epithelium
            2. Punctate keratopathy
            3. Corneal edema
            4. Neovascularization
            5. Stromal scarring
        ii. Stage II - a recurrent or persistent epithelial defect (PED)

1. Most common superior half of the cornea
2. Typically, oval in shape
3. Margins are smooth and rolled due to impaired epithelial healing

iii. Stage III – corneal ulcer
1. Stromal involvement
2. Melting
3. Perforation

6. Management of NK
   a. Goal is to promote corneal healing and avoid complications
   b. Preservative free eye drops, gels and ointments
   c. Treat ocular surface diseases (dry eye, blepharitis, exposure keratitis, limbal stem cell deficiency)
   d. Avoid topical NSAIDs
      i. No benefit
      ii. Can further decrease corneal sensitivity
   e. Stage based approach
      i. Stage 1 - Punctate keratopathy
         1. Goal - Avoid epithelial breakdown
         2. Treatment
            a. Frequent use of preservative free artificial tears
            b. Lubricant ointment
            c. Autologous serum
            d. Therapeutic soft contact lens
      ii. Stage II – PED
         1. Goal - Promote PED healing and prevent the development of a corneal ulcer
         2. Treatment includes all of the above for stage I
            a. Patching/tape tarsorrhaphy
            b. Amniotic membrane grafting
            c. Tarsorrhaphy, gold weight, or botulinum induced ptosis
            d. Topical Nerve Growth Factor
            e. Scleral lens
            f. Antibiotic eye drops to prevent bacterial infections
            g. Caution with topical corticosteroids. May could induce stromal melting.
      iii. Stage III – Corneal ulcer
         1. Treatment includes all of the above for stages I and II
            a. If stromal melt, N-acetylcysteine, oral tetracycline and medroxyprogesterone
      iv. Surgical options
         1. Corneal neurotization
            a. transfers the supraorbital or supratrochlear nerve to either directly or indirectly with a nerve graft to the neurotrophic cornea
         2. Amniotic membrane transplantation
         3. Conjunctival flap

7. NK Complications

    a. Secondary infection
        i. Microbial keratitis
    b. Poor wound healing
    c. Recurrence
    d. Corneal scarring
        i. Loss of vision
    e. Delayed treatment
        i. Lack of patient symptoms
8. NK clinical cases
    a. Herpetic eye disease
        i. Management amniotic membrane
    b. PED
        i. Management scleral lens
    c. Topical anesthetic abuse
        i. Management topical nerve growth factor and contact lens
    d. Descemetocele
        i. Management: Failed: temporal tarsorrhaphy, amniotic membrane, gold weight. Success: Scleral lens 12 x 2, followed by scleral daily wear, tape tarsorrhaphy, hyperosmotic NaCl ointment

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