ACNE VULGARIS

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Summary

Acne vulgaris causes much emotional trauma, social embarrassment and cosmetic disfiguration in teenage girls and boys. The multifactorial etiology, pathogenesis and clinical features of this condition are narrated. The mechanism of comedo formation is briefly discussed. Recent concepts in the management of this chronic malady are critically reviewed.

KEY WORDS : Acne Vulgaris, Comedo Formation, Acneiform Eruption, Therapeutic Measures.

Acne vulgaris is a universal blemish of adolescence and is one of the most common dermatologic problems. As a matter of fact, it has been mentioned that no individual makes the transit through adolescence without a few comedones and pustules[1]. Despite various modalities of treatment available, acne continues to be an incurable disease. However, the condition can be controlled to a large extent till remission occurs spontaneously. The amount of emotional trauma, social embarrassment and cosmetic disfiguration caused by acne in teenage girls and boys is enormous. During the past few years, several new developments have taken place in the treatment and in understanding of etiopathogenesis of acne. This topic has been reviewed extensively in several excellent papers and commentaries in the western literature. As far as ascertained, no comprehensive review appeared on this subject in recent Indian literature and hence, we felt it necessary to highlight the important aspects of this problem.

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Received for publication on 9—9—1982

Etiology

Although the basic etiology of acne vulgaris is not exactly known, several interesting considerations that may play a role in the causation of acne have been proposed. The role of heredity in acne has been considered by Hamilton et al[2]. It is difficult to deny the importance of genetic factors in determining the susceptibility of an individual to acne, since the condition is seen to affect several members in the family in many instances. Androgens are mentioned to play an important role in the production of acne[3]. It has been postulated that di-hydrotestosterone, which is a very potent androgen, can mediate changes in the thickness and composition of keratin, permeability of pilosebaceous epithelium and production as well as composition of sebum[4]. There is evidence that human skin contains specific androgen receptors, some of which are

believed to be located in the sebaceous glands. In predisposed young persons, a temporary increase in local di-hydrotestosterone formation occurs due to increase in 5-alpha reductase activity and this has been blamed to produce acne[6]. Not only the adrenal but also the gonadal androgens take part in the stimulation of sebaceous gland activity. Estrogens possess an inhibitory effect on the sebaceous gland, probably by suppressing the androgen synthesis[6]. The "sebotropic" pituitary hormone has not yet been demonstrated in human beings and its exact significance is not clear.

Pochi and Strauss[7] observed excessive sebum production in acne patients and this is more in several cases. Free fatty acids (FFA) and squalene which are normal constituents of sebum have been shown to induce comedo formation in animal experiments[8,9]. Plewig et al[10] described that a sudden change in the intrafollicular concentration of FFA could cause irritation of follicular epithelium resulting in rapid production of cells, which leads to the formation of a microcomedo. However, it may be important to note that the role of FFA in the pathogenesis of acne has been recently questioned[11]. No striking differences were observed in the viscosity of sebum in acne cases and normal controls[12]. Morello et al[13] found a significant decrease in the sebum levels of linoleic acid of acne patients. Since the deficiency of essential fatty acids can give rise to hyperkeratosis, it has been suggested that linoleic acid deficiency may play an important role in the pathogenesis of acne.

The major part of the microbial flora of a sebaceous follicle is formed by *Propionibacteria*, *Micrococcaceae* and *Pityrosporon*, of which the predominant are the *Propionibacteria*. The group *Propionibacteria* have been divided into 3 types, *P. acnes*, *P. granulosum* and *P. avidum*[14]. Significantly higher number of *P. acnes* were found in acne lesions, although they may occur in normal follicles also[15]. Many strains of *P. acnes* and *S. epidermidis* have been observed to hydrolyse triglycerides into free fatty acids through lipase production. In addition to lipases, *Propionibacteria* have been shown to produce other enzymes such as proteases, lecithinases and hyaluronidases[16]. These enzymes are thought to be important in the pathogenesis of acne but their exact role has not been explained. Puhvel et al[17] found an increased immediate hypersensitivity reaction to *P. acnes* antigen in acne cases. In nodulo-cystic acne, increased serum antibody levels to *P. acnes* have been demonstrated. Massey et al[18] stated that local presence of *P. acnes* could lead to local activation of alternate complement pathway with local generation of C3b leading to chemotaxis and local release of lysozomal enzymes. Complement activation has also been implicated in causation of acne by Dahl et al[19]. However, the above findings do not substantiate the rarity of acne before puberty and their regression after certain age.

Kenyon[20] noted that emotional disturbances may result in a significant aggravation of acne lesions and in fact, an increase in FFA levels has been observed during the periods of emotional stress[21]. Some dietary factors like chocolates, nuts, fried foods, tomatoes, cola drinks and shellfish have been presumed to cause an exacerbation of acne[22] but it is pertinent to note, that the studies of Anderson[23] could not substantiate this belief. Premenstrual flare of acne has been observed by Williams and Cunliffe[24]. Contact with mineral oils, pomades and topical corticosteroids may cause aggravation of acne[25]. It may be important to note that some

drugs like iodides, bromides, lithium, INH, corticosteroids, chloralhydrate, thiouracil and even tetracycline have been noted to produce acne-like lesions (acneiform eruptions[26]).

Pathogenesis

Acne rarely develops in certain regions of the body suggesting that, there may be limiting forces possibly related to androgen receptors, critical mass of sebum or bacteria, pore-size of the follicle, surface temperature, sebum viscosity, biochemical composition of sebum or any other unknown factor[27]. All follicles do not develop acne and those containing terminal hairs are particularly immune. Commonly, acne occurs in sebaceous follicles present on the face, chest and back. These follicles have a deep and cavernous infundibular canal, a tiny hair and large sebaceous glands. The infundibular part, which extends from the follicular orifice above to the entrance of the sebaceous duct below, is divided into two parts. The terminal one-fifths (acroinfundibulum) is continuous with the epidermis and keratinizes in the same fashion with a sturdy horny layer. The lower four-fifths (infrainfundibulum) produces only a thin and imperfect horny layer, whose cells slough sooner or later. The initial lesion of acne (comedo) begins in the infra – infundibulum[1],[27]. Kligman[1] studied the mechanism of comedo formation in detail. Two important events have been observed to occur during this process :– (1) A decrease in the dehiscence of horny cells that stick together tightly and form a solid mass which steadily expands. Numerous keratinosomes present in the normal infundibulum of a follicle, show a marked reduction in number during comedo formation. This has been blamed to be responsible for the decrease in the lysis of intercellular cementing substance and poor dehiscence of horny cells (2) Hyperproliferation of the follicular epithelium. When the horny cells stick together, they form an impacted mass that distends the lumen of the follicle forming a microcomedo. When it grows to a size of 1 mm, the microcomedo becomes visible as a closed comedo. With the expansion of horny mass, the lining epithelium becomes thinned out due to pressure. Comedones undergo one of the two fates. They may rupture and incite an inflammatory reaction or they transform into open comedones. Later, the horny mass protrudes through the orifice in the open comedone and the tip darkens due to melanin deposition with gradual thickening[28]. The shrunken sebaceous glands continue to secrete sebum throughout the life of a comedo that streams to the surface through tortuous bacteria-filled channels inside the comedo[1].

Clinical Features

The primary site of acne is the face and to a lesser extent the back and shoulders. The lesions may be either inflammatory or non-inflammatory and the latter may be either open (black-heads) or closed comedones (white-heads). The open comedones are seen as flat or slightly raised papules with a central follicular impaction of black keratin and lipid. The closed comedones are, however, difficult to visualize. Comedones are the primary lesions of acne[29]. The inflammatory lesions vary from small papules with an erythematous areola to indolent pustules and large tender fluctuant nodules and cysts. All these lesions show an inflammatory infiltrate in the dermis histologically and their clinical appearance depends upon the size and location of the infiltrate. The scars in acne are irregular in shape.

The diagnosis is based on the mode of onset, distribution and appearance of the clinical lesions. Sudden or late onset and an unusual distribution may

be due to the acneiform eruption induced by drugs or exogenous acneigenic agents. Like-wise, acne has to be differentiated from rosacea, perioral dermatitis, certain tuberculids, Pityrosporon folliculitis and adenoma sebaceum[30].

Treatment

The assessment of therapeutic efficacy of various medications used in the treatment of acne is a difficult task. There is a great fluctuation in the natural course of acne and the response to placebo therapy is considerable[30]. An explantion of the disease process to the patient makes the therapy more useful and meaningful. The patient must be informed that a careful and continued attention to the treatment which may run to longer period at times, helps in reducing the severity of lesions and excessive scarring. The internal consumption and external contact with acneigenic agents must be avoided. The patient should be instructed not to scratch or squeeze the lesions and to avoid undue local heat in the from of steaming and hot fomentations, as this could result in excessive vasodilation. Keeping the face dry by frequent washings with a soap, preferably medicated, is useful.

Topical Therapy

Judiciously administered topical therapy acts an an adjuvant to systemic agents and produces greater therapeutic improvement. Most of the topical remedies used in acne act as peeling agents by producing dryness and desquamation. These include the conventional sulfur, salicylic acid and resorcinol lotions and the recently introduced retinoic acid and benzoyl peroxide[31].

Retinoic acid (vitamin A acid) is comedolytic[32] and has been shown to reverse the altered pattern keratinization in acne[33]. This is of particular value in comedonal acne[34]. In an electron microscopic study, it has been demonstrated that retinoic acid could result in loosening of an experimentally induced cohesive horny mass and expell it from the follicle within 7 days[35]. Care has to be taken about exposure to sun, as this could produce aggravation of sunburn. The concentration of 0.05% produces the desired effect without undue irritation[36]. Several workers observed good therapeutic results with this drug in acne[37-44]. Topical preparations containing lactic acid/lactate lotion are found to be useful in the management of acne and available in the Indian market as Eclin(R) lotion. Lactic acid is a known antibacterial agent produced by the skin.

Topical benzoyl peroxide is now probably the most common topical remedy used in the treatment of acne in western countries. It is a powerful antibacterial agent and its action is probably related to a decrease in the bacterial flora and an accompanying reduction in the hydrolysis of triglycerides into free fatty acids. Excellent results were obtained with this drug in the treatment of acne[45,46]. The response is better if this agent is used in combination with systemic tetracycline and topical vitamin A acid[47]. Recently, several investigators observed encouraging results with the lotions of topical tetracycline[34], erythromycin[37] and clindamycin[48] in the treatment of acne.

Systemic Therapy

Systemic antibiotics have become the mainstay in the treatment of acne for the last two decades. Oral tetracycline is the most frequently used drug. Although, tetracycline does not alter the sebum production in acne, it has been found to decrease the concentration of free fatty acids, probably by suppressing the number of *P. acnes*[11]. It can also inhibit the neutrophil chemotaxis[49]. In the

beginning, it can be given in the dose of 500 mg to 1000 mg/day and slowly the dose may be reduced depending upon the clinical improvement. Prolonged treatment with oral tetracycline may result in Gram-negative folliculitis in addition to the other known side effects[50]. Oral erythromycin[51], clindaycin[52] and minocycline[53] were also found to be effective in the treatment of acne. It is important to note that, use of systemic antibiotics in smaller doses can lead to increased incidence of resistant strains of bacteria, while full doses can lead to toxicity on prolonged therapy. A combination of sulfa-methoxazole with trimethoprim was observed to be useful in acne by Strauss and Pochi[54]. Dapsone was mentioned to be of particular value in the management of haemorrhagic acne lesions[55].

Estrogens prescribed in the form of oral contraceptives have been found useful in some female cases[27]. However, their side effects must be considered and weighed against their variable beneficial effects[31,56]. The safety of antiandrogens in acne has not yet been established. Cyproterone acetate along with estradiol was found to be effective in a few female acne patients[57].

Oral retinoids (retinoic acid), given in the dose of 2 mg/Kg/day for a period of 4 months, resulted in marked improvement of acne[58]. Oral zinc sulphate has been reported to be useful in acne by several workers[59-62]. Ghorpade et al[63] observed low plasma zinc levels in acne vulgaris and acne lesions following significant improvement of treatment with oral zinc sulphate, 220 mg three times per day for 3 months.

Physical Therapy

The beneficial effect of ultraviolet light in acne results from desquamation[29]. Natural sunlight provides the best source of UV radiation. The reduction in the sebaceous gland size following X-ray therapy is not permanent and acne may recur. Thyroid carcinoma has been reported in acne, following X-ray therapy[64] and hence, this line of treatment is not recommended. Cryotherapy may be given by a local application of precipitated sulfur, powdered dry ice and acetone or by brushing across the skin with a piece of solid carbon dioxide that has been dipped in acetone or alternately by using liquid nitrogen[31]. Intralesional triamcinolone acetonide, 0.05 to 0.25 ml per lesion, may be used in the treatment of severe nodulo-cystic acne. Acne surgery consisting of mechanical removal of comedones and draining of chronic pustules and cysts, helps in the rapid involution of the lesions. Acne scarring can be improved by a properly planned dermo-abrasion or periodic applications of carbon dioxide snow softened to the consistency of a slush with acetone at weekly or fortnightly intervals[30].

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