**Abstract**

**Introduction**

Keratoacanthoma (KA) was first described in 1889 by Sir Jonathan Hutchinson as a ‘crateriform ulcer of the face’. KAs are rapidly growing, cutaneous tumours with atypical histological features similar to squamous cell carcinoma (SCC) that resolve leaving an atrophic scar. KAs are either follicular KAs arising in hair-bearing skin or non-follicular KAs arising in the palm and sole. Nearly all KAs are solitary lesions, less than 2 cm in diameter and arising on skin exposed to the sun. The term ‘giant keratoacanthoma’ is applied to a tumour greater than 2–3 cm in diameter. Xeroderma pigmentosum (XP) is a rare, autosomal recessive genodermatosis characterised by deficient DNA repair, photosensitivity, severe solar sensitivity, cutaneous pigmentary changes and xerosis developing before the age of two years. Early development of mucocutaneous and ocular lesions, solar keratoses, cutaneous horns, KA, SCC and basal cell carcinoma, basal-quamous carcinoma, atypical fibroxanthoma, malignant melanomas and angiomas, have been reported. We present a case of a 50-year-old female patient, a known case of XP, with a large, solitary dome-shaped lesion on her right cheek.

**Case report**

A 50-year-old female patient, a known case of xeroderma pigmentosum, presented with a large, dome-shaped, crateriform lesion over her right cheek that had been present for the last four months. Histological examination showed an exophytic lesion with a large central keratin-filled crater surrounded by deep bulbous nodules of proliferating squamous cells that had abundant keratin with a lip of normal epidermis. The demarcation was discrete except for tiny foci of deep infiltration at the periphery. However, immunohistochemistry for p53 revealed strong positivity only in the basal layer of the infiltrating islands, weak Ki67 staining. Loss of Bcl-2 and E-cadherin but preserved desmoglein in the infiltrative areas (Figure 1). Additionally, immunohistochemistry for p53 revealed strong positivity only in the infiltrate was lymphoplasmacytic infiltrate admixed with polymorphs and eosinophils, was seen at the peripheral edge. Parakeratosis within the crater and micro-abscesses were seen towards the periphery. The cells showed mild anisonucleosis, prominent nucleoli and infrequent mitosis. The advancing edges at the base and sides of the lesion were distinct except for focal irregular areas with cords of squamous cells infiltrating the underlying dermis. A dense lymphocytic infiltrate admixed with polymorphs and eosinophils, was seen at most of the tumour interphase, however, the infiltrate was lymphoplasmacytic in the infiltrative areas (Figure 1). Additionally, immunohistochemistry for p53 revealed strong positivity only in the basal layer of infiltrating islands with weak Ki67 staining. Loss of Bcl-2 and E-cadherin but preserved desmo-
Discussion
KA is seen in 3% of all reported cases of XP but giant KA is uncommon. KA is a self-limiting epithelial proliferation with a strong clinical and histopathological similarity to well-differentiated SCC. Exposure to excessive sunlight is the most frequently incriminated factor in the aetiology of both KA and XP with 95% of the solitary lesions found on the sun-exposed areas like the face, head and extremities.

Men are more commonly affected than women. Lesions pass through the stage of proliferative phase, maturation phase and final resolving phase in which KAs reabsorb and expel the keratogenous core and eventuate into a scar with variable atrophy. However, this case showed a rapidly increasing size with no involution. Kern et al. observed that almost all of the confirmed KAs had invaginating keratin-filled craters with epidermal proliferation at the sides and the bottom of the lesion, and significant atypia and mitotic activity was rare, while SCCs showed considerable cellular anaplasia, pleomorphism and many displayed significant mitotic activity unlike this case. Cribier et al. evaluated 14 histological criteria, mainly based on the architecture of the tumours to differentiate KA from SCC. Epithelial lip, (as seen in this case) and sharp demarcation between tumour and stroma have been described as distinctive features of KA. However, this demarcation was focally not seen in this case thus increasing the difficulty in ruling out SCC. It was also suggested that atypical or difficult cases should be treated as SCC as clear-cut distinction is not possible in such cases; however, a clear distinction and diagnosis were made in this case.

Cain et al. compared the clinical, histological and immunohistochemical differences using antibodies to proliferating cell nuclear antigen, and wild-type and mutant-type p53 protein but found no significant statistical differences. However, Kerschmann et al. observed that 80% KA showed nuclear staining with anti-p53 antibody that was distributed along the outermost layers of the aggregates of neoplastic cells, similar to what was observed in our case, while 60% of the SCCs were uniformly p53 positive. Mean Ki-67 proliferation fraction was higher for KA than for SCC (55% vs. 46%), but this difference was not statistically significant. Connolly et al. concluded that immunohistochemistry for p53 and Ki-67 may help distinguish between a subungual SCC and a subungual KA. Loss of Bcl-2 expression with tumour maturity in KA has been reported as seen in this case. Desmoglein 1 and 2 have demonstrated the down-regulation.

Figure 1: a. Central keratin-filled crater surrounded by an epidermal lip (H&E 100×). b. Solid lobules of proliferating squamous cells in the base with abundant keratin (H&E 100×). c. Solid lobules of proliferating squamous cells in the base with lymphocytic infiltrate at the interface (H&E 400×). d. Focal irregular areas with cords of squamous cells infiltrating the underlying dermis with lymphoplasmacytic infiltrate at the interface (H&E 400×).
and up regulation of catenin in SCC but not in KA as also observed by us, and CD44 appears to be up regulated in KAs.

Conclusion

Giant KA can sometimes mimic SCC, both clinically as well as histologically. Immuno-staining with p53, Ki-67, Bcl-2, E-cadherin and desmoglein has to be conducted to differentiate between the two potential diagnoses, as in this case. However, in our case, a close follow-up with absence of any local recurrence or metastasis supported the diagnosis of giant KA with borderline features masquerading as SCC.

Abbreviations list
KA, keratoacanthoma; SCC, squamous cell carcinoma; XP, xeroderma pigmentosum.

References

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