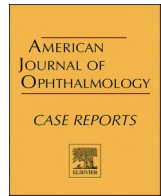




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Case report

# Successful management of chronic Blepharo-rosacea associated demodex by lid scrub with terpinen-4-ol

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## ABSTRACT

**Purpose:** To report a successful treatment of chronic rosacea associated ocular demodicosis with lid scrub containing terpinen-4-ol (T4O).

**Observations:** A 72-year old woman presented with recurrent and refractory ocular erythema, irritation, dryness, and photophobia despite conventional medical treatment (artificial tears, hypochlorous acid lid hygiene, doxycycline, and erythromycin) for 5 years. Examination revealed facial erythema, telangiectasias on cheeks, nose and lids, and cylindrical dandruff (CD) on bilateral upper and lower lashes. Epilation sampling confirmed demodicosis. After treatment with lid wipe containing T4O (Cliradex, Biotissue, Miami, FL) over face and lids, ocular discomfort, CD, facial and eyelid erythema, telangiectatic vessels were significantly reduced. Complete eradication of demodex mites and resolution of symptoms and signs lasted 8 months of follow-up.

**Conclusions:** This case suggests that T4O is effective in treating chronic rosacea associated ocular demodex blepharitis.

## 1. Introduction

Demodex mites (*Demodex folliculorum* and *Demodex brevis*) are the most common ectoparasites infesting the pilosebaceous unit of the skin. Unbeknownst to many, Demodex prevalence increases with age and demodex infestation (termed demodicosis) has been implicated in several diseases of the skin, including rosacea and blepharitis.<sup>1</sup> Although the pathogenic role of demodex in the development of rosacea has not been fully elucidated, there is a strong correlation of comorbidity between demodex and symbiotic *Bacillus oleronius* in facial rosacea and chronic blepharitis.<sup>1</sup> Rosacea has been suggested to be a risk factor for demodicosis in the eyelashes.<sup>2</sup> In addition, demodex complicates the clinical course and was found more prevalent in patients with chronic severe rosacea compared to rosacea without demodex involvement.<sup>3</sup> These mites may link to the chronicity of disease by stimulating the inflammatory process which subsequently leads to tissue damage and

aggravation of telangiectasias.<sup>1,4</sup>

Previously, it was reported eyelid scrubs with tea tree oil (TTO) are effective in reducing demodex counts and ocular surface inflammation. Such effect was attributed to terpinen-4-ol (T4O), which was found to be the most active component in eradicating demodex.<sup>5</sup> Importantly, T4O was found to be safe and effective in killing microorganisms not only related to common ocular but also skin infectious diseases.<sup>6</sup> However, there was no reported case of resolution of rosacea with ocular features after T4O treatment. We speculate that rosacea associated with ocular features and demodex is very easily overlooked. Herein we report the first case of using T4O wipe to achieve successful treatment of facial rosacea and chronic demodex blepharitis.

## 2. Case report

A 72-year-old woman presented with a significant past history of

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rosacea with ocular manifestations, dry eye disease, blepharitis and meibomian gland dysfunction. She had persistent eyelid erythema, irritation, dryness, and photophobia despite medical treatment of artificial tears, erythromycin, punctal plugs, cyclosporine, hypochlorous acid lid hygiene (Avenova, Novabay, Emeryville, CA, USA), and systemic doxycycline for 5 years. Examination revealed fixed erythema of facial skin, telangiectasias on cheeks, nose (Fig. 1a) and bilateral upper and lower eyelids (Fig. 1b). Slit lamp examination revealed bilateral cylindrical dandruff (CD) on the upper and lower lashes, trace conjunctival injection, mild inferior superficial punctate keratitis and rapid tear breakup time. The remaining killing demodex through competitively ophthalmic exam was unremarkable. The patient was consented to have microscopic examination of epilated eyelashes containing cylindrical dandruff, which detected a total of 15 demodex in the right eye and 16 in the left.

The patient was treated with T4O lid wipes (Cliradex®; Biotissue, Miami, FL) twice per day on both lids and surrounding periocular area. One month after treatment, the patient had significant reduction in facial and eyelid erythema (Fig. 1c). Slit lamp exam showed reduction of in CD in both eyes (Fig. 1d). In addition, her initial superficial punctate keratitis had resolved in both eyes. At 2 months follow up, the patient had significant reduction of eye irritation and dryness. Furthermore, the patient had complete resolution of facial and periorbital erythema and absence of telangiectatic vessels (Fig. 1e) with no CD along the lid margins (Fig. 1f). At 4 months follow up, patient remained asymptomatic. Exam showed no facial and periorbital erythema or telangiectasia. Her Ocular Surface Disease Index (OSDI) score improved from 37 (baseline) to 15. Repeat microscopic examination of epilated lashes showed absence of demodex. At 8 months, the patient remained asymptomatic, no appearance of facial skin erythema and telangiectasia without any additional therapy. Repeat microscopic examination of epilated lashes confirmed eradication of demodex, defined by the consecutive negative results spanning beyond two mite life cycles.

### 3. Discussion

Both rosacea and demodex blepharitis are common in older



**Fig. 1. Changes of Face and Lids following T4O Scrub.** (a, b) Significant facial, periorbital erythema, abundant cylindrical dandruff (CD), and telangiectatic vessels on the lid margin at baseline before treatment. (c, d) Reduction of facial and periorbital erythema, telangiectatic vessels and CD at 1 month after treatment. (e, f) Disappearance of facial and periorbital erythema, telangiectatic vessels, and CD at 2 months after treatment.

populations. Their coexistence and potential to exacerbate each other makes the diagnosis and treatment more challenging, often masquerade as other disease entities. Popular treatment for rosacea are systemic doxycycline, azelaic acid, Isotretinoin, metronidazole, pulsed dye laser, and avoid potential triggers such as excess UV exposure.<sup>7</sup> As for blepharitis management, the conventional treatment modalities have targeted largely on the symptoms such as hyperthermic therapy, topical and systemic antimicrobial therapy for bacterial etiologies, topical steroids, lid hygiene with baby shampoo, and hypochlorous acid. Other treatments such as pilocarpine gel, ivermectin and metronidazole have been reported in treating demodex.<sup>3,8</sup> Nonetheless, despite a myriad of similar conventional therapies, our case did not notice any relief for 5 years. Recent studies suggested demodex complicates the course of rosacea. We speculate that such failure might be resulted from combination of facial rosacea<sup>1,3,4,9</sup> and demodicosis blepharitis<sup>1</sup> that conventional treatment modalities are not demodicidal.<sup>1,7,10</sup> With a large body of evidence that indicates improvements in blepharitis with T4O, studies suggested that eradicating demodex can also lead to resolution of chronic severe rosacea cases,<sup>3</sup> similar to that of demodex associated blepharitis.<sup>6</sup>

Our case initially had demodex blepharitis associated with rosacea in the presence of diagnostic skin manifestations<sup>11</sup> including centrofacial erythema, facial telangiectasia, and ocular features<sup>11</sup> of eyelid telangiectasia, slight conjunctival injection and punctate keratitis. Once demodex was eradicated with T4O, not only blepharitis but also facial rosacea was cured at the same time. Our patient exhibited complete resolution of facial skin erythema and telangiectasias on cheeks, nose and bilateral upper and lower eyelids besides the improvement of ocular symptoms and signs. The promising therapeutic effect of T4O on facial rosacea further supports that the underlying cutaneous inflammation of rosacea likely leads to blepharitis. Therefore, the fact that both ailments (rosacea and blepharitis) improved simultaneously is not surprising. There is also evidence suggesting the pathogenic role of demodicosis in rosacea. A recent meta-analysis demonstrated demodex mites may play a role in different phenotypes of rosacea including erythema, telangiectatic, and papulopustular.<sup>12</sup>

One theory regards Demodex mites as a vector carrying bacteria to produce superantigens, cause mechanical obstruction in follicles, and activate the Toll-like receptor 2 (TLR2).<sup>9</sup> Thus, the innate immune response is enhanced to produce more pro-inflammatory mediators, such as IL-8, and IL-12p70 to activate CD4<sup>+</sup> T helper cells and macrophages and foster Langerhans-cell infiltration.<sup>9</sup> T4O possesses anti-parasitic, and anti-inflammatory properties by suppressing superoxide production and pro-inflammatory cytokines which may also explain the rapid resolution of symptoms in this case.<sup>13</sup> Consequently, we believe that the success of our case can be credited to the use of T4O, which has been reported as the key active ingredient in T4O to kill mites.<sup>5</sup> Besides killing demodex through competitively blocking the neurotransmitter terminating enzyme acetylcholinesterase (AChE) in parasites,<sup>14</sup> T4O also exerts antibacterial and antifungal effects.<sup>6</sup> This is especially desirable since part of rosacea pathogenesis directly involve *Staphylococcus epidermidis* and *Bacillus oleroniensis*.<sup>7</sup> From this case we speculate that demodex is a common link between these two disease entities and very easily overlooked. Future controlled trials are needed to substantiate what we have reported in this single case.

### Patient consent

This report does not contain any personal information that could lead to the identification of the patient.

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## Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

## Declaration of competing interest

Dr. Scheffer Tseng is the founder and a shareholder of Tissue Tech Inc. that holds patents on use of tea tree oil for the treatment of demodicosis. Sean Tighe is an employee of TissueTech. The following authors have no financial disclosures: (H.Y, A.C.)

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