

Rosacea-like Demodicosis Mimicking Cutaneous Lymphoma

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Demodex mites may play a pathogenic role when present in excessive numbers or when penetrating into the dermis. There are two types of mites. *Demodex folliculorum* is usually found in the follicular infundibulum, and *D. brevis* in sebaceous ducts and meibomian glands (1, 2). Pityriasis folliculorum is one of the typical skin manifestations of Demodex, and is characterized by facial erythema with follicular plugs and scale producing a “nutmeg-grater” or “sandpaper-like” appearance. Histologically, the eruption exhibits perivascular and diffuse dermal infiltration of lymphocytes without granuloma formation.

Rosacea-like demodicosis is another representative eruption characterized by follicular scaling, sudden onset, rapid progression, and no history of flushing (3, 4). In addition, meibomian gland dysfunction and keratoconjunctivitis may occur as eye lesions (5). Notably, there may be eyelid involvement, called demodectic blepharitis. Biopsies show a primary perifollicular infiltrate of mononuclear cells, with possible granulomatous inflammation. Demodicosis gravis represents a more severe form of demodicosis and shows intriguing granulomatous rosacea. Biopsies show granulomas with central caseation necrosis and foreign-body-type multinucleated giant cell (3, 4).

We report here two patients with rosacea-like demodicosis who had indurated lesions with massive lymphocytic infiltrates on the eyelids, forehead and cheeks and congestion of the eyes.

CASE REPORTS

Case 1

A 55-year-old healthy man had a one-year history of pruritic skin eruption on the face, which was treated with corticosteroid ointment without therapeutic effect. Subsequently, he developed blepharodema and sclera-oedema on the left cheek, acnerosacea-like rash with red papules and telangiectasia on his lower jaw, and congestion on his left eye. On examination, the patient had sclera-oedematous lesions on the left eyelids, left upper cheek and two subcutaneous nodules around his glabella (Fig. 1a). A skin biopsy specimen from the cheek showed a dense lymphocytic infiltrate around hair follicles (Fig. 2a). In serial sections, multiple Demodex mites were packed inside the infundibulum and sebaceous glands. The lymphocytes were positive for CD3, CD4, and partially CD8, and negative for CD20, CD30, CD56, CD79a, TIA-1, granzyme B and Epstein-Barr virus (EBV)-encoded RNA (EBER). Although the infiltrate consisted of small lymphoid cells without atypia, oligoclonal pattern of T-cell receptor (TCR) gene rearrangement was detected in the biopsy specimen by a PCR-based detection method. In another specimen from a subcutaneous nodule on

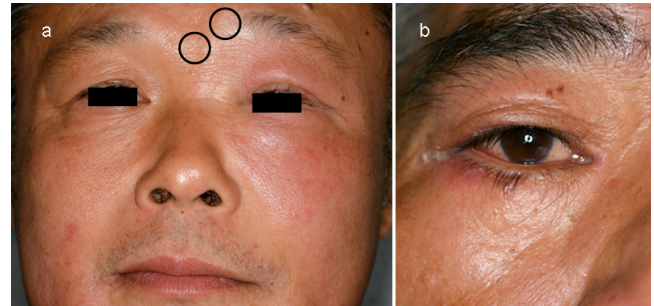


Fig. 1. (a) Blepharodema and sclera-oedema on the left aspect of the face and two subcutaneous nodules around the glabella (circles) (case 1). (b) Sclero-oedema of the nose, erythema on the inferior eyelid, and congestion on the right eye (case 2).

the forehead, there was sarcoidal granuloma, with Langhans and foreign-body-type multinucleated giant cells in the dermis and subcutaneous tissue (Fig. 2b). Periodic acid-Schiff (PAS), Grocott and Ziehl-Neelsen stains were negative.

Laboratory investigations revealed normal blood chemistry, including serum glucose and angiotensin-converting enzyme, and humoral and cellular immunity. Soluble IL-2 receptor level was normal, and thymidine kinase activity was slightly elevated (8.5; normal <5 U/l). Titres of antibodies against EBV and human immunodeficiency virus (HIV), and copies of EBV were unremarkable. Magnetic resonance imaging of the

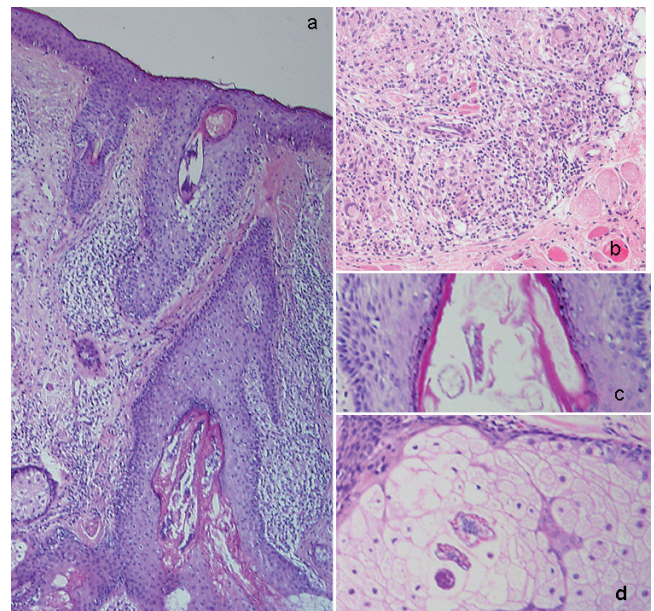


Fig. 2. (a) In a specimen from the cheek, there is a dense perifollicular lymphocytic infiltrate and multiple Demodex mites are present inside the infundibulum. (b) In a specimen from the glabella, there is sarcoidal granuloma consisting of Langhans and foreign-body-type multinucleated giant cells (case 1). (c) In a specimen from the nose, Demodex mites are present inside the hair follicles. (d) Demodex in sebaceous glands (case 2).

head revealed hypertrophy of subcutaneous tissue around his left eyelid and cheek, but no abnormalities in the nasal cavity, paranasal sinus or orbit. Chest and abdominal CT disclosed neither lymphadenopathy nor pulmonary involvement. We thus ruled out tuberculoid sarcoidosis and leprosy. The patient was treated with oral ivermectin and topical crotamiton, which markedly improved blepharoeidema and facial sclera-oedema and subcutaneous nodules. We again performed skin biopsy from his cheek, and there was a slight perifollicular infiltrate without granuloma. No TCR gene rearrangement was detected in the specimen, suggesting that Demodex mites played a pathogenic role for the monoclonal infiltration of T cells.

Case 2

A 64-year-old healthy man presented with a 6-month history of indurations on the nose and right cheek. He also had erythema on his inferior eyelid margin, with scaling at the root of eyelash and congestion on his right eye (Fig. 1b). No lymphadenopathy was found. Laboratory investigations revealed no humoral or cellular immunodeficiency, and no elevation of antibodies against EBV antigens. Skin biopsy from his nose showed a dense perifollicular lymphocytic infiltrate and the presence of Demodex mites inside hair follicles (Fig. 2c) and sebaceous glands (Fig. 2d). TCR gene rearrangement was not present in the biopsy specimen. The patient was treated with oral minocycline, and sclerosis of the nose, blepharitis and congestion on his right eye disappeared dramatically.

DISCUSSION

In the two patients with demodicosis, rosacea-like eruptions, blepharitis and conjunctivitis are the known lesions caused by Demodex. Demodex blepharitis is often misdiagnosed as other corneal and external diseases, and should be kept in mind on seeing refractory blepharitis, conjunctivitis and keratitis in adult patients or blepharoconjunctivitis and recurrent chalazia in young patients (5). Massive infiltration of lymphocytes and monoclonal expansion of T cells was a novel finding in our patients. It is known that the pathogenic mechanisms of demodicosis include sequential occurrence of the following events: (i) occlusion of hair follicles and sebaceous ducts by the mites or possible reactive hyperkeratosis; (ii) host's cell-mediated immune reactions by the mites or their waste products; (iii) further foreign body granulomatous reaction to the chitinous skeleton of mites; and (iv) possible modulation by a vector role for bacteria (3). Superantigens produced by *Staphylococci* and *Streptococci* are also implicated in the induction of rosacea (6).

Demodex may feed on follicular and glandular epithelial cells, leading to direct damage of the lid. *D. fol-*

liculorum has been reported to consume epithelial cells at the hair follicle, which results in follicular distension, and subsequent formation of loose or misdirected lashes. The resultant trichiasis may induce trauma to the corneal epithelium (5). On the other hand, *D. brevis* can mechanically block the orifices of meibomian glands, giving rise to meibomian gland dysfunction with lipid tear deficiency (7), and ophthalmologically, *D. brevis* increases evaporation of tears and causes keratoconjunctivitis. *D. brevis* usually burrows deep into the sebaceous and meibomian glands, and its chitinous exoskeleton may act as a foreign body causing granulomatous reaction, which causes recurrent and refractory chalazia (8, 9).

In the two cases described here, facial sclera-oedema and blepharoeidema with histological massive lymphocytic infiltration mimicked cutaneous lymphoma. The treatment of Demodex was therapeutically effective for the congestion of the eyes as well as the skin lesions in both cases. The disappearance of monoclonality of T cells may provide evidence for stimulation of certain populations of T cells with mite antigen. The cases described here suggest that rosacea-like demodicosis occasionally resembles cutaneous lymphoma, and the eye lesions may be informative for suspecting demodicosis.

The authors declare no conflicts of interest.

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