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Clinical-pathological Study of Rosacea in a Small Cohort of Saudi Arabia

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Abstract. Although rosacea is a common disease, it is rarely biopsied. There are few reports on the histopathological changes in rosacea in literature, but no attempt has been made in Saudi Arabia, to correlate such changes with clinical findings. In the present study, our aim was to analyze the clinical diversity and histological alteration of rosacea in a small cohort. The study included eight patients with a diagnosis of rosacea. A skin biopsy with 4 mm punch was performed in each case from the clinically involved area. The patients had broad clinical spectrum of lesions ranging from erythematous telangiectatic plaque to rhinophyma. No histological pattern was found to be unique for rosacea. *Demodex* mite infestation, which is considered to be significant in literature, was found not to be a contributing factor. Rosacea demonstrates a wide range of clinical presentation. Elastoid degeneration was an outstanding feature due to the ultraviolet sensitivity of the disease and the fact that our sunrays are potentially damaging all year round.

Keywords: Rosacea, *Demodex* mite, Elastoid degeneration.

Introduction

Rosacea is one of the most enigmatic inflammatory chronic cutaneous disorders, usually affecting fair skinned, middle-aged individuals. It

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involves primarily the convexities of the central face (cheeks, nose chin and central forehead)[1]. For a diagnosis of rosacea, one or more of the following primary features concentrated on the convex areas of the face is required: flushing (transient erythema), non transient erythema, papules and pustules, and telangiectasia. Secondary features include burning or stinging, edematous plaques, a dry appearance, ocular manifestations and phymatous changes[2,3]. In addition to the diversity of clinical manifestations, the precise etiopathogenesis of rosacea remains unknown. Various factors have been suspected of contributing to this condition, which include excessive sun exposure[4], vascular abnormalities[5], *Demodex* mite presence, gastro-intestinal disturbances, emotional stress, chronic, hormonal influences[6], matrix degeneration[7] and pilosebaceous unit abnormality[8]. In order to develop a standard system, in 2002, the National Rosacea Society created a standard classification system[9] and a grading system[1] for rosacea, that can serve as an instrument to investigate the manifestations, for both the clinicians and researchers. Although the diagnosis of rosacea is easily established clinically based on the characteristic morphology, distribution and microscopically by a combination of several histopathologic criteria, the atypical clinical manifestation can be overlooked or misdiagnosed.

The aim of the present study was to analyze the clinical diversity and histologic alterations of rosacea in a small cohort of Saudi Arabia.

Patients and Methods

The retrospective study included eight patients with rosacea from the outpatient clinic of King Khalid University Hospital (KKUH), Riyadh, during a five year period. The patients' ages ranged from 15 years to 65 years (median approximately 45 years). The face was exclusively affected, most commonly involving cheeks and forehead. All patients had a combination of both erythematotelangiectatic and papulopustular types of Rosacea. Only one single male patient had an additional rhinophymatous type. The final diagnosis was based on clinical evaluation and histologic findings. A skin biopsy with a 4 mm punch was performed in each case from the clinically involved area. All biopsy specimens included the subcutaneous tissue. The specimens were routinely processed and stained with Hematoxylin and Eosin, Verhoeff-Van Gieson stain, Giemsa stain and periodic acid-Schiff stains. Multiple sections on every biopsy specimen (15 serial sections on average) were

examined under light microscopy. The selected histological criteria were evaluated semi-quantitatively from grade 0-3 into absent, mild, moderate and severe. Parameters like granuloma, epidermal atrophy, and necrotic keratinocytes were recorded as either absent or present.

As *Demodex* mite is normally present in hair follicle in healthy individuals without any skin lesion. The presence of at least three parasites in the hair follicle or keratin layer as significantly positive for mite was considered. Elastoid degeneration in the dermis was characterized by curling and fragmentation of elastic fibers, forming mass of degenerated fibers throughout the dermis.

Results

Clinical Data

The present study consisted of 8 patients (5 males and 3 females, one of them pregnant) and the age range was between 15-65 years.

The lesions predominated on the cheeks (5 cases), forehead (4 cases) while periorbital and perioral regions were involved in 1 case. Ocular rosacea was reported in one patient who had blepharitis. Flushing affecting the malar region was a common complaint among all patients. Six patients complained of itching, while scaling and coexistent seborrheic dermatitis was noted in five patients. Differential diagnosis included seborrheic dermatitis; 5 cases, systemic lupus; 1 case, *Polymorphus* light eruption; 1 case and lupus miliaris disseminatus faciei; 1 case. ANA was done and was negative in patients suspected to have connective tissue disease.

Histological Data

The epidermis showed mild spongiosis in seven (87.5%) cases lymphocytic exocytosis in five cases and epidermal atrophy with loss of rete ridges in three cases. Necrotic keratinocyte and *Demodex* mite was detected in the keratin layer and within hair follicle in only one case.

In the dermis, the most prominent and consistent finding was the presence of mixed lymphocytes and neutrophils (67.5%) or mononuclear (32.5%) inflammatory cell infiltrating predominantly in the perivascular area. One case showed severe perifollicular pattern with a predominance of lymphocytes with occasional neutrophils and plasma cells in a

perifollicular array in the dermis and subcutis (Fig. A and B). Elastoid degeneration was present in 6 (75%) cases varying from moderate to severe in 83% cases and mild to absent in the rest. Another striking feature was the presence of irregularly dilated vascular channels seen in 87.5% cases. Dermal edema was an inconsistent finding, being present in only half of the cases. Non-specific epitheloid granuloma consisting of aggregate of epitheloid histiocytes, lymphocytes and giant cell surrounding destroyed follicle was noticed in one case only.

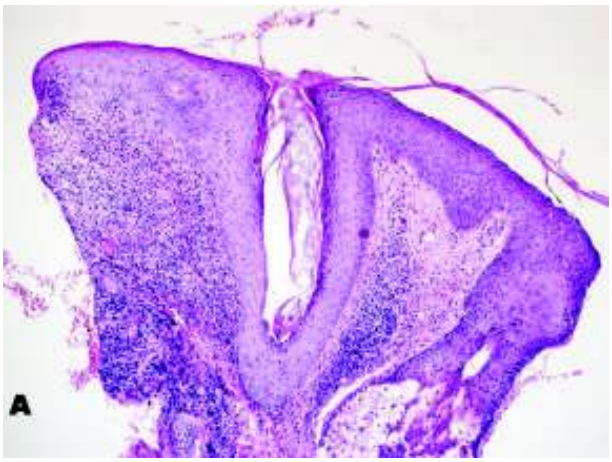

Fig. A. **A dense polymorphous inflammatory infiltrate is present in the dermis with overlying epidermal spongiosis and parakeratosis (Hematoxylin and Eosin x 100).**

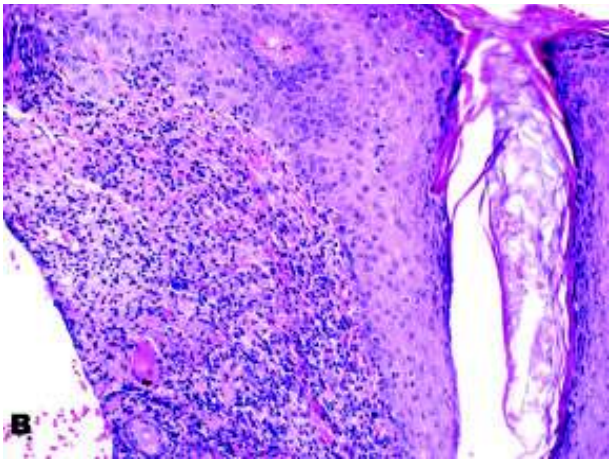

Fig. B. **An intense perifollicular inflammatory infiltrate is comprised of lymphocytes, histiocytes and eosinophils (Hematoxylin and Eosin x 200).**

Discussion

Six out of eight patients in our study were between 30-60 years of age which confirms the literature data that rosacea is a disease of middle age[10,11]. It is observed that women are affected more commonly then males in the early stage of disease, however males progress to the advanced stage more often than females[11]. In this study, males out-numbered females and the lesion was in advanced stage. All patients had combined persistent erythematous telangiectatic and papulopustular subtypes. Only one patient had Rhinophyma, *i.e.,* hyperplasia of nasal sebaceous glands and connective tissue. Rhinophyma is seen almost exclusively in males over 40 years of age[10]. All the lesions were located on face and sun exposure was important exacerbating feature, seen in almost all the cases. This in accordance with others authors[12-14] who reported disease exacerbation and worsening of symptoms by sunlight. This advocates the pathogenetic role of solar radiation in the development and progression of rosacea in a way that ultraviolet radiation in susceptible individuals may cause distortion of collagen structure; alter lymphatic and blood vessel function by damaging the dermal support network of elastic and collagen fibers[15]. Other exacerbating factors, also quoted by many authors previously[12] included heat, stress, spicy foods and excessive sweating. The presence of scaling and itching was the most common presenting symptoms, seen in 87.5% of the cases. The co-existent 'Seborrheic Dermatitis' was observed in 62.5% cases. The combination of rosacea and seborrheic dermatitis was also reported in 23% patients by Aroni *et al.* in 2004[16].

Our histologic findings did not differ from the one reported in the literature[16]. In this study, moderate to severe solar elastosis was the consistent finding, in accordance with the fact that sunlight is the most frequent reported aggravating factor[4,12,16]. Moderate to severe inflammation, either mixed or mononuclear was seen in the dermis in 62.5% cases. Vascular dilatation accompanied by perivasular inflammation was observed in all the cases. However, the significant infestation of *Demodex* mite along with granuloma formation was seen in only one case of pregnant female. In seven out of eight cases, there was little or absent local inflammation around the appendages. Only one case that presented clinically with rhinophyma showed severe inflammation around appendages. As supported previously by some authors[13,16,17], as well as in this study, no statistically significant relationship was seen

between the presence of *Demodex* mite, histological perifolliculitis or granuloma formation. Thus, whether *Demodex* is truly pathogenic or simply an inhabitant of follicles in rosacea prone skin remains the subject of future study.

The analysis of our data indicates that there is no histopathological pattern unique to rosacea supporting this to have a multi-factorial origin. The most prominent and consistent histologic finding was the solar elastosis and sunlight was the most frequently reported aggravating factor. However, many aspects of rosacea require further investigation and additional future studies to elucidate the role of certain factors in the exact pathogenesis of the disease, which in turn will aid in the development of specific therapy to treat rosacea patient more effectively.

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دراسة الروابط السريرية النسيجية لمرضى الوردية في مجموعة صغيرة من المملكة العربية السعودية

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المستخلص . تعتبر الوردية من أكثر الأمراض التي يتم علاجها من قبل أطباء الجلد، وحيث إن المرض يمكن تشخيصه سريريًا، فمن النادر أن تؤخذ خزعات لمعاينتها نسيجيًا. كما ولوحظ وجود دراسات قليلة متركزة على التغيرات النسيجية لمرضى الوردية ومثل هذه الدراسات شبه منعدمة في المملكة العربية السعودية حسب درايتنا.

كان الهدف من هذه الدراسة تحليل مظاهر المرض والتغيرات النسيجية المرافقة في مجموعة من المرضى.

تضمنت الدراسة ٨ حالات من مرضى الوردية، وفي كل حالة تم أخذ عينة بقياس ٤ ملم من المناطق المتأثرة بالمرض. لقد تنوعت المظاهر السريرية في مرضى الوردية واشتملت على الحمراء، وتورم الأنف ونموه، مع عدم وجود نمط نسيجي متفرد بمرض الوردية. كما لم يتبين أهمية عث ديمودكس كعامل مساعد في ظهور المرض، كما هو معروف. قد تبين من تحليل بيانات هذه الدراسة عدم وجود نمط نسيجي فريد لتشخيص مرض الوردية، مما يدعم تعدد أسبابه. وقد لوحظ تحلل شديد في ألياف الايلاستين بفعل الطاقة الشمسية. وقد كان هذا التحلل من أبرز علامات هذا المرض في مجموعة الدراسة. يعتبر ضوء الشمس من أهم عوامل

تدهور المرض، ولهذا يجب أن تتضمن الخطط العلاجية لهذا المرض الحماية الفائقة من الشمس.