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CASE REPORT

Inverted Follicular Keratosis in Young Adult: A Rare Entity in the Differential Diagnosis of Skin Tumors

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Introduction: Inverted follicular keratosis (IFK) is a rare benign tumor arising from the follicular infundibulum, typically presenting as a solitary lesion on the head and neck of older adults. The actual incidence of inverted follicular keratosis is likely underreported due to frequent misdiagnosis as more common cutaneous lesions, including seborrheic keratosis, verruca vulgaris, or pyogenic granuloma.

Case Presentation: We reported a rare case of IFK in a 26-year-old male with a solitary, asymptomatic, pedunculated lesion on the scalp. The patient presented with a 0.7 cm-sized lesion demonstrating intermittent bleeding and slow growth over three years. The lesion was initially diagnosed clinically as a pyogenic granuloma, reflecting its solitary skin lesion and bleeding tendency. On dermoscopy, white structureless amorphous areas with amorphous central keratinous plugs and blood spots were seen. The diagnosis of inverted follicular keratosis was established following histopathological examination, which revealed characteristic features of IFK, including endophytic proliferation and squamous eddies. This case underscores the diagnostic complexity of IFK, which can mimic both benign and malignant cutaneous tumors.

Conclusion: IFK, while rare in young patients, should remain a differential diagnosis for scalp lesions across all age groups. Recognition of its dermoscopic and histopathologic features is critical to avoid misclassification and to guide appropriate management. Histopathologic assessment remains essential for establishing a definitive diagnosis.

Keywords: infundibulum tumor, inverted follicular keratosis, young adult

Introduction

The pilosebaceous apparatus consists of the hair follicle, sebaceous gland, and, in certain areas, apocrine glands, along with the arrector pili muscles. This apparatus is primarily concentrated in the head and neck, with hair follicles predominantly on the scalp and sebaceous glands on the face, chest, and upper back. Consequently, tumors arising from these structures tend to occur predominantly in these anatomical regions and are mostly benign.[1] Appendage tumors typically present as solitary or multiple dermal papules or nodules with minimal epidermal change, appearing skin-colored, pink, or bluish.[2] Appendage tumors are uncommon and often present with non-specific clinical characteristics, making definitive diagnosis reliant on excision followed by histopathological analysis.[1,2]

Inverted follicular keratosis (IFK) is a rare benign follicular infundibular tumor classed as a less organized hamartomas form,[1,3] first identified by Helwig in 1954.[4] It typically presents as a solitary, small, skin-colored to pink papule, most commonly occurring on the head and neck region of elderly males. Its classification is controversial, with some considering it a variant of seborrheic keratosis or verruca vulgaris.[4] IFK remains a rarely reported entity, with a particularly limited number of documented cases occurring in younger individuals.[5,6] A 10-year retrospective study from Tunisia reported 13 cases of inverted follicular keratosis, including three in young male patients, underscoring the exceptional rarity of IFK in younger individuals, where atypical morphologic features such as central polylobulation may further complicate clinical diagnosis.[6]

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Inverted follicular keratosis is often clinically indistinguishable and is typically diagnosed only after histopathological evaluation following excision.[6] Prior research reported that accurate pre-excisional diagnosis occurs in less than 2% of cases.[6] Clinically and histopathologically, IFK may mimic malignant neoplasms such as squamous and basal cell carcinoma. Accurate differentiation between IFK and malignant neoplasms is essential, as their management strategies differ significantly. Although commonly reported in older adults, IFK in young individuals is exceedingly rare and may present with atypical clinical features, making early recognition and reporting particularly important to broaden the clinical spectrum and improve diagnostic awareness. Herein, we present a case of IFK in a young male patient.

Case Presentation

A 26-year-old male presented to the Dermatovenereology Clinic with a three-year history of an asymptomatic, slowly enlarging, solitary lesion on the parietal aspect of his scalp. Initially, the lesion's slow growth went unnoticed, becoming apparent only through its persistence and slight enlargement. Intermittent spontaneous bleeding was reported, with precipitating factors such as trauma or scratching.

Dermatological examination revealed a solitary, well-defined, round, reddish-pink pedunculated mass with an irregular surface and minimal crusting measuring 0.7 × 0.7 × 0.5 cm on his scalp (Figure 1A and B), with no other similar lesions elsewhere. The lesion exhibited an irregular, verrucous surface with crusting, but no evidence of friability. After two weeks of topical imiquimod therapy, an approximate 40% reduction in lesion size was noted (Figure 1C); however, complete resolution was achieved following total surgical excision (Figure 1D). The patient's medical and family history were unremarkable, and routine laboratory tests were within normal limits. On dermoscopy, white structureless amorphous areas with amorphous central keratinous plugs and blood spots were seen (Figure 2). Pyogenic granuloma was the presumed clinical diagnosis before excision.

The result of histopathological examination showed hyperparakeratosis, parakeratosis, acanthosis, and an endophytic proliferation, with prominent squamous eddies formed by cleft formation at the periphery (Figure 3). Keratin horn pearls were seen. The subepithelial layer consists of fibrocollagenous connective tissue stroma with lymphocyte inflammatory cells and dilated blood vessels. Based on histological features, a diagnosis of IFK was established.

Given the patient's initial preference for a non-surgical approach, topical 5% imiquimod cream was initiated three times weekly at bedtime, supported by prior reports demonstrating substantial regression of IFK with similar regimens. Two weeks following the application of imiquimod, approximately 40% regression of the lesion was seen. A mild local adverse reaction was present with a tingling sensation shortly after imiquimod application, but tolerance soon increased. Due to intermittent bleeding of the lesion, the patient subsequently underwent complete surgical excision of the lesion under local anesthesia at his request. The patient was fully informed about the diagnosis, treatment options, potential risks, and expected outcomes, and provided written informed consent prior to both medical therapy initiation and surgical excision.

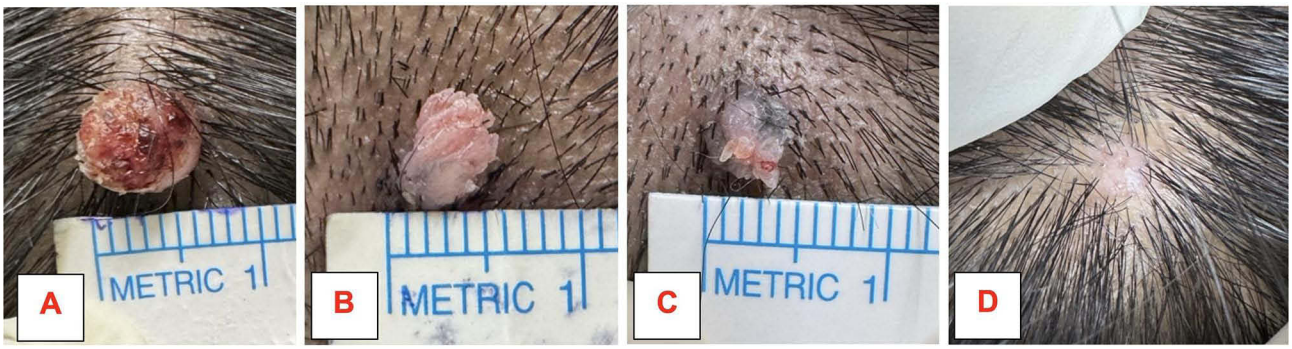

Figure 1 A solitary, round, reddish-pink pedunculated mass with minimal crusting measuring 0.7×0.7x0.5 cm with an irregular surface on the scalp (**A**) Verrucous surface of the lesion after shave biopsy (**B**) Regression of the lesion was observed after 2 weeks of 5% imiquimod application (**C**) No lesion were seen 46 days after complete excision (**D**).

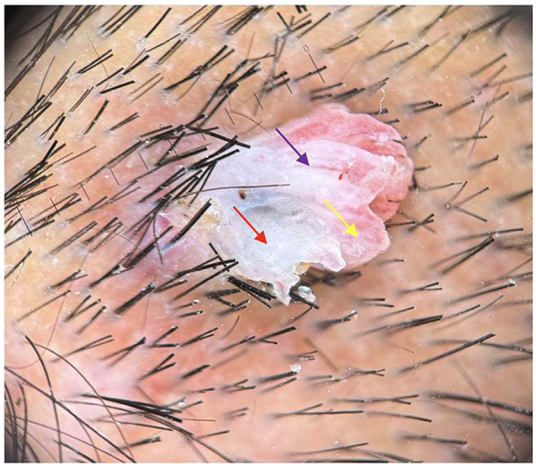

Figure 2 Dermoscopy showed hairpin vessel (purple arrow) with milky red (yellow arrow) and amorphous white area (red arrow).

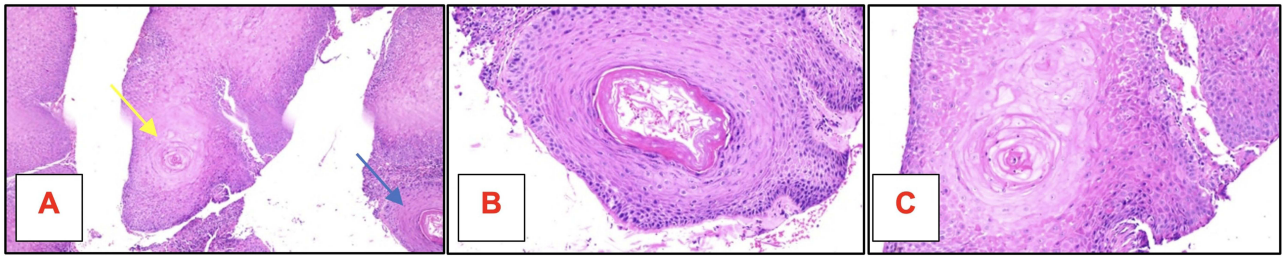

Figure 3 Histopathological examination of the skin lesion revealed squamous eddies (blue arrow) and horn pearls (yellow arrow) at 40x magnification (**A**), with higher magnification highlighting squamous eddies (**B**) and horn pearls (**C**) at 100x.

Discussion

Inverted follicular keratosis is a localized hyperkeratotic lesion associated with the pilosebaceous orifice that typically presents as a solitary, firm, white-tan to flesh-colored hyperkeratotic nodular or filiform verrucous lesion ranging in size from 0.3 to 1 cm in diameter and is asymptomatic.[1,4,7,8] Although rare, lesions may reach sizes up to 8 cm and may present with inflammation and pruritus.[1,7] More than 50% of the lesions exhibited a central keratotic area, and an ulcerated center was described in several cases.[6] Ninety-two percent of the lesions are located in sun-exposed areas.[6] About 90% of cases involve the head and neck, with the cheeks and upper lip being the most frequently affected areas.[4,7] Involvement of the eyelids has also been reported.[4] A significant association was found between lesion location and patient age, with older patients showing more lesions on the lower extremities, upper extremities, and neck.[9] In younger patients, IFK has been reported to occur on the face (nasal, periocular), neck, trunk, genital, and lower extremities, with the scalp being the most common site (50%).[9–11] IFK is more prevalent among males, Caucasians, and older individuals.[1,4,7] Incidence in individuals younger than 30 years accounted for only 7.5% of cases.[10] Although IFK typically manifests as a solitary lesion, multiple lesions of IFK have been reported in individuals with Cowden syndrome.[12] In this case, the patient was a young male with a solitary pedunculated lesion on the scalp, consistent with literature describing a typical predilection of IFK in young patients.

Duperrat and Mascaro proposed that the tumor originates from the hair follicle infundibulum, although its exact etiology remains unclear.[7] The pathogenesis of IFK appears multifactorial, with long-term UVB exposure to epidermal keratinocytes playing a pivotal role.[9] UV-induced DNA damage and reactive oxygen species generation contribute to oxidative injury and mutations, while repeated exposure suppresses DNA repair mechanisms, leading to cumulative genetic alterations.[9] Additionally, UV damage triggers pro-inflammatory cytokine production (IL-1β, TNF-α), promoting keratinocyte proliferation and abnormal differentiation.[9] A prior report of vulvar IFK in a young patient noted a history of frequent perineal shaving and total body tanning, leading to speculation that repetitive trauma or abrasion may

contribute to tumor development.[13] The classification of IFK is still uncertain, with ongoing debate about whether it is a separate condition or related to viral warts, seborrheic keratosis, or Cowden syndrome; the absence of human papilloma virus in most recent cases undermines previous suggestions of a viral cause.[6,12,14]

Inverted follicular keratoses are primarily endophytic tumors characterized by lobular or finger-like epithelial projections into the dermis,[14] though some may exhibit a dominant exophytic component.[4] Mehregan identified four histological growth patterns: 1) a papillomatous wart-like variant with exophytic growth and surface keratinization; 2) a keratoacanthoma-like type with peripheral buttressing and a central mixed epithelial mass; 3) a solid nodular form that is mainly endophytic with lobulated epithelial masses; and 4) a rare cystic variant featuring intra-tumoral clefts and small cyst formation.[4] Each tumor lobule consists of peripheral basaloid cells and central keratinizing squamous cells, with mitotic figures commonly observed in the basaloid component.[4,7]

In the majority of IFK cases, the diagnosis is not clinically suspected prior to histopathological confirmation.[6] IFK is defined by the squamous eddies, which are concentric whorls of squamous cells that may demonstrate central keratinization with keratohyalin and keratin.[1,4,14] Squamous metaplasia with abundant eosinophilic cytoplasm is commonly observed.[6] The proliferation of keratinocytes appears to encircle one or more follicular canals that connect to the infundibulum of the hair follicle and extend to the surface.[1,7] Peripheral cleft formation and focal acantholysis may also be observed, while melanin pigmentation tends to be minimal.[4] The underlying dermis may contain a mild lymphohistiocytic infiltrate and telangiectatic vessels, particularly in filiform variants.[4] The overlying epidermis commonly exhibits hyperkeratosis, parakeratosis, keratinous plugs, and occasionally a cutaneous horn.[4,6] Immunohistochemically, suprabasal layers show an increased number of Bcl-2-positive dendritic cells, corresponding with a higher density of CD1a+ cells.[4] IFK was established in this patient by the presence of squamous eddies with endophytic proliferation found on histopathological results.

Vascular pattern analysis is a critical component in the differential diagnosis of non-pigmented skin tumors.[15] Therefore, supplementary modalities such as dermoscopy have been recommended to improve diagnostic accuracy, as they may exhibit specific features suggestive of inverted follicular keratosis.[6,16] It commonly reveals a keratoacanthoma-like pattern, characterized by radially arranged hairpin, glomerular, or arborizing vessels surrounding a white, amorphous central area.[4,6,15] Another frequent pattern features a yellowish-white amorphous central region with radially oriented vascular structures. A less common pattern shows a yellowish-white central area with milky red globules.[4] The presence of a whitish halo surrounding vessels is a strong indicator of epithelial differentiation in neoplasms and is typically absent in melanocytic tumors.[17,18] A previous study reported that although the majority of dermatoscopic and vascular features do not differ significantly between Fitzpatrick skin phototypes II–III and IV–V, certain elements vary by phototype, with pink structureless areas and blood spots on ulceration occurring more commonly in lighter skin types, whereas blue–grey coloration is significantly more frequent in darker phototypes.[19] To date, no published studies have reported defined sensitivity or specificity metrics for the dermoscopic diagnosis of IFK, and no dermoscopic pattern differences between young and elderly patients have been described in the existing literature. Dermoscopy of the lesion in this patient revealed a keratoacanthoma-like pattern, characterized by hairpin vessels encircling a central white amorphous area, accompanied by milky-red globules.

Reflectance confocal microscopy (RCM) enabled the exclusion of a melanocytic tumor by demonstrating the absence of key diagnostic features, such as a cobblestone pattern or pagetoid cells in the epidermis, and meshed, ringed, or clod-like structures, edged papillae, or dermal nests at the dermoepidermal junction.[15] In IFK, RCM may present nonspecific findings, including epidermal projections, superficial keratotic scale, and hairpin or glomerular vessels.[4,15] In some cases, a lobular epidermal configuration with an irregular honeycomb pattern of the granular and spinous layers, displaying variability in line brightness and hole size, may be observed. Although these irregularities may raise suspicion for squamous cell carcinoma, the diagnosis of IFK is confirmed by biopsy.[4]

The clinical differential diagnosis for IFK comprises pyogenic granuloma, seborrheic keratosis, trichilemmoma, verruca vulgaris, a range of follicular adnexal tumors, basal cell carcinoma, squamous cell carcinoma, and malignant melanoma.[4,7,20,21] Squamous eddies accompanied by an intense chronic inflammatory cell infiltrate in IFK resemble those in irritated seborrheic keratosis; however, the predominantly endophytic growth pattern and involvement of the dermis, along with increased numbers of Bcl-2 positive dendritic cells help differentiate it from seborrheic keratoses.[4,6,7]

It also has structural similarities with trichilemmoma, an endophytic, lobulated epithelial tumor often centered around a follicular structure.[4,7] However, trichilemmomas are characterized by glycogen-rich clear cells, a palisaded basal layer, and a thickened basement membrane.[4,7] Human papillomavirus is typically absent in inverted follicular keratosis, arguing against its classification as a verruca vulgaris variant, though some warts may exhibit overlapping histologic features.[4] Mitotic figures may be rarely seen in inverted follicular keratosis, although prominent cellular atypia typical of squamous cell carcinoma is not present.[1,6,7] While squamous eddies may resemble horn pearls found in squamous cell carcinoma, they can be differentiated by their smaller size, higher frequency, and distinct borders.[6] Immunohistochemical analysis using the anti-Ki-67 antibody may be conducted to assess the proliferative activity of the lesions, revealing a low proliferation index consistent with benign pathology and effectively excluding basal cell carcinoma and squamous cell carcinoma.[5] Another study reported that the immunohistochemical profile characterized by mosaic p16 staining, wild-type p53 expression, and uniformly negative HPV testing reinforces the interpretation of IFK in young adults as a benign, non-HPV-associated lesion with no evidence of malignant potential.[19] Rarely, increased pigmentation may lead to clinical misdiagnosis as malignant melanoma.[4]

Complete surgical excision remains a well-established and effective therapeutic modality for IFK; nonetheless, recent reports have demonstrated the efficacy of topical 5% imiquimod as a non-surgical alternative treatment.[21,22] Imiquimod exhibits antitumor and antiviral properties,[23] along with antiangiogenic effects, by upregulating endogenous antiangiogenic mediators such as tissue inhibitors of matrix metalloproteinases and downregulating proangiogenic factors, including basic fibroblast growth factor and matrix metalloproteinases.[21] It also induces cytokine production through activation of antigen-presenting cells, including monocytes, macrophages, and dendritic cells, via stimulation of toll-like receptors 7 and 8.[19,24] Initially, the patient was prescribed topical 5% imiquimod, resulting in approximately 40% reduction in lesion size after two weeks of treatment. However, due to episodic bleeding triggered by scratching and concern about the persistence of the lesion, the patient elected to undergo complete surgical excision.

Inverted follicular keratoses are generally stable and persistent but can occasionally undergo spontaneous regression.[7] However, IFK has been documented to recur within weeks following incomplete excision, although recurrence is not consistently observed in all cases.[1,4] On the other hand, no instances of invasive growth or metastasis have been reported in the literature following surgery.[22]

Conclusion

This case report documents IFK in a young patient, a condition predominantly observed in older adults, expanding the current understanding of its age distribution and reinforcing the importance of including IFK in the differential diagnosis across all age group. The presence of scalp lesions in young patients should prompt clinicians to include IFK as a possible diagnosis and pursue thorough evaluation. Owing to its clinical similarity to both benign and malignant tumors, accurate identification of IFK necessitates a comprehensive diagnostic strategy that integrates thorough clinical assessment, histopathological confirmation, and dermoscopic evaluation, thereby facilitating precise diagnosis and guiding optimal patient management.

Abbreviations

IFK, inverted follicular keratosis; RCM, reflectance confocal microscopy.

Ethics Approval and Consent to Participate

This study had obtained ethical clearance from the Research Ethics Committee of Dr. Hasan Sadikin General Hospital No. DP.04.03/D.XIV.4.4/2866/2025. Written informed consent was obtained from the patient to participate in this case report.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images. Approval has been obtained from Dr. Hasan Sadikin General Hospital to publish the case details.

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Disclosure

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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