Case Record 12

Toxic Epitheliopathy

Symptoms misinterpreted by patient as Dry Eye and mismanaged as such.

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Introduction – poor clinical nomenclature

The presentation for this patient was one of toxic epitheliopathy due to long-term excessive use of preserved artificial tears; the symptoms being misinterpreted by the patient as representing dry eye. Poor nomenclature, vague clinical use of the term ‘dry eye’ coupled with poor patient education were potential contributors to the presentation. It is therefore impossible to discuss this case of toxic epitheliopathy without a consideration of the vague nomenclature associated with ‘Dry Eye’ conditions.

The term ‘dry eye’ is misleading for patients and can lead to mismanagement and exacerbation of the problem. Albietz (2001) suggests that a dry eye results from any anomaly in a gland associated with tear production or an anomaly in lid and/or blinking function in which the quantity and/or quality of the tear film is adversely affected and there is an inability to maintain a healthy ocular surface. Inflammatory and sensory feedback loops also modulate the ocular responses (Heath 2007, Mann 2007). These complex and multifactorial processes lead to two functional outcomes : tear deficient dry eye and evaporative dry eye (O’Toole 2005).
Albietz (2001) reports that a quarter of patients presenting for routine eye examinations describe symptoms of ‘dry eye’, however, only 3 % of patients have a tear deficient dry eye. The same author reports that 40% of the general population show signs of meibomian gland dysfunction.

The term ‘dry eye’ therefore does not reflect this disparity in prevalence of aetiologies resulting in what is clinically described as ‘Dry Eye’. Albietz (2001) suggests that ‘tear film and ocular surface disorders’ is a more suitable term; within our clinic the simpler term of ‘reduced tear quality’ seems to better reflect the functional impact for the patient.

Correct diagnosis is essential if the condition is to be managed appropriately (Albietz 2001). Mann (2007) suggests the mainstay of treatment for ‘dry eye’ remains the instillation of artificial tears and yet the vast majority of cases involve increased evaporative stress rather than reduced tear volume (Albietz 2001). In this case of toxic epitheliopathy, it seems likely that the pathological spiral commenced years before with lubricants prescribed for a low-grade evaporative condition labelled ‘dry eye’.

22nd November 2006

The primary presenting complaint was variable/blurry vision.
The patient was under HES care for glaucoma and has used Xalatan® nocte since 2002. Coincidentally, she reported being diagnosed with dry eye 20 years ago and has used a range of lubricants, currently Viscotears® liquid gel.

Slit lamp examination with fluorescein revealed diffuse, pan-corneal superficial punctate epitheliopathy. The pattern and extent of the staining suggested a toxic reaction; when questioned more closely the patient admitted that her eyes had felt so irritable that she had been instilling the viscotears® up to 10 times per day.
The pattern of staining due to drop toxicity tends to be pan-corneal (Albietz 2001, Bruce and Loughnan 2003, Catania 1995). Bruce and Loughnan (2003) mention Dry Eye, Blepharitis and Exposure Keratopathy as differential diagnoses, while Ostler (1993) also includes many viral agents and Staphyloccocal blepharokeratitis. Apart from some viral pathogens those mentioned tend to demonstrate characteristically different staining patterns. Blepharitis is certainly associated with toxic corneal reactions but the resultant staining is typically confined to the zone of lid/globe apposition (Onofrey, Skorin and Holdeman 1997).

Excipients listed for Xalatan® includes benzalkonium chloride while multi-dose Viscotears® incorporates cetrimide (Electronic Medicines Compendium 2007). The specific product characteristics (SPC) of Xalatan® (emc 2007) include the warning that benzalkonium chloride has been reported to cause punctate keratopathy and/or toxic ulcerative keratopathy. No equivalent warning for cetrimide is included in the SPC for preserved Viscotears®, although toxicity is documented (Albietz 2001, Diebold et al 1998). Further, dosage for viscotears, both preserved and unpreserved, is 1 drop 4 times daily or as required (BNF 2007, emc 2007). No warnings of toxicity effects if over-used are included, but Bruce and Loughnan (2003) and O'Toole (2005) state that preserved drops should not be used more than four times per day. Gels and ointments also increase the corneal contact time enhancing the potential for adverse preservative reactions (Mann 2007).
Some glaucoma medications have been shown to have intrinsic corneal toxicity (Albietz 2001, Bruce and Loughnan 2003, Fraunfelder 2006). The SPC for Xalatan® (emc 2007) lists punctate epithelial erosions as a common side effect, however this is transient and usually asymptomatic. Rarely, however, symptomatic corneal oedema and erosions have been

reported. Sudesh et al (1999) describe four cases of toxic corneal reactions to Latanoprost.

Regardless of the reported reactions to Xalatan® and its' excipient, the over use of Viscotears® was considered the most likely cause for the clinical presentation.

Plan

The patient was due to be reviewed by her ophthalmologist the following week; an accompanying report was given.
Use of Viscotears® was stopped until this review. The patient was advised on the problem and leaflet given.

7th January 2007 Review

The clinical appearance and subjective symptoms were much improved. While maintaining preserved Xalatan® nocte, the ophthalmologist recommended non-preserved viscotears®.
While some irritability and visual blurring was still experienced the patient was much more comfortable.
Slit lamp showed a significant reduction in the superficial, epithelial staining. Phenol Red thread was 22mm and the tear meniscus was regular and estimated at 0.4mm, suggesting that this patient did not have a tear deficient dry eye. Having confidently concluded that the problem was purely evaporative, no further advice for tear deficiency was given.

Plan

General advice, with support material, on photophobia (Heath 2004) and contrast sensitivity (O'Toole 2005), a consequence of tear/epithelial disruption was given.
Use of all ocular medications re-enforced.
Routine review for six months.

22nd December 2007

At this check visual quality was reported as good, while ocular comfort was excellent. Overall the patient was very pleased but still reported slight variability in vision and improving vision with blinking. While single dose viscotears® was still prescribed the patient used it as little as once a week, supporting the view that the original presentation was toxicity related and not dry eye. No fluorescein or Lissamine Green staining of the ocular surfaces was noted but very mild Lid Wiper Epitheliopathy and slightly poor meibomian gland expression were.

The only ocular surface anomaly now was very mild posterior blepharitis. While mild, the persisting slight visual symptoms, coupled with an appreciation of the ocular discomfort possible, made the patient enthusiastic to pursue a long-term lid hygiene regime.

Plan

Blepharitis advice on lid scrubs was given with written instructions. Non-preserved palliatives as required but mainstay of treatment lid hygiene techniques.
Routine reviews recommended.

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