



Case Report

Demodex Folliculorum can Cause Pyogenic Granuloma of Conjunctiva

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Abstract

An elderly Caucasian female with a history of oral lichen planus and functional nasolacrimal obstruction underwent bilateral Dacryocystorhinostomy (DCR). Eight months later tearing symptoms recurred, right greater than left, and a right lower medial eyelid inflammatory process was clinically correctly diagnosed as pyogenic granuloma. Excision and drainage without pathology was performed but the inflammation continued despite topical therapy with steroids and antibiotics. Clinical suspicion of conjunctival lichen planus prompted serial topical mitomycin-C applications effecting slight improvement over six-months. Persistence of the lesion led to a biopsy initially interpreted as pyogenic granuloma and subsequent step-sections of the specimen demonstrated a cyst containing probable parasite debris. A second deeper biopsy three months later revealed only granulation tissue. Thereafter the problematic area gradually healed. Controversy as to what parasite was responsible prompted a Center for Disease Control consult resulting in an unexpected diagnosis of *Demodex folliculorum*. **Methods:** We reviewed all clinical and pathology records related to this case. She had not traveled out of her home area or visited any agricultural fair or farm and did not remember any insect bites. **Results:** Parasitic debris was initially thought consistent with the external cuticle of a fly larva such as *Oestrus Ovis* [Sheep bot fly]. Eventual consultation with the Center for Disease Control resulted in a diagnosis of inflammation residual to *Demodex folliculorum* migration into conjunctival stroma. **Conclusion:** Persisting conjunctival inflammation can be due to *Demodex folliculorum* stromal invasion to locations far from eyelid skin, the common site of mite infestation.

Case Report

An otherwise healthy 78-year-old Caucasian female with a history of oral lichen planus presented to RRW on 8/18/08 (Figure 1) with a one-year history of continual bilateral tearing, greater on the right. There was no pain or foreign body sensation. She was sensitive to lacrimal probing, which demonstrated anatomically patent lacrimal drainage systems but with copious reflux from the non-cannulated

punctum bilaterally justifying a diagnosis of functional nasolacrimal system obstruction. Bilateral Dacryocystorhinostomies (DCR) were performed on 8/19/09. The surgical procedures were initially successful through five months post-operatively during which she was tearing free. However, by eight months post DCR the tearing had recurred bilaterally. In addition, a conjunctival inflammatory process was obvious on eversion of her right lower eyelid (Figure

2). Non-response to topical lubrication steroids and antibiotics prompted an initial incision and drainage for presumed pyogenic granuloma or chalazion without pathology. The inflammatory process slowly recurred including a purulent appearing microcyst (Figure 3) leading to a conjunctival biopsy sent to Eye Pathology at UCI 11/18/2010, one-year following the DCR. Clinical photos before the first excision revealed a purulent micro-cyst, correlating with the histology demonstrating a pyogenic granuloma (Figure 2-4). Pathologic study revealed incompletely excised micro-nodules of acutely and chronically inflamed granulation tissue partially covered by conjunctiva with focal pseudoepitheliomatous hyperplasia, necrosis and crush artifact. Step-sections of the deeper portions of the first specimen revealed non-polarizing membranous debris, suggestive of chitin of insect or parasite origin, within a well-defined fibrous envelope (Figure 5). In spite of treatment by multiple other ophthalmologists, topical steroids, antibiotics, and twelve serial 0.02% mitomycin-C topical applications over six months recommended by consultants who suspected conjunctival lichen planus, the lesion persisted leading to a second deeper excisional biopsy three months later revealing only granulation tissue. After this second biopsy the area eventually healed with no recurrence.

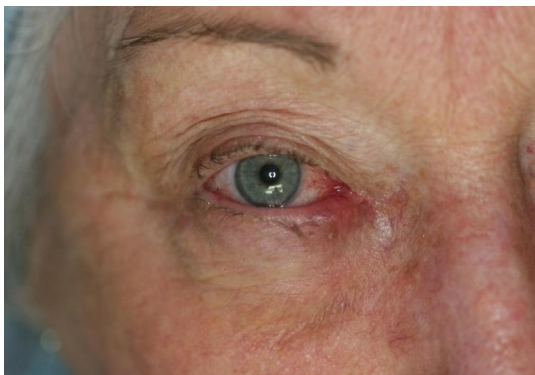


Figure 1: Initial clinical appearance of right lower eyelid inflammation 8/18/2008.



Figure 2: Appearance of everted right lower eyelid 8-months after DCR demonstrating inflammation and scarring residual to incision and drainage prior to biopsy with pathology.



Figure 3: Subsequent appearance several days after Fig. 2 including a small cyst containing purulent material.

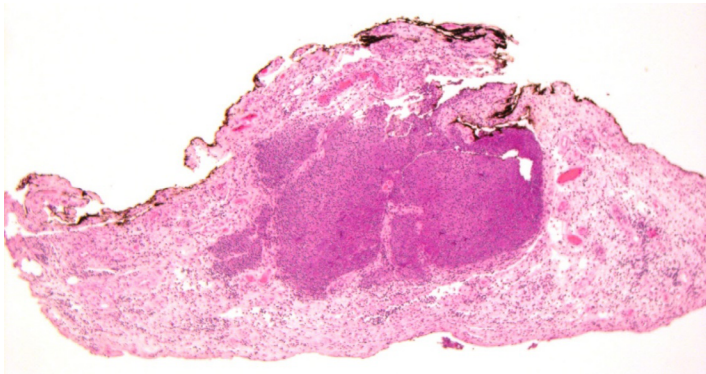


Figure 4: Photomicrograph of H&E-stained section after first biopsy with pathology, received 11/18/2010 illustrating partially necrotic abscess-like inflammatory reaction consistent with clinical appearance in Fig. 3. Black ink placed at gross exam delineates margin of excision. (Original magnification X 200)

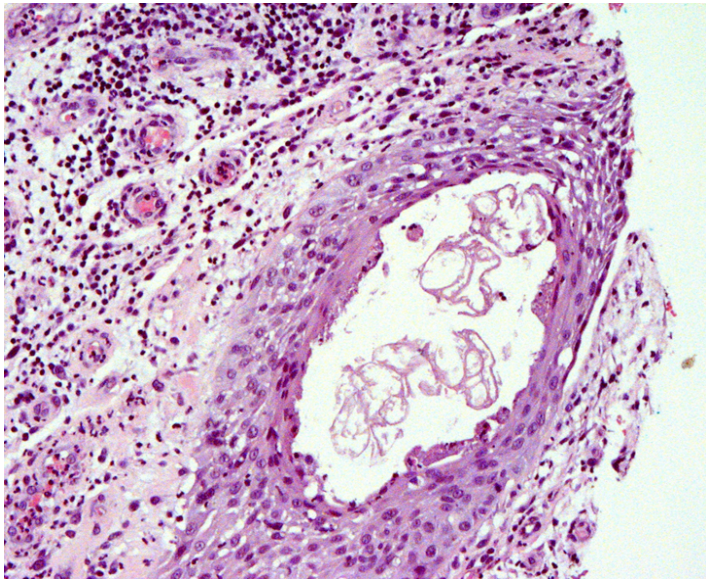


Figure 5: Photomicrograph of H&E-stained deeper step-section of same tissue block as in Fig. 4, revealing a cystic epithelial inclusion with intraluminal remnants of the parasite, and a background of capillary proliferation and a mixed inflammatory infiltrate typical of pyogenic granuloma (original magnification X 200)

Methods

We reviewed all clinical and pathology records related to this case. She had not traveled out of her home area or visited any agricultural fair or farm and did not remember any insect bites.

Results

Parasitic debris, initially thought consistent with the external cuticle of a fly larva such as *Oestrus Ovis* [Sheep bot fly], was suspected but consultation with the Center for Disease Control resulted in an unexpected diagnosis of inflammation residual to a *Demodex folliculorum* mite migration into conjunctival stroma.

Discussion

Two species of ectoparasite arthropod mites *Demodex Folliculorum* and *Demodex Brevis* commonly infest human eyelids and skin generally (demodicosis) worldwide [1-4]. Most frequently, as in the examples here, (Figure 6, 7) they are incidental findings during biopsy for various other reasons. *D. folliculorum* (length 0.3-0.4 mm) commonly in eyelid or body hair follicles and *D. brevis* (length 0.15-0.2 mm) preferring the sebaceous Zeis glands associated with eyelid hair follicles or sebaceous glands of the face and chest. *D. brevis* is also thought capable of destroying meibomian glands [1]. Although usually asymptomatic, the more common *D. folliculorum* may be associated with chronic blepharitis and may aggravate lid hyperemia, meibomian inflammation, chalazion formation, dry eye, and Rosacea [1]. Clinical signs include distension and increased fragility of cilia follicles and debris collars around the bases of eyelashes. A 2013 publication by Huang et al. suggested these infestations may increase recurrence of pterygia after excision [5]. *Demodex* infestation has a strong association with various types of dermatitis including rosacea and acne. Based on recent genetic studies of mitochondrial DNA it seems the human variety of *D. folliculorum* has a common ancestry with similar mites of dogs [6]. Of interest, the life cycle of *D. folliculorum* is only approximately one week. It feeds primarily on blood or plasma, the secretions of sebaceous glands and epithelial cells [1]. Females lay 20-24 eggs of 50–60-micron length. The hatchlings morph into nymphs and then pass through two stages into adults. They avoid sunlight and are generally only actively mobile at night, moving at approximately 16 mm/hour. Their aversion to light causes them to retract into cilia spaces during slit lamp examination making it unlikely they can be viewed by the examiner. *D. folliculorum* has dagger-like teeth capable of penetrating the host cells and in addition can secrete lytic enzymes to predigest its food [1]. While obviously a superbly adapted parasite deserving respect for its survival ability, *D. folliculorum* causes direct damage to human hair follicles, and dermal epithelium. *D. brevis* can block meibomian glands causing granulomatous inflammation secondary to chitin debris, perhaps a significant unrecognized contribution to chalazion occurrence [1]. Mites may also be associated with bacterial species including *Propionibacterium* and *Staphylococcus aureus* that play substantial roles in many serious dermatologic diseases.

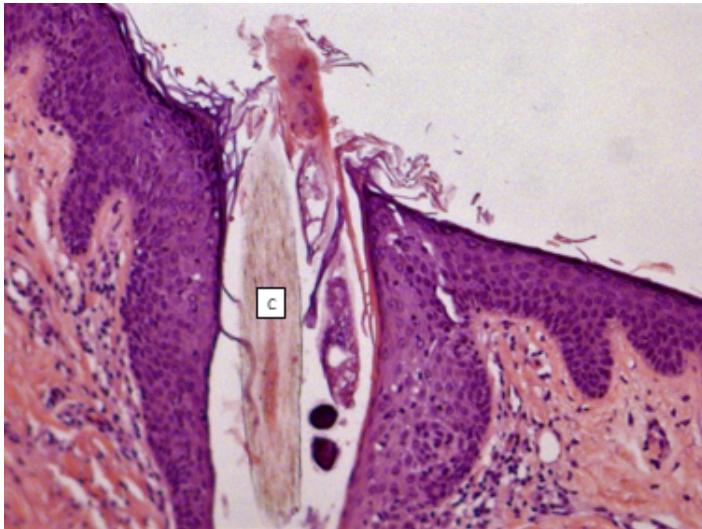


Figure 6: Photomicrograph of *Demodex folliculorum* in a different case with one or more mites in a hair follicle adjacent to cilia (c) in left upper eyelid skin found incidentally during histopathology examination after biopsy for chronic inflammation. Several mites typically share the same follicle and often contain basophilic accumulations consistent with egg sacs. (H&E original magnification X 200)

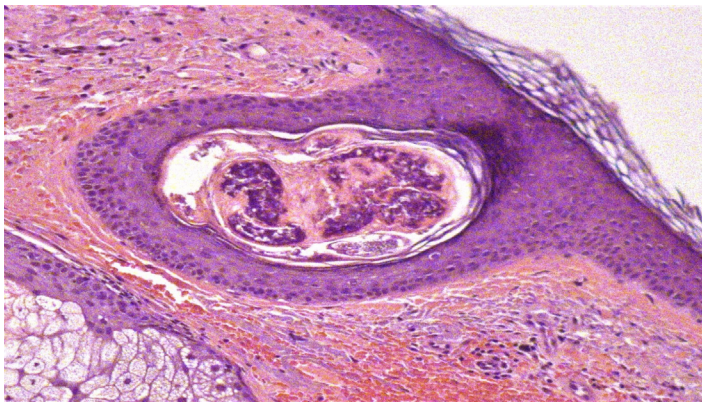


Figure 7: *Demodex folliculorum* from a separate case seemingly encysted near the surface of an elderly man's upper eyelid. Step or serial sections usually reveal that the surrounding epithelium connects to the surface epithelium. Numerous basophilic egg sacs are present within the organism. Incidental finding in biopsy for suspected eyelid neoplasm (H&E photomicrograph original magnification X 200.)

The incidence of ocular *Demodex* in otherwise healthy children in an epidemiological survey in South China found a 12% infection rate among those 3-14 years of age. Undoubtedly

demodicosis is likely to be far more prevalent among children of the same ages in underprivileged regions with poor hygiene, malnutrition or immune deficiency [7].

This patient's age and history were inconsistent with parasitic infection such as *Oestrus ovis* but compatible with demodicosis. Her several interval applications of topical Mito Mycin-C (MMC) intended as therapy for lichen planus conjunctivitis, never documented by biopsy, could have modified the inflammatory reaction to the parasite, most likely decreasing the intensity of an inflammatory reaction that could have limited its migration into deeper conjunctival tissues. Histopathology findings did not resemble the rare chronic conjunctival inflammation including symblepharon and scarring associated with lichen planus.

Histologically, we identified a pyogenic granuloma (aka lobular capillary hemangioma) which is a reactive tumor-like lesion characterized by localized vascular proliferation and mixed acute and chronic inflammatory infiltrate intermixed with fibroblasts [8-9]. The overlying epithelium usually demonstrates hyperplastic changes and variable degree of ulceration. This benign lesion can develop in response to trauma, infection, medication, chronic irritation, viral oncogenes, hormonal influence, and microscopic arteriovenous anastomoses. Prior studies indicate that the eyelid is the most common location of periocular lobular capillary hemangioma, followed by conjunctiva [9]. Herein, we describe a case of pyogenic granuloma arising in the palpebral conjunctiva associated with *Demodex folliculorum*. The patient had a history of DCR and multiple topical MMC treatments including steroids, antibiotics and a chemotherapeutic agent which could have altered the local microenvironment and immune status. Secondary immunodepression might have played a role in the migration of the parasite from the eyelid margin into the conjunctiva and subsequent pyogenic granuloma.

The most unusual feature of this case compared to many we have seen was its deep conjunctival invasion to a large distance from surface eyelid skin and inciting a pyogenic granuloma. Early and repeat pathologic tissue evaluation of atypical and recalcitrant conjunctival lesions is highly recommended. This example reminds eyecare providers to consider mite infestation as possibly responsible for granulomatous conjunctival lesions.

The remarkably high incidence of *D. folliculorum* human infections stratified by increasing age documented by a serial section study of healthy eyelids compared to eyelids demonstrating blepharitis [10]. Mite infestations increased by decade from age 20 years at 20% to 30% at 50 years and to 50% at 80 years. Healthy eyelids contained at least one mite in every tenth lash and eyelids with blepharitis contained at least one mite in every sixth lash, consistent with mite-induced blepharitis.

Treatment of *D. folliculorum* infestation can be difficult requiring lengthy therapy but control is possible with patient cooperation in-office or with instructions at home.

Suggestions from various sources

In office treatment regimens

- 70% alcohol brushed vigorously across external lid margin
- 3 weekly visits with above shown to decrease symptoms and number of observed mites at home treatment:
- Lid hygiene with diluted baby shampoo eye scrubs twice daily
- Antibiotic ointment at bedtime to lid surfaces to impede mite motility
- Alternatively, Mercury oxide 1% ointment to base of eyelashes at bedtime to trap mites as they emerge
- Pilocarpine gel (toxic to mites by impeding respiration and motility)

Although many studies have reported treatment results for Human demodicosis utilizing a variety of therapies including Tea Tree Oil (TTO), soaps, antibiotics, Intense Pulsed Light (IPL), Permethrin, an anti-Scabies drug, Ivermectin an antiparasitic drug and even biologics. Caution should prevail to ensure that the treatment is not more harmful than the disease, especially in patients with compromised immunity. One systematic review and meta-analysis involving an exhaustive literature search concluded that topical and systemic Ivermectine are promising treatments based on quantified decrease in mite numbers over treatment for weeks to months. Nearly a 100% decrease in mite numbers was achieved utilizing topical Ivermectin, TTO, Permethrin, IPL, and baby shampoo [11].

The UCI Internal Review Board does not require an IRB approval for a single clinical-pathologic case report.

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