Rosacea: 244 Tunisian cases

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LA TUNISIE MEDICALE - 2010 ; Vol 88 (n°08) : 597 - 601

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RÉSUMÉ

Prérequis: La rosacée est une dermatose faciale chronique fréquente, d'étiologie mal comprise, de stades différents et de pronostic variable. Il existe peu d'études épidémiologiques nord-africaine et en particulier tunisiennes qui se sont intéressées à cette affection.

But : Déterminer le profil épidémio-clinique, histologique, les modalités thérapeutiques et l'évolution de la rosacée en Tunisie.

Méthodes: Une étude rétrospective de tous les cas de rosacée collectés au service de dermatologie de l'hôpital Charles Nicolle de Tunis a été conduite entre Janvier 1990 et Mai 2003.

Résultats: 244 patients ont été inclus. Le diagnostic a été retenu sur des critères cliniques dans 185 cas et histologiques dans 59 cas. La prévalence était de 0.2%. Le sex ratio H/F était de 0,4. L'âge moyen des patients était de 49 ans. Les facteurs déclenchant le plus souvent cités étaient: l'exposition solaire (64%) et la chaleur (25%). La durée moyenne entre le début des symptômes et la première consultation était de 20 mois. La répartition des patients selon les stades était: érythémato-télangiectasique (12%), papulo-pustuleuse (69%), et rhinophyma (3.7%). La rosacée granulomateuse a été diagnostiquée chez 8 patients et la rosacée stéroïdienne dans 28 cas. La rosacée oculaire a été observée dans 41 cas. Les modalités thérapeutiques incluaient: traitement topique (1.6%), systémique (85%), systémique et topique (5%) et chirurgical (1.2%).

Conclusions: La rosacée est une dermatose fréquente en Tunisie ou la majorité de la population sont de phénotype IV-V. Elle affecte le plus souvent les femmes d'âge moyen. La plupart de nos malades présentaient une rosacée au stade papulo-pustuleux (69%). Des études épidémio-cliniques nord-affricaines supplémentaires sont nécessaires pour étayer nos résultats.

Mots-clés
Face,c dermatose, épidémiologie

SUMMARY

Background: Rosacea is a common, chronic facial dermatosis of uncertain etiology, several well-defined types and variable progression. There is a paucity of epidemiologic studies from North African countries especially in Tunisia.

Aim: to determine epidemiological, clinical, histological features, treatment and outcome of rosacea in a Tunisian study.

Methods: A retrospective study of all rosacea cases diagnosed in the outpatient Dermatology Department of Charles Nicolle hospital of Tunis was conducted between 1990, January and 2003, May.

Results: Our study included 244 patients. The diagnosis of rosacea was made on symptoms and clinical features in 185 cases and on histological findings in 59 patients. The hospital prevalence of rosacea was 0.2%. The sex ratio M/F was 0,4. Patient's Mean age was of 49 years. Triggered factors mentioned included most often: sun exposure (64%) and thermal stimuli (25%). Mean duration between the onset of symptoms and the first consultation was about 20 months. The rosacea subtypes were: erythematotelangiectatic type (12%), papulopustular rosacea (69%), and rhinophyma (3.7%). Granulomatous rosacea was diagnosed in 8 patients and steroid rosacea in 28 cases. Ocular rosacea was observed in 41 cases. Treatment modalities included: topical treatment (1.6%), systemic treatment (85%), systemic and topical treatment (5%) and surgical procedures (1.2%).

Conclusions: Rosacea seems to be a frequent dermatosis in Tunisia where most of the population is phenotype IV-V. It affects mostly middle-aged women. Most of our patients present with papulo-pustular rosacea (69%). More epidemiological and clinical studies in North African countries should be conducted to emphasize these results.

Key-words
Face, dermatosis, epidemiology

Rosacea is a common, chronic facial dermatosis of uncertain aetiology and variable progression. Several well-defined types of rosacea are described including erythematotelangiectatic rosacea, papulopustular rosacea, phymatous rosacea and ocular rosacea. There is a paucity of epidemiologic studies, especially in North African countries (1). The purpose of this study was to determine epidemiological, clinical, histological features, treatment and outcome of rosacea in a Tunisian study.

PATIENTS AND METHODS

A retrospective study of all rosacea cases diagnosed in the outpatient Dermatology Department of Charles Nicolle hospital of Tunis was conducted between 1990, January and 2003, May (13 years and five months). The diagnosis of rosacea was made on symptoms and clinical features in 185 cases. A skin biopsy was made in 59 patients with atypical clinical presentation and led to the diagnosis. Six patients were excluded after new histological examination of skin biopsies.

For each patient, we look for: sex, age, country area, phototype, co-morbidities, symptoms (itching, flushing), precipitating factors (solar exposition, drugs, and thermal stimuli), localizations of lesions, clinical stage, ocular involvement, treatment modalities, response to treatment and complications dealing with rosacea or treatment.

RESULTS

Our study included 244 patients. The hospital prevalence of rosacea was 0.2%. Sixty nine men and 175 women were enrolled in the study (sex ratio H/F 0.4). This female preponderance (71%) was noted both overall and for each of the 10-year age-group strata (Fig.1). Patient's Mean age was of 49 years [extremes: 21 and 85 years]. The mean age was 51.4 years in men and 48 years in women. Both sexes reached peak prevalence with the 41-50-year age group (Fig.1). Patients were originated from the north of the country in 86% of cases, from the center in 7% of cases and from the south in 7% of cases. Review of photographs of 29 patients allows us to know approximately the phenotype: 27 patients had brown skin, dark eyes and black hairs, 2 patients had clear skin and eyes and blonds hairs.

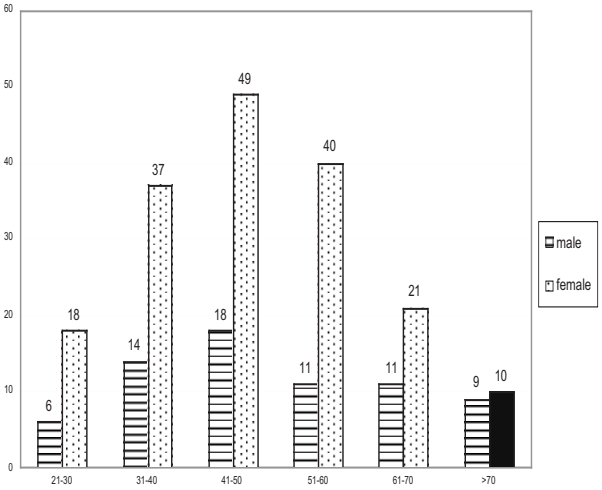
Co-morbidities were recorded in 54 patients: diabetes (13 patients), hypertension (10 cases), gastritis and duodenal ulcer (5 cases), heart failure (4 cases), inflammatory bowel disease (2 cases), chronic renal failure (3 cases), rheumatoid arthritis (3 cases), thrombocytopenia (2 cases), herpes zoster (2 cases), dysthyroidy (2 cases) and others (14 cases). Eleven patients have received systemic corticosteroids when rosacea begun.

Sixty patients were asked which factors trigger skin changes according to them. They mentioned most often: sun exposure (64%) and thermal stimuli (25%).

Mean duration between the onset of symptoms and the first consultation was obtained in 207 cases and was about 20 months [extremes: 3 days and 20 years].

The most common sign of rosacea was erythema, seen in 199 patients (81.5%). Flushing was present in 32 patients (13.1%) and itching in 45 cases (18.4%). Cutaneous manifestations affected: cheeks (148 cases), forehead (57 cases), chin (32 cases), perioral region (11 patients) and upper eyelid (3 cases). Unilateral lesions were found in 28 patients. Extrafacial lesions were seen in 7 patients: upper chest (4 cases), ears (2 cases), forearms (2 cases) and hands (1 case).

Figure 1 : Distribution of patients according to age and sex



The rosacea subtypes were: erythematotelangiectatic type (12%), papulopustular rosacea (69%), and rhinophyma (3.7%). All patients with rhinophyma were men.

Granulomatous rosacea was diagnosed based on clinical and histological findings in 8 patients. Twenty eight cases of steroid rosacea were recorded during the period of the study. In 23 cases, corticosteroids were an aggravating factor of a preexisting rosacea and in 5 cases they induced rosacea. All patients with steroid rosacea were women.

Ocular rosacea was observed in 41 cases. They included 33 women and 8 men with a mean age of 48.5 years. Unilateral ocular involvement was seen in 5 cases. Thirty three patients had conjunctivitis. Blepharitis was diagnosed in 3 patients, keratitis in 1 patient, irritated eyes in 3 patients and watery eyes in 1 patient. Only eleven patients were referred to ophthalmologist.

Histological examination of 59 skin biopsy-specimens of patients with rosacea was performed. Epidermal changes were: hyperplasia (5 cases), atrophy (6 cases), spongiosis and exocytosis (10 cases). Telangiectasias were rarely present in 5 cases, moderately distributed in 39 cases and markedly distributed in 5 cases. Edema of the papillary and reticular dermis was observed in 18 cases. Actinic elastosis in the dermis was moderate in 31 cases and important in 4 cases. Biopsy revealed an infiltrate of the dermis mainly consisting in lymphocytes and histiocytes in 39 cases (66%), neutrophils in 2 cases (3%), epithelioid cells in 17 cases (29%) and plasmocytes in 15 cases (23%). This infiltrate was diffuse in 30 skin biopsies

(50.5%), perifollicular in 20 cases (34%) and perivascular in 8 cases. The inflammatory infiltrate was in the upper dermis in 12 patients (20%), upper and middle dermis in 33 patients (56%) and in all dermis in 13 cases (22%). Demodex folliculorum was isolated in 10 cases (17%). Hyperplasia of sebaceous glands was observed in 8 cases. Lymphangiectasis was seen in 2 skin biopsies. A fibrosis of the dermis without inflammatory infiltrate was observed in a case of rhinophyma. According to the clinical and anatomopathologic findings, we classified those 59 cases of rosacea as: erythematotelangiectatic type (8 cases), papulopustular type (39 cases), rhinophyma (4 cases) and granulomatous rosacea (8 cases).

Treatment modalities included: topical treatment: 4 cases, systemic treatment: 208 cases, systemic and topical treatment: 12 cases and surgical procedures: 3 cases. Systemic therapy is summarized in Table I. Mean duration of treatment was of 45 days. Clinical evolution of lesions is summarized in Table II. Eighty eight patients were lost to follow-up. A clinical improvement was obtained in 88% of patients. A recurrence was noted in 46 cases after low dose treatment or off treatment. During the period of follow-up, one patient with rhinophyma developed three lesions with basal cell carcinoma on the nose.

DISCUSSION

Our study showed that: (i) rosacea seems to be a frequent dermatosis in Tunisia where most of the population is phenotype IV-V, (ii) it affects mostly middle-aged women (sex ratio 0.4), (iii) most of our patients presented with papulopustular rosacea subtype (69%), (iiii), cyclines and oral metronidazole were the most used treatment modalities with a good result.

In fact, rosacea represents 0.2% of dermatological outpatient cases in our study. In a prospective Tunisian study of 28.244 patients attending a number of public or private dermatological outpatient clinics in Tunis from June 1999 to July 2000, rosacea represents 0.3% of all skin disorders (1). Epidemiological data on North African populations are scanty. In the world, it affects 10% of the population (2). Its prevalence is 2.2% of all skin diseases in a cohort of 48.665 employees in Germany (3). An estimated 13 million Americans are affected by the disease (4). The disease equally affects both genders but men with rosacea are more prone to the development of thickening and distorting phymatous skin changes (5). In our study, a female preponderance (71%) is noted. A female preponderance is also noted in the United States and in Sweden (6, 7). This apparently female predominance is probably related to the greater medical request from women because of the esthetic damage.

In the United States, the mean age of patients with rosacea was of 50 years (6). The mean age of our patients was of 49 years (51.4 years for men and 48 years for women). Both sexes reach peak prevalence with the 41-50-year age group and prevalence decreases thereafter (Fig.1). Patients with rosacea are younger in our study. This is probably due to genetic predisposition and ultraviolet radiation damage in our sunny weather.

Rosacea can occur in all racial and ethnic groups, although fair skinned persons of Celtic and northern European origins are thought to be particularly prone to the disorder (7). The disease

Tableau 1 : Systemic treatment modalities according to rosacea subtype.

	Rosacea subtype					
Treatment	**Erythemato-telangiectatic**	**Papulo-pustular**	**rhinophyma**	**Granulomatous**	**steroid**	**Total**
Metronidazole	7	74	1	2	9	93
Doxycyclins	3	13	0	2	4	22
Tetracyclins	10	37	3	1	5	56
Metronidazole and cyclins	2	27	2	2	3	36
Erythromycin	0	1	0	0	0	1
Total	22	152	6	7	21	208

Tableau 2 : Efficacy of treatment according to rosacea subtype

Rosacea subtype	**Total improvement**	**Partial improvement**	**No improvement**	**Total**	**Percentage**
Erythemato-telangiectatic	3	8	2	13	8,3%
Papulopustular	15	82	14	111	71,2%
Phymatous rosacea	0	3	1	4	2,5%
Granulmatous rosacea	0	6	1	7	4,5%
Steroid	4	16	1	21	13,5%
Total	22	115	19	156	100%

is rather uncommon in persons with dark skin (8). In our study, the patient's skin phototype are not mentioned. But, when we reviewed photos of 29 patients, 27 of them had brown skin. So it seems that rosacea predominates in high phototype in our report.

Rosacea affects approximately 2% (south Europe) to 10% (northern Europe) of different white populations worldwide (7). Our study showed that in contrast to the other African countries, especially black Africans, rosacea is a frequent dermatosis in Tunisia. Unfortunately, epidemiological studies on other North African populations are not available.

The cause of rosacea remains unknown. Proposed etiological mechanisms can be grouped into the following categories: vasculature, climatic exposures, matrix degeneration, chemicals and ingested agents, pilosebaceous unit abnormalities, and microbial organisms.

The association between rosacea and migraine has been first reported by Cunliffe in 1976 (9). In Sweden, 27% of patients in the rosacea group were found to suffer from migraine compared with 13% in the control group ($p<0.001$) (7). In our retrospective study, patients were not asked whether they had migraine or not. An association between rosacea and gastrointestinal disease such as gastritis and duodenal ulcer (10), an increased prevalence of Helicobacter pylori infection in patients with rosacea and dermatological improvement in patients treated with antibiotics for this infection lead some authors to consider rosacea as one of the extragastric symptoms of Helicobacter pylori infection (11, 12). In our study, 5 patients suffered from gastritis/duodenal ulcer but we didn't establish a causal relation. Many triggering factors of rosacea are reported in the literature. In the study of Jaworek et al, 69 patients with rosacea were asked which factors triggers skin changes according to them. Patients mentioned most often: stress (58%), sun exposure (56.5%), alcohol (33.3%), exercise (29%), drinking coffee (21.7%) and hot meals (20.3%) (13). In fact, many authors have endorsed the notion that rosacea results from the caustic effects of climatic exposures that damage both cutaneous blood vessels and dermal connective tissue (14, 15). The pivotal role of sunlight is supported by the distribution of erythema and telangiectasias on the facial convexities. In addition, actinic elastosis is prominent in skin biopsy specimens from rosacea patients (16). In contrast, epidemiologic studies demonstrate that only 17% to 31% of rosacea patients report worsening of symptoms by sunlight (7, 17). In our study, 60 patients were asked which factors trigger skin changes according to them. They regarded the sun as the most strongly aggravating factor of rosacea (64%).

The prolonged use of topical steroids may reproduce many of the characteristic signs and symptoms of papulopustular rosacea (18). A regular use of corticosteroids on the face is reported by 11% of our patients. Although not currently reported, 11 patients received systemic corticosteroids in our study before the onset of rosacea. Other medications have been reported to induce rosacea such as amineptin (19), tacrolimus ointment (20) and acetazolamide (21).

Clinically, most of our patients have papulopustular rosacea (69%) with a significant proportion of ocular rosacea (18%). In our study, ocular rosacea is probably misdiagnosed because of the lack of specialized examination. In the literature, it occurred in 3% to 58% of patients with rosacea (22-24).

Granulomatous rosacea is characterized by periorificial yellow, brown, or red monomorphic papules or nodules that can lead to scarring (25). Eight cases of granulomatous rosacea (3.3%) have been described in our study, which emphasizes the rarity of the disease.

There are few reports of the histological changes in rosacea. A recent study of 73 patients with rosacea attempts to correlate such changes with clinical findings. Histological examination showed that there is no histological pattern unique to rosacea (26). In a study of 108 biopsy specimens, Marks et al. found hair follicle abnormalities in only 20% of the 74 papules or papulopustules subjected to biopsy (27). In addition, perifollicular inflammatory infiltrates are found in only 51% of these specimens. Ramelet et al. find that the all 75 specimens contained perivascular infiltrates, while only 13 (17%) were judged to be predominantly periadnexial (28). While in our study, the infiltrate was diffuse in 30 cases (50.5%), perifollicular in 20 cases (34%) and perivascular in 8 cases (13,5%). It is, also, documented that rhinophyma is characterized by sebaceous hyperplasia, fibrosis, follicular plugging, and telangiectasia. In the present study, sebaceous hyperplasia is observed in 8 patients (4 patients had rhinophyma). Ramelet et al., noted that telangiectasias are observed in all cases (28) and in our patients they are observed in 83% of cases. A recent study is conducted to evaluate microvessel density and total vascular area in clinically involved and uninvolved skin with rosacea. An important statistical correlation is found between high vascular density, papulopustular rosacea, disease duration, granuloma formation in the dermis and the presence of ocular manifestations (29).

Actinic elastosis is noted in all the cases in the study of Ramelet et al. (16) and in 59% of our cases. This is probably related to the fact that our patients had pigmented skin. Several studies suggest that the simple identification of Demodex is by no means proof of pathogenesis. It is the density of mites significantly higher in patients with rosacea or their extrafollicular location (30, 31). In our study, these mites were observed in only 17% of our patients.

Metronidazole 0.75% lotion, cream, and gel and 1.0% metronidazole cream and gel are all efficient treatments. Combination treatment with oral antibiotics is also efficient. Maintenance treatment with topical metronidazole decreases relapses and allows for longer intervals between flares (32).

In this study, cyclines and oral metronidazole are the most prescribed treatments with a good response and a good tolerance for the two treatments. The mainstay of therapy is surgical correction as in our three patients. Careful follow-up is mandatory as basal cell carcinoma may be associated with rhinophyma.

Laser reported studies on rosacea-associated telangiectasia and erythema are limited. The most commonly applied system is the flash lamp-pumped pulsed dye laser. Rhinophyma can be treated with CO2 lasers (33). We recommend using more these procedures in the future.

CONCLUSION

Rosacea is a common condition characterized by transient or persistent central facial erythema, visible blood vessels, and often papules and pustules. Many aspects of rosacea require further investigation. The contribution of a genetic predisposition to sun damage, responses to other climatic conditions, and flushing responses should be studied. Epidemiologic data can contribute to these investigations. It is our hope that this manuscript will stimulate some of these efforts.

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