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A Case of Refractory Rosacea with Ultra-high-density Demodex Folliculorum Colonization and the Features of Reflectance Confocal Microscopy and Dermoscopy

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Abstract: *Rosacea is a chronic inflammatory dermatosis that primarily affects the facial vasculature, nerves, and pilosebaceous units. This case report describes a case of refractory rosacea associated with ultra-high-density Demodex folliculorum (DF) colonization and its specific skin imaging findings. The patient was a middle-aged man with a 1.5-year history of facial erythema, papules and pustules with itching and dryness. Reflectance confocal microscopy (RCM) revealed that the number of DF reached an average of 40 within an area of 4 mm² and that the perifollicular keratinocytes were arranged in multilayered concentric circles. The patient received conventional treatments such as oral doxycycline and hydroxychloroquine for more than 3 months with poor efficacy, but his condition improved significantly after 1 month of combined anti-mite therapy. The density of DF in this rosacea case was significantly higher than previously reported and it might be induced by DF. In addition, the presence of perifollicular keratinocytes arranged in multilayered concentric circles under RCM was an extremely rare feature that has not been reported before. Dermatologists should evaluate DF when available and add anti-mite therapy if necessary. RCM and dermoscopy, as non-invasive testing techniques, play a positive role in the assessment of DF, inflammation, vascularity, and follicular abnormalities and can assist in the diagnosis, treatment options, and efficacy evaluation of rosacea.*

Keywords: *Rosacea; Demodex folliculorum; Reflectance confocal microscopy; Dermoscopy*

1. Introduction

Rosacea is a chronic inflammatory disease characterized by persistent erythema, paroxysmal flushing, papules, pustules, and telangiectasia of the midface, as well as phymatous changes and ocular symptoms. Skin sensitivities such as burning, tingling, and itching often accompany these manifestations[1,2]. The pathogenesis of rosacea remains unclear. Recent studies have found that DF is involved in the pathogenesis of rosacea by activating certain immune responses and exacerbating neurogenic inflammation[3,4]. Various degrees of DF infection have been reported in some rosacea patients[5]. In recent years, dermoscopy and RCM have been used as non-invasive examination tools to assist in the diagnosis and evaluation of therapeutic efficacy for a wider spectrum of diseases. We present a case report of refractory rosacea associated with ultra-high-density DF colonization, and the occurrence of this rosacea might be induced by DF. In addition, we describe rare and previously unreported manifestations observed through RCM in this patient. We also review the relevant literatures to illustrate the RCM and dermoscopic features of rosacea and discuss the clinical significance of dermatologic imaging techniques in rosacea, hoping to provide some clinical enlightenment.

2. Clinical Data

A 48-year-old Chinese man complained of " facial erythema, papules, and pustules for 1.5 years". Erythema appeared on his nose 1.5 years ago without obvious predisposing factors. Subsequently, the erythema gradually spread to his forehead and jaw, accompanied by scattered red papules and pustules with itching and dryness. Approximately a year ago, the patient was diagnosed with rosacea at the local hospital and was treated with oral doxycycline and hydroxychloroquine for more than 3 months. Although the pustules resolved, there was no significant improvement in the erythema. Half a month ago, the patient felt that the itching worsened and his cheeks burned when exposed to heat or excitement,

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without oral ulcer, muscle and joint pain, or ocular symptoms. The patient was healthy previously and denied any history of infectious diseases, allergies, or similar familial diseases. Physical examination showed multiple erythema with scattered red papules and pustules on the bilateral cheeks, periocular area, nose, right forehead, and left jaw, accompanied by telangiectasia on the cheeks and phymatous changes on the nose and left jaw(Figure 1). RCM showed focal edema in the stratum spinosum and some dilated follicular infundibulum. The superficial dermis showed prominent dilated vessels, quickened blood flow velocity, and increased vascular density. The presence of various degrees of inflammatory cell infiltration around the blood vessels in the dermal papillary layer and superficial dermis was observed. In addition, the number of DF reached an average of 40 within an area of 4 mm^2, and the perifollicular keratinocytes were arranged in multilayered concentric circles(Figure 2). Dermoscopy showed lots of vascular polygons and linear vessels on the red background of his cheeks and glabella region, with yellow halos around the hair follicles and scattered black vellus hairs and white scales. The left jaw and nose showed red diffuse structureless areas, punctate vessels and linear capillaries, yellow-white homogeneous pustules, follicular keratotic plugs, and diffuse white halos around the hair follicles(Figure 3). Microscopic examination was positive for Malassezia spores.

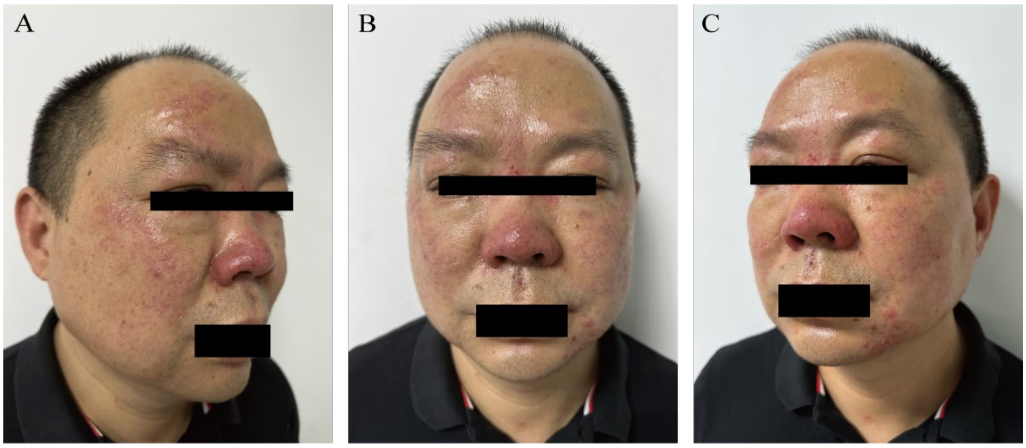

Figure 1: (A-C)Clinical images showed multiple facial erythema with scattered red papules and pustules, accompanied by telangiectasia on the cheeks and phymatous changes on the nose and left jaw.

Combined with the clinical history, skin lesions, and imaging examinations, the patient was diagnosed as rosacea with ultra-high-density DF colonization. Given the patient's poor response to previous treatment, a combination of oral ornidazole, topical lincomycin cream and sulfur cream, along with water-oxygen therapy using metronidazole solution was administered as anti-mite therapy. A follow-up visit showed that the patient's condition of erythema, pustules, and itching was significantly improved after 1 month of treatment.

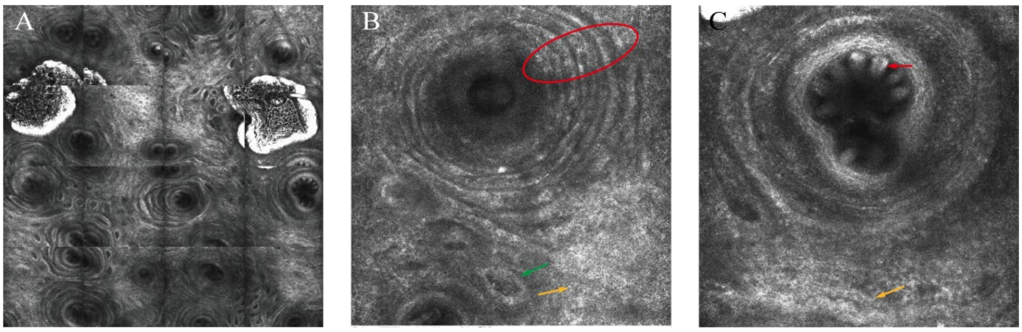

Figure 2: RCM mosaic (2×2mm^2, z=92.96um) (A) and RCM single images (0.5×0.5mm^2, z=92.96 & 83.82um) (B-C) of the cheek. (A) The mosaic revealed lots of Demodex mites and concentric structures. (B) The perifollicular keratinocytes arranged in multilayered concentric circles (red circle), dilated blood vessels (green arrow), and inflammatory cell infiltration (yellow arrow). (C) Many bright round-like structures (red arrow) in the dilated follicular infundibulum, corresponding to DF, and inflammatory cell infiltration (yellow arrow).

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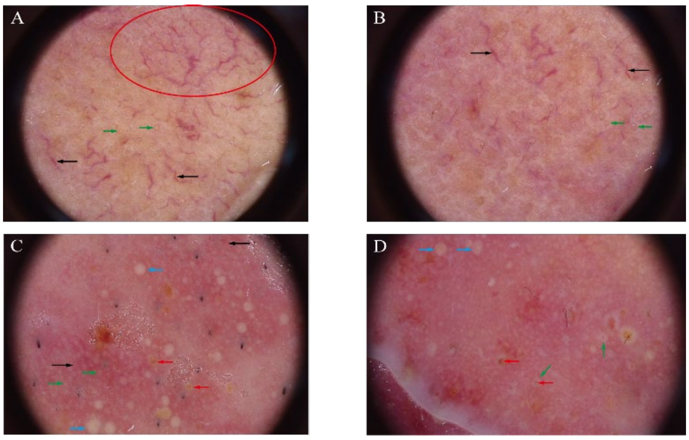

Figure 3: (A-D) Facial dermoscopic features. (A) The right cheek revealed a reddish background with numerous polygonal vessels (red circle), linear vessels (black arrows), perifollicular yellow halos (green arrows), and scattered white scales. (B) The glabella revealed a red background, linear vessels (black arrows), and perifollicular yellow halos (green arrows). (C) The left jaw revealed red diffuse structureless areas, numerous punctate vessels (black arrows), yellow-white homogeneous pustules (blue arrows), diffuse perifollicular white halos (green arrows), and follicular keratotic plugs (red arrows). (D) The nose revealed red diffuse structureless areas, linear or reticular vascular shadows, yellow-white pustules (blue arrows), perifollicular white halos (green arrows), and follicular keratotic plugs (red arrows).

3. Discussion

As a facial inflammatory dermatosis, rosacea mainly occurs in young and middle-aged women, with a global prevalence rate of approximately 5.46%[1,6]. In 2002, the National Rosacea Society's Expert Committee categorized rosacea as four subtypes: erythematotelangiectatic rosacea (ETR), papulopustular rosacea (PPR), phymatous rosacea (PHR), and ocular rosacea. However, because different subtypes can coexist or transform into each other and recent studies suggest that evaluating rosacea based on clinical phenotypes may improve the accuracy of diagnosis and treatment, the classification criteria for rosacea have gradually changed from subtype-based to phenotype-based[1,2]. This case is a middle-aged man with erythema, telangiectasia, papules, pustules, and phymatous changes that could not be classified into any of the traditional subtypes, further demonstrating the necessity of this phenotype-based classification criterion.

The pathogenesis of rosacea remains uncertain, but it is currently thought to be associated with genetics, microorganisms, neurovascular dysfunction, immune dysfunction, and disrupted skin barrier[1,2]. DF is a common symbiotic saprophytic mite that parasitizes hair follicles in human skin. Studies have shown that DF can aggravate neurogenic inflammation mediated by the activation of TRPV1-NGF-TRKA pathway in rosacea lesions, and that Demodex mites and Demodex-associated bacterial proteins may activate certain innate and adaptive immune responses involved in the pathogenesis of rosacea[3,4,7]. DF colonization also occurs in normal skin, but Demodex infection is typically defined as Demodex density of 5 mites/cm² or higher[3,5]. As a non-invasive and reusable imaging tool that provides real-time images at nearly cellular histologic resolution, RCM can objectively and precisely detect and quantify DF in vivo[8]. A meta-analysis conducted by Chang et al.[5] found that the prevalence and degree of Demodex mite infestation were significantly higher in rosacea patients than in healthy controls and patients with other facial dermatoses. The average density of Demodex mites was 71.0 mites/cm² (range: 1.9-376.8 mites/cm²) in rosacea patients and 8.7 mites/cm² (range: 0.06-89.6 mites/cm²) in healthy controls. The average number of DF in this patient was 40 within an area of 4 mm², and the Demodex density was significantly higher than the highest value previously reported. In addition to ultra-high-density DF colonization, the patient's condition improved significantly after the addition of anti-mite therapy, indicating that the patient's rosacea was closely related to DF and might be induced by DF.

The diagnosis of rosacea is mainly based on dermatologist's subjective identification of medical history and clinical features, but its clinical manifestations are similar to facial inflammatory dermatoses such as acne and seborrheic dermatitis. As new non-invasive techniques, RCM and dermoscopy can assist in the diagnosis of skin lesions by providing real-time and in vivo examination[8]. Studies have reported that RCM examination of rosacea reveals spongiform edema, Demodex colonization in the follicular infundibulum, dilated capillaries and venules in the dermis, quickened blood flow velocity, and increased vascular density[8,9]. The dermoscopic features of ETR are mainly vascular changes, which are red background and vascular polygons. Compared with ETR, PPR has milder vascular changes and more follicular abnormalities, mainly manifested as vascular polygons or linear vessels, pustules, follicular keratotic plugs, pigmented structures, and yellow scales. PHR mainly manifests as orange diffuse structureless areas, white halos around hair follicles, and branched vessels[10,11]. These imaging features play a great guiding role in the diagnosis of rosacea.

The clinical manifestations, RCM and dermoscopic features of this patient were consistent with rosacea, but the Demodex density of up to 40 mites/4 mm² is rare in rosacea. More particularly, the perifollicular keratinocytes were arranged in multilayered concentric circles, resembling onion skin-liked structure. Thus, the RCM manifestations of this rosacea case are very rare in clinical practice and have not been reported in the literature before. The term of concentric structures has mainly appeared in the RCM features of verruca plana. Studies have found that the RCM feature of verruca plana is characterized by rose-like concentric structures that are rarely seen in other dermatoses[12]. The reason for the appearance of this structure in this case is unknown, but it may be related to the long-term extrusion or stimulation caused by the ultra-high-density DF colonization in hair follicles. The dermoscopic manifestations were diverse in different parts of the patient, which was related to the complex and diverse clinical phenotypes.

The patient had poor response to conventional therapy, but his condition was significantly improved after combined anti-mite therapy, indicating that anti-mite therapy was important for this patient. DF played an important role in the pathogenesis of this rosacea case and it might be induced by DF. Dermatologists should be aware of this potential association, actively evaluate DF when available, and add anti-mite therapy if necessary. RCM can non-invasively and accurately detect and quantify DF, evaluate inflammation and vascular changes, and identify some histological changes. Dermoscopy can easily observe the background color, vascular condition, and follicular abnormality[8]. These two imaging techniques can not only assist in the diagnosis of rosacea, but also help to make therapeutic scheme. They are also valuable in efficacy evaluation and have great potential for clinical promotion and application.

References

[1] Gallo R L, Granstein R D, Kang S, et al. Standard classification and pathophysiology of rosacea: The 2017 update by the National Rosacea Society Expert Committee[J]. Journal of the American Academy of Dermatology, 2018, 78(1): 148–155.

[2] van Zuuren E J, Arents B W M, van der Linden M M D, et al. Rosacea: New Concepts in Classification and Treatment [J]. American Journal of Clinical Dermatology, 2021, 22(4): 457–465.

[3] Lacey N, Russell-Hallinan A, Zouboulis C C, et al. Demodex mites modulate sebocyte immune reaction: possible role in the pathogenesis of rosacea[J]. The British Journal of Dermatology, 2018, 179(2): 420–430.

[4] Lee S G, Kim J, Lee Y I, et al. Cutaneous neurogenic inflammation mediated by TRPV1-NGF-TRKA pathway activation in rosacea is exacerbated by the presence of Demodex mites[J]. Journal of the European Academy of Dermatology and Venereology: JEADV, 2023, 37(12): 2589–2600.

[5] Chang Y-S, Huang Y-C. Role of Demodex mite infestation in rosacea: A systematic review and meta-analysis[J]. Journal of the American Academy of Dermatology, 2017, 77(3): 441-447.e6.

[6] Gether L, Overgaard L K, Egeberg A, et al. Incidence and prevalence of rosacea: a systematic review and meta-analysis[J]. The British Journal of Dermatology, 2018, 179(2): 282–289.

[7] McMahon F, Banville N, Bergin D A, et al. Activation of Neutrophils via IP3 Pathway Following Exposure to Demodex-Associated Bacterial Proteins[J]. Inflammation, 2016, 39(1): 425–433.

[8] Logger J G M, de Vries F M C, van Erp P E J, et al. Noninvasive objective skin measurement methods for rosacea assessment: a systematic review[J]. British Journal of Dermatology, 2020, 182(1): 55–66.

[9] Huang Y, He J, Zhang S, et al. A novel multi-layer perceptron model for assessing the diagnostic value of non-invasive imaging instruments for rosacea[J]. PeerJ, 2022, 10: e13917.

[10] Fei W, Han Y, Li A, et al. Summarization and comparison of dermoscopic features on different subtypes of rosacea[J]. Chinese Medical Journal, 2022, 135(12): 1444.

[11] Trave I, Micalizzi C, Gasparini G, et al. Dermoscopy of papulopustular rosacea and comparison of dermoscopic features in patients with or without concomitant Demodex folliculorum[J]. Clinical and Experimental Dermatology, 2021, 46(8): 1434–1440.

[12] Lu Q, Wang S, Wu T, et al. Dermatoscopy and Reflective Confocal Microscopy for Facial Seborrheic Keratosis, Verruca Plana, and Nevus Pigmentosus[J]. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP, 2021, 30(4): 450–454.