

# Keratoacanthoma of the lip: A case report with emphasis on histogenesis

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## Abstract

Keratoacanthoma (KA) is a benign epithelial tumor which presents clinically as a proliferating dome-shaped keratin-filled crater. The lesion occurs predominantly upon sun-exposed areas of the body and is known to arise from hair follicle. Actinic rays are a major contributing factor in the etiology. It simulates grossly as well as microscopically a low-grade squamous cell carcinoma. KAs occur habitually on the mucous membrane as well, but their origin in these cases is debatable, owing to the lack of hair follicles in these sites. Our report is an attempt to demonstrate the cells that could be responsible for initiation of this lesion on the oral mucosa.

**Keywords:** Ectopic sebaceous gland, follicular infundibulum, keratoacanthoma

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## INTRODUCTION

Keratoacanthoma (KA) is a relatively common benign, proliferative lesion, which involves cutaneous tissues and less frequently the mucosal surfaces. KAs are frequently found on sun-exposed areas suggesting that actinic rays among other etiologic factors are largely responsible for the lesion. It is believed that cutaneous lesions arise from hair follicles, while the occurrence of KA on mucosal surfaces suggests its possible origin from ectopic sebaceous glands or surface epithelium. KA is a self-limiting lesion that undergoes spontaneous regression and is known to heal by scarring. Here, we report the case of a KA presenting on the lower lip with an attempt to throw light on its pathogenesis.

## CASE REPORT

A 45-year-old female was referred for evaluation of an asymptomatic nodule on the lower lip of 4-week duration. Clinical examination revealed a well-defined, nontender, ulcerated, nodular growth measuring approximately 1 cm × 1 cm on the lower lip vermilion [Figure 1]. Oral hygiene was fair. There was no report of local trauma, and the patient presented no parafunctional habits. The patients' medical, family and social history was noncontributory.

An excisional biopsy was performed under local anesthesia. Histopathological examination of H- and E-stained section revealed a hyperkeratotic, hyperplastic epithelium with parakeratin plugging in some areas. The underlying connective tissue stroma showed multiple areas of

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epithelial tissue entrapment with cystic degeneration in the center and keratinization [Figures 2 and 3]. Periodic acid–Schiff (PAS)-stained section showed glycogen granules in the superficial epithelium. The epithelial proliferations in the connective tissue did not exhibit PAS positive glycogen granules though [Figure 4].

The lesion healed with no scarring over 5 weeks, but the patient was lost to follow-up later.

## DISCUSSION

KA is a benign, rapidly proliferating epithelial growth seen in older age groups (between the ages of 45 and 69 years) with a male preponderance.<sup>[1-4]</sup>

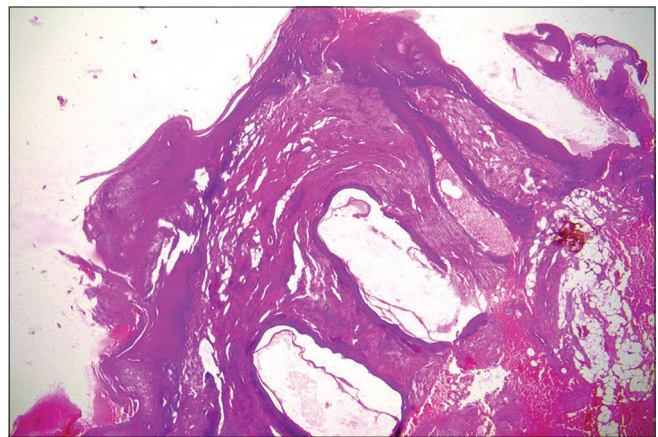
It arises on the sun-exposed parts of the body chiefly face, neck and forearms, especially in light-skinned individuals,<sup>[5]</sup> as a self-limiting proliferation of the hair follicle apparatus called follicular infundibulum.<sup>[2]</sup> The etiologic factors

implicated include irritation in the form of actinic rays, trauma, tars, virus, immunocompromised status and genetic factors (which are commonly responsible for squamous cell carcinoma [SCC] too).<sup>[6]</sup>

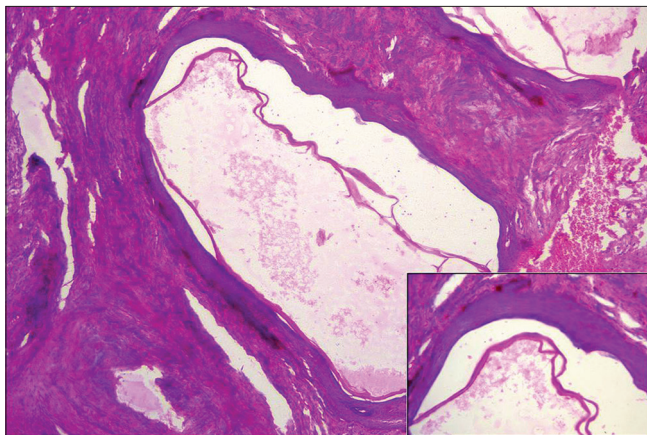
KA typically presents as a dome-shaped lesion with a central crater filled with keratin. This condition is thought to represent a proliferation of the infundibular portion of hair follicles rather than epidermis. In the normal hair follicle, the cells have a programmed ability to be deleted by apoptosis. Thus, it is suggested that KA represents a temporary derangement of the normal regulatory apoptotic mechanism in the follicles. TUNEL results in a study have shown that these aberrant cells do undergo complete apoptosis but by another mechanism.<sup>[7]</sup> It is believed that KA cells can differentiate into cells that are similar to outer root sheath cells of the hair follicle, further supporting the possibility that cutaneous KAs arise from hair follicles. Furthermore, it is seen that KA



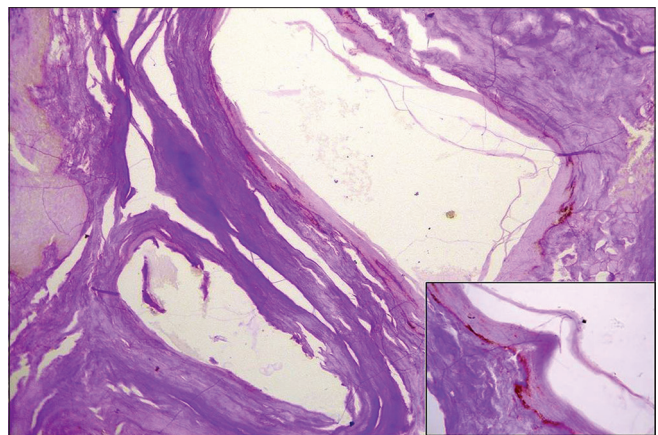
**Figure 1:** Clinical image shows noduloulcerative growth with keratin plugging seen on left vermilion of the lower lip



**Figure 2:** Histopathological image shows hyperkeratotic epithelium with parakeratin plugging overlying connective tissue stroma with epithelial proliferations superficially in the stroma (H&E, x40)



**Figure 3:** Histopathological image shows epithelial tissue entrapment with cystic degeneration in the center and keratinization (H&E, x100). Inset (H&E, x400)



**Figure 4:** Histopathological image shows periodic acid–Schiff-stained section showing negative staining for glycogen granules (H&E, x100). Inset (PAS, x400)

follows a cycle similar to the life cycle of a hair follicle, i.e., cycles of proliferation (anagen), regression (catagen) and quiescence (telogen).<sup>[1,3]</sup>

KA has been reported to have three clinical stages: (i) Proliferative, (ii) mature and (iii) involucional or resolving. Ghadially has classified KA as Type I, bud shaped if it is of upper follicular origin; Type II or dome shaped and Type III or berry shaped if the lesion is of lower follicular origin.<sup>[4,8]</sup> Apart from solitary and multiple forms, the various other types of morphologic and syndromic forms of KA are: Agglomerate KA, KA centrifugum marginatum, giant KA, subungual KA, mucous membrane KA (including the intraoral variety), multiple KAs of the Fergusson Smith types, multiple persistent KAs, generalized eruptive KAs of Grzybowski,<sup>[9]</sup> KAs in Torre syndrome, KA in xeroderma pigmentosum and KAs in nevus sebaceous of Jodassohn.<sup>[4]</sup>

KA of the lip is usually a solitary, circular ulcerated nodule with central keratin plug that occurs at the vermilion border of the lip. Occurrence of solitary KA on vermilion portion of lips is now widely recognized, and it is debatable as there are no hair follicles in oral mucosa. Some report its possible origin from surface epithelium,<sup>[4,5]</sup> whereas others suggest that since oral mucosa lacks hair follicles, the KA may develop from ectopic sebaceous glands.<sup>[4]</sup>

PAS stain with or without diastase is a special stain demonstrating cytoplasmic glycogen content and stromal hyalinized basement membrane in cutaneous adnexal lesions. The outer two epidermal cell layers of hair bulb (from which KA is thought to occur) consist of large, glycogen-rich cells which can be diagnosed with PAS stain,<sup>[10,11]</sup> thus helping in the determination of cells of origin of the lesion. To understand the histogenesis of mucous membrane KA occurring on the lip, we analyzed PAS staining in the lesion.

Staining for PAS was negative in the present case, reinforcing that origin of KAs of lip could be from ectopic sebaceous glands rather than from a hair follicle.

The epithelial entrapments in the connective tissue, typifying epithelial proliferation in the stroma displayed cystic spaces with keratinization. Previously, cystic appearance in KA has been reported in two recurrent cases, attributing it to a proliferative signal being switched in a remnant of the infundibular cyst focus, resulting in the cystic appearance.<sup>[12]</sup> This left us to deliberate whether the lesion in our case was a recurrent one with the patient having overlooked its occurrence the first time or was it a *de novo* lesion displaying cystic appearance.

KA must be considered for its clinical and histopathological similarity with SCC. The morphologic features and growth pattern of a KA are distinct. However, in a perplexing case, histopathology is the mainstay in differentiating between the two lesions.<sup>[13]</sup> Advanced studies directed at differentiating KA and SCC have shown that expression of cell proliferation markers, telomerase activity and apoptotic and cell adhesion marker are markedly more in SCC, categorizing KA and SCC as two distinct entities.<sup>[7,14,15]</sup> Schwartz considered KA as an aborted malignancy that only rarely progresses into invasive SCC.<sup>[8]</sup>

Different treatment modalities proposed for KA are cryotherapy, electrodesiccation, irradiation, 5-fluorouracil, curettage, radium implantation, cautery, hydrocortisone and antibiotic ointments, podophyllin and topical photodynamic therapy which have been tested to varying extents. However, complete excision has proved to be the treatment of choice as it facilitates healing without scarring and also allows histopathological assessment of the complete lesion.<sup>[10]</sup>

## CONCLUSION

KA is a common benign cutaneous lesion which occasionally presents itself on the mucous membrane. It is known to originate from follicular infundibulum, but mucosa is devoid of hair follicles. This report of KA of the lip is an attempt to clarify this unsolved query. Through PAS staining, we concluded that KA of oral mucosa in all probabilities arises from ectopic sebaceous glands and not hair infundibulum. Furthermore, KA has striking clinical familiarity with SCC, and a certain way of differentiating them is by histopathology. The mainstay in treatment is complete excision as it facilitates healing without scarring and also allows histopathological evaluation of the lesion.

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## Conflicts of interest

There are no conflicts of interest.

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