DOI: 10.24938/kutfd.1609752 Kırıkkale Üniversitesi Tıp Fakültesi Dergisi 2025;27(2):246-249
Case Report Olgu Sunumu

LATE-ONSET NEVUS COMEDONICUS IN AN ADULT PATIENT WITH DIABETES MELLITUS

Erişkin bir Diyabetes Mellitus Hastasında Geç Başlangıçlı Nevüs Komedonikus

Metin ÖZASLAN[1] Zeliha ÇELİK[2]

[1] *Dermatology Clinic, Konya Numune Hospital, KONYA, TÜRKİYE*
[2] *Pathology Clinic, Konya Numune Hospital, KONYA, TÜRKİYE*

ABSTRACT

Nevus comedonicus (NC) is classically defined as a malformation of the pilosebaceous unit characterized by dilated follicular ostia and comedone-like hyperkeratotic follicular plugs. In addition to the classical type, inflammatory NC (NC suppurativa) is accompanied by inflammatory lesions and has been rarely reported in the literature. We report a case of late-onset NC suppurativa on the midline of the forehead in a 47-year-old male patient with diabetes mellitus (DM). Skeletal, central nervous system, dental, and ophthalmologic examinations for NC syndrome were normal. The coexistence of NC suppurativa and DM may not be incidental. Regular monitoring of patients with NC suppurativa for signs of DM could be beneficial. Future studies should include diagnostic tests for DM in all patients with NC suppurativa to clarify the potential link with DM.

Keywords: *Diabetes mellitus, epidermal nevus, hair follicle, hamartoma, hidradenitis suppurativa*

ÖZ

Nevus komedonikus (NC) klasik olarak dilate foliküler ostia ve komedon benzeri hiperkeratotik foliküler tıkaçlarla karakterize pilosebase ünitenin bir malformasyonu olarak tanımlanır. Klasik tipin yanı sıra, inflamatuar lezyonların eşlik ettiği inflamatuar NC (NC süpürativa) literatürde nadiren bildirilmiştir. 47 yaşında diyabetes mellituslu (DM) bir erkek hastada alın orta hattında yerleşen geç başlangıçlı NC süpürativa olgusu sunulmuştur. Hastanın NC sendromu için yapılan iskelet sistemi, merkezi sinir sistemi, diş ve göz muayeneleri normaldi. NC süpürativa ve DM birlikteliğinin tesadüfi olmayabileceğini düşünüyoruz. NC suppurativa hastalarının DM belirtileri açısından düzenli olarak izlenmesi yararlı olabilir. Gelecek çalışmalarda DM ile ilişkiyi netleştirmek için NC süpürativa'lı tüm hastalarda DM açısından tanısal testler yapılmalıdır.

Anahtar Kelimeler: *Diyabetes mellitus, epidermal nevüs, kıl folikülü, hamartom, hidradenit süpürativa*

Correspondence / Yazışma Adresi: **Dr. Metin ÖZASLAN**
Dermatology Clinic, Konya Numune Hospital, KONYA, TÜRKİYE
Phone / Tel: +905549385225 **E-mail** / E-posta: metinozaslanx@gmail.com
Received / Geliş Tarihi: 30.12.2024 **Accepted** / Kabul Tarihi: 11.04.2025

KÜ Tıp Fak Derg 2025;27(2):246-249
Doi: 10.24938/kutfd.1609752

INTRODUCTION

Nevus comedonicus (NC) is classically defined as a malformation of the pilosebaceous unit characterized by dilated follicular ostia and comedone-like hyperkeratotic follicular plugs. In addition to the classical type, inflammatory NC (NC suppurativa) is accompanied by inflammatory lesions (e.g., papules, pustules, and cysts) and has rarely been reported in the literature.[1]

CASE REPORT

A 47-year-old man presented with an irregularly circumscribed hyperpigmented plaque with nodules and a cystic lesion measuring approximately 4×4 cm in diameter on the midline of the forehead (Figure 1).

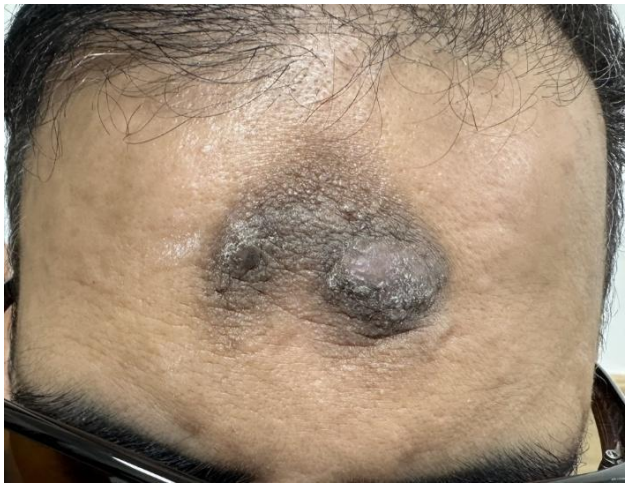

Figure 1: Irregularly circumscribed hyperpigmented plaque containing nodules and a cystic lesion.

The lesion had developed 2 years previously. The patient routinely noticed that the cystic lesion regressed and recurred every 4-6 months. No family history of similar lesions was reported, and the patient's oral mucosa examination was normal. The patient's diabetes mellitus (DM) was inadequately controlled despite treatment with oral metformin. Microbiological analysis of the aspirated material from the cystic lesion revealed no microbial growth. Hematological parameters were within normal limits. Routine biochemical investigations were unremarkable, with the exception of an elevated fasting blood glucose level of 180 mg/dL and a hemoglobin A1c (HbA1c) of 7.6%. Histopathologic examination of the biopsy obtained from the edge of the cystic lesion, including the perilesional skin, showed minimal acanthosis and minimal elongation of the rete in the epidermis, inflammation and pigmented melanophages in the superficial dermis, and some ruptured cystic hair follicles surrounded by dense neutrophil-rich inflammation in the deep dermis (Figure 2).

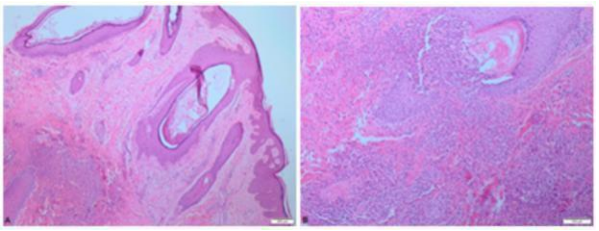

Figure 2: Histopathology of nevus comedonicus: **(a)** details with large follicles containing lamellated keratin but absent hair shafts; the epidermis is hyperkeratotic and may show a combination of atrophy and acanthosis (hematoxylin & eosin stain × 40); **(b)** ruptured follicle and inflammatory granulation tissue (hematoxylin & eosin stain × 100).

Based on these findings, the patient was diagnosed with NC complicated by a hidradenitis suppurativa (HS)-like lesion (NC suppurativa). Evaluation for NC syndrome, including skeletal, neurological, dental, and ophthalmologic assessments, yielded normal findings. As the patient refused medical treatment, he was referred to the plastic surgery department for surgical excision of the lesion, but was subsequently lost to follow-up.

DISCUSSION

NC can be localized anywhere on the body in a dermatomal, blaschkoid, unilateral, bilateral, or interrupted distribution. The majority of cases are diagnosed at birth or before puberty. Adult-onset NC is rare, as in our case.[2] NC infrequently arises secondary to posttraumatic events, bacterial or viral cutaneous infections, and various inflammatory dermatoses.[3] In our case, there was no history of trauma, infection, or skin disease before lesion presentation.

The etiopathogenesis of nevus comedonicus (NC) remains poorly understood. However, emerging evidence suggests that somatic mutations in the NEK9 (never in mitosis gene A-related kinase 9) may interfere with follicular differentiation, while upregulation of ABCA12 (ATP-binding cassette subfamily A member 12) may alter sebaceous gland architecture, both contributing to the development of NC.[4,5] Fibroblast growth factor receptor 2 (FGFR2) signaling has also been reported to play a critical role in the development of the pilosebaceous unit. Overstimulation of FGFR2 signaling increases interleukin-1 (IL-1) alpha expression and triggers acne vulgaris, acne formation in Apert syndrome, and NC development.[6] Until recently, it was known that NC was not associated with systemic diseases, except for NC syndrome, which is accompanied by skeletal, brain, eye, and dental anomalies. However, Mazzella et al. reported obesity comorbidity in a patient with NC and acne vulgaris.[7] In that study, the relationship of FGF signaling with metabolic syndrome and acne via the mTOR pathway was emphasized. Considering that activation of the mTOR pathway leads to insulin resistance and DM[8], it

KÜ Tıp Fak Derg 2025;27(2):246-249
Doi: 10.24938/kutfd.1609752

may be possible that the FGF–mTOR relationship may lead to NC and DM comorbidity in our case. Other possible mechanisms behind the comorbidity of NC and DM may involve increased levels of the proinflammatory cytokine IL-1 and disruption of the neurogenic locus notch homolog (Notch) signaling pathway, both of which are linked to comedogenesis.[4,6] IL-1 contributes to DM by causing insulin dysregulation and pancreatic beta-cell apoptosis, while disruption of Notch signalling impairs insulin metabolism and plays a key role in the development of insulin resistance and DM.[9,10]

Chronic hyperglycemia-related microvascular damage can reduce oxygen and nutrient supply to hair follicles, leading to follicular damage. This is linked to hair thinning, decreased hair density, slower hair growth, and androgenetic alopecia.[11] The effects of insulin on sebaceous glands can be summarized as follows: It promotes hypertrophy and hyperplasia of the sebaceous glands, activates lipogenic transcription factors to stimulate de novo lipogenesis, and increases sebum production. In cases of insulin resistance, the sebum increase driven by de novo lipogenesis can trigger local inflammation and infundibular epithelial proliferation.[12] In our patient, hyperglycemia and insulin resistance likely contributed to follicular damage, excessive sebum production, and an inflammatory response. While sebum overproduction and infundibular hyperkeratosis typically cause comedone formation, chronic inflammation and microvascular dysfunction may have disrupted follicular integrity, leading to early rupture or a direct progression to nodular and suppurative lesions, contributing to NC development.

HS is a chronic, recurrent, inflammatory disease affecting apocrine glands. HS-like lesions (such as inflamed nodules, abscesses, sinus tracts, ulcers, and scars) accompanying NC have rarely been reported in the literature.[1,13–15] The critical role of follicular occlusion in the pathogenesis of both NC and HS may explain the coexistence of lesions from both diseases. In our case, the presence of HS-like cystic lesion clinically, sterility of the cyst aspiration material, and suppurative inflammation around ruptured cystic hair follicles on histopathology can be listed as findings in favor of HS. Unlike cases with NC and HS-like lesions reported in the literature, where HS-like lesions are typically localized in the folds, trunk, or buttocks, similar to classical HS, the lesion in our case is localized on the face, which is rarely affected by classical HS. The reason for this unusual localization remains unclear; however, uncontrolled DM, known to be associated with chronic inflammation and immune dysregulation, may contribute to this unusual localization.

Sharma et al. proposed the term “NC suppurativa” for HS-like lesions accompanying NC due to features such as resistant clinical course, frequent recurrence, and affecting quality of life compared to NC.[1] Our case is compatible with NC suppurativa because of recurrent HS-like cystic lesions that negatively affect social life. Most NC suppurativa cases present in childhood with comedones. However, in our case, the lesion developed in adulthood without comedones. This delayed onset may be due to the initially normal functioning of the pilosebaceous unit in the absence of DM, with cumulative DM-related changes over time impairing follicular integrity and eventually leading to lesion development. Although sebum overproduction due to insulin resistance can promote follicular occlusion, chronic inflammation and microvascular dysfunction may have disrupted keratinization, causing follicular damage. This could have prevented comedone formation while promoting nodular and suppurative lesions. Due to the lack of long-term follow-up, we could not assess whether new lesions, particularly comedones, developed over time.

While NC usually does not require treatment except for cosmetic concerns, NC suppurativa necessitates treatment due to its resistant clinical course. Management options for NC suppurativa include oral retinoids, cryotherapy, ablative laser therapies, and surgical excision; however, therapeutic outcomes remain variable and unpredictable.[1] Moreover, the frequency of disease recurrence in long-term follow-up after treatment has not been adequately investigated.

In conclusion, we suggest that the coexistence of NC suppurativa and DM may not be incidental. Regular monitoring of patients with NC suppurativa for signs of DM could be beneficial. Future studies should include diagnostic tests for DM, such as fasting glucose and HbA1c, in all patients with NC suppurativa to clarify the potential link with DM.

Researchers' Contribution Rate Statement: Concept/Design: MÖ; Analysis/Interpretation: MÖ, ZÇ; Data Collection: MÖ, ZÇ; Writer: MÖ, ZÇ; Critical Review: MÖ; Approver: MÖ, ZÇ.

Conflict of Interest: The authors have no conflicts of interest to declare.

Support and Acknowledgment: No financial support was received from any institution or person.

Informed Volunteer Consent Form: The patient provided written informed consent for the publication of this case report.

REFERENCES

1. Sharma S, Sahu P, Dayal S, Yadav A, Brar K. Nevus comedonicus suppurativa: A report of a novel entity. *J Clin Aesthet Dermatol*. 2020;13(6):36-39.
2. Zanniello R, Pilloni L, Conti B, Faa G, Rongioletti F. Late-onset nevus comedonicus with follicular epidermolytic

hyperkeratosis-case report and review of the literature. *Am J Dermatopathol*. 2019;41(6):453-455.
3. Grimalt R, Caputo R. Posttraumatic nevus comedonicus. *J Am Acad Dermatol.* 1993;28(2 Pt 1):273-274.
4. Levinsohn JL, Sugarman JL; Yale Center for Mendelian Genomics; McNiff JM, Antaya RJ, Choate KA. Somatic mutations in NEK9 cause nevus comedonicus. *Am J Hum Genet.* 2016;98(5):1030-1037.
5. Liu F, Yang Y, Zheng Y, Liang YH, Zeng K. Mutation and expression of ABCA12 in keratosis pilaris and nevus comedonicus. *Mol Med Rep*. 2018;18(3):3153-3158.
6. Melnik B, Schmitz G. FGFR2 signaling and the pathogenesis of acne. *J Dtsch Dermatol Ges*. 2008;6(9):721-728.
7. Mazzella C, Fabbrocini G, Luciano MA, Cacciapuoti S. Nevus comedonicus with acne vulgaris and obesity. *Dermatol Pract Concept*. 2019;10(1):e2020006.
8. Laplante M, Sabatini DM. mTOR signaling at a glance. *J Cell Sci.* 2009;122(Pt 20):3589-3594.
9. Banerjee M, Saxena M. Interleukin-1 (IL-1) family of cytokines: Role in type 2 diabetes. *Clin Chim Acta.* 2012;413(15-16):1163-1170.
10. Eom YS, Gwon AR, Kwak KM, et al. Notch1 has an important role in β-cell mass determination and development of diabetes. *Diabetes Metab J.* 2021;45(1):86-96.
11. Miranda JJ, Taype-Rondan A, Tapia JC, Gastanadui-Gonzalez MG, Roman-Carpio R. Hair follicle characteristics as early marker of type 2 diabetes. *Med Hypotheses.* 2016;95:39-44.
12. Okoro OE, Camera E, Flori E, Ottaviani M. Insulin and the sebaceous gland function. *Front Physiol.* 2023;14:1252972.
13. Dufour DN, Bryld LE, Jemec GB. Hidradenitis suppurativa complicating naevus comedonicus: The possible influence of mechanical stress on the development of hidradenitis suppurativa. *Dermatology.* 2010;220(4):323-325.
14. Qian G, Liu T, Zhou C, Zhang Y. Naevus comedonicus syndrome complicated by hidradenitis suppurativa-like lesions responding to acitretin treatment. *Acta Derm Venereol.* 2015;95(8):992-993.
15. Manikavachakan N, Siddaraju MN, Rajendran SC, Venkataraman A. Extensive nevus comedonicus, complicated with recurrent abscesses, successfully treated with surgical resurfacing. *J Cutan Aesthet Surg.* 2018;11(1):33-37.