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Adult-Onset Solitary Verrucous Epidermal Nevus Without Blaschkoid Distribution: A Clinicopathological Diagnostic Challenge

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Abstract: Verrucous epidermal nevus (VEN) is a benign keratinocytic hamartoma that usually appears in childhood and follows Blaschko's lines. Adult-onset solitary VEN without Blaschko line distribution is rare and may clinically mimic other verrucous lesions, including verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma. **Objective:** This case report aims to describe an atypical adult-onset solitary VEN without Blaschko line distribution and emphasize the importance of clinicopathological correlation in establishing the diagnosis. **Case:** A 27-year-old man presented with a progressively enlarging verrucous plaque on the left lateral malleolus for one year. The lesion was hyperkeratotic, well-demarcated, and associated with pruritus. Clinical differential diagnoses included verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma. Complete surgical excision was performed, followed by histopathological examination. **Discussion:** Histopathological findings showed hyperkeratosis, papillomatosis, focal hypergranulosis, acanthosis, and basal hyperpigmentation without koilocytosis, horn cysts, cytologic atypia, or invasive growth. These findings confirmed the diagnosis of VEN and excluded infectious and malignant verrucous lesions. **Conclusion:** Solitary adult-onset VEN without Blaschko line distribution is a rare diagnostic challenge. Histopathological examination is essential for accurate diagnosis, while excisional biopsy may serve both diagnostic and therapeutic purposes in localized lesions.

Keywords: verrucous epidermal nevus; Blaschko's lines; histopathological examination; excisional biopsy; verrucous lesion.

INTRODUCTION

Verrucous epidermal nevus (VEN) is a benign keratinocytic hamartoma that generally appears during infancy or childhood and commonly follows Blaschko's lines. Although VEN is not a life-threatening disorder, its clinical relevance lies in its ability to mimic various acquired verrucous lesions, including verruca vulgaris, seborrheic keratosis, inflammatory linear verrucous epidermal nevus, and verrucous squamous cell carcinoma. This diagnostic challenge becomes more important when the lesion occurs as a solitary

adult-onset plaque without a typical linear or Blaschkoid distribution. In clinical practice, solitary verrucous lesions in adults often raise concern because they may represent infectious, benign neoplastic, premalignant, or malignant processes. Therefore, accurate identification is essential to prevent misdiagnosis, inappropriate treatment, unnecessary anxiety, or delayed recognition of malignant lesions. Epidermal nevi are estimated to occur in approximately 1–3 per 1,000 individuals, but adult-onset non-Blaschkoid solitary presentations remain uncommon and underreported.

Previous studies on epidermal nevi can be grouped into at least three major categories. First, clinical and case-based studies have emphasized that VEN and related epidermal nevus variants typically present as hyperkeratotic, papillomatous, or verrucous plaques with a linear or Blaschkoid pattern, although rare adult-onset cases have been reported (Dağtaş et al., 2025; Johnson et al., 2024; Nayak et al., 2022). Second, histopathological studies have described the main microscopic features of VEN, including hyperkeratosis, papillomatosis, acanthosis, rete ridge elongation, and variable hypergranulosis, which are important for distinguishing VEN from verruca vulgaris, seborrheic keratosis, and verrucous carcinoma (Alaziz & Najim, 2021; Mishra et al., 2015; Verzì et al., 2019; Ye et al., 2023). Third, molecular and genetic studies have explained epidermal nevi as mosaic disorders caused by postzygotic somatic mutations, particularly involving FGFR3, HRAS, KRAS, NRAS, and PIK3CA pathways (Hafner, 2014; Hafner et al., 2012; Morren et al., 2024; Zuntini et al., 2023). However, despite these contributions, previous literature has not sufficiently emphasized solitary adult-onset VEN without Blaschko line distribution, especially in lesions clinically resembling acquired verrucous tumors on the lower extremity.

This case report aims to describe an atypical presentation of solitary adult-onset verrucous epidermal nevus located on the left lateral malleolus without Blaschko line distribution. Specifically, this report seeks to explain the clinical diagnostic challenge, describe the histopathological findings, compare the lesion with relevant differential diagnoses, and highlight the role of clinicopathological correlation in confirming the diagnosis. By presenting this case, the article contributes to the limited literature on non-Blaschkoid adult-onset VEN and provides practical insight for clinicians when evaluating solitary verrucous lesions in adult patients.

The main argument of this report is that solitary verrucous lesions in adults should not be diagnosed solely based on clinical morphology, particularly when the presentation is

atypical and does not follow the classical Blaschkoid pattern of epidermal nevus. Although adult-onset solitary VEN is rare, it should remain an important differential diagnosis when histopathological findings reveal hyperkeratosis, papillomatosis, acanthosis, focal hypergranulosis, and basal pigmentation without koilocytosis, horn cysts, cytologic atypia, or invasive growth. Therefore, histopathological examination is essential not only to establish the diagnosis of VEN but also to exclude infectious and malignant verrucous conditions. In localized atypical cases, complete surgical excision may serve both diagnostic and therapeutic purposes.

CASE PRESENTATION

Patient Information

A 27-year-old male patient presented to the Dermatology and Venereology Clinic at the Yogyakarta Islamic Hospital PDHI with a lump on his left ankle. One year prior to his hospitalization, the patient had complained of a pink lump the size of a pinhead on his left ankle. The lump was itchy but not painful or prone to bleeding.

Four months prior to presentation, the lesion progressively enlarged and evolved into a well-demarcated, hyperkeratotic verrucous plaque with a brownish pigmentation and an irregular, slightly cerebriform surface. The patient reported associated pruritus without pain, ulceration, or spontaneous bleeding. No systemic symptoms such as fever, arthralgia, or weight loss were noted. The patient works as a construction worker and regularly wears half-ankle boots without socks, which may contribute to chronic friction and localized irritation. He denied any prior history of similar lesions or a family history of related dermatologic conditions.

Physical Examination

His general condition was good, with normal consciousness (compos mentis) and stable vital signs, and general health status within normal limits. Dermatological examination revealed a solitary tumor with a hyperkeratotic verrucous surface, erythematous, measuring 1.2 × 1 cm, with well-defined borders, soft consistency, and associated superficial erosions and a thin crust (Figure 1). The patient was diagnosed with verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma.

Figure 1. Clinical appearance of the lesion on the left lateral malleolus showing a solitary hyperkeratotic verrucous plaque with well-defined borders, superficial erosion, and thin crusting.

The lesion appeared as a solitary verrucous plaque with progressive enlargement over one year. Clinically, the hyperkeratotic surface, irregular morphology, and superficial erosion raised suspicion for several acquired verrucous disorders, including verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma. The absence of a linear or Blaschkoid distribution contributed to the diagnostic challenge because classical verrucous epidermal nevus commonly follows Blaschko's lines.

Diagnostic Assessment

The patient underwent complete surgical excision of the lesion followed by histopathological examination. Prior to the procedure, the patient underwent a general clinical evaluation and received an explanation regarding the procedure, including its risks and possible complications. Written informed consent was obtained. The patient was positioned in the left lateral decubitus position, and the operative field was prepared using 1% povidone-iodine antisepsis (Figure 2A). Local anesthesia was achieved by intralesional injection of 1 mL of 2% lidocaine. The lesion was completely excised, and the specimen was submitted for histopathological examination. Hemostasis was achieved adequately, and the wound was closed using five interrupted non-absorbable sutures and covered with a sterile dressing (Figure 2B).

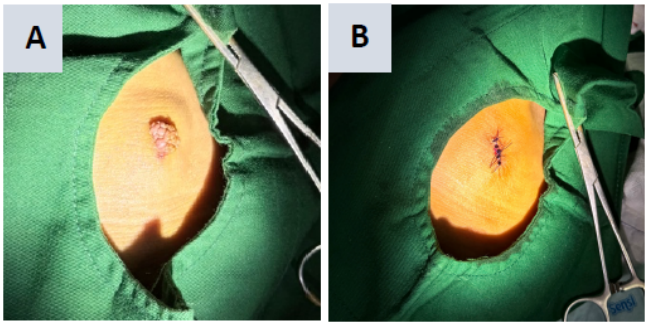

Figure 2. Surgical excision procedure. (A) Preoperative appearance after antiseptic preparation with povidone-iodine; (B) postoperative wound closure using interrupted non-absorbable sutures with minimal bleeding.

Figure 2 illustrates the surgical excision procedure performed to obtain a definitive diagnosis and remove the lesion therapeutically. Figure 2A shows the lesion after antiseptic preparation, while Figure 2B shows the wound closure after complete excision using interrupted non-absorbable sutures.

Postoperatively, the patient was instructed to keep the wound clean and dry and was scheduled for follow-up on the tenth postoperative day. At follow-up, the wound showed good healing without pain or bleeding, and the sutures were removed (Figure 3).

Figure 3. Postoperative follow-up on day 10 demonstrating satisfactory wound healing after suture removal.

Figure 3 demonstrates the postoperative condition on day 10, showing satisfactory wound healing without signs of infection, bleeding, or wound dehiscence. This finding supports that complete surgical excision was an effective and safe management approach in this localized lesion.

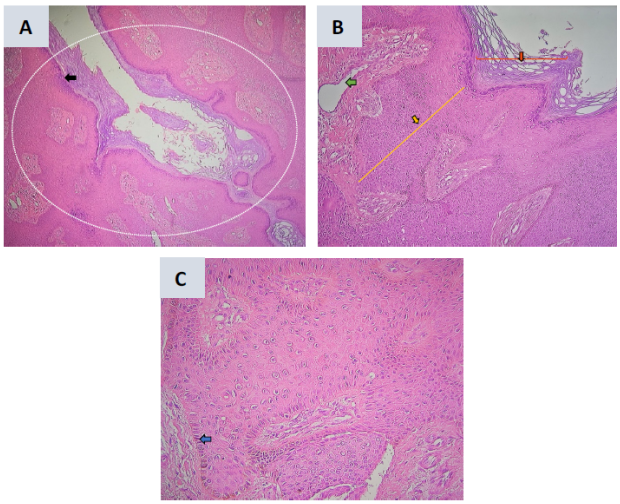

Figure 4. Histopathological findings of verrucous epidermal nevus stained with hematoxylin and eosin (H&E). (A) Low-power magnification (4×) showing papillomatosis and focal hypergranulosis; (B) medium-power magnification (10×) demonstrating irregular acanthosis and hyperkeratosis; (C) high-power magnification (40×) revealing increased basal layer pigmentation.

Figure 4 confirms the histopathological diagnosis of verrucous epidermal nevus. Figure 4A shows papillomatosis and focal hypergranulosis, Figure 4B demonstrates irregular acanthosis and hyperkeratosis, and Figure 4C reveals increased basal layer pigmentation. These findings support the diagnosis of VEN and help exclude verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma.

Histopathological examination revealed hyperkeratosis, papillomatosis, focal hypergranulosis, and acanthosis (Figure 4A, 4B), accompanied by increased melanin pigmentation within the basal layer (Figure 4C). The dermis showed perivascular inflammatory infiltrates composed predominantly of lymphocytes and histiocytes. No sebaceous gland proliferation, viral cytopathic changes, or evidence of malignancy was identified. Based on these findings, a diagnosis of verrucous epidermal nevus (VEN) was established, while verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma were excluded.

DISCUSSION

Verrucous epidermal nevus (VEN) is a benign epidermal hamartoma that may mimic several verrucous skin disorders both clinically and histologically. Typical lesions usually

appear during childhood and follow Blaschko's lines. In contrast, solitary lesions arising in adulthood without linear or Blaschkoid distribution are uncommon and may complicate clinical diagnosis (Alaziz & Najim, 2021; Gazali et al., 2024).

The clinical presentation in this patient demonstrated several characteristic features of VEN, although the adult-onset manifestation and absence of Blaschkoid distribution rendered the diagnosis clinically challenging. The lesion appeared as a solitary, slowly progressive hyperkeratotic verrucous plaque with well-defined borders and a slightly cerebriform surface localized on the lateral malleolus. Such morphology reflects abnormal epidermal keratinocyte proliferation and is consistent with the verrucous phenotype commonly described in keratinocytic epidermal nevi. Nevertheless, unlike the classical presentation of VEN that usually develops during infancy or early childhood along Blaschko's lines, the present lesion emerged during adulthood without linear configuration, thereby broadening the recognized clinical spectrum of VEN and increasing the possibility of misdiagnosis as acquired verrucous dermatoses or malignant proliferations (Dağtaş et al., 2025; Johnson et al., 2024).

The lesion's gradual enlargement over one year, accompanied by pruritus and superficial erosion, further contributed to the diagnostic dilemma. Clinically, these features overlapped with verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma. Previous studies have emphasized that atypical adult-onset epidermal nevi may clinically mimic infectious, inflammatory, and neoplastic conditions, particularly when lesions are localized and non-Blaschkoid in distribution. In this context, clinicopathological correlation becomes essential to avoid both underdiagnosis and overtreatment (Dağtaş et al., 2025; Morren et al., 2024).

Histopathological examination in this case strongly supported the diagnosis of VEN. Microscopic findings demonstrated marked hyperkeratosis, papillomatosis, focal hypergranulosis, and irregular acanthosis of the stratified squamous epithelium accompanied by increased basal layer pigmentation. These findings correspond to the characteristic epidermal hyperplasia and disordered keratinization pattern observed in verrucous epidermal nevus. Papillomatosis with elongated rete ridges explains the clinically verrucous and cerebriform appearance of the lesion, whereas hyperkeratosis accounts for the thickened hyperkeratotic surface observed on physical examination. Additionally, focal hypergranulosis and basal hyperpigmentation are frequently reported histologic features in keratinocytic epidermal nevi and further support the diagnosis

(Dağtaş et al., 2025; Verzì et al., 2019).

Importantly, several histopathological findings helped exclude other differential diagnoses. The absence of koilocytosis or viral cytopathic changes argued against verruca vulgaris, while the lack of horn cysts made seborrheic keratosis less likely. Furthermore, no cytologic atypia, infiltrative growth pattern, or malignant keratinocyte proliferation was identified, thereby excluding verrucous squamous cell carcinoma. Recent literature has consistently emphasized that histopathological confirmation remains the gold standard for diagnosing atypical or adult-onset VEN because clinical morphology alone may be insufficient, especially in non-Blaschkoid presentations (Dağtaş et al., 2025; Johnson et al., 2024).

The lesion's gradual progression from a discrete papule to a hyperkeratotic plaque further contributed to its misleading clinical morphology. This evolution parallels that of several benign and malignant keratinocytic proliferations, reinforcing the limitations of morphology-based diagnosis. Additionally, chronic mechanical irritation particularly repeated friction associated with occupational footwear may have acted as a local promoting factor, promoting keratinocyte proliferation and altering the clinical morphology of the lesion. Such environmental modulation of phenotypes is increasingly recognized as an important contributor to atypical dermatologic presentation (Aghajani et al., 2026; Morren et al., 2024).

Definitive diagnosis in this context relies on histopathological evaluation. The constellation of findings hyperkeratosis, papillomatosis, focal hypergranulosis, and acanthosis with basal layer hyperpigmentation is consistent with VEN and reflects disordered epidermal differentiation. Crucially, the absence of koilocytosis excluded viral etiology, while the lack of horn cysts, cytologic atypia, and infiltrative growth effectively ruled out seborrheic keratosis and verrucous carcinoma (Montanari et al., 2024; Ye et al., 2023). These observations underscore the indispensable role of histopathology in resolving diagnostic ambiguity and preventing both overdiagnosis and undertreatment.

In the present case, the lesion demonstrated overlapping clinical features with several acquired verrucous disorders. However, histopathological examination revealed findings characteristic of VEN, including hyperkeratosis, papillomatosis, focal hypergranulosis, and acanthosis, without evidence of viral cytopathic changes or malignant transformation. The comparison between the principal differential diagnoses and the findings observed in this case is summarized in Table 1.

Table 1. Differential diagnosis of solitary verrucous lesions and comparison with the present case.

Differential Diagnosis	Clinical Features	Histopathological Features	Reason for Exclusion
Verruca vulgaris	Hyperkeratotic papules or plaques with rough verrucous surface, commonly associated with HPV infection.	Papillomatosis, hyperkeratosis, hypergranulosis, and characteristic koilocytosis.	No koilocytosis or viral cytopathic changes were identified.
Seborrheic keratosis	Well-demarcated pigmented verrucous plaques with a stuck-on appearance.	Hyperkeratosis, acanthosis, papillomatosis, and horn cysts or pseudohorn cysts.	No horn cysts or pseudohorn cysts were observed histologically.
Verrucous squamous cell carcinoma	Slow-growing exophytic verrucous tumor that may ulcerate or bleed.	Endophytic growth, cytologic atypia, and invasive squamous proliferation.	No cytologic atypia, infiltrative growth, or malignant features were identified.
Verrucous epidermal nevus (final diagnosis)	Hyperkeratotic verrucous plaque, usually present since childhood.	Hyperkeratosis, papillomatosis, acanthosis, and focal hypergranulosis.	Histopathological findings were fully consistent with VEN.

Previous studies have demonstrated that adult-onset and non-Blaschkoid presentations of verrucous epidermal nevus are uncommon clinical variants that may closely resemble acquired verrucous dermatoses, resulting in diagnostic difficulty. Clinicopathological correlation therefore remains essential to distinguish VEN from infectious, benign, and malignant verrucous proliferations. Several reports have emphasized that atypical epidermal nevi in adulthood may represent delayed phenotypic expression of postzygotic mosaic mutations influenced by environmental or mechanical factors, including chronic friction and localized trauma (Morren et al., 2024; Nayak et al., 2022).

At the molecular level, epidermal nevi are understood to arise from postzygotic somatic mutations that result in genetic mosaicism, with recurrent alterations described in FGFR3, HRAS, KRAS, and PIK3CA (Morren et al., 2024; Zuntini et al., 2023). The phenotypic heterogeneity of VEN reflects the timing, distribution, and clonal expansion of these mutations. While classical Blaschkoid patterns correspond to embryologic cell migration, deviations such as localized, non-linear, or delayed-onset lesions may occur when mutational events arise outside typical developmental windows or remain clinically silent for extended periods. In this framework, adult-onset presentation may not represent

a true de novo process, but rather late clinical expression influenced by cumulative factors such as trauma, inflammation, or epidermal hyperproliferation (Aghajani et al., 2026; Morren et al., 2024; Zuntini et al., 2023).

Collectively, this case underscores the necessity of integrating clinical suspicion with histopathological confirmation when encountering atypical verrucous lesions. Failure to recognize such variants may lead to diagnostic misclassification, inappropriate management, or unwarranted concern for malignancy. In localized disease, complete surgical excision remains a rational and effective strategy, providing both diagnostic certainty and definitive treatment. The favorable postoperative outcome in this patient, without recurrence or complications, further supports the role of excision as a reliable therapeutic modality in atypical VEN presentations (Waldman et al., 2022)

Study Limitations

Several limitations were identified in this case report. This study involved only a single patient, limiting the ability to generalize the findings to broader populations. As a descriptive case report, the study cannot establish causal relationships or determine prevalence and incidence patterns of atypical adult-onset VEN. Second, molecular and genetic analyses were not performed. Although the discussion referenced mosaic mutations involving FGFR3, HRAS, KRAS, and PIK3CA pathways as possible mechanisms underlying atypical epidermal nevus presentations, these mutations were not confirmed in the present patient. Consequently, the proposed pathogenic explanation remained theoretical rather than directly demonstrated.

Ethical Consideration

Ethical principles were observed throughout the management and reporting of this case. The patient underwent a comprehensive clinical evaluation and received a clear explanation of the procedure, including its benefits, risks, and potential side effects, after which written informed consent for the surgical intervention was obtained. Additionally, written informed consent for the publication of clinical images and case details were obtained from the patient. Patient confidentiality and anonymity were strictly maintained by excluding personally identifiable information. The authors declare no conflicts of interest related to this publication. All procedures were conducted in accordance with standard dermatological and surgical practices, including proper antiseptic preparation,

anesthesia administration, tissue sampling, postoperative care, and follow-up monitoring.

CONCLUSION

This case report shows that solitary adult-onset verrucous epidermal nevus without Blaschko line distribution is a rare presentation that may create significant diagnostic difficulty. The main finding of this case is that clinical morphology alone is insufficient to distinguish VEN from other solitary verrucous lesions, such as verruca vulgaris, seborrheic keratosis, and verrucous squamous cell carcinoma. Histopathological examination remains essential to confirm the diagnosis and exclude infectious or malignant conditions.

The scientific contribution of this report lies in documenting an atypical non-Blaschkoid adult presentation of VEN and emphasizing the importance of clinicopathological correlation in evaluating solitary verrucous lesions. This case also supports the role of complete excisional biopsy as both a diagnostic and therapeutic approach for localized lesions with uncertain clinical features.

However, this report is limited by its single-case design and the absence of molecular or genetic analysis to confirm possible mosaic mutations associated with epidermal nevus. Further studies involving more cases, longer follow-up, and molecular evaluation are recommended to better understand the pathogenesis and clinical spectrum of adult-onset non-Blaschkoid VEN.

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