Synchronous Squamous and Basal Cell Carcinoma in Oculocutaneous Albinism: A Rare Co-occurrence

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ABSTRACT

Oculocutaneous albinism (OCA) is a rare autosomal recessive disorder characterized by generalized deficiency of melanin pigment, which normally protects against ultraviolet (UV) radiation–induced DNA damage. Consequently, affected individuals are predisposed to cutaneous malignancies, most commonly squamous cell carcinoma (SCC), whereas basal cell carcinoma (BCC) occurs less frequently. The synchronous occurrence of SCC and BCC in a single patient with OCA is exceedingly uncommon.

We report a 41-year-old male with OCA who presented with ulcerated lesions over sun-exposed areas. Histopathological examination revealed two distinct tumors. One lesion showed features of SCC with nests and sheets of malignant squamous cells demonstrating nuclear pleomorphism and keratinization, and tumor cells exhibited strong nuclear positivity for p40 (ΔNp63 isoform of p63), confirming squamous differentiation. The second lesion demonstrated basaloid tumor nests with peripheral palisading and stromal retraction clefts, consistent with BCC, and showed cytoplasmic positivity for B-cell lymphoma 2 (BCL-2).

This case highlights the importance of careful clinical evaluation, histopathological examination, and immunohistochemistry in identifying synchronous malignancies in OCA. Early diagnosis and strict photoprotective measures are essential to reduce morbidity in individuals genetically susceptible to UV-induced skin cancers.

Keywords: Oculocutaneous albinism; squamous cell carcinoma; basal cell carcinoma; synchronous skin malignancy; ultraviolet radiation; photoprotection; histopathology; immunohistochemistry.

INTRODUCTION

Oculocutaneous albinism (OCA) is an inherited disorder resulting from mutations in genes involved in melanin biosynthesis and melanosome formation, such as tyrosinase (*TYR*), OCA2, tyrosinase-related protein 1 (*TYRP1*), and solute carrier family 45 member 2 (*SLC45A2*)[1,2]. Melanin absorbs both UVA and UVB radiation and also functions as a free-radical scavenger, thereby limiting oxidative DNA damage.[2]. In the absence of melanin, individuals with OCA are extremely sensitive to sunlight and have an increased risk of developing actinic keratoses and skin cancers, particularly in tropical regions with intense solar exposure [3,4].

Among the cutaneous malignancies in OCA, SCC is the most prevalent, with a predilection for chronically sun-exposed areas[3,4]. BCC, although less frequent, also develops due to cumulative actinic damage and aberrations in the Hedgehog signalling [pathway7,8].

The simultaneous occurrence of both SCC and BCC in the same patient is extremely rare and has been reported only sporadically in the literature [5-7]. This case report presents a rare instance of synchronous SCC and BCC in a patient with OCA and emphasizes the diagnostic role of immunohistochemical (IHC) markers p40 and BCL-2.

Case Presentation

A 41-year-old male farmer with a known history of oculocutaneous albinism presented with generalized depigmentation of the skin and hair, along with erythematous, ulcerated plaques over sun-exposed areas of the right wrist and right dorsolateral aspect of the forearm (Figure 1). The lesions bled easily on minimal trauma. The patient reported chronic occupational sun exposure without consistent use of photoprotective measures.

Two lesions were biopsied for histopathological evaluation. The right wrist lesion showed skin with an infiltrative epithelial tumor arising from the epidermis and extending into the dermis (Figure 2). The tumor was composed of nests, cords, and sheets of malignant squamous epithelial cells exhibiting nuclear pleomorphism, vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm with individual cell keratinization (Figure 3). On IHC, the tumor cells showed strong nuclear positivity for p40, confirming squamous differentiation consistent with squamous cell carcinoma (SCC) (Figure 4).

The right dorsolateral forearm lesion showed a tumor arising from the basal layer of the epidermis extending into the dermis (Figure 5). The tumor was composed of nests and lobules of basaloid cells with hyperchromatic nuclei, scant cytoplasm, peripheral palisading, and retraction clefts between tumor nests and stroma (Figure 6). IHC showed cytoplasmic positivity for BCL-2, supporting the diagnosis of basal cell carcinoma (BCC) (Figure 7).

Immunohistochemistry

Formalin-fixed, paraffin-embedded tissue sections (3–4 μm) were used for immunohistochemical analysis. Sections were deparaffinized in xylene and rehydrated through graded alcohol. Heat-induced epitope retrieval was performed using citrate buffer (pH 6.0). Immunostaining was carried out using a horseradish peroxidase (HRP) polymer detection system with diaminobenzidine (DAB) as chromogen and hematoxylin counterstain. Appropriate positive and negative controls were run with each batch.

The tumor cells in the first lesion showed diffuse strong nuclear positivity for p40, confirming squamous differentiation. The second lesion demonstrated diffuse cytoplasmic positivity for BCL-2 within basaloid tumor nests, supporting basal cell carcinoma.

The patient underwent wide local excision of both lesions with histologically free margins. The postoperative period was uneventful. At 6-month clinical follow-up, no evidence of local recurrence or regional lymphadenopathy was identified. The patient was counselled regarding strict lifelong photoprotection and regular dermatological surveillance.

DISCUSSION

OCA represents a spectrum of genetically heterogeneous conditions characterized by melanin deficiency in the skin, hair, and eyes [1,2]. The lack of melanin eliminates the natural UV-protective barrier, rendering patients vulnerable to actinic injury, DNA damage, and subsequent neoplastic transformation[2]. Among the skin cancers, SCC is the most common in albino patients, with a reported incidence of up to 30% in equatorial regions[3]. In contrast, BCC is less frequent, accounting for about 5–10% of skin cancers in albinos[4].

SCC primarily develops due to UVB-induced mutations in the *TP53* tumor suppressor gene, leading to keratinocyte dysplasia and malignant transformation[2]. BCC arises mainly through aberrant activation of the Hedgehog signaling pathway, particularly mutations in *PTCH1*, which drive uncontrolled proliferation of basal keratinocytes[7].

The carcinogenesis in OCA is fundamentally related to impaired UV-induced DNA damage protection. Ultraviolet radiation generates reactive oxygen species and DNA photoproducts, activating DNA damage response pathways[10,11]. Activation of apoptosis signal-regulating kinase-1 (ASK1) triggers downstream p38 and JNK signaling cascades, resulting in cell-cycle arrest mediated through p21 and other checkpoint regulators. In normal skin, melanin attenuates this process by absorbing ultraviolet radiation and scavenging free radicals[2].

In OCA, the absence of melanin leads to persistent DNA damage, checkpoint dysregulation, genomic instability, and accumulation of mutations in keratinocyte stem cell populations, predisposing to multiple keratinocyte malignancies. These mechanisms collectively contribute to actinic field damage and facilitate the development of multiple independent keratinocyte carcinomas[10,11].

The synchronous appearance of both tumors in an individual with OCA, as in this case, suggests cumulative UV-induced damage acting on different target cells within the epidermis[2,8].

Histologically, the coexistence of basaloid and squamous differentiation raises the possibility of basosquamous carcinoma. However, in the present case the two tumors were spatially distinct and showed classic independent morphological features without a transition zone. The squamous lesion demonstrated overt keratin pearl formation and diffuse p40 positivity, while the basaloid lesion showed peripheral palisading, stromal retraction clefts, and diffuse BCL-2 expression, favoring two synchronous primary tumors rather than a single biphasic neoplasm[9].

Other differential diagnoses considered included keratoacanthoma, trichilemmal carcinoma, proliferating trichilemmal tumor, and pseudoepitheliomatous hyperplasia arising in actinic keratosis. Keratoacanthoma typically shows a crateriform architecture with glassy keratinocytes and pushing margins. Trichilemmal tumors exhibit clear cell change with trichilemmal keratinization lacking a granular layer. Pseudoepitheliomatous hyperplasia lacks significant cytologic atypia and destructive stromal invasion. The presence of marked atypia, infiltrative growth, and supportive immunohistochemistry confirmed true malignancy in both lesions[9].

IHC is valuable in confirming the dual diagnosis. p40, an isoform of p63, is a highly specific nuclear marker for squamous differentiation and helps distinguish SCC from its histological mimics. BCL-2, an anti-apoptotic cytoplasmic protein, shows strong expression in BCC and assists in differentiating it from SCC and adnexal tumors[9]. Early recognition and accurate differentiation are crucial for guiding appropriate management and prognostication[12].

This case emphasizes the need for regular dermatological surveillance, prompt biopsy of any suspicious lesion, and rigorous photoprotection using broad-spectrum sunscreens, protective clothing, and avoidance of peak UV exposure.

To the best of our knowledge, synchronous occurrence of spatially separate squamous cell carcinoma and basal cell carcinoma in a patient with oculocutaneous albinism remains rarely documented in the literature. The present case highlights that multiple independent keratinocyte malignancies may arise simultaneously in OCA due to field cancerization from chronic ultraviolet exposure. Recognition of this possibility is important because clinically similar lesions may represent histologically distinct tumors requiring separate pathological evaluation.

CONCLUSIONS

The synchronous occurrence of SCC and BCC in oculocutaneous albinism is exceedingly rare but clinically important. This case highlights the need for a high index of suspicion and early histopathological and immunohistochemical confirmation using p40 and BCL-2. Rigorous photoprotection, patient education regarding sun avoidance, and regular clinical follow-up are essential to reduce morbidity in individuals with OCA.

Limitations

This report is limited by its single-case design and short follow-up duration. Molecular genetic testing and tumor mutational profiling were not performed, and therefore the specific genetic subtype of oculocutaneous albinism and molecular alterations within the tumors could not be determined. Larger studies incorporating molecular subtyping are required to better understand tumor biology in patients with OCA.

Ethics statement:

Written informed consent was obtained from the patient for publication of clinical details and clinical images. The study was conducted in accordance with the principles of the Declaration of Helsinki. As this report

describes a single observational case without experimental intervention or patient identifiers, formal institutional ethics committee approval was not required as per institutional policy.

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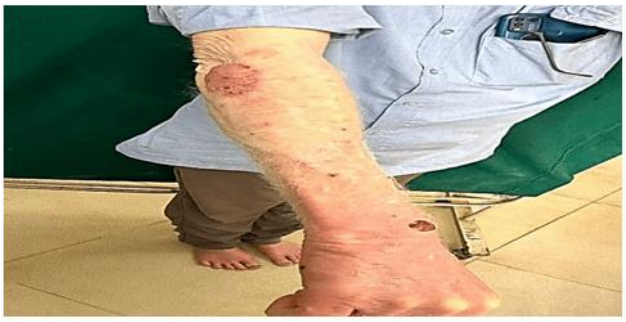

Figure 1:
Clinical photograph showing generalized cutaneous and hair depigmentation consistent with oculocutaneous albinism, along with erythematous, ulcerated plaques over the right wrist and right dorsolateral forearm.

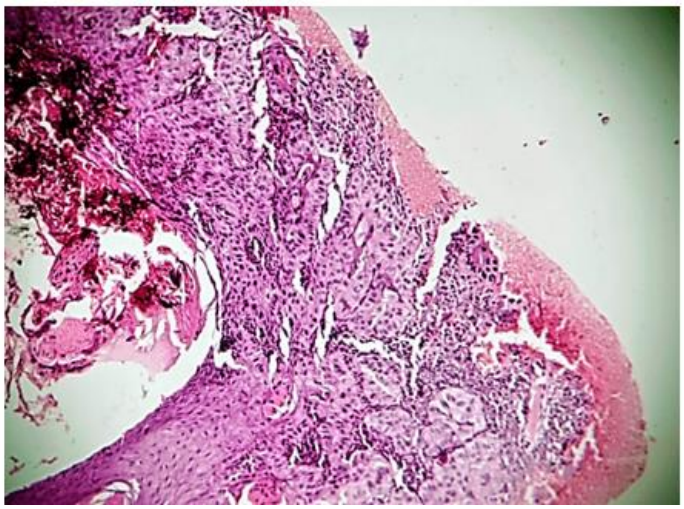

Figure 2:
Low-power photomicrograph of the right wrist lesion showing an infiltrative epithelial tumor arising from the epidermis and extending into the dermis (H&E, 100x).

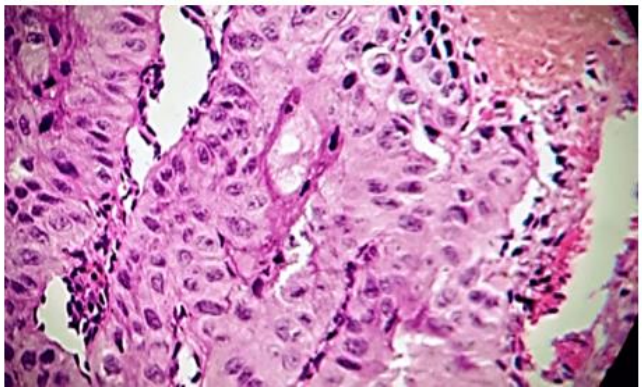

Figure 3:
High-power view of the squamous cell carcinoma displaying nests and sheets of malignant squamous cells with nuclear pleomorphism, vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm with individual cell keratinization (H&E, 400x).

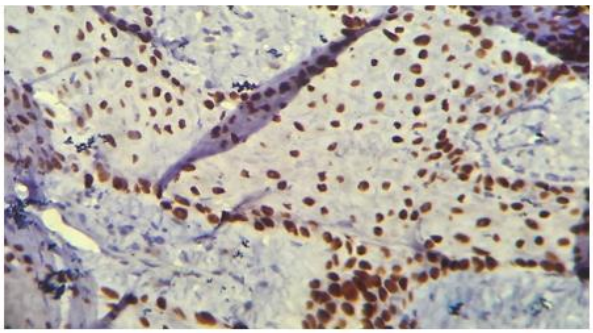

Figure 4 (SCC – IHC):

Tumor cells show diffuse strong nuclear immunoreactivity for p40 (ΔNp63 isoform of p63), confirming squamous differentiation consistent with squamous cell carcinoma (IHC, 100× magnification).

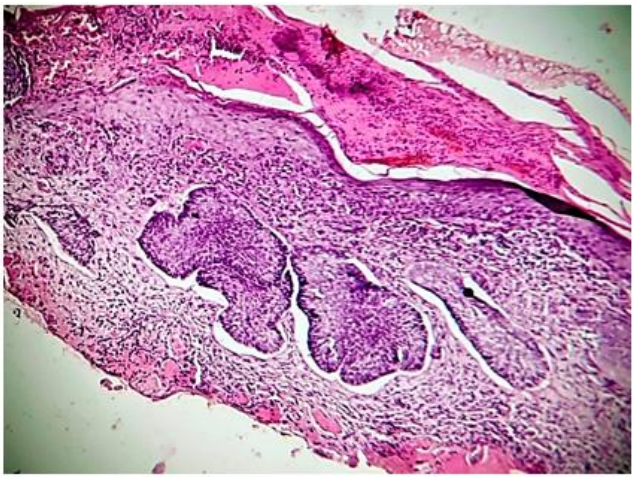

Figure 5:
Low-power photomicrograph of the right dorsolateral forearm lesion showing a tumor arising from the basal layer of the epidermis and extending into the dermis (H&E, 100x).

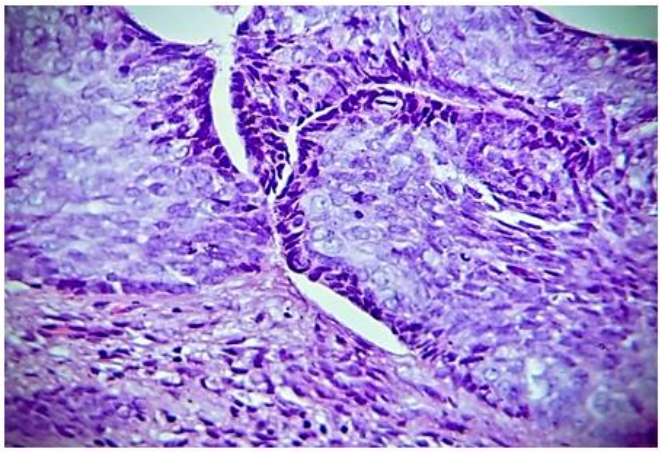

Figure 6:
High-power view of basal cell carcinoma composed of basaloid cell nests with hyperchromatic nuclei, peripheral palisading, and characteristic retraction clefts between tumor nests and surrounding stroma (H&E,400x).

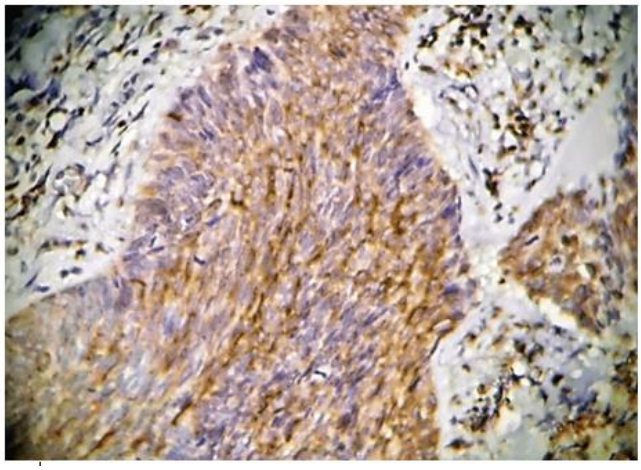

Figure 7: Immunohistochemistry revealed cytoplasmic positivity for BCL-2, a specific marker for basal cell carcinoma, supporting the diagnosis of BCC (IHC 100X)