

Corneal Deposits Associated with Oral Isotretinoin

Sevillano C^{1*}, Dios E², Rodríguez-López V³ and Lázaro V⁴

¹Medicine Degree, Ophthalmology Service, Complejo Hospitalario de Pontevedra

²Medicine Doctor, Ophthalmology Service, Complejo Hospitalario de Pontevedra

³Medicine Degree, Centro de Salud de Villagarcía de Arousa

⁴Medicine Doctor, Radiology Service, Complejo Hospitalario de Pontevedra

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Introduction

Isotretinoin can involve some ocular side-effects such as blepharitis (11- 40%), dry eye (10-20%) and different corneal alterations (8-17%) [1,3-5]. Most of these side effects have shown to be completely reversible [2-5]. In the case of corneal disease, previous reports do not distinguish clearly between infiltrate, opacity and keratitis. To our knowledge, this is the first description of stromal corneal deposits in a patient treated with oral isotretinoin.

Case Report

A 20 year old woman was referred to our clinic because of pain, tearing and photophobia in her left eye. She was diagnosed of rosacea and had been treated on oral isotretinoin for 7 months (accumulated dose: 6000 mg). A year ago she had suffered an exacerbation of a seborreic blepharitis that was treated with oral tetracyclines. She referred other episodes with similar symptoms that were diagnosed as phlyctenula. She was an occasional soft contact-lens wearer (twice a week) with good tolerance.

Best corrected visual acuity was 20/20 in both eyes with a -0.75 spheric correction lens in her left eye. Intraocular pressure, pupil reflex, ocular motility and funduscopy were unremarkable. There were no skin

signs of active rosacea. In the biomicroscopy, no blepharitis or anterior chamber reaction were found, but there was a whitish, granular infiltrate in the medium stroma of the cornea in her left eye, with superficial limbar neovascularization and perilesional inflammatory reaction. The infiltrate was 3 x 1.5 mm and fluorescein test was negative. It was also thicker centrally (Figure 1). A diagnosis of phlyctenula was made.

The symptoms of the patient improved partially after treatment with fluormetolone every 6 hours and ciprofloxacin every 8 hours, but the infiltrate grewed, so fluormetolone was changed to metilprednisolone every 4 hours. However, the infiltrate worsened and reached the pupil area (Figure 2). After 3 weeks without improvement, both topical and oral treatment (fluormetolone, ciprofloxacin and oral isotretinoin) were

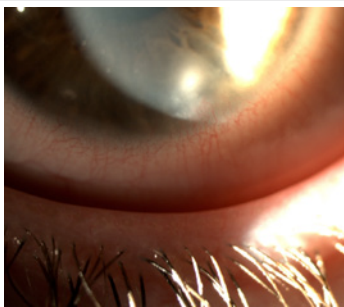


Figure 1: Whitish stromal infiltrate diagnosed as phlyctenula. Note the lack of signs of blepharitis.



Figure 2: Lesion reaching the pupil border area in spite of topical treatment.

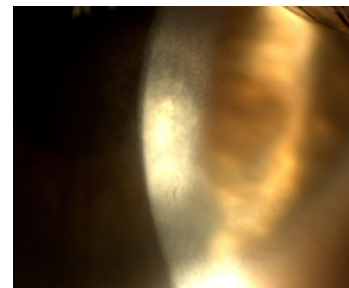


Figure 3: Stabilization of the lesion after stopping oral retinoid. Ghost vessels and fibrosis.

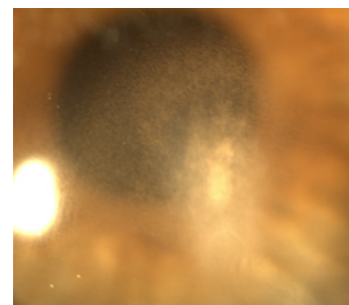


Figure 4: Mottled brownish stromal appearance larger than the initial infiltrate.

***Corresponding author:** Carlos Sevillano Torrado, Hospital Provincial de Pontevedra, calle Loureiro Crespo s/n; 36001 Pontevedra, Tel: +34 61987950; E-mail: seviojos@hotmail.com

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discontinued and 14 days later, the lesion became inactive with ghost vessels and no symptoms (Figure 3). One month later, the infiltrate had a granular brownish mottled appearance (Figure 4) and has been stable ever after a follow-up period of 22 months. Visual acuity is 20/20 and no symptoms are referred.

Discussion

Isotretinoin is a retinoid used mainly for the treatment of cystic acne, usually in oral administration [1-5]. Several ocular surface adverse side effects (dry eye, blepharitis...) have been described with its use [1,3-5]. Corneal alterations such as limbar infiltrates, opacities and keratitis have also been observed. Although a clear distinction between these terms has not been established, they are thought to be dose-dependent and to appear with more than 2 mg/kg daily dose [3,5]. However, corneal alterations have been described at more usual doses, as low as 1 mg/kg [2-5]. Corneal alterations are usually reversible when the drug is discontinued [1-4], generally 2 months after being discontinued [3,4].

The World Health Organization define the isotretinoin side-effects as certain (keratitis and opacities), possible (ulcers) and improbable (limbar infiltrates) [1], without a description of each lesion. Blackman et al. [5] found epithelial keratitis in 30% of their patients, probably in relation with the blepharoconjunctivitis induced by the retinoid, but with no direct corneal involvement. Ellies et al. [2] described a reversible stromal infiltrate and Fraunfelder et al. [3] differentiated between rounded and whitish subepithelial opacities and triangular limbar phlyctenula.

In our case, granular brownish material was observed in the corneal stroma, and the corneal infiltrate was classified as irreversible opacity due to possible corneal deposits of isotretinoin, without histopathologic confirmation because of the invasive character of this

test (best corrected visual acuity was 20/20). No corneal topography was carried out because no changes in visual acuity, glare or poor light adaptation were referred by the patient. Deposits developed on a previous phlyctenular lesion, but were observed growing out of the phlyctenula and were only stabilized when oral isotretinoin was stopped.

A differential diagnosis was made with interstitial keratitis, corneal scarring after phlyctenula and other corneal diseases such as autoimmune keratitis. Although we cannot conclude completely that keratitis was caused by isotretinoin, it is reasonable to think this association have been observed.

We think it is necessary to define in each case the morphologic characteristics of lesions, their depth and localization, so that an accurate classification can be made and consequently a more suitable treatment can be worked out. Our case presents a description, though it lacks of a histological study, of stromal deposits in relation with the use of oral isotretinoin.

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