

**CRAIOVA MEDICAL AND PHARMACEUTICAL
UNIVERSITY**

DOCTORAL THESIS

SUMMARY

**WHAT'S NEW IN DIAGNOSIS AND
TREATMENT OF CHRONIC AND
HYPERTROPHIC ACNEE**

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CRAIOVA – 2013

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A. GENERAL PART

INTRODUCTION

Rhinophyma is representing the stage IV of rosaceous evolution, determining a major unaesthetic aspect at face level, the nose becoming deformed with a caricatured aspect, with an enlarged volume, with protuberances, the individual having a monstrous aspect of the face. The rhinophyma is an affection with a low frequency that is specific to males.

The disease begins within 50 years old, on a predisposing ground, preexistent rosacea acne, possibly with juvenile acne history.

The rhinophyma incidence is bigger in western countries, in American continent where almost 13 million people are diagnosed with rosacea acne in early stages.

Behind this affection a great influence has the ethnic character. It is a rarity between African populations but is more prevalent between Indian populations.

In Romania, because of low frequency and natural history, the majority of patients are presenting themselves because of unaesthetic aspect and not for functional disorders.

Through time, there were incriminated more factors like steroids hormones excess (androgens) [1,2], presence of Demodex parasite folliculorum [1], vitamins deficiency (vitamins from B group) [3]. From clinical point of view, the nose of affected patients, usually men, appears erythematous, with an increased volume, with dilated pits and telangiectasias. Recurrent papules and pustules are frequently presented. In severe forms were observed also erythematous nodules.

Were reported cases of rhinophyma evolution to malignization (squamous carcinoma).

CHAPTER I

NASAL PYRAMID ANATOMY

The nasal pyramid or the external nose are part of nasal formations that are composing the first segment of superior breathing airways and has a triangular form .

It has in its structure an *anterior edge* – behind the nose- that begins from nasal base, from the point named nasion to the top of the nose and which separate the two lateral faces of nasal pyramid that are expanding to the nasogenien and nasopalpebral groove building the other two edges of nasal pyramid. The third angle of nasal pyramid is profound and continues itself with nasal pits. The base of nasal pyramid is crossed by the two narinas.

To the nasal pyramid is described a cutaneous external surface, a mucosal-cutaneous internal

surface that is continuing the respiratory mucosa of nasal pits, and between these two surfaces are external to internal disposed the others plans of the region: sub-cutaneous fatty conjunctive tissue; muscular plan; the oseto- cartilaginous skeleton.

The inferior part of anteorlaterals faces is mobile and forms nose's wings. From the top of the nose to posterior part a cutaneous line begins, the nasal septum together with the free margins of nose's wing is bounding the two apertures – narinas-. The most lateral parts of narinas are creating the alar points.

The skin, thin and mobile in the superior part, is becoming thick and confluent in the inferior part of the region. It is highly vascularised presenting a lot of sebaceous glands at this level, that area of the nose being the one that suffers the rhinophyma modifications. In its superior area it breaks itself easily and in the inferior part is stick to underlying fibro- cartilaginous plan from this level.

The conjunctive-fatty subcutaneous tissue is weakly represented finding himself especially in the superior part of the region and lacking at nose's wings and top of the nose level.

The muscular plan is build of four skin-like muscles that are not representing any modification in the context of a hypertrophic chronic acne. The four skin-like muscles are: procerus muscle (pyramidal of the nose), nasal muscle (m. nasalis); - the elevating muscle of the superior lip and nose's wing (m. levator labii superioris et alaeque nasi); the septum depressor muscle (m.mirtiformis).

Osteo- cartilaginous frame

The nose is sustained by an osteo-cartilaginous frame. The bonny area of this frame is composed by frontal processes of cheek bones, by appropriate nasal bones, anterior nasal spine and palatines process of cheek that are including the piriform aperture. The skeleton of inferior part of the nose is cartilaginous being composed by lateral nasal cartilages (cartilago nasi lateralis) and alar cartilages (cartilago alaris major). The remained space between these cartilages is rounded by a fibrous membrane in which bigness can be found a variable number of cartilaginous nodules: accessories nasal cartilages; minor alar cartilages (cartilagine alares minores) situated behind the big ones and closer of the nasogenien channel, vomerian cartilages; sesamoidal cartilages situated between lateral cartilages and the big alar cartilages. In the nasal septum's thickness it is found the septal cartilage of the nose (cartilago septi nasi) [4].

The osteo-cartilaginous frame is kept totally in the case of hypertrophic chronic acne.

The arteries of nasal region are represented by dorsal artery of the nose (artera dorsalis nasi) that represents the terminal branch of ophthalmic artery which at its turn is terminal branch of internal carotid artery.

The angular artery terminal branch of facial artery or external maxillary is originating from the place where the artery is going superficially beyond the square muscle of the superior lip and nasal muscle and it is directing to medial angle of the eye.

CHAPTER II

MICROSCOPICAL STRUCTURE OF SKIN

The epidermis is a tissue that is finding itself in a permanent change, renewal, it presents in the squamous epithelium which the main cells are represented by keratinocytes. Through this are found other cellular elements with different origin from the keratinocytes developed in mature epidermis, the melanocytes or pigment formation cells which had their origins in the neural apex, Langerhans cells which is an immune-competent cell that has its origins at bone marrow level and lymphocytes. The epidermis is split in five layers from profound to superficial so: -basic layer-; spiky layer or polyedric cells; grained layer (Unna's); lucidum layer; horny layer.

The dermis or the corion is a conjunctive structure where are blood vessels and lymphatic ones are located, the nerves and nervous terminations but also cutaneous appurtenances: hair, sebaceous and perspiratory gland. Structural a superficial derma or papillary exists, represented by dermic papilla and conjunctive tissue located under dermic and profound or even reticular dermis that comes in report with the hypo-dermis.

The Hypo-dermis or subcutaneous cellular tissue is formed from lax conjunctive tissue or areolar, were, often, are found adipose panniculus separated by conjunctive septum. These septums are accompanying the nervous and vascular branches and, on other half, it adheres to muscular fascias or periost.

The pilo-sebaceous apparatus is bud from the hair spring and by pilous follicle that has as appurtenances a sebaceous gland and an erector muscle.

The sebaceous glands, holocrine type, are, altogether, attached to hair springs situated in the angle from these and erector muscle. Sebaceous glands hairless are located al gland's lips level, penis foreskin and minor labia.

Ovoid or piriform shape, they are simple alveolar type or rarely branched. Formed from a secretory part, doubled by a conjunctive sheath and by a duct that opens itself at hair spring level. The glandular epithelium advance peripheric with active nucleus and rare lipid inclusions and big central cells with picnotic nucleus with clear vacuolar cytoplasm hard loaded with fat. The excretory channel is formed by cells disposed on one or two lines.

The sebum is the result of central cells disintegration, their secretion being of holocrine type.

The perspiratory glands that arise from the epidermis through some sprouts which are developing themselves in the stable and underlying hypoderm. The perspiratory glands are

tubuloglomerular type formed by a secretory component similar to glomerula and from an excretory channel more or less sinuous which opens itself at the surface of tegument, circulating through an inter-epidermic apex which stands between two dermic papilla.

CHAPTER III

ACNEE ROSACEA AND RHINOPHYMA

Definition

The acne rosacea is a chronic inflammatory disease that affects the convex zones of the face characterized by flushing, persistent, telangiectasias, unexpected inflammatory episodes where the edema, the papules and the vesicles are highlighted.

The acne rosacea is an illness more frequently founded to persons with white skin kelts [6], type I-II Fitzpatrick compared with the ones with dark skin, the Mediterranean, but, even so, the disease can appear also at personas with type IV-V Fitzpatrick.[7,8]

The pathogeny of rosacea acne is not know totally, but were identified a large number of agents with a major contribution, without absolutely proving the prevalence of some of them: infectious agents, exposure to UV radiation and to climatic conditions, thermal radiation, pharmacological agents, alimentary and a long chain of immunologic agents that seem to have a bigger contribution.

RHINOPHYMA

Definition and history

The rhinophyma is a mutating affection of the nose, it is considered to be the most severe manifestation of the final stage of rosacea acne, being characterized by a non-painful hyperplasia and progressive of sebaceous glands and conjunctive tissue of the nose. This augmentation of grotesque aspect is usually limited to the inferior 2/3 of the nose.[9]

The name came from the Greek words "Rhis" meaning nose and "phyma" meaning increase.

The diagnosis is not a difficult one, the injuries being visible from the beginning phase of the illness. Usually, the patient presents in a late evolutive stage, only in the moment when the esthetic aspects begin to be serious and when respiratory problems appear. The positive diagnosis of Rhinophyma can be done on the anamnesis and clinical exam, without supplementary clinical investigations. In inconclusive cases, the reliability diagnosis is assured by the hystopathological exam after the biopsy of the tegument.

Being a chronically disease with an insidious start and a long term evolution, initially it appears with a light and progressive congestion of nasal lobe, the hypertrophy and the apparition of telangiectasias. Afterwards the sebaceous gland's porosity begins to distend the nasal lobe tegument having an orange skin aspect.

In state period the nose lobe tegument hypertrophies itself considerably taking a poli-lobe aspect, cauliflower-like of blue-red color with much expanded sebaceous gland porosity.

The local clinical exam highlights an increased nose, with red erythematous teguments, with tumoral zones of variable dimension, that originate on nasal tegument, without extension of the tumor inside nasal cavity. The narinas can be blocked by a large volume of tumoral formations that can dive on narinas orifices. [10]

B. PERSONAL PART

CHAPTER IV

STUDY OBJECTIVES

In the present work I wanted to effectuate:

1. A retrospective clinical-statistical study regarding the stage IV of acnee rosacea, that highlights the next aspects of the affection: - establishing the incidence on a seven years period with sex distribution, origins, age groups; -evaluating the modifying risk factors; determining the evolutive particularities and prognostic of Rhinophyma and apparitions of some eventual neoplasias at nasal pyramid tegument level modified by rhinophyma; the specification of the surgical intervention's early character to obtain favorable and esthetic results of a better quality.

2. A histological study on excised parts of the biologic material from patients with Rhinophyma in order to highlight: - modification of sebaceous glands; - modification of pilo-sebaceous follicles; modification of dermal vessels; the presence of perifollicular inflammatory process; with the purpose to split in four characteristic types: glandular form; fibrous form; - fibro-angiomatos form; actinic form.

3. Regarding the treatment I assigned a special attention because the technical progress came up with a lot of news in surgical resolution. Regarding the aesthetic aspect that the nose has for the beauty of the face, the surgical techniques appointed a faster recuperation and the absence of scars, appreciating the narinas trough limiting the hypertrophic modification of nasal tegument to the snot,

but by the gigantic dimensions of sebaceous glands were affected also the breath and also the alimentation of patients, an additional argument to assign a bigger attention for maintain the narinas border.

CHAPTER V

CLINICAL AND STATISTICAL STUDY OF RHINOPHYMA

DURING 2006-2012

The clinico-statistical study I've conducted was a retrospective epidemiological study conducted in an interval of 7 years, respectively between 2006-2012, having studied all cases of Rhinophyma admitted to the Emergency County Hospital Craiova to E.N.T. Clinic and Clinic of Plastic Surgery .

The distribution of the 51 cases of Rhinophyma by age, revealed that this condition was met by people aged between 35 and 84 years. By the age of 55, Rhinophyma is rare (2 cases in total) accounting about 4%.

After the age of 55 years the number of cases increased significantly, Rhinophyma recorded the following situation: between 55 and 64 years there have been 6 cases, accounting for 11.76 %, between 65 and 74 years were recorded 28 cases, representing 55 %, between 75 and 84 years, 15 patients, representing 29.24 % .

Regarding the distribution of Rhinophyma after gender, in the clinical and statistical study conducted, the doctoral student noted that there is a significant difference between the cases occurred in males and females. Thus revealed that Rhinophyma occurred with overwhelming frequency in males (94 % - 48 cases) and rarely in females (6% - 3 cases) . Increased incidence of the disease in men is attributed to their influence on androgen.

From the total of the patients, most patients went to the doctor for this condition, in the range of 6-8 years from the first signs of the disease - 16 patients, followed by a total of 12 patients who went between 9-11 years , and 10 patients within 3-5 years, 6 patients in the range 12 to 14 years , 5 patients were submitted after 15 years, the fewest in number, 2 went in the first two years. Based on clinical observations, patients were divided in: Rhinophyma classic form, the nose was enlarged, with prominent pilosebaceous orifices, but with the profile still kept, 15 patients representing 29% and severe form that included 36 patients (71%) with a significant distortion of the nose .

Of the 51 patients, 19 patients (37%) abused of alcohol, 23 (45%) drank occasionally , and 9 (18%) did not consume at all.

CHAPTER VI

The treatment of Rhinophyma

The patients diagnosed by clinical and laboratory tests with Rhinophyma received surgery. The types of surgery have been applied to patients admitted to the E.N.T. Clinic and Plastic Surgery Clinic of Emergency County Hospital Craiova, were both classic and dermabrasion intervention, depending on the size and the degree of Rhinophyma, the patient's social and intellectual status.

Both classical surgery and dermabrasion were performed under general anesthesia with oro-tracheal intubation.

The surgery consisted in the classic excision of Rhinophyma and the coverage of the tegumentary defect with free split or full thickness skin.

Decortication was performed by the cleavage space, starting from the top area between the skin and pericondrum, respecting the pericondrum's integrity. At the bottom husking was performed using dissecting scissors for the strong adhesion between skin and alar cartilages large and small. This cartilage damage can lead to further deformation of the nose.

After excision, intraoperative appearance is given by the pericondrum discovered entirely with a pearly white look, being able to view and septum. If the nostrils are moving apart from each other, we apply a transnasal wire through the nostrils to close them together and keep them close to the septum.

To cover the remaining tegumentary defect, depending on the size of the Rhinophyma, was used either full thickness skin graft harvested from the retroauricular region, or free split skin graft from the internal face of the arm.

Next the skin was applied to the defect, tailored to the size of the defect, wire sutures left long. Over the graft was applied a compress in a single layer and wet, then added 3-4 layers of a folded compress, to the area between the alars large and small, were sometimes added chopped compresses moistened with saline. On top of these were added 2-3 dry compresses and the long wires were tied over the compresses to achieve a slightly compressive dressing and not modify any position, preventing the sliding of the graft on the recipient bed.

CHAPTER VII

Histological aspects in Rhinophyma

The studied pieces were from 24 patients that were hospitalized in the Clinic of Plastic Surgery and E.N.T. Clinic of Emergency County Hospital Craiova after the surgical removal.

The biological material, respectively the fragments of the tumor tissue from the nasal pyramid, were processed by conventional histological techniques for inclusion in paraffin, technique that allowed us to carry out serial sections of 3- 5 μ thickness that can be stained and studied optimal with the optical microscope. Staining used was Hematoxylin-Eosin.

After studying the histopathological findings I divided the patients in the common and severe form of the disease.

Common form of the disease

Histopathological results show a normal thick epidermis with dilated acroinfundibuli. The superficial and middle dermis revealed a large number of piriform sebaceous lobules connected to the widely dilated infundibulum. There were observed infundibular cysts filled with cornified cells. Surrounding stroma was edematous, rich in fibrocystic cells with sources of inflammatory infiltrate composed by lymphocytes and plasma cells. In some specimens the inflammatory infiltrate was rich, characteristic of a suppurative folliculitis, either granulomatous or both. In the superficial dermis was observed the dilation of the capillaries, venules and the lymphatic vessels. Moderate fibrosis was observed in the superficial dermis and the level of cross-emphasizing perifollicular. Solar elastosis was unsteady present. In the superficial dermis elastic fibers were reduced.

Severe form of disease

Histopathological results showed a thinned epidermis, devoided of the Rete ridges network with just a few easy dilated acroinfundibuli, significantly thickened dermis with severe reduction or absence of pilosebacei follicles, occasional infundibular cysts. For each patient, depending on the specimens examined, there were areas in which the stroma was intense fibrosis with irregularly arranged collagen bundles and areas where the stroma was edematous with large amounts of mucin. Between collagen bundles highlighted an increased number of spindle cells with irregular, hyperchromatic nuclei with large pleomorphism. Multinucleated cells were identified, some of which had multilobate cores. Most cells had insufficient and poorly defined cytoplasm. Mast cells were present in large numbers. In the deep dermis capillaries, venules and lymphatics were dilated. Inflammatory infiltrate composed of lymphohystocyte cells was insufficient. The elastic fiber network was destroyed.

CHAPTER VIII

DISCUSSIONS AND CONCLUSIONS

Corroborating the results of the three studies, the following clinical and histological correlations were established.

This study showed that the condition affects mainly the males - 94% of the data consistent with the literature, showed that male/female ratio of Rhinophyma between is 12/1 and 30/1 [11]. The increased incidence of the disease in men is attributed to their influence on androgen.

Regarding distribution by age, the highest incidence was in the age range 65-74 years -55% of cases, according to the literature.

According to our study the clinical form associated with the disease duration, disease is more severe as the disease duration is longer. Other authors have shown that there is no correlation between the clinical presentation and disease duration [12].

In our study, dermabrasion is used in small lesions in the common form, especially. In severe forms was practiced shelling and free split skin plasty. According to other authors, when the lesion is large, classical surgical excision is required [11]. Dissection must comply the nasal perichondrium cartilage in order to avoid the risk of chondrolisis [13].

The main complication that can occur is the chondrolisis of nasal cartilage, to avoid this complication stop using electric scalpel and electrocoagulation wich could compromise perichondral vascularization[14].

My study shows that histopathological changes on Rhinophyma are different and correlate with the clinical picture of the disease. Histologically the classical type of the disease shows predominance sebaceous hyperplasia with asymmetric, dilated infundibulum with occasional cysts, telangiectasias in the superficial dermis and perifollicular infiltrate composed of lymphocytes, histiocytes and plasma cells. In Rhinophyma severe histopathological changes observed many similarities to those seen in elephantiasis, caused by chronic lymphedema. Our results confirm the literature [15].

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