Rosacea: A study of clinical patterns, blood flow, and the role of *Demodex folliculorum*

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Background: Rosacea is a common facial eruption that has various clinical presentations.
Objective: We studied blood flow in lesional skin and explored the role of *Demodex folliculorum* in patients with rosacea.
Methods: A survey of clinical presentations was made in 108 patients with rosacea. Facial blood flow was studied by laser-Doppler flowmetry. The presence of *Demodex* was determined by microscopy of skin samples.
Results: The sex incidence was equal. The incidence peaked in the fourth and seventh decades of life. Lymphedema was common and was seen in 26 patients. Rhinophyma was present in 15 patients, mostly men. Eleven patients were black, an unexpectedly high number. Laser-Doppler flowmetry showed that lesional blood flow was three to four times that of control subjects. *Demodex folliculorum* was found in 20 of 25 rosacea patients examined but in only 2 of 20 control subjects.
Conclusion: The findings indicate that the papillary dermal vasculature is dilated in rosacea. *Demodex* may be present. These findings give no definitive clue as to the origin of the disease.
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The differentiation of rosacea from acne vulgaris is credited to Unna (cited in Marks[1]) but little is known about the origin of the former. Its increased prevalence in lighter-skinned races and the histologic findings of elastotic degeneration suggest a role for solar irradiation,[2] but this does not seem to be the entire explanation. The occurrence of rosacea-like lesions in carcinoid syndrome[3] and the presence of elevated substance P levels in some patients with rosacea[4] raise the possibility that inflammatory mediators may be involved in the pathogenesis of the disease. Histologic examination shows dilatation of small dermal blood vessels with thickened walls,[5] although there is debate whether the cutaneous blood flow is increased.[5, 6]

The development of rosacea is often but not invariably multiphasic. It frequently starts with flushing and proceeds to erythema and telangiectasia, to papules and pustules, and finally, in a small proportion of patients, to rhinophyma.[7] A lymphedematous variant of rosacea is said to occur only occasionally.[1] Rosacea usually responds to therapy with tetracycline but shows a relapse rate of 69% in 2 years.[8] When patients are assessed 10 years after onset, more than half still have evidence of disease.[9] Lymphedema, keratitis, and rhinophyma are bad prognostic signs.[9] The mite, *Demodex folliculorum,* has been demonstrated in increased numbers in the hair follicles of patients with papular and pustular rosacea,[10] but the significance of this is uncertain as a histologic study demonstrated the mite in only 19% of skin biopsy specimens.[11]

In this study we examined the clinical presentation of rosacea in a large group of patients, particularly with regard to their age, sex, and race and their response to treatment. In addition, we studied blood flow and the presence of *D. folliculorum* in rosaceous skin.

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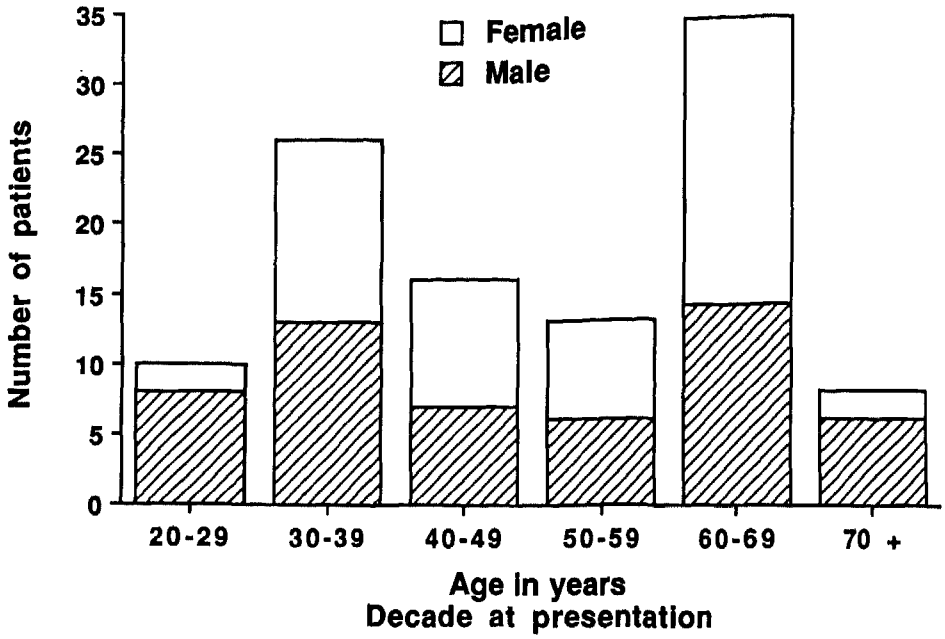

Fig. 1. Sex and age at presentation for 108 patients with rosacea.

MATERIAL AND METHODS

During an 18-month period, 108 patients were diagnosed as having rosacea. Ninety-three of these were personally interviewed by one of us (S. S.); details of the remaining 15 were obtained from notes. Data regarding age at presentation, sex, race, symptoms, signs, associated conditions, treatment, and response to therapy were obtained.

An assessment of the blood flow in affected facial skin was made with laser-Doppler flowmetry in 25 patients with rosacea and in equivalent areas in 15 age-, sex-, and race-matched normal control subjects. A PeriFlux Pf2B laser-Doppler machine (Perimed, Stockholm, Sweden) was used, with a filter setting of 4 K Hz and a gain of ×3. Measurements were done under identical conditions of temperature and humidity and recorded graphically for later analysis.

The presence of *D. folliculorum* was assessed in 25 patients with rosacea and in 20 age-, and sex-matched control subjects. *D. folliculorum* was looked for in eyelashes, in sebum, and in the follicular keratin plug. Three eyelashes were plucked from the lower eyelid with mosquito forceps and examined with a microscope after being placed on a microscope slide and mounted with glycerine. Sebum was expressed from a rosaceous area (usually the side of the nose), smeared onto a microscope slide, and examined. A follicular keratin plug was dislodged from an area of rosacea, mounted in 40% potassium hydroxide solution, and examined as already described.

Ethical approval for the aforementioned studies were obtained from the Ethical Committee of the Royal Hallamshire Hospital, Sheffield.

RESULTS

Presentation

The age of presentation ranged from 21 to 87 years and showed a bimodal distribution with peaks in the fourth and seventh decades (Fig. 1). The sex incidence was equal with 55 men and 53 women. However, there was a predominance of women with rosacea in the fourth, fifth, and sixth decades, whereas at the opposite ends, men predominated (i.e., in the less than 30-year age group, 8 of 10 were men and in the 70-year age group, more than 6 of 8 were men). The occurrence of rosacea at the extremes of age was associated with the use of potent topical corticosteroids on the face.

The most common sign of rosacea was erythema, seen in 105 of the 108 patients. Papules and pustules were found in 90 and 72 patients, respectively, and telangiectasia was recorded in 54. Flushing was present in 45 patients. Lymphedema occurred in 26, two thirds of whom were men. The lymphedema affected the forehead and eyelids in several patients. Fourteen of the 15 patients with rhinophyma were men.

Bilateral cheek involvement was the most common presentation and was present in 89 patients.

The entire face was involved in three patients. Unilateral disease was seen in eight patients. Disseminated rosacea was found in six patients, who had lesions on the arms, shins, and trunk. A bald scalp was involved in four subjects. Ocular complaints were recorded in 38 patients.

The most frequently reported exacerbating factors were heat or the sun (cited by 34 patients), the use of topical corticosteroids (cited by 32), alcohol (in five) and, in women, an oral contraceptive, pregnancy, or menstruation (cited by 13). Fifty-eight subjects gave a history of migraine and six had a family history of rosacea. Nine patients had both rosacea and seborrheic dermatitis.

The skin type and racial background were assessed in 80 patients. Thirty-nine had skin types I or II and 11 had skin type VI (blacks).

Treatment

Most patients had already received some treatment before referral. In their initial consultation at our clinic tetracycline was prescribed in 79 cases, erythromycin in 16 cases, metronidazole in three, and isotretinoin and trimethoprim-sulfamethoxazole in two instances each. The most common topical therapy was 1% clindamycin solution, prescribed in 14 patients. Tetracyclines improved rosacea in 69 of 79 patients; erythromycin was of benefit in 9 of 16, and topical clindamycin was effective in 8 of 14 cases.

Twenty-one of the 26 patients with lymphedematous rosacea showed some response to treatment with tetracycline, although many had relapses if therapy was discontinued.

Laser-Doppler flowmetry

Affected facial skin in 25 patients with rosacea showed a mean percent flux value that ranged from 10 to 25 units (mean 18.52, median 20) compared with a range of 3 to 6 units (mean 4.13, median 4) for equivalent facial areas in 15 control subjects.

Studies on *D. folliculorum*

Twenty of the 25 patients with rosacea examined were infested with *D. folliculorum* compared with only 2 of the 20 control subjects. Men and women were equally represented. Changes in the infested rosacea patients were scaly erythematous-telangiectatic (14), papulopustular (5), and lymphedematous (1). The five rosacea patients who were not infested had the nonscaly, erythematous-telangiectatic variant. The two controls who had *Demodex* were lightly infested (one or two mites each). Sebum contained more *Demodex* mites than keratin, which had more than the eyelashes.

DISCUSSION

The peak decades for age at presentation in our study were the fourth and seventh as compared with the fourth and fifth decades reported in other series.[12, 13] Our finding of an equal sex incidence but with a majority of women around the menopausal years agrees with the observation of Sobye.[12] This suggests a possible hormonal influence on the disease, supported by our finding of the deleterious effect of oral contraceptives and pregnancy on rosacea. Men were in the majority at the extremes of life and their rosacea may have been induced by topical corticosteroids.[14] Certain presentations have a male bias; for example, two thirds of the 26 patients with lymphedema and all but one of the 15 with rhinophyma were men. In our series, extrafacial (peripheral) rosacea was more common than expected but always occurred with facial disease and was mainly seen on the limbs.[15, 16] As expected,[1] patients with fair skin (type I or II) were the most commonly affected group, but our study confirms a recent report that rosacea is not as uncommon in blacks as was previously supposed.[17]

Tetracyclines remain the treatment of choice in rosacea, and, in common with other authors,[8, 9, 18] we found them to be effective in the majority of patients (87%). We observed tetracycline to have some effect even in the lymphedematous type, the most difficult of the variants to treat.[1] Only one of our patients received topical 0.75% metronidazole (with benefit), although since that experience we have had success with this preparation and are able to confirm its efficacy.[19]

The laser-Doppler flowmetry demonstrated that the total movement of red blood cells in the flush areas of rosaceous skin was increased three- to fivefold in comparison with normal control subjects. Previous studies have shown conflicting results: some have demonstrated an increase,[6] whereas others have found a decrease.[5] The most likely explanation of the increased laser-Doppler flow is dilatation and engorgement of the papillary dermal vessels. The possibility of increased vascularity cannot be excluded although histologic studies have found no evidence of a proliferation of dermal blood vessels.[5] Dilatation of the dermal blood vessels may result from damage

to the supportive connective tissue of the papillary dermis.[20] However, the recent finding of increased substance P levels in rosacea patients raises the possibility that circulating vasodilator substances have an effect. Our finding that half our patients suffered from migraine provides some evidence that these patients have a vasculature prone to vasodilatation. The association with migraine confirms previous observations.[13, 21]

D. folliculorum was present in 20 of 25 of our rosacea patients, including those with the scaly erythematous telangiectatic, papulopustular, and lymphedematous variants, but not the nonscaly erythematous-telangiectatic type. Despite the finding of the mite in a minority of skin biopsy specimens from rosacea,[11, 22] other authors have found *Demodex* to be increased in rosacea, particularly of the papulopustular type.[10] Whether the mite has a part in initiating rosacea or simply finds the lesions of rosacea a convenient home is still uncertain. However, it is possible that the *Demodex* mite can stimulate an inflammatory reaction that ultimately results in connective tissue damage and telangiectasia.[20]

The rarity of rosacea in the young, its occurrence in sun-exposed sites, and the frequency in the fair-skinned person suggest that solar-induced degeneration of connective tissue is important in its origin. The flushing, association with migraine, histologic vasodilatation, and increased skin blood flow indicate vascular reactivity. The presence of *Demodex* and granulomatous histologic characteristics point to an immunologic phenomenon, possibly as a secondary event.

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