Brief Overview about ATROPHIC POST ACNE SCARS

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Abstract

Background: Acne vulgaris (AV) is a chronic inflammatory disease affecting the pilosebaceous apparatus. Clinically, it is characterized by two main categories of lesions: non-inflammatory (closed and open comedones) and inflammatory (papules, pustules, nodules, and cysts). Physical and psychological problems are often encountered in acne patients, with post acne scars being the most disfiguring sequelae. Scarring is a consequence of abnormal healing following damage to the sebaceous follicle during acne inflammation. Acne scars are classified into atrophic and hypertrophic types. Atrophic scars are further subdivided into rolling, icepick, and boxcar subtypes. Several modalities are used for these scars, including chemical peeling, dermabrasion, microneedling, platelet-rich plasma (PRP), laser resurfacing, subcision, and punch elevation technique. Atrophic post-acne scars present as depressions secondary to fibrous contractions. They are classified into three types: boxcar, icepick, and rolling scars. Boxcar scars are round to oval depressions with sharply demarcated vertical edges and a flat bottom. Icepick scars are deep and narrow, sharply demarcated tracts that extend to the deep dermis. Rolling scars are wide, shallow, or deep depressions with gently sloped edges. Acne scar treatment has traditionally used a variety of techniques, and innovative modalities are always being developed to achieve the best outcomes.

Keywords: Interleukin 17; Atopic Dermatitis; Mometasone Furoate; Borgasone.

Introduction

Acne vulgaris (AV) is a chronic inflammatory disease affecting the pilosebaceous apparatus. Clinically, it is characterized by two main categories of lesions: non-inflammatory (closed and open comedones) and inflammatory (papules, pustules, nodules, and cysts). Physical and psychological problems are often encountered in acne patients, with post acne scars being the most disfiguring sequelae (**1).**

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Epidemiology

Acne vulgaris is a highly prevalent skin disorder that affects approximately 85% of young people. Puberty is the age at which AV typically manifests; however, neonatal, infantile, and post-adolescent acne are also possible. Females usually experience more severe disease than males. In addition, females are more likely to seek medical advice and have cosmetic concerns than males **(3)**

Up to 95% of AV patients have mild to moderate scarring, whereas 30% have severe scarring. Atrophic scars represent 80-90% of all acne scars, while keloidal or hypertrophic scars represent the remaining 10-20%. The majority of people with cystic acne or post-acne scars have at least one parent with severe acne (**4)**

Pathogenesis of Acne Vulgaris

In AV, the target organ is the pilosebaceous unit. The majority of sebaceous follicles are found on the face (900 glands/cm2), upper chest, and back. These areas are where AV is most likely to be distributed. The pilosebaceous unit consists of the keratinized follicular infundibulum, the hair, the convoluted sebaceous gland, and the sebaceous duct that joins the gland with the infundibulum **(5).**

The pathogenesis of AV is multifactorial, with six major factors involved in its pathogenesis **(6):**

- **A.** Genetic factors.
- **B.** Hormonal factors.
- **C.** Hyperseborrhea.
- **D.** Follicular hyperkeratinization.
- **E.** Bacterial proliferation.
- **F.** Inflammation.

A. Genetic factors

Several genetic factors have been associated with an increased risk of AV and its subsequent scarring. These factors include the alteration of transcription genes encoding pro-inflammatory cytokines and antimicrobial peptides. The aberrant expression of tumor necrosis factor (TNF)-β, ovo-like transcriptional repressor-1 (OVOL-1), follistatin, and transforming growth factor (TGF)-2 genes has been associated with severe cases of acne. These cytokines play a crucial role in tissue inflammation, scarring, androgen metabolism, and keratinocyte differentiation **(6)**.

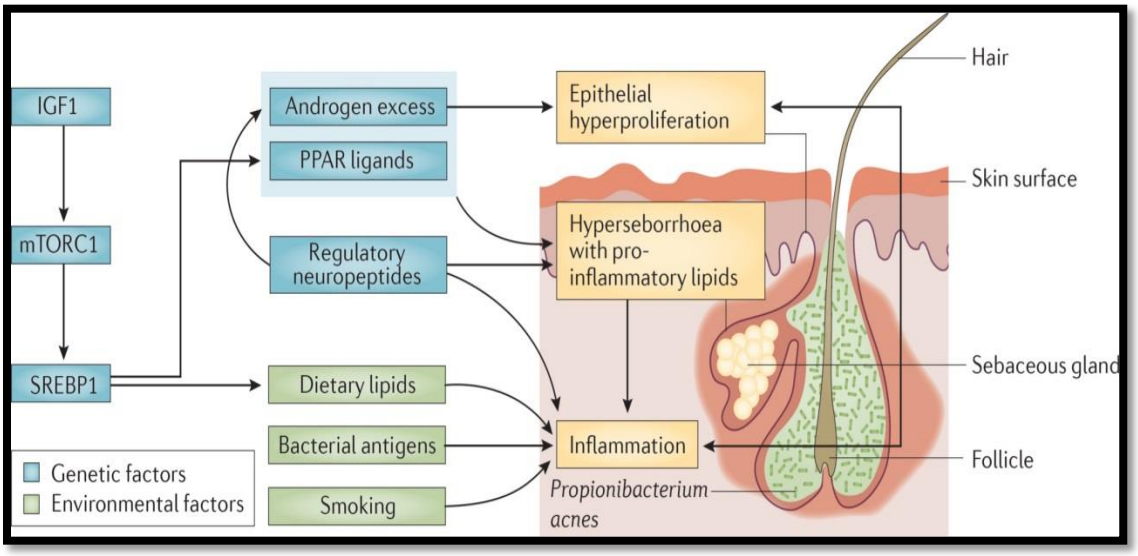

Figure (1): Aspects of acne pathogenesis**.** IGF1, insulin-like growth factor-1; mTORC1, mammalian target of rapamycin complex-1; PPAR, peroxisome proliferator-activated receptor; SREBP1, sterol regulatory element-binding protein-1 **(6)**.

A. Hormonal factors

Acne vulgaris usually develops with the onset of puberty due to increased androgen production by the adrenals and gonads and/or increased sensitivity of androgen receptors. AV patients frequently have higher levels of testosterone, dihydrotestosterone (DHT), and dehydroepiandrosterone-sulfate (DHEA-S) compared to healthy controls **(7).**

Furthermore, compared to uninvolved skin, acne-prone skin usually exhibits a higher density of androgen receptors (ARs) and a higher activity of 5α-reductase that converts testosterone to DHT (**8**). Several skin cell types, including keratinocytes, sebocytes, fibroblasts, endothelial cells, sweat gland cells, and dermal papillae cells, have cytoplasmic ARs **(9).**

Meanwhile, the role of estrogens in AV pathogenesis remains unclear. Although estrogens do not have a direct effect on the activity of sebocytes, they may have an indirect effect by interfering with the androgen control of these cells. Progesterone may inhibit the activity of free androgens in vivo and block ARs. Also, estradiol can lower the level of bioactive androgens by increasing the level of sex hormone-binding globulin **(10).**

B. Hyperseborrhea

In AV patients, hyperseborrhea is caused by increased androgen activation, which stimulates sebocyte proliferation and differentiation as well as lipid synthesis. The proliferation and differentiation of sebocytes are mediated by the inhibition of the Wnt/β-catenin signalling pathway, while lipogenesis is increased by the AR-dependent activation of mTOR **(9).**

In the pilosebaceous gland, triglycerides are hydrolyzed into free fatty acids and glycerol under the effect of lipase produced by Cutibacterium acnes (C. acnes), formerly known as Propionibacterium acnes (P. acnes). Once released into the skin through follicular breakdown, these free fatty acids are cytotoxic and induce inflammation **(11).**

C. Follicular hyperkeratinization

In AV patients, there is increased proliferation and reduced shedding of intrafollicular keratinocytes, causing obstruction of the pilosebaceous unit with retention of secretions leading to the formation of comedones**.** This abnormality may result from high androgen levels, altered sebum composition, and increased levels of the pro-inflammatory cytokine interleukin (IL)-1 **(9).**

A. Bacterial proliferation

There is a marked increase in C. acnes colonization during puberty, which correlates with the maturation of sebaceous glands. C. acnes may disrupt follicular keratinocyte differentiation and induce an inflammatory response, leading to the formation of comedones and inflammatory acne lesions, respectively **(12).**

B. Inflammation

Cutibacterium acnes produces proteases, which attenuate the follicular wall and cause inflammation, and chemotactic factors, which initially chemoattract CD4-lymphocytes and then neutrophils and monocytes to acne lesions. Moreover, these bacteria activate toll-like receptor (TLR)-2 on monocytes, leading to stimulation of the innate immune system with subsequent production of pro-inflammatory cytokines, including IL-8, which attracts neutrophils to the pilosebaceous unit **(5).**

Pro-inflammatory cytokines, such as IL-1, IL-8, IL-12, and defensins, are then produced by the recruited inflammatory cells, leading to the formation of inflammatory papules, pustules, and, in severe cases, cysts and nodules **(13).**

C. Other factors

Foods with a high glycaemic index, dairy products, chocolate, and fatty foods have been associated with AV. On the other hand, fatty acids, vegetables, and fruits tend to protect against AV **(14).** Studies have also shown that vitamin D deficiency, high-dose vitamin B6 and vitamin B12 supplements, and whey protein supplements may be associated with acne (**15**).

The role of smoking in acne pathogenesis is controversial. Nicotine in cigarette smoke has been suggested to activate receptors on keratinocytes, inhibiting wound healing and inducing acne. On the other hand, smoking has also been suggested to reduce inflammation and hence protect against inflammatory acne (**16**).

Oxidative biomarkers (e.g., lipid peroxidation final products) have been found to be higher in AV lesions and positively correlated with acne severity. Contrarily, lower levels of antioxidant enzymes (e.g., superoxide dismutase and catalase) have been detected in AV patients (**17**).

Pathogenesis of Post Acne Scars

The infra-infundibular inflammatory process, follicular rupture, and perifollicular abscess formation, which characterize acne lesions, also stimulate the wound healing process, which is one of the most complex biological processes. It involves soluble chemical mediators, extracellular matrix components, parenchymal resident cells such as keratinocytes, fibroblasts, endothelial cells, nerve cells, and infiltrating blood cells such as lymphocytes, monocytes, and neutrophils, collectively known as "immune-inflammatory cells". Wound healing may result in scarring, which may be atrophic or hypertrophic **(18).**

The wound healing process progresses through three stages:

(1) Inflammation: This stage is characterized by vasodilatation. Also, melanogenesis might be triggered. Therefore, this stage is crucial for the development of post-acne erythema and post-inflammatory hyperpigmentation. Additionally, a number of blood cells, including granulocytes, macrophages, neutrophils, lymphocytes, platelets, and fibroblasts, get activated and produce inflammatory mediators that prepare the area for granulation tissue formation (**19**).

(2) Granulation Tissue Formation: In this stage, damaged tissues are repaired and new capillaries are formed. Neutrophils are replaced by monocytes that change into macrophages and release several growth factors, including platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), and TGF-α/β, which stimulate the migration and proliferation of fibroblasts. Production of new collagen by fibroblasts begins approximately 3-5 days after the wound is created. At first, type III collagen is dominant, with a small percentage (20%) of type I collagen. Later, the balance of collagen types shifts in mature scars to be similar to that of unwounded skin, with approximately 80% of type I collagen (**19**).

(3) Matrix Remodeling: In this stage, matrix metalloproteinases (MMPs) and tissue inhibitors of MMPs are produced by fibroblasts and keratinocytes. MMPs are enzymes that break down the extracellular matrix (ECM) and work together to produce a lytic cascade for ECM remodelling. As a result, atrophic or hypertrophic scars can develop when the ratio of MMPs to tissue inhibitors of MMPs is disordered (**20**).

Clinical Features

Atrophic post-acne scars present as depressions secondary to fibrous contractions. They are classified into three types: boxcar, icepick, and rolling scars. Boxcar scars are round to oval depressions with sharply demarcated vertical edges and a flat bottom. Icepick scars are deep and narrow, sharply demarcated tracts that extend to the deep dermis. Rolling scars are wide, shallow, or deep depressions with gently sloped edges. Different scar types are typically seen in the same individual, making differentiation difficult. Furthermore, post-inflammatory erythema (PIE) may exacerbate the appearance of acne scars in individuals with light skin, making PIE treatment a crucial initial component of therapy **(21)**

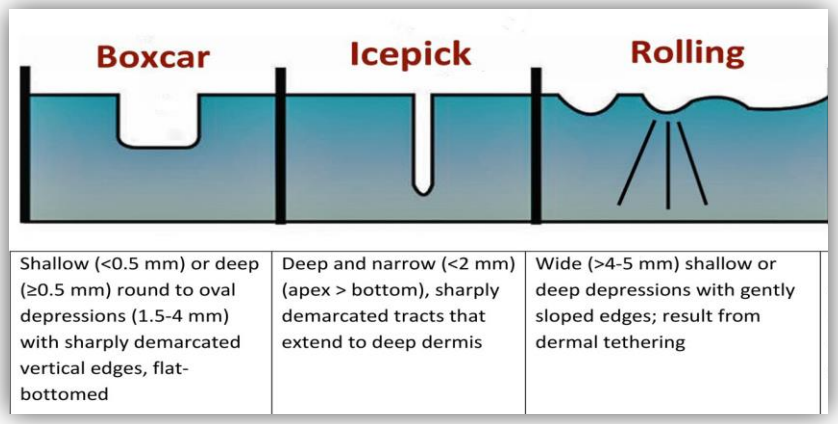

Figure (2): Types of atrophic post-acne scars (**21**).

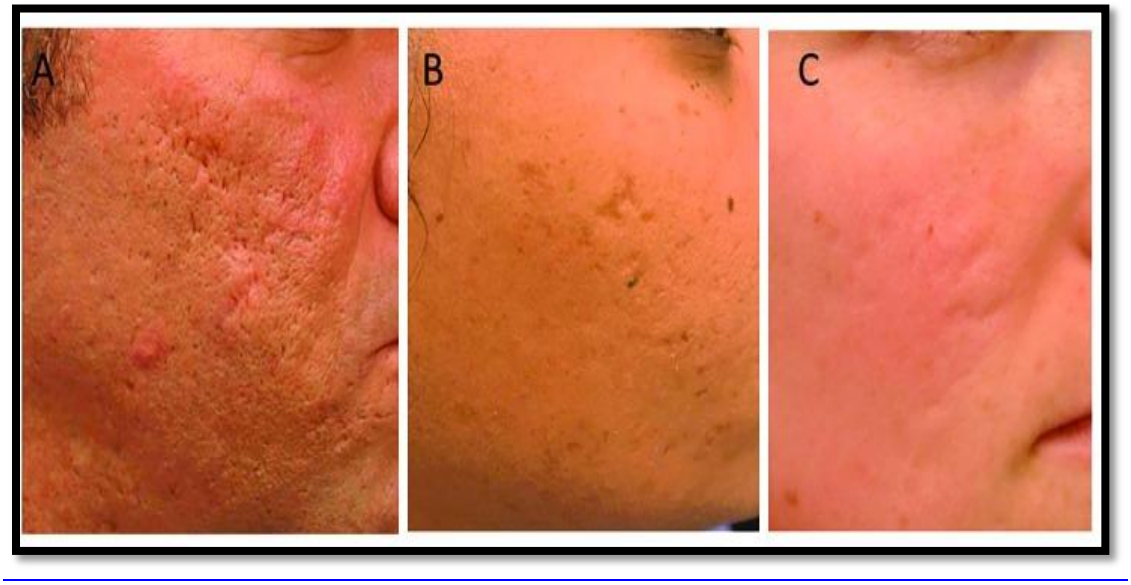

Figure (3): The three types of atrophic acne scars: (A) icepick, (B) boxcar, and (C) rolling **(21)**

Treatment

Acne scar treatment has traditionally used a variety of techniques, and innovative modalities are always being developed to achieve the best outcomes. The classification of several approaches used for the treatment of acne scars is illustrated in **(22).**

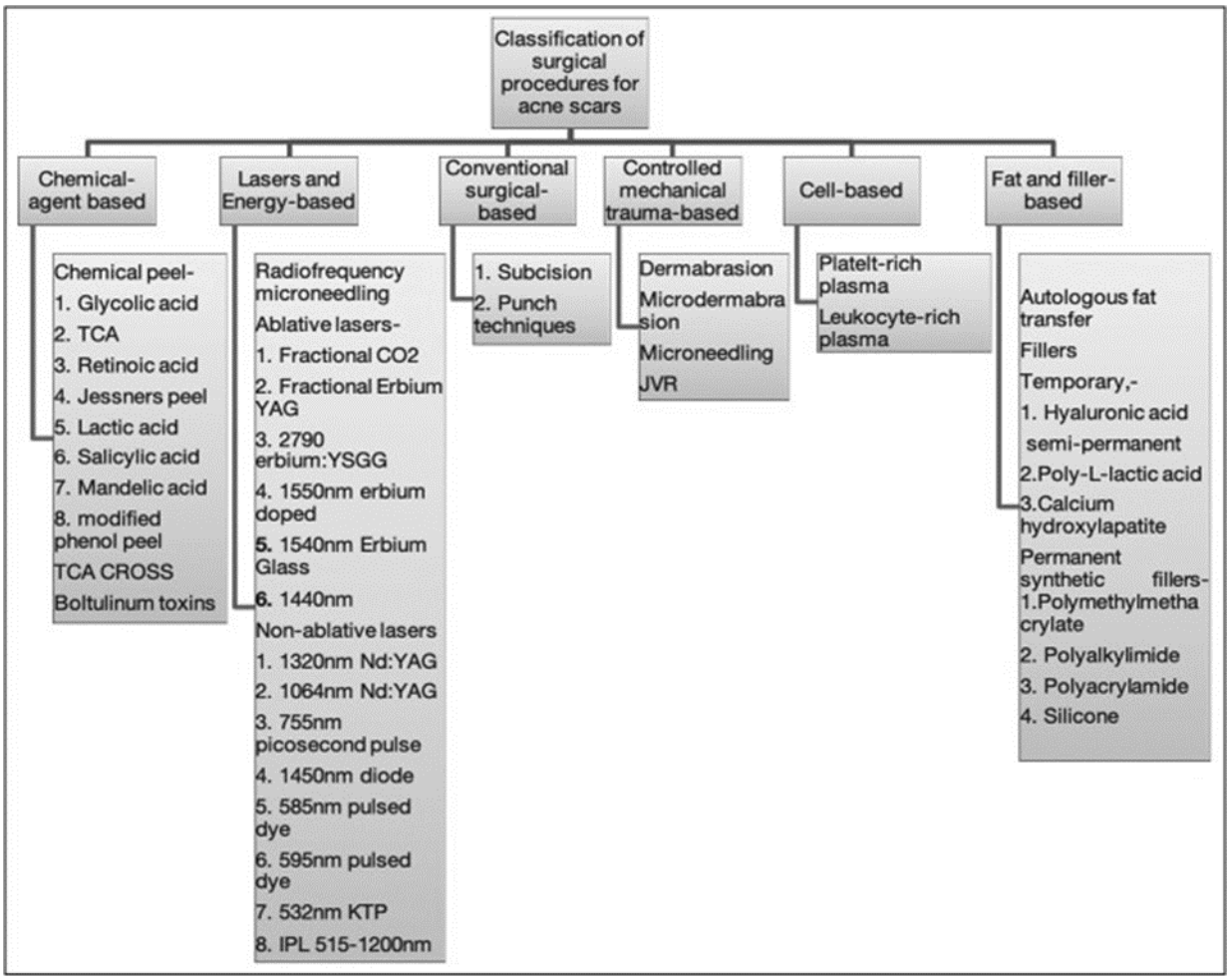

Figure (4): Classification of surgical modalities for acne scars. CROSS, Chemical reconstruction of skin scars; JVR, Jet volumetric remodeling TCA, Trichloroacetic acid **(22).**

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