Dermatology Practical & Conceptual

An Aggressive Case of Infundibulocystic Squamous Cell Carcinoma on the Upper Lip: A Hybrid Pathology of Well-Differentiated and Infiltrative Variants

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Introduction

Infundibulocystic squamous cell carcinoma (icSCC) is a rare skin adnexal neoplasm, originating from the infundibulum of hair follicles. Histologically, it displays follicular differentiation and comprises three distinct variants; well-differentiated, less-differentiated, and infiltrative forms [1,2]. The highly differentiated pathology of icSCC may hold mild-to-moderate phenotype, but often possesses aggressive clinical presentation, alerting a prognostic and therapeutic perspective. We describe for the first time such a case of icSCC with a hybrid histology of well-differentiated and infiltrative variants, whose clinical course showed an aggressive behavior but prompt regression to a concurrent chemoradiation therapy, possibly retaining reminiscent of hair cycle.

Case Presentation

An 82-year-old Japanese man presented with a month-history of a small nodule on the upper lip, which rapidly enlarged after diagnostic skin biopsy. Examination revealed a 3 × 2 cm, reddish indurative plaque with keratotic surface on the upper lip (Figure 1A). Dermoscopy revealed reddish homogeneous area with tiny white cystic structures, resembling milia-like cysts (Figure 1B). Previous histological findings showed a keratin-filled cystic structure with irregular shaped, epithelial walls that invaded into the deep dermis, suggesting well-differentiated SCC, although the diagnosis of keratoacanthoma remains likely (Figure 2A).

He underwent excisional biopsy with safety margin for the conclusive diagnosis. Histology revealed a volcano-like

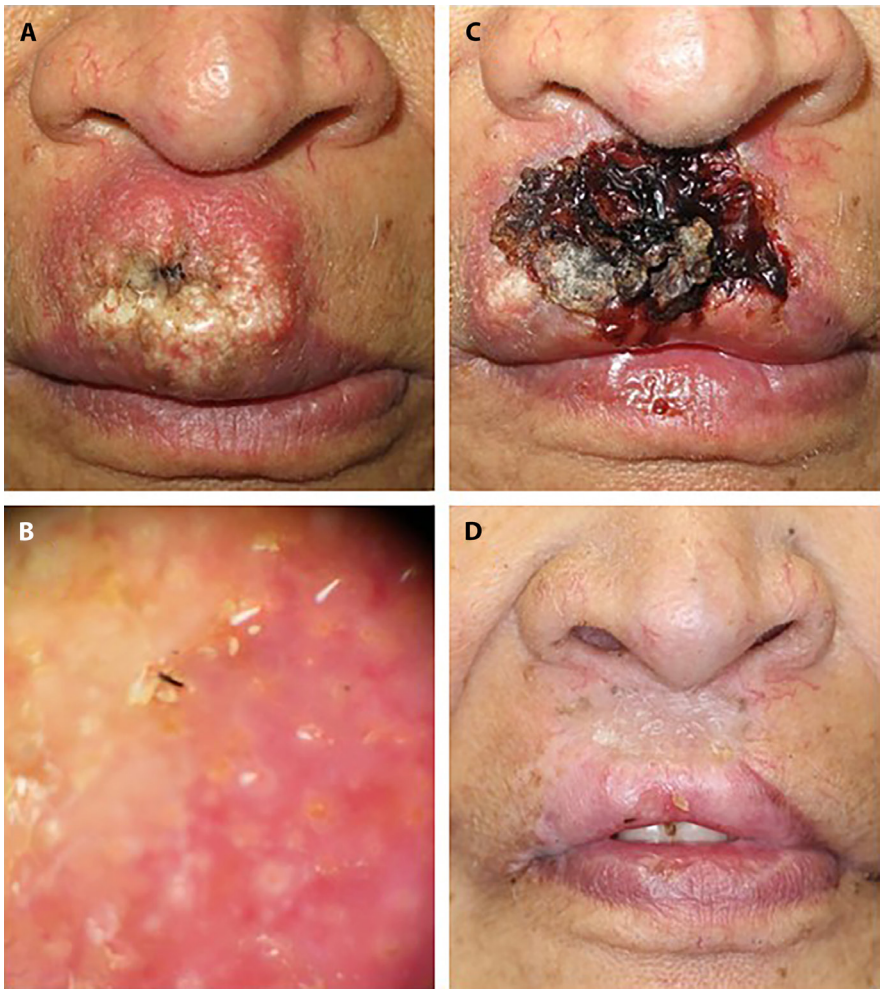

Figure 1. Time-course clinical view and dermoscopic findings.

(A) A 3 cm × 2 cm, reddish indurative plaque with whitish keratotic surface on the upper lip.
(B) A reddish homogeneous area with scattered tiny white cystic structures, similar to millia-like cysts.
(C) Three weeks after marginal resection of the tumor, a local recurrence developed and rapidly enlarged, covering almost the entire upper lip and part of the nostril.
(D) The tumor size and invasiveness were dramatically reduced and disappeared leaving a well-healed scar by four courses of chemotherapy with docetaxel and irradiation.

opening of the central keratin-filled plug invaginated by epidermal lipping that arose from the follicular infundibulum (Figure 2, B and C), similar to those of keratoacanthoma. The neighboring epidermis was irregularly thickened with various sized nests and endophytic infundibular cysts, invading into the deep dermis and peripheral nerve sheath (Figure 2, D-G). The tumour nests were mostly consisted of eosinophilic glassy-pale keratinocytes with slight-to-moderate nuclear atypia (Figure 2H). The former histopathology was compatible with well-differentiated icSCC and the latter was infiltrative one. Immunohistochemistry showed intense staining of CK16 (Figure 2I) and β-catenin (Figure 2J), follicular infundibulum markers [2], and Bcl-xL (Figure 2K), a candidate biomarker for distinguishing SCC from keratoacanthoma [3].

Three-weeks after resection, a local recurrence of the tumour developed and rapidly enlarged, which covered almost the entire upper lip and part of the nostril (Figure 1C). Enhanced CT scanning showed no evidence of metastasis. Considering the aggressive clinical activity, age, and affected skin sites, we employed a combined chemoradiation therapy with docetaxel (25mg/m^2 monthly) and electron beam, achieved a dramatic reduction and completed disappearance leaving a well-healed scar (Figure 1D).

Conclusions

To date, there have been only 5 case reports of icSCC, including ours (Table 1) [2,4,5]. Their affected skin sites were the exposed area. Recurrence or metastasis were unclearly stated. Our case displayed abrupt local recurrence within 3-weeks after complete resection and rapid regression during chemoradiation therapy. The bipolar clinical course may in part reflect a possible transition of two key life-stages of the hair follicle (eg, anagen and catagen).

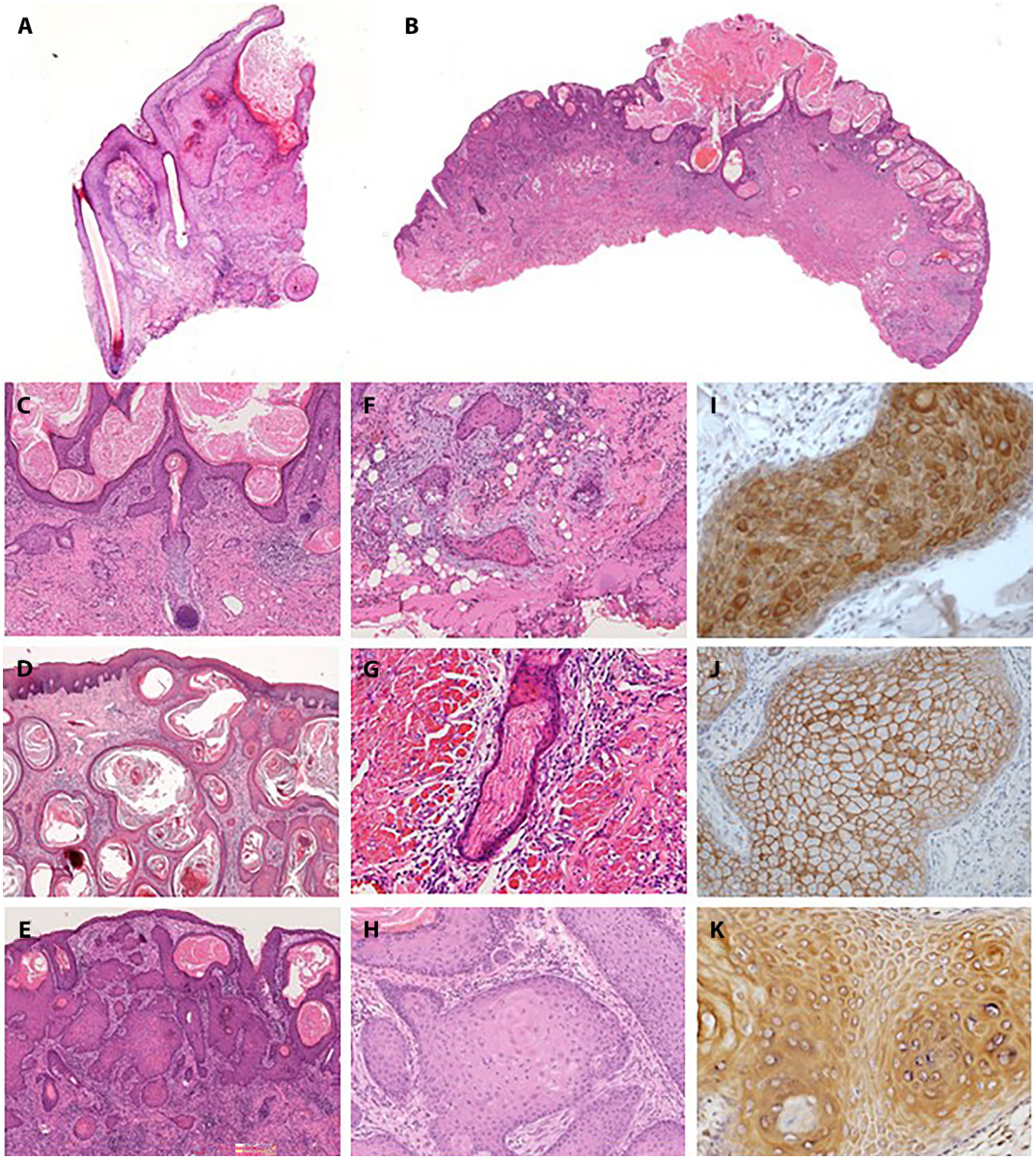

Figure 2. Histopathological features (hematoxylin-eosin and immunohistopathological staining).

(A) A punch biopsy pathology showing a keratin-filled cystic structure with irregular shaped, epithelial walls that invaded into the deep dermis (original magnification, x20).
(B) A volcano-like opening of the central keratin-filled plug invaginated by a thinner epidermal lipping architecture similar to that of keratoacanthoma (x20).
(C) Tumor nests and infundibular cysts arose from the follicular infundibulum (x40).
(D) Numerous micro- or dilated infundibular cysts of various shapes that infiltrated into the deep dermis (x40).
(E) Irregularly and asymmetrically thickening of the epidermis with various sized neoplastic cords or nests from the wall of the follicular infundibulum throughout the dermis (x40).
(F and G) The tumor nests invaded into the deep dermis (x100) and peripheral nerve sheath (x200), respectively.
(H) The nests were mostly consisted of eosinophilic glassy and pale keratinocytes with slight to moderate nuclear atypia (x200).
(I) Broad and intense expression of CK16 in the deeply situated neoplastic components (x100).
(J) Membrane-dominated staining of b-catenin with jigsaw-like nuclear/cytoplasmic pattern in the whole neoplastic components (x100).
(K) Cytoplasmic staining of antiapoptotic protein Bcl-xL was observed in the nest (x100).

An infundibulocystic biology towards carcinogenic transition proposes the involvement of two major molecular cascades, namely oncogenic RAS and Wnt/β-catenin pathways [6]. An imbalance of two signaling pathways may affect the stability of hair infundibulum regeneration, responsible for the carcinogenic state and possibly aggressive clinical behavior in our case.

The overall prognosis and definitive diagnosis of icSCC remain inconclusive. The aggressive clinical behavior in our case may be attributed to a rare pathological hybrid possessing well-differentiated and infiltrative characters, with direct activation of the oncogenic Wnt signaling pathway by β-catenin overexpression.

Table 1. Summary of infundibulocystic squamous cell carcinoma a thus far reported in the literature.

Case	Authors	Age/ Sex	Site	Size (cm)	Treatment	Local recurrence	Metastasis	Clinical features	Follow-up (yr)	References
1	Misago N, et al	79/M	Upper lip	3	N.D.	None	None	Erythematous keratotic plaque	1.5	2
2	Misago N, et al	56/M	Upper lip	2.5	N.D.	None	None	Erythematous keratotic plaque	2	2
3	Kim SM, et al	67/M	Posterior ear	2	Excicion	N.D.	None	Flat nodule, keratotic plaque	N.D.	4
4	Suma A, et al	72/M	Left helix of ear	2	Excicion and postoperative external beam radiotherapy	None	None	Solitary, crusted, flesh-colored, rubbey mass	3.5	5
5	Our case	82/M	Upper lip	3	Marginal resection, chemoradiation therapy	+	None	Reddish indurative plaque with a whitish keratotic surface	1	this report

N.D., not described.

To date, there have been only 5 case reports of icSCC, including ours. Their affected skin sites were the exposed area. Recurrence or metastasis were unclearly stated.

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