Alqalam Journal of Medical and Applied Sciences. 2025;8(2):907-910
https://doi.org/10.54361/ajmas.258254

Review article

Keratoacanthoma of the Head and Neck: A Mini Review

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Abstract
Keratoacanthoma (KA) is a keratinocyte-derived, rapidly growing skin neoplasm. A well-differentiated lesion often exhibits spontaneous regression. KA typically presents as a dome-shaped lesion with a central keratin plug, demonstrating a symmetrical, well-circumscribed architecture histologically. This review discusses the epidemiology, clinical presentation, histopathology, differential diagnosis, and management of KA with emphasis on lesions occurring in the head and neck region.
Keywords. Keratoacanthoma, Clinical Presentation, Histopathology, Immunohistochemical.

Introduction

Keratoacanthoma (KA) is a skin tumor that closely resembles Squamous Cell Carcinoma (SCC). It typically appears on sun-exposed areas such as the face, forearms, and hands, mostly affecting middle-aged and older adults. Arises in the pilo-sebaceous apparatus and pathologically mimics SCC [1]. There are still Strong debates concerning the classification of keratoacanthoma as a variant of invasive SCC. Dermatopathologists refer to the lesion as SCC, keratoacantoma-type. It is usually detected as a single dome-shaped nodule with a central crater filled with keratin. It is a fast-growing lesion that regresses and confines spontaneously [2]. KA refers to a type of lesion that typically undergoes three distinct phases. Initially, there is a rapid growth phase lasting about 6 to 8 weeks. This is followed by a stationary phase, during which the lesion stops growing. Finally, there is an involution phase lasting approximately 4 to 6 weeks, during which the lesion regresses spontaneously. Once it resolves, it often leaves behind a scar that is atrophic and hypopigmented [3]. This condition is most commonly seen in older adults with fair skin, particularly in areas frequently exposed to the sun, such as the lips (including the vermilion border), cheeks, nose, and the backs of the hands. Lesions are frequently found on the head and neck region are particularly concerning due to aesthetic and functional implications [1].

Epidemiology

KA typically affects older adults, with peak incidence in individuals over 60 years and a male predilection. It is more prevalent in fair-skinned populations with a history of chronic sun exposure. Additional risk factors include immunosuppression (e.g., post-transplant patients), exposure to carcinogens, trauma, and genetic syndromes such as Muir-Torre [4]. The lesion shows no significant gender predilection, although it is slightly more common in males.

Clinical features

KA presents as a solitary, rapidly growing, dome-shaped papule or nodule with a central keratin-filled crater. Lesions most frequently occur on sun-exposed sites—particularly the face, scalp, ears, and neck. Most KAs are 1–2 cm in diameter but may reach larger sizes if untreated. Though typically asymptomatic, they may ulcerate or become secondarily infected [5]. The exact cause of keratoacanthoma remains vague, although several factors have been considered for the onset of the skin tumor have been considered. Keratoacanthoma is noted to have a similar etiology to squamous cell carcinoma. Prolonged unprotected sun exposure is the most implicated risk factor in keratoacanthoma, and fair-skinned individuals [6].

Histopathology

Microscopically, KA displays a symmetrical, crateriform architecture filled with keratin and surrounded by proliferating squamous epithelium. The margins are usually well-defined and non-infiltrative, which helps differentiate KA from SCC. However, overlapping histological features make definitive diagnosis difficult in some cases. In such situations, complete excision is recommended to rule out malignancy [7].
The microscopic examination displayed: The lesion consists of hyperplastic squamous epithelium with a central, crater-like depression extending into the underlying connective tissue. Keratin accumulation, forming keratin pearls, was evident, and individual cell keratinization was occasionally observed, primarily in the upper regions of the lesion [4]. The superficial epithelium along the lateral border appeared histologically normal. The lesional epithelial cells exhibited mild atypia and cellular pleomorphism. In the fibroconnective tissue, infiltration of chronic inflammatory cells—mainly lymphocytes—may be present [8].

Received*: 13-03-2025 -* ***Accepted****: 10-05-2025 -* ***Published****: 20-05-2025*

Differential Diagnosis

The primary clinical and histologic differential diagnosis is well-differentiated SCC. Other considerations include basal cell carcinoma, verruca vulgaris, cutaneous horn, and molluscum contagiosum. Distinction from SCC is critical due to differing prognoses and management [9].

Keratoacanthoma exoendophytic lesion with a central horn-filled crater overhanging 'lips' of epithelium rarely ulcerated abundant pale staining cytoplasm of keratinocytes, intraepithelial abscesses within the lesion, acantholytic cells within the intraepithelial abscesses often, gland-like formations rare, lack of anaplasia, sharp outline between tumor nests and stroma absence of stroma desmoplasia [10].

SCC is predominantly endophytic with no horn-filled crater, no epithelial, lips commonly ulcerated, acantholytic cells form without associated neutrophils, and pseudo glandular formations. Often, anaplasia is common.

Immunohistochemical staining of SCC reveals strong expression of COX-2 and Telomerase and complete absence of desmoglein and Syndecan-1[11]. KA COX-2 and Telomerase exhibit weak expression where whereas desmoglein and Syndecan-1 show high expression [10].

Management

Surgical excision is the preferred treatment, both for diagnostic confirmation and therapeutic removal. Mohs micrographic surgery is often utilized for lesions in cosmetically or functionally sensitive areas [12]. Alternative therapies include: Cryotherapy, which is effective for small lesions. Intralesional therapy using Methotrexate or 5-fluorouracil injections for selected cases. Topical agents such as Imiquimod cream for superficial or regressing lesions and radiotherapy are considered for patients unfit for surgery [13].

Prognosis

KA generally has an excellent prognosis after complete excision. Recurrence is uncommon, but close monitoring is advised, especially in immunosuppressed patients or when histologic ambiguity exists. Although KA is usually benign, transformation into invasive SCC has been reported, warranting caution in management [14]. which undergoes progressive peripheral growth with atrophy in the center of the lesion. It is often solitary, but multiple KCMs have been described occasionally. Unlike the solitary KA, KCM shows no tendency toward spontaneous resolution [14].

Subungual KA is a rare, destructive variant of keratoacanthoma that seldom regresses spontaneously. It may involve the distal tissue under the nail or the proximal nail fold, and sometimes also affects the underlying bone [15].

Syndrome-associated keratoacanthoma:

Multiple Ferguson-Smith keratoacanthoma (familial keratoacanthoma)

This is a rare autosomal dominant, mapped to chromosome 9, self-healing type of keratoacanthoma, with lesions arising in early adulthood.

Muir-Torre syndrome

Keratoacanthoma may be a component of Muir-Torre syndrome, which is a cancer-associated genodermatosis with multiple sebaceous neoplasms (adenomas, adenocarcinomas), keratoacanthomas, and gastrointestinal malignancies (most commonly colon), although other carcinomas have been reported (genitourinary, pulmonary, endometrial. MTS has an AD pattern of inheritance.

Genetic mutations in two of the DNA mismatch repair genes (MLH1 and MSH2) have been found in some sporadic cases of KA as well as in 70% of Muir-Torre syndrome-associated KA. Germline mutations associated with Muir-Torre syndrome result in microsatellite genomic instability, which can alter tumor suppressor gene expression, leading to the development of multiple malignancies in the syndrome (visceral and dermal malignancies).

KA of the lip is derived from outer root sheath cells (ORS), particularly those associated with the upper part of ORS, the infundibulum.

The Grzybowski generalized eruptive (Kas)

Kas is a rare condition of unknown etiology. Kas of this type is smaller, 2-3 mm in size, and more numerous than the Ferguson-Smith variant. Patients usually present with thousands of lesions. Grzybowski KAs often have a military appearance and have a predilection for the eyelids, palms, soles, and oral mucous membrane. These lesions usually resolve spontaneously but often leave scarring and affect middle-aged adults. Clinical behavior: & metastatic potential. Unlike SCC, the lesion exhibits spontaneous healing. Over several months. This regression may be immunologically mediated.

The tumor exhibits unpredictable and aggressive growth in some instances, leading to local destruction. In immunosuppressed patients, cases of metastasis of (KA) to distant organs have been reported. Perineural invasion is observed in 1% to 4% of KA cases. Complications include extension into facial muscles, involvement of cranial nerves, invasion of the cavernous sinus, and metastasis to the parathyroid gland, as

Received*: 13-03-2025 -* ***Accepted****: 10-05-2025 -* ***Published****: 20-05-2025*

well as local structures. Recurrence of keratoacanthoma (KA) occurs in up to 8% of cases, particularly when lesions are found on the fingers, hands, lips, or ears, with trauma often being a contributing factor [16].

Histogenesis of Keratoacanthoma

Keratoacanthoma (KA) is a unique skin tumor that has been the subject of extensive research regarding its origin and development. The prevailing theory suggests that keratoacanthomas arise primarily from the outer root sheath of hair follicles, particularly in sun-exposed areas of the skin. This aligns with observations that KA often occurs in older individuals with significant sun exposure, indicating a potential link between ultraviolet radiation and tumor development [17]. This hypothesis is supported by both histological features and molecular findings that suggest follicular differentiation.

Immunohistochemistry has played a pivotal role in elucidating the origin of keratoacanthoma (KA), supporting its differentiation from squamous cell carcinoma (SCC) and reinforcing its derivation from the infundibular portion of the hair follicle. The following markers have been especially informative:

KA shows strong expression of cytokeratin 17 (CK17), which is characteristic of the outer root sheath and infundibulum of hair follicles. Cytokeratins 1 and 10 (CK1/10), markers of infundibular differentiation, are also commonly expressed.

Immunohistochemical Profile

The immunohistochemical (IHC) profile of keratoacanthoma is crucial for distinguishing it from squamous cell carcinoma (SCC). Studies have shown that keratoacanthomas exhibit distinct patterns of protein expression, which can aid in the diagnosis and understanding of their behavior [18].

p53 and Ki-67: Both proteins are expressed in keratoacanthomas, but their expression patterns differ from those in SCC. In KA, the expression of Ki-67, a marker of proliferation, tends to decrease during the involution phase of the tumor, contrasting with SCC, where higher levels are maintained [19].

p21 (WAF-1/CIP1): This protein is associated with cell cycle regulation and is found to be expressed in keratoacanthomas, particularly during the maturation and regression phases. Its expression may reflect the differentiation status of the tumor [20].

Bcl-2: This anti-apoptotic protein has been studied in the context of KA and SCC, with varying levels of expression noted. The presence of Bcl-2 may indicate the tumor's ability to evade apoptosis, a feature that could contribute to its growth dynamics [19].

Conclusion

Keratoacanthoma is a unique lesion that requires careful clinical and histopathological evaluation, particularly when occurring in the head and neck region. Given the diagnostic challenge it presents, prompt excision with histologic review remains the gold standard. Further research into its molecular characteristics may clarify its relationship to SCC and guide future therapeutic approaches.

The immunohistochemical profile of keratoacanthoma—particularly its expression of CK17, CK1/10, limited Ki-67 proliferation, basal p53 pattern, and variable β-catenin activation—supports its derivation from the infundibular epithelium of the hair follicle. These findings reinforce its distinction from SCC and other epidermal neoplasms.

Conflict of interest. Nil

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Received: *13-03-2025* - ***Accepted***: *10-05-2025* - ***Published***: *20-05-2025*

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Received*: 13-03-2025 -* ***Accepted****: 10-05-2025 -* ***Published****: 20-05-2025*