

## Original Article

# Histopathologic Study of Rosacea and the Role of Demodex Folliculorum

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### ABSTRACT

**Background and Objective:** Rosacea is a common and ill-defined disease and Demodex folliculorum has been reported in rosacea in a number of clinical studies. Since demodex mite is present in many healthy individuals, the mite may have a pathogenic role only when it is present in high densities. Therefore, in this study, the possible role of demodex folliculorum and the importance of mite density were investigated using an elliptical incisional skin biopsy technique.

**Materials and Methods:** Thirty-nine patients with rosacea, twenty-five females, 14 males, and 41 age- and sex-matched healthy individuals as control were included in the study. With the incisional skin biopsy of face, we studied six sections of each sample. We also studied the number of follicles, mite density, epidermal changes, solar elastosis, inflammatory cells in the dermis and their pattern, granuloma formation, and vascular changes.

**Results:** Varying degree of vasodilatation, solar elastosis, and inflammatory infiltrate were found in all patients. The infiltrate was lympho-histiocytic in 29 cases, lympho-plasmacytic in 6 cases, neutrophilic, especially around hair follicles in 2 cases, and eosinophilic infiltration mixed with mononuclear cells in 2 cases. The number of D. folliculorum was statistically significant.

There was also a significant difference between males and females regarding the number of mite in rosacea in relation to age ( $p = 0.047$ ). There was also granuloma around appendages in 3 cases and granuloma around hair follicle in 2 cases. One case in the latter group had degenerated demodex cuticle.

**Conclusion:** Rosacea is a multifactorial disease and high densities of demodex are important in the form of hypersensitivity reaction to antigens or granuloma formation in response to its cuticle or destructed hair follicles. The individual properties may modify the severity of inflammatory response to demodex.

**Key words:** Rosacea, Demodex folliculorum

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## Introduction

Rosacea is a common chronic dermatosis characterized by varying degrees of flushing, erythema, telangiectasia, edema, papules, pustules, ocular lesions, and rhyphomas<sup>1</sup>. Etiology and pathogenesis of rosacea are still unknown and multifactorial. Many possible causes have been described including the disease or contributing factors to its manifestation such as genetic predisposition, abnormal vascular reactivity, changes in vascular mediating mechanisms, *Helicobacter pylori* infection, *Demodex folliculorum* infestation, seborrhea, sunlight, hypertension, and psychogenic factors (1).

Rosacea shows a wide spectrum of clinical presentations which vary over time and age. *Demodex folliculorum* (DF) has been reported in rosacea in a number of clinical studies. Since the *Demodex* mite is also present in many healthy individuals, the mite may have a pathogenic role only when it is present in high densities (2). Although some reports claim a significant association of mites in rosacea biopsies, but other studies have not supported this claim. The mites may represent an important cofactor in heightening disease severity (3)

In the present study, the possible role of DF and the importance of mite density were investigated using a standard elliptical incisional skin biopsy technique.

## Materials and Methods

Thirty-nine cases with a diagnosis of rosacea were included in the study. The cases were obtained from Sina hospital (Hamedan University, Hamedan). It is a dermatology and pathology center in western Iran. The slides were reviewed and the diagnosis of rosacea was confirmed according to the criteria of Levers text book of skin pathology (3). The tissue was obtained by an incisional skin biopsy for evaluation.

Twenty-five of cases were females, fourteen were males, and 41 were age- and sex-matched healthy skin biopsies as control group. They had biopsied for other reasons and they did not have rosacea or other inflammatory dermatosis. We analyzed six

sections of each sample (section with a thickness of 4-5 micron and stained with H and E and PAS. We studied the epidermal changes, number of follicles, mite density, and solar elastosis, inflammatory cells in the dermis and their pattern, granuloma formation, and vascular changes (2,4). The number of follicles in each section calculated and averaged *Demodex* in each follicle was considered for each patient.

The including criteria for rosacea was observed. None of the control cases had pityriasis folliculorum or pustular folliculitis of face since *demodex* has a role in their pathogenesis.

## Results

The mean age of rosacea and non-rosacea dermatosis groups was 45.3 and 43.1 years respectively. It was the research plan that two groups were age-matched. Varying degree of vasodilatation, solar elastosis, and inflammatory infiltrate were found in all patients. The infiltrate was lymphohistiocytic in 29 cases, lympho-plasmacytic in 6 cases, neutrophilic, especially around hair follicles in 2 cases, and eosinophilic mixed with mononuclear cells in 2 cases. The number of *D. folliculorum* was three in each follicle of 17.9% of rosacea group and 8% of control group. Meanwhile, 12.8% of cases had two samples of D.F in rosacea group and control revealed 2.4% of such samples.

In addition, 30.8 % had only one *demodex* in each follicle and 38.5 % had not any *demodex* in their follicles in rosacea group, but non-rosacea group revealed 84.5% of cases without D.F. (Table 1).

**Table 1. Number of Demodx in the skin of rosacea and non-rosacea patients**

Total	rosacea	Non-rosacea	Mean number of demodex
Number (%)	Number (%)	Number (%)	
50 (62.5)	15 (38.5)	35 (85.4)	0
17 (21.2)	12 (30.8)	5 (12.2)	1
6 (7.5)	5 (12.8)	1 (2.4)	2
7 (8.8)	7 (17.9)	0 (0)	3
80 (100)	39 (100)	41 (100)	Total

The number of demodex was also 1.103 in each follicle in rosacea group and 0.171 in control group with a significant difference ( $p = 0.000043$ ) (Table 2). There was also significant difference in the number of mite in rosacea group related to age (it was 0.545 in the group with an age less than 40 years and was 1.308 in the group with an age greater than 40 years ( $p = 0.047$ )). This was non-significant in non-rosacea group (0.118 mite per follicle versus 0.509 mite per follicle ( $p = 0.53$ )). There was granuloma unrelated to appendages in three of cases and granuloma around hair follicle in two of cases. In this respect, one of the latter groups revealed degenerated Demodex cuticle.

**Table 2. Comparison of mean number of demodex in face skin of rosacea and non-rosacea groups**

Group	Rosacea	Control
Number	39	41
Mean number of demodex	1.103	0.171
SD	1.119	0.442
T-value	4.943	
P-value	0.000042	

## Discussion

Rosacea is a multifactorial disease. Among its pathogenic factors, a causative role has been postulated for the hair follicle mites *Demodex folliculorum* and *Demodex brevis* (4). Recent studies have shown a significant increase in Demodex in rosacea group in comparison with controls (49.8 versus 10.8 with six biopsies of face with cyanoacrylic glue (5)). Another study revealed 86% for demodex in rosacea patients (6). Two other studies also revealed scanty mite in patients. For these groups, it was two out of 75 patients and 14 out of 74 cases (6,7). Georgala (7) revealed demodex in 16 out of 18 cases. All of the patients were treated with anti-mite therapy. In addition, Bonnar (5) demonstrated 49.8 mites per 10 cm<sup>2</sup> surface of face. It was significantly higher than non-rosacea group. It was 10.8 mites per 10 cm<sup>2</sup>.

Our study revealed 1.103 mites per follicle in

patients and 0.171 in non-rosacea, with age and sex matched. It was statistically significant. Our study based on histological examination of skin biopsies and it was possible to be done by standardized skin surface biopsy (SSSB) where cyanoacrylate glue is used to sample the horny layer and follicular contents (3). The presence of five or more mites per square centimeter by SSSB is considered significant (3). Hypersensitivity reaction to mite antigens has an important role. Georgala revealed that delayed hypersensitivity reaction, possibly triggered by antigens of follicular origin has a causative role.

The hypersensitivity reaction triggered by mite antigens may lead to granuloma formation. Ramelet (4) revealed the role of demodex in granulomatous form of rosacea. We find granuloma unrelated to hair follicle in three cases, two cases had granuloma around hair follicle, and one of them revealed degenerated Demodex cuticle. These cases had eosinophilic infiltration mixed with mononuclear cells. The pathogenesis of Demodex-related disease may be related to 1) blockade of hair follicle and sebaceous duct, 2) mite serving as a vector for bacteria, 3) foreign body reaction to mite, 4) and induction of host immunity by the mite or its waste (3). These finding demonstrate a strong association, but not cause and effect.

To conclude, rosacea is a multifactorial disease and high densities of demodex are important, in the form of hypersensitivity reaction to antigens or granuloma formation in response to its cuticle or destructed hair follicles. The individual properties may modify the severity of inflammatory response to demodex.

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