Nascent verrucous hyperplasia – A transition to cutaneous squamous cell carcinoma

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ABSTRACT
Cutaneous squamous cell carcinoma is a common global cancer with ultraviolet light recognized as the most significant risk factor. The other definite or plausible risk factors include immunosuppression, infection with oncogenic viruses, exposure to toxins, chemicals, chronic inflammatory skin disease and a high body mass index.

This case highlights the rarity of the pathology in terms of size, the subtle transition of verrucous hyperplasia to cutaneous squamous cell carcinoma over a period of time and the fallibility of the frozen section report in deciding the optimum resection margins. The initial innocuous presentation represented a diagnostic challenge as it can be mistaken for other benign entities. A correlation between the history, clinical presentation, tumor biology and the histopathological characteristics helped us to unlock the jigsaw puzzle of approaching a rare condition with a modification in the surgical approach.

1. Introduction
Tumours of long standing duration or multiple surgical procedures violate the tumour biology. Cutaneous squamous cell carcinoma is a common global cancer with ultraviolet light as the major risk factor. The case illuminates the subtle transitions of benign lesion transforming into malignancy.

2. Case report
A 48-year-old female presented to us with an outsized fungating growth in the left side of the face. The swelling had initially marked its presence 20yrs back, was a small nodule, asymptomatic with a slow progression. An excisional biopsy was done in 2011 and included a complete removal with the histopathology report suggestive of verrucous hyperplasia. It reappeared 2 years later, asymptomatic, other than her aesthetic concerns. It has had an indolent course since then with a snail pace progression in its size. She had been chewing smokeless tobacco for about 4 years prior to the appearance of the growth and has reformed since then. The medical history was unremarkable.

On clinical examination, the well-demarcated exophytic growth in the left side of the face. The swelling had initially marked its presence 20yrs back, was a small nodule, asymptomatic with a slow progression. An excisional biopsy was done in 2011 and included a complete removal with the histopathology report suggestive of verrucous hyperplasia. It reappeared 2 years later, asymptomatic, other than her aesthetic concerns. It has had an indolent course since then with a snail pace progression in its size.

A PET CT and the previous MRI had ruled out bony erosion and intracranial extension. A 4.9 × 2.8 × 5.8 cm large cutaneous ulceroproliferative exophytic polypoidal mass lesion is seen arising from the left nasolabial region (Fig. 3). In view of the long-standing history...
increased propensity for subclinical metastasis [1]. Some of the was considered due to the high-risk tumour features that have an and recurrence from the previous excisional biopsy, neck dissection was considered due to the high-risk tumour features that have an increased propensity for subclinical metastasis [1]. Some of the high-risk features include depth of invasion 2 mm, poor histological differentiation, high-risk anatomic location (face, ear, pre/postauricular, genitalia, hands, and feet), perineural involvement, recurrences, multiple cutaneous SCC tumors, and immunosuppression. The AJCC defines a cutaneous SCC as a higher-risk lesion when its diameter grows beyond 2 cm and can be an independent risk factor for metastatic disease [2, 3].

Wide local excision, reconstruction with Radial forearm free flap and conchal cartilage to restore the alar cartilage defect (Fig. 4). Nasal ala has a complex tridimensional anatomy, the anatomically distinct layers and recurrence from the previous excisional biopsy, neck dissection was considered due to the high-risk tumour features that have an increased propensity for subclinical metastasis [1]. Some of the high-risk features include depth of invasion 2 mm, poor histological differentiation, high-risk anatomic location (face, ear, pre/postauricular, genitalia, hands, and feet), perineural involvement, recurrences, multiple cutaneous SCC tumors, and immunosuppression. The AJCC defines a cutaneous SCC as a higher-risk lesion when its diameter grows beyond 2 cm and can be an independent risk factor for metastatic disease [2, 3].

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(External skin, internal nasal lining and the intervening fibro-fatty tissue) [4] necessitate a composite reconstruction to provide symmetry and preserve nasal function. There were twin defects to be reconstructed: Exernal lining defect of the cheek region and the complex defect in the ala of the nose which included the external skin, alar cartilage and internal lining. Conchal cartilage was harvested from the Left ear to reconstruct the alar cartilage defect and sandwiched it using the skin of the Radial artery free flap to cover both on the outer and inner side, thereby achieving a good cosmetic outcome (Fig. 5).

The final biopsy report showed an exophytic growth composed of neoplastic squamous cells arranged in lobules, nest with keratinization and an invasive front, features are suggestive of a well-differentiated squamous cell carcinoma (Fig. 6). This is in contrast to the classical histopathological image of a verrucous carcinoma characterized by multiple, round-shaped proliferations of well-polarized squamous cells with little atypia and rare mitotic figures.

She has been on a regular follow up for 6 months with no signs of locoregional recurrence (Fig. 7).

3. Discussion

The distinctive proliferation of the epithelium which gets heaped above the surface is a hallmark of verrucous lesions. Verrucous hyperplasia, Proliferative verrucous leukoplakia, Verrucous carcinoma, Hybrid verrucous carcinoma are the heterogeneous patterns that can perplex the clinician with the camouflage of verrucous appearance, hence it is recommended that all verrucous lesions be surgically excised to confirm an accurate diagnosis. The most ideal site for an incisional biopsy in verrucous carcinoma is the periphery of the verrucous carcinoma where the surrounding epithelium dips downward [5, 6, 7, 8, 9, 10].

Our patient had an initial excisional biopsy (2011) with histopathologic analysis of the suggestive of verrucous hyperplasia. It is unlikely that the malignant component would have been missed considering the in toto removal of the lesion. The reappearance of the growth after 2 years and untreated thereafter can transform the tumour biology with an increased predilection to malignancy. Recurrent tumors are more biologically aggressive and have reported metastatic rates as high as 30% [11].

Considering the large tumour size, prolonged duration, surgical manipulation and discordance of the earlier histopathological report (2011-Verrucous hyperplasia) with the current clinical presentation, a provisional diagnosis using a frozen section was essential.

A specific fragment from the tumor was incised and sent for frozen section. The tissue is freezeed at -30 °C, sectioned using cryotome and stained with routine Hematoxylin-Eosin (HE) staining. The multiple initial bits of tissue followed by an excisional biopsy sent for the frozen section was suggestive of verrucous hyperplasia (Fig. 8). Discordance of the pathological finding and a suspicious malignant clinical presentation kept us in dilemma regarding the optimum surgical margins.

In our case despite the whole of the tumour being excised and sent for frozen section our pathologists were unable to decrypt the presence or absence of malignant cells. A possible explanation to this would be that the cut sections for rapid frozen might have probably not been a representative part of the tumour with its basement membrane. The inadequacy of frozen to assess bony margins, interpretive error, sampling error and occasionally missed positive margins are the inherent flaws of use of a frozen section [12].

In view of the ambiguous frozen interpretation, a conventional approach of treating a verrucous lesion was not considered. The wide surgical margins considering the lateral spread, infiltrative potential, local aggressiveness helped us to overcome the histological surprise of Squamous cell carcinoma. Limitations of rapid frozen and a clinician suspicion of aggressive tumour biology prompted us to go for a wide
Fig. 3. 4.9 × 2.8 × 5.8 cm large cutaneous ulceroproliferative exophytic polypoidal mass lesion arising from the left nasolabial region.
local excision and reconstruction. This would avoid revision of the surgical margins if the final histopathology report was squamous cell carcinoma.

Tumours of a long-standing duration or a surgical intervention followed by a recurrence violate the tumour biology and enable the tumour to gallop with vengeance [13]. The case reminisces us of the fact that a long-standing history of disease with recurrences following surgical interventions are red flags of malignant transformation repudiating the indolent nature of the primary tumour.

Depletion of the ozone layer, rise in the UV index, increased vulnerability to environmental and dietary carcinogens and declining immune surveillance mechanism in the aging population [14, 15] are potential risk factors for cutaneous squamous cell carcinoma.

Due to the paucity of cases reported it is essential to understand the
limitations of a rapid frozen, subtle transformation of tumour biology with increasing size and depth, its aggressiveness following the initial surgical trauma, all this underlines the significance of documenting each new case.

4. Patient consent

The patient provided her consent to the medical faculty of HCG group for diagnostic and therapeutic procedures with an understanding that her clinical images will be utilized for research activities and publications in journals/conferences.

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