Follicular scales, scalp and ocular involvement in patients with papulopustular rosacea: prevalence and association with Demodex mite proliferation

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Abstract

Facial follicular scales, dandruff, scalp itching and ocular alterations are lesser-known signs of rosacea and demodicosis. The aim of this prospective original study was to investigate the presence of these signs and symptoms in patients with almost-clear, mild and moderate papulopustular rosacea (PPR) and to study the differences between Demodex-positive (D+) and Demodex-negative (D-) rosacea. Twenty-seven out of 60 patients (45%) presented follicular scales, 24 (40%) ocular involvement and 22 (36.67%) scalp involvement. Follicular scales were more frequently observed in mild and moderate than in almost-clear rosacea (P<0.001). Itching of the scalp was more frequently reported in patients with moderate rosacea than in those with mild disease (P=0.05). Follicular scales (P=0.002) and scalp itching (P=0.05) were more frequently reported in D+ than in D- patients. Among D+ patients, scalp itching was more frequently reported in mild than in almost clear rosacea (P=0.01) and ocular symptoms associated to scalp itching were more frequently reported in moderate than in almost-clear rosacea (P=0.05). We suggest looking for these signs and symptoms in all patients with PPR, because they can be a sign of a more severe form of rosacea or of demodicosis.

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Introduction

Papulopustular rosacea (PPR) is characterized by multiple, small, dome-shaped erythematous papules and pustules arising on erythematous skin in a centrofacial distribution.[1,2] Human demodicosis is a skin condition caused by an increased proliferation of Demodex mites in the pilosebaceous unit and in the dermis. Demodicosis can be a primary disease or a complication of pre-existing facial dermatoses, such as rosacea. It is characterized by signs and symptoms like pustular folliculitis, papulopustular scalp eruption or only itching and a non-specific facial eruption.[3] In the literature, it was observed that patients with PPR and/or demodicosis can present other clinical signs, such as facial follicular scales, dandruff and scalp pruritus in addition to the well-known classical features.[4] However, there is a lack of studies evaluating the frequency of these symptoms in PPR and in demodicosis. The aim of this study was to investigate the presence of the additional signs of follicular scales, scalp and ocular involvement in patients with almost-clear, mild and moderate PPR and to investigate the differences between Demodex-positive (D+) and Demodex-negative (D-) PPR.

Materials and Methods

We conducted a prospective study at the Dermatology Centre of Ospedale Policlinico San Martino IRCCS in Genoa (Italy). The diagnosis of rosacea was made by an experienced dermatologist and it was based on the clinical signs described by the National Rosacea Society expert panel:[1] i) fixed centrofacial erythema in a characteristic pattern that may periodically intensify; ii) papules and pustules (with or without telangiectasias, flushing and ocular

manifestations).[4] Subjects that had been treated with specific therapies during the previous six months and overlap cases were not included in the study. Patients with an history of seborrheic dermatitis or affected by it were excluded. Additionally, scalp symptoms (pruritus, burning and dandruff) and ocular involvement (conjunctivitis, haemorrhagic conjunctival injection and dry eye) were evaluated in all patients.[4] To study Demodex mites count, a standardized skin surface biopsy (SSSB) was performed by a trained dermatologist. SSSB is a sampling method in which 1 cm^2 of the superficial part of the horny layer and of the follicular content of the skin is recovered.[5] Following SSSB test, microscopic examination was undertaken with ×10 and ×40 magnifications. Every sample with ≥5 Demodex/cm^2 (D/cm^2) was considered positive (D+).[5] To assess disease severity, we applied the Investigator Global Assessment score (IGA score). The IGA score is a 0 to 4 scale: IGA 0 = no inflammatory lesions, no erythema; IGA 1 = very few small papules/pustules, very mild erythema; IGA 2 = few small papules/pustules, mild erythema; IGA 3 = several small or large papules/pustules, moderate erythema; IGA 4 = numerous small or large papules/pustules, severe erythema.[6]

Descriptive statistical analyses were performed, and data were shown as median [range], mean (standard deviation), or number (percentage). Continuous variables with normal distribution were analyzed using Student's t test. For categorical variables, data were analyzed using the χ^2 test and Fisher's exact test.

The study was approved by the local Ethical Review Board (Comitato Etico Regione Liguria. N. Registro CER Liguria: 492/2020).

Results

In total, 60 Caucasian patients, including 33 women (55%) and 27 men (45%) with a mean age of 57±14.7 years, range 30-81 years, were enrolled.

Twenty-seven out of 60 patients (45%) presented with follicular scales, 24 (40%) with ocular involvement (redness, pruritus, foreign body reaction, and conjunctival inflammation), 22 (36.67%) with scalp involvement (erythema, dry scaling and itching) and 11 (18.33%) with ocular and scalp involvement.

Of the 60 patients, 31 (51.67%), 16 (26.67%) and 13 (21.66%) patients had an IGA score of 1, 2 and 3 respectively. No patient had an IGA score of 0 or 4.

The additional symptoms classified by IGA score and the Demodex status are summarized in Table 1. Patients with an IGA score of 2 and 3 had a higher frequency of follicular scales than patients with IGA 1 (62.5% *vs* 19.35%, p<0.01 and 84.61% *vs*. 19.35%, p<0.001). Patients with IGA 3 reported more frequently itching of the scalp than patients IGA 2 (61.54% *vs*. 25%, P=0.05). There was no significant correlation between IGA score and ocular symptoms (p=0.13, p>0.999, p=0.14).

Using SSSB, Demodex mites were found in 20 (33.33%) of the 60 patients, seven of whom had IGA 1, seven had IGA 2 and nine had IGA 3 rosacea.

D+ patients presented more follicular scales (60% *vs*. 37.5%, P=0.002) and scalp pruritus (55% *vs* 27.5%, P=0.05) than D- patients. There was no significant correlation between D+ and D- PPR and ocular involvement (p=0.6)

Among D+ patients, those with an IGA score of 2 reported more scalp pruritus than IGA 1 patients (100% *vs* 20%, p=0.01) and patients with IGA3 showed more ocular symptoms associated to scalp pruritus than patients with IGA1 (100% *vs* 20%, p=0.05).

Discussion

To the best of our knowledge, no previous research has investigated the incidence of follicular desquamation, scalp and ocular symptoms in PPR of different degrees with and without concomitant Demodex infestation. Forton *et al.*, in 2019, identified these signs as clues to the presence of Demodex in facial dermatoses in both primary and secondary demodicosis.[4] The association between Demodex and rosacea is common although its pathogenesis is unknown and controversial.[7-9]

Follicular scales are keratin fragments which cover hair follicles and can be observed with dermoscopy in rosacea.[10] In our study, follicular scales were the most frequent additional sign of rosacea and they were more common in severe rosacea and in D+ patients. In addition, follicular scales were found in the almost clear PPR, thus representing an early sign of rosacea. In Demodex infestations, the follicular, superficial and small scales correspond to the epistosome of the parasite protruding from the follicular orifice. Forton *et al.* demonstrated an association of follicular desquamation with facial telangiectasias in patients with rosacea showing that desquamation may be a sign of rosacea itself.[4]

Regarding scalp involvement, 36.67% of patients presented erythema, dry scaling, and itching of the scalp. These symptoms and signs were statistically more frequent in patients with moderate rosacea and in D+ patients. Scalp itching in patients with rosacea has been reported by Forton *et al*., who have considered it like a little-known diagnostic sign of Demodex proliferation. Rosacea is associated with a reduction in long-chain saturated fatty acids,[11] with a decrease of skin hydration,[11,12] and alteration of the lipid film quality.[13] These mechanisms may contribute to the pathogenesis of both rosacea and scalp involvement. Moreover, we hypothesized that Demodex infestation could have a role in

Table 1. Signs and symptoms of papulopustular rosacea divided by the Investigator Global Assessment score.

Signs and symptoms of PPR		IGA 1=31 (51.66)		IGA 2=16 (26.67)		IGA 3=13 (21.67)		Total 60
Follicular scales	D+(%)	1 (16.67)	6 (19.35)	6 (60)	10 (62.5)	5 (45.45)	11 (84.61)	12 (20)
	D−(%)	5 (83.33)		4 (40)		6 (54.55)		15 (25)
Ocular symptoms	D+(%)	1 (12.5)	8 (25.81)	4 (57.14)	7 (43.75)	5 (55.56)	9 (69.23)	10(16.67)
	D−(%)	7 (87.5)	3 (42.86)		4 (44.44)		14(23.33)	
Scalp symptoms	D+(%)	2 (20)	10 (32.26)	4 (100)	4 (25)	5 (62.5)	8 (61.54)	11(18.33)
	D−(%)	8 (80)		0 (0)		3 (37.5)		11(18.33)
Ocular and scalp symptoms	D+(%)	1 (20)	5 (16.13)	2 (100)	2 (12.5)	4 (100)	4 (30.77)	7 (11.67)
	D−(%)	4 (80)		0 (0)		0 (0)		4 (6.67)

PPR, papulopustular rosacea; IGA, Investigator Global Assessment; D+/−, Demodex-positive/negative.

rosacea of the face as well as in the desquamation of the scalp. Although high proliferation of Demodex mites has been only associated with scalp folliculitis and favus on the scalp,[14] we suppose that the scalp itching in PPR may be due to an increased Demodex proliferation promoted by the increased sebum production which occurs after puberty. However, there are no studies which investigate the concentration of mites on the scalp in rosacea patients. We did not investigate the presence of Demodex on the scalp because conventional sampling appears to be painful and we preferred to define the entity of scalp involvement in PPR before resorting to SSSB or alternative techniques.

Ocular involvement was associated with D+ severe facial rosacea in the presence of scalp problems. More than 50% of patients with cutaneous rosacea show ocular rosacea,[15] 20% of which report ocular before cutaneous symptoms.[16] Several studies have shown the presence of Demodex on the eyelashes and eyelid edge, both areas with high density of sebaceous glands and hair follicles. The mite is capable of triggering a TLR-2 mediated inflammatory response and of mechanically blocking follicles (*D. folliculorum*) and sebaceous glands (*D. brevis*) leading to chronic blepharitis, inflammation of the conjunctiva, corneal lesions, and meibonian gland dysfunction.[17] In a study on patients with rosacea, Demodex-positivity on the face did not correlate with eyelash infestation; however, those with rosacea and concomitant symptoms of blepharitis had a higher incidence of ocular Demodex than patients without rosacea.[18] Consequently, Demodex sampling is important in all patients with rosacea and ocular symptoms to avoid empiric treatment with topical corticosteroids, which may mask Demodex infection and induce chronic blepharitis.[16] Application of topical ivermectin to the eyelids of these patients can improve ocular rosacea symptoms.[19] In the literature, there are no studies that associate ocular and scalp symptoms in PPR. However, hypothesizing a common etiopathogenetic mechanism mediated by Demodex in sebaceous glands and hair follicles, our finding is not surprising.

Our study has different limitations: we did not have patients with severe rosacea (IGA4), and we performed a clinical eye assessment without instrumental ophthalmic evaluation.

Conclusions

We suggest looking for follicular scales, scalp and ocular involvement in all patients with papulopustular rosacea because these can be signs of a more severe form of disease or of a demodicosis in patients with papulopustular rosacea. Moreover, it would be appropriate to investigate Demodex infestation on the scalp with SSSB or with a less invasive method to evaluate a possible correlation between scalp symptoms and demodicosis.

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