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OVERVIEW OF NEVUS COMEDONICUS CAUSES AND MANAGEMENT

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Abstract

Introduction: *A rare kind of epidermal nevus is called nevus comedonicus (NC). It is a part of the nevus comedonicus syndrome, a neurocutaneous condition with symptoms affecting the eyes, the skeleton, and the nervous system. Histopathology and clinical examination are used to make diagnoses. There is new information on signaling pathways in illnesses linked to acne that may also affect NC. Contrary to acne-related comedones, the epithelium is frequently hyperkeratotic and occasionally acanthotic, making comedo extraction more difficult. Dermatologists need to be aware of any potential connections between NC and extracutaneous findings like NCS and skin cancers. Complete surgical excision is the best treatment option. Future advancements in laser technology could make them an option. Targeted therapy will become an option in the future when molecular etiology is more understood. Better patient outcomes and a higher quality of life may result from the proper diagnosis and treatment of nevus comedonicus.*

Aim of the study: *The present review describes nevus comedonicus examination and therapy and briefly explains the function of the interprofessional team in treating individuals with this condition.*

Methodology: *The review is a comprehensive research of PUBMED from the year 1895 to 2018*

Conclusion: *Any patient presenting with lesions indicative of nevus comedonicus should be checked for signs of nevus comedonicus syndrome. Patients need to be warned about the likelihood of sporadic flares. Although there are currently no clear randomized control trials that can predict therapeutic success with any certain modality, patients must be made aware of all of their alternatives in order to make an educated choice.*

Keywords:*Nevus comedonicus, Epidermal nevus syndrome, Tyrosine kinase receptors, Rare skin disorders,*

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INTRODUCTION:

A very uncommon skin condition is nevus comedonicus (NC). Clinically, NC is distinguished by follicular apertures that are closely spaced, dilated, and have keratinous plugs that resemble classic comedones. It is a rare variety of epidermal nevus that typically favors the face and neck region. Kofmann initially provided a description of the condition in 1895 and proposed the term "comedo nevus." NC can be inherited or developed later in life, most frequently at the age of 10 years. The nevus comedonicus syndrome (NCS), which Engber first used in 1978, includes NC. The prevalence of NC has been reported to range from 1 in 45,000 to 1 in 100,000, irrespective of race and gender. There is no distinct predilection for gender; both men and women might be affected. No evidence of higher incidence within a particular ethnic group has been found. [1,2]

NC is typically asymptomatic and most frequently affects the face and neck region, with the genital area, palms, and soles as an exception. Clinically, NC manifests as a honeycomb pattern of clustered, dilated, blocked follicular ostia. Lamellated keratinaceous material is seen in the blocked ostia. They resemble black dots, but unlike acne comedones, the substance cannot be easily removed manually. The distribution of NC lesions may be unilateral, bilateral, linear, interrupted, segmental, or blaschkoid.[1,3]

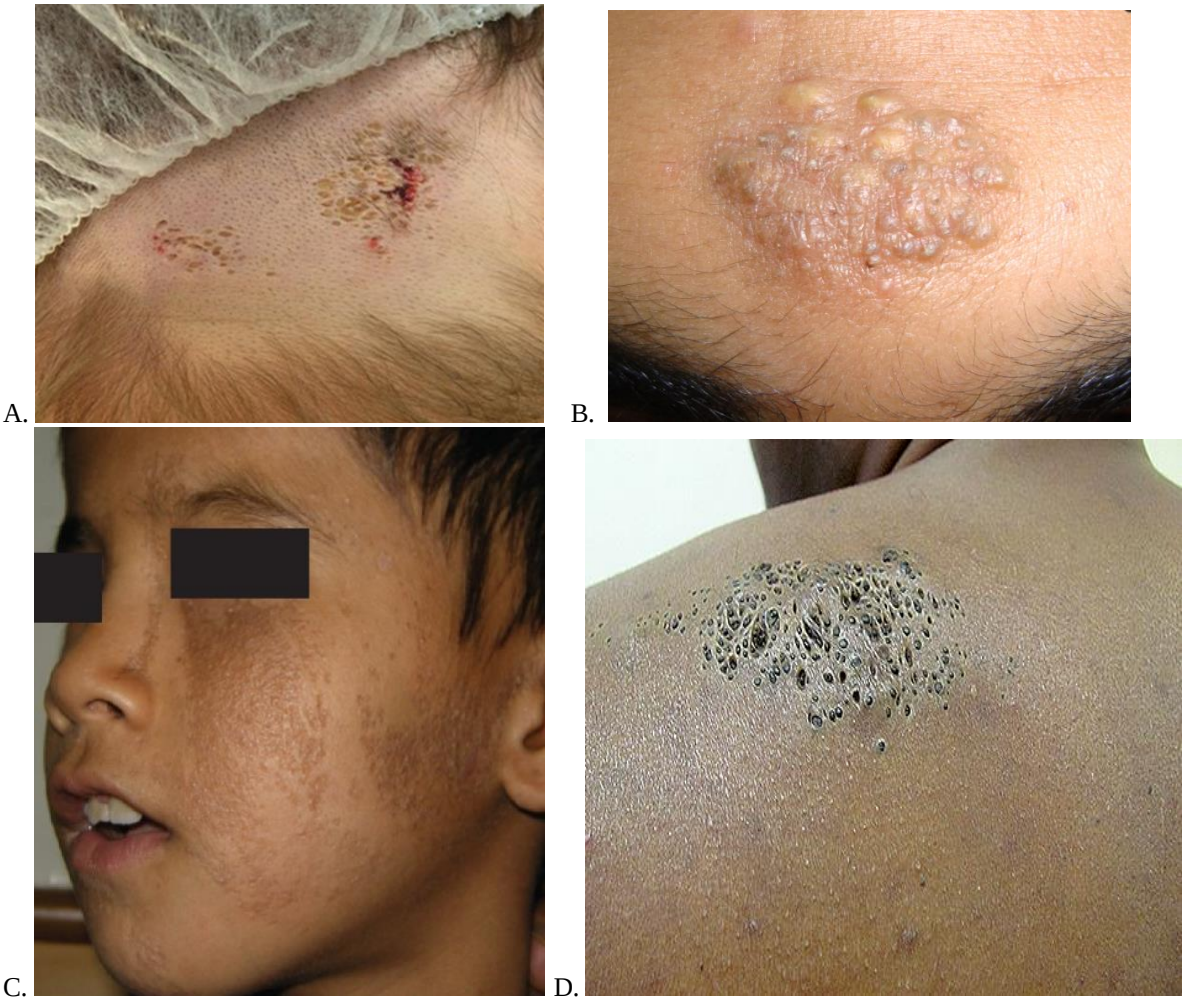

Figure 1 Nevus comedonicus lesion on (A) Scalp, (B) Forehead, (C) Unilaterally on Face and (D) Unilaterally suprascapular region.[4-6]

Etiology

The precise etiology is still unclear. The epidermal nevus, known as nevus comedonicus is thought to originate from the hair follicle. The alternative theory holds that it is a hamartoma generated from the pilosebaceous unit's mesodermal region. It has been suggested that genetic mosaicism contributes to the etiology of nevus comedonicus.[7]

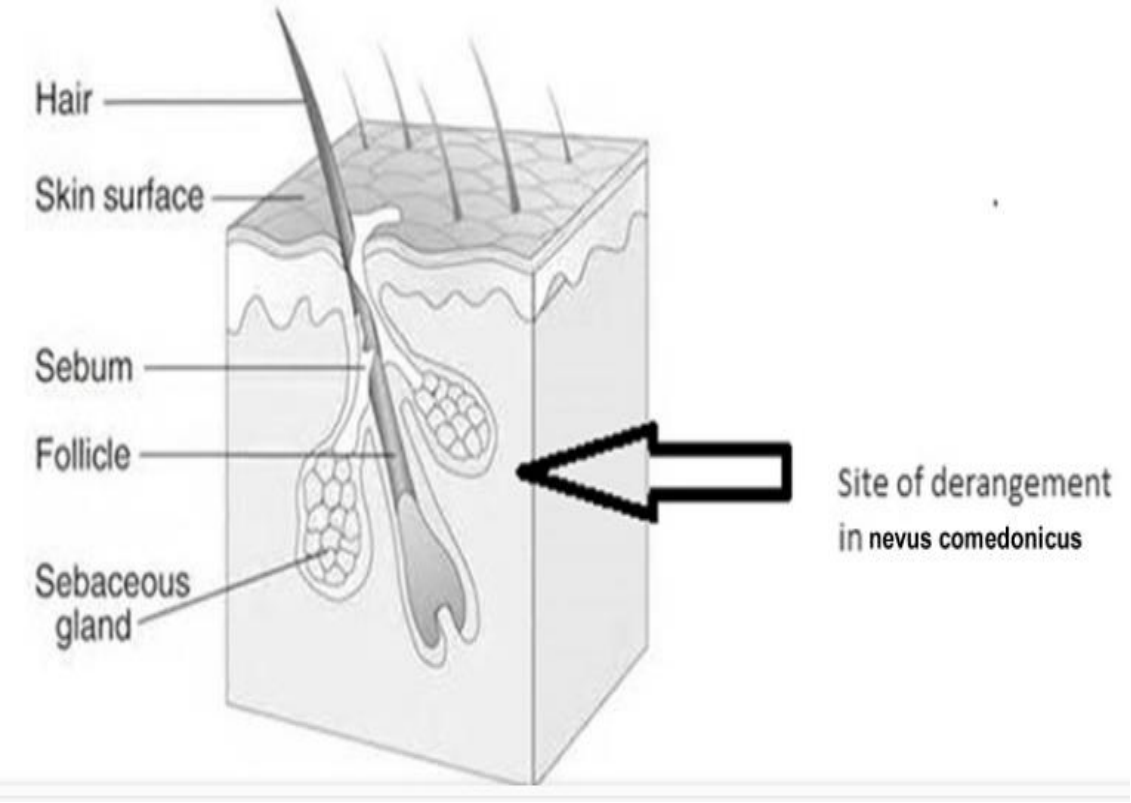

Figure depicting the origin and sire of nevus comedonicus.[4]

However, somatic NEK9 mutations in nevus comedonicus were detected by whole-exome sequencing, each of which affected highly conserved residues in the kinase or RCC1 domains. All of the variants increased phosphorylation at Thr210, a crucial step in NEK9 kinase activation, and were gain of function alterations. The researchers discovered that the development of comedones in nevus comedonicus is characterized by the loss of follicular differentiation markers, the expansion of keratin-15-positive cells from the bulge to the entire sub-bulge follicle and cyst, and ectopic expression of keratin 10, a marker of interfollicular differentiation absent from healthy follicles. These results point to NEK9 as a potential regulator of follicular homeostasis and suggest that NEK9 mutations in nevus comedonicus alter normal follicular differentiation.[8]

Fibroblast growth factor (FGF) and FGF receptor-2 (FGFR2) interaction is a critical mechanism for mesenchymal-epithelial interplay in the development of pilosebaceous units. A group of tyrosine kinase receptors is known as FGFR. Only epithelial cells, such as sebocytes and keratinocytes in the epidermis, contain FGFR2b. NC pathogenesis may be influenced by excessive FGFR2 signaling and elevated interleukin-1 expression. Segmental acne patients with somatic mutations as Ser252Trp substation have been found. Another option for NC is -Secretase, which is present in the epithelium of human hair follicles. Without this enzyme, hair follicles completely transform into epidermal cysts.[9]

Diagnosis and Management

In most cases, the diagnosis is clinical. In suspected cases of NC syndrome, a thorough examination of the eyes, skeletal system, and central nervous system are necessary. A skin sample reveals the usual dilated, keratin-filled follicular ostia. A higher expression of proliferating cell nuclear antigen, intercellular adhesion molecule-1 (ICAM-1), HLA-DR, and CD68 has been observed in immunohistochemistry investigations. The number of Langerhans cells has grown, according to electron microscopy. [10]

However, in cases of atypical presentations, other conditions should be taken into consideration as differentials. These include atypical acne (such as segmental acne and other mosaic acneiform conditions), other acneiform conditions like chloracne, and Favre-Racouchot syndrome (i.e., nodular elastosis with cysts and comedones). In most cases, the diagnosis is clinical. In suspected cases of NC syndrome, a thorough examination of the eyes, skeletal system, and central nervous system are necessary. A skin sample reveals the usual dilated, keratin-filled follicular ostia. A higher expression of proliferating cell nuclear antigen, intercellular adhesion molecule-1 (ICAM-1), HLA-DR, and CD68 has been observed in immunohistochemistry investigations. The number of Langerhans cells has grown, according to electron microscopy. [10]

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Dermoscopy has reportedly recently been found to be helpful in the diagnosis of nevus comedonicus. The common comedonal lesions are highlighted by dermoscopy. Numerous round or barrel-shaped, homogeneous patches in light and dark brown with noticeable keratin plugs are some of the typical dermoscopy findings mentioned.[11]

Treatment

Although the spontaneous remission of nevus comedonicus has not been reported, vigorous treatment is not advised because the condition is largely benign. Treatment is typically saved for cosmetic purposes or in cases of problems like cysts or abscess formation. It may also be necessary to receive cosmetic therapy for the post-inflammatory scars. Topical and systemic retinoids are available as treatment alternatives. For their anti-inflammatory properties, topical steroids, salicylic acid, or 12% ammonium lactate are occasionally used with these. In NC, ablative lasers and surgical excision have both been tried. Interleukin-1-alpha inhibitors, anti-gamma-secretase medications, and FGFR inhibitors are some of the more recent therapy options being investigated. [12]

FGFR inhibitors with antivascular activity may be of interest. Interleukin-1 receptor inhibitors, such as anakinra, and monoclonal antibodies against the interleukin itself, can be categorized as interleukin-1 inhibitors. There are no data available at this time for NC. A further intriguing medicinal target is -secretase; future therapies may involve the stimulation of this enzyme with agents like general control nonderepressible 2 (GCN2), a subunit of eukaryotic translation factor 2 kinase. [12]

Contrary to superficial shaving, comedo extraction, and dermabrasion procedures, localized NC can be eliminated surgically with good aesthetic results. Complex decongestive therapy, which includes manual lymph drainage and compression clothing, improves the healing process if linear NC is surgically removed from the limbs. The use of repeat-filling or self-filling osmotic tissue expanders is another option for larger lesions to provide a surplus of skin for defect closure. Larger lesions may require transplantation for defect closure. [13]

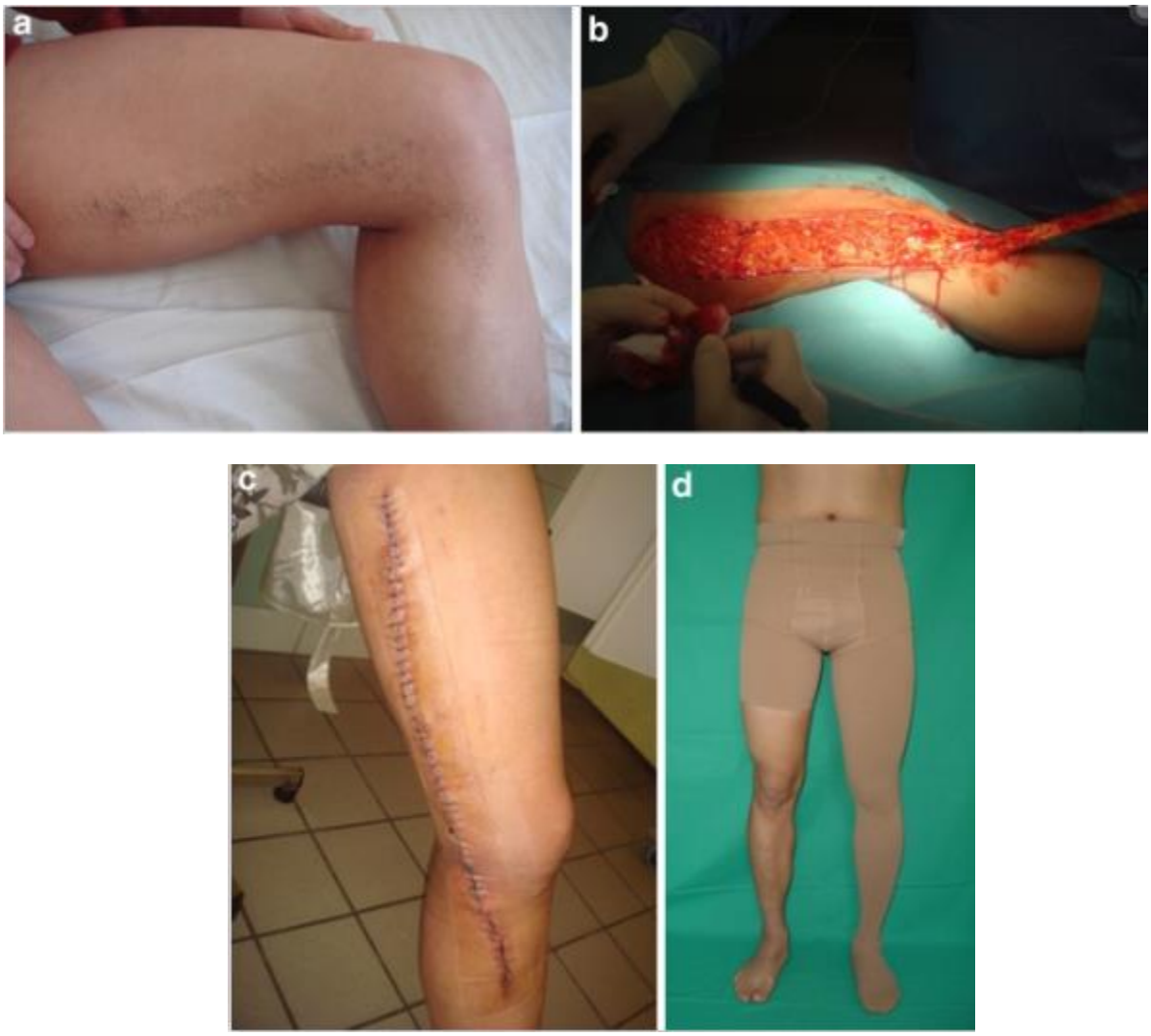

Figure A. linear nevus comedonicus with multiple follicular openings. B Surgical excision. C. Three weeks after surgical excision. D Use of compression garments to avoid postsurgical lymphedema. [4]

Some patients have shown improvement after receiving laser therapy from 2,940–nm erbium YAG, 10,600–nm ultra pulsed CO2, or 1,450–nm diode lasers. However, skin depression will continue. Delayed relapses are frequently experienced after erbium YAG laser therapy. The 1,450 nm diode lowers seborrhea and shrinks sebaceous glands in contrast to ablative lasers. NC may be treated using a 1,450 nm diode laser and a 1,550 nm erbium-doped fiber laser combination. [14]

CONCLUSION:

Any patient presenting with lesions indicative of nevus comedonicus should be checked for signs of nevus comedonicus syndrome. Patients need to be warned about the likelihood of sporadic flares. Although there are currently no clear randomized control trials that can predict therapeutic success with any certain modality, patients must be made aware of all of their alternatives in order to make an educated choice.

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