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Case Report

Synchronous cutaneous malignancies in a patient with vitiligo: A rare case report

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Abstract

Background: Synchronous malignancies of skin are quite rare and association of these synchronous malignancies with vitiligo have never been reported. Here we present a case with synchronous presence of basal cell carcinoma, squamous cell carcinoma and basosquamous carcinoma at different anatomical locations in a patient with vitiligo.

Case Report: A 78-year-old male presented to Dermatology OPD with history of raised lesions over nose, lip, and chest for 1 month. Patient was a known case of vitiligo but was not on any medication or PUVA therapy. Punch biopsy was taken from these lesions and sent to Department of Pathology for histopathological examination. Microscopic examination from the sections from nose biopsy revealed histopathological features consistent with Basal Cell Carcinoma. Sections from lip biopsy revealed histopathological features consistent with Squamous Cell Carcinoma. Sections from chest lesion revealed histopathological features of a poorly differentiated carcinoma, basosquamous carcinoma was kept as first possibility.

Conclusion: Our patient, an elderly male with Vitiligo, without history of PUVA, developed synchronous non-melanotic malignancies. Genetic and epigenetic factors might have led to this carcinogenesis. Our case contributes to the awareness of development of synchronous non melanotic malignancies in vitiligo patient.

Keywords: Synchronous malignancies, Vitiligo, Squamous cell carcinoma, Basal cell carcinoma, Basosquamous carcinoma.

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1. Introduction

Synchronous malignancies of skin are quite rare and association of these synchronous malignancies with vitiligo have never been reported. Here we present a case with synchronous presence of non-melanocytic malignancies basal cell carcinoma, squamous cell carcinoma and basosquamous carcinoma at different anatomical locations in a patient with vitiligo.

2. Case Report

A 78-year-old male presented to Dermatology OPD with history of raised lesions over nose, lip and chest since 1 month. He first developed the lesion over chest, which gradually increased in size. Simultaneously, he developed lesion over lower lip and over nose near left nasolabial fold. There was history of spontaneous ulceration, bleeding and crusting over these lesions. Patient was a known case of vitiligo but was not on any medication or PUVA therapy. On examination, these lesions were well to ill defined, elevated crusted lesions, ranging in size from (1x1) cm to (2X1) cm. Punch biopsy was taken from these lesions and sent to Department of Pathology for histopathological examination. Sections from biopsy were processed and slides were stained with hematoxylin and eosin. Microscopic examination from the sections from nose biopsy revealed histopathological features consistent with Basal Cell Carcinoma. Sections from lip biopsy revealed histopathological features consistent with Squamous Cell Carcinoma. Sections from chest lesion revealed histopathological features of a poorly differentiated carcinoma, basosquamous carcinoma was kept as first possibility. (**Figure 1**, **Figure 2**, **Figure 3**) As immunohistochemistry was not available at our institution so it could not be performed.

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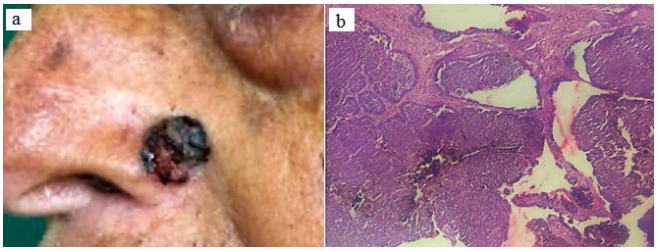

Figure 1: a: lesion over nose; **b:** Histopathological image showing features of basal cell carcinoma (H&E,10x)

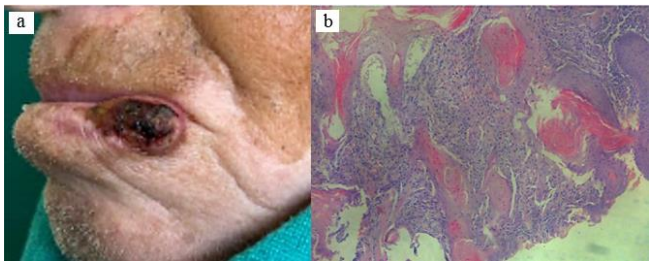

Figure 2: a: lip lesion; **b:** histopathological features of squamous cell carcinoma are seen (H&E,10x)

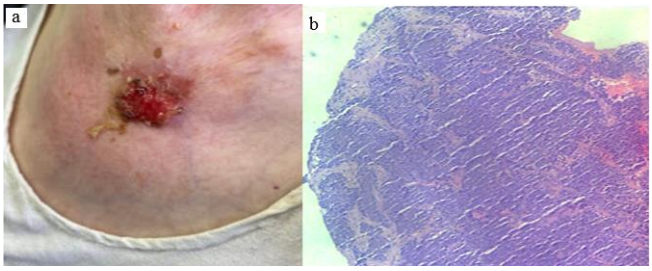

Figure 3: a: chest lesion; **b:** histopathological features of poorly differentiated carcinoma are seen (H&E,10x)

3. Discussion

Malignancies are said to be synchronous when more than two primary malignancies are diagnosed at the same time in the same individual at different anatomical locations while excluding the possibility of metastasis from the primary malignancy.

Warren and Gates have defined the criteria for classifying a tumor as "second primary malignancy." Diagnostic criteria require each cancer to be proven malignant by histopathological examination, and there should be at least 2 cm of normal mucosa between the tumors, if they are in same location. They should also be separated in time by at least 5 years, and the possibility of metastasis should be excluded.[1] However, our patient had three different primary malignancies detected at the same time at different anatomical locations.

Tumorigenesis involves successive "hits," leading to a cascade of events which culminate into neoplastic transformation of the cells. Genetic susceptibility, smoking, occupational hazards, dietary intake, sun exposure and aging are the known factors which are linked to each other, and they play interacting roles in the development of various cancers. The possible mechanisms involved in the development of synchronous malignancies are defective immune surveillance systems, inherent faulty gene expression, tumour suppressor genes, and many other possible etiologies.

Vitiligo is an acquired skin disorder characterised by idiopathic destruction of melanocytes, resulting in achromic macules. Melanin absorbs light, filters UV rays, and protects skin against the harmful effects of UV radiation. So, it is expected that absence of melanin increases cutaneous carcinoma risk.[2]

However, literature suggests that Vitiligo is associated with reduced risks of BCC and SCC, as well as internal malignancies.[3,4] Possible reason given for this association was that vitiligo patients are advised sun protection and there is an overexpression of epidermal wild-type p53 and Mdm2, which is a negative regulator of p53. However, our patient, a known case of vitiligo, contrary to the above developed three different synchronous malignancies.

Kim et al in his study demonstrated association of cutaneous malignancies (melanotic and non-melanotic) with vitiligo in Korean population.[5] He attributed it to possible ethnic differences in the susceptibility to skin cancer.

Basal Cell Carcinoma (BCC) arise from immature, pluripotent cells associated with the hair follicle in response to sun damage. Ultraviolet (UV) radiation can cause direct DNA damage, indirect DNA damage through reactive oxygen species, and immune suppression. Melanin absorbs UV-A and causes damage to DNA generation of free radicals. UV-B damages DNA and RNA with C/T or CC/TT transition. UV exposure also causes suppression of the cutaneous immune system. There is excessive activation of the sonic hedgehog (HH) pathway, either through the inhibition of the transmembrane protein PTCH or the activation of SMO. Most common gene alteration is PTCH1 gene followed by mutations in P53 and CDKN2A locus.[6]

Squamous cell carcinoma can arise from keratinocytes due the damage caused by UV radiation and P53 gene mutations. p53 is a transcription factor that plays a major role in maintaining genomic stability. Following cellular insults, p53 regulates the expression of its target genes and causes cell cycle arrest, apoptosis, senescence, DNA repair, or changes in metabolism. Environmental factors lead to alteration of the epigenetic status of the cells. Association of SCC with gene-specific promoter hypermethylation has been reported in literature.[7]

Actinic keratosis is a precursor of squamous cell carcinoma, and our patient had vitiligo, but as per a study comparing long-term actinic damage in sun exposed vitiligo and normally pigmented skin, there was no significant increase of chronic actinic damage in skin devoid of melanin pigments.[8] The squamous cell carcinoma lesion developed in

less than a month, and there was no precursor lesion in this case.

Basosquamous carcinoma (BSC) is rare skin cancer that shares the characteristic features of both basal and squamous cell carcinoma. It has never been reported in patients of vitiligo. Chang et al. suggested that BSCs exhibit PTCH1 and SMO mutations. These mutations commonly associated with BCC.[9] This supported the hypothesis that the sonic hedgehog (HH) signalling pathway serves as the primary driver mutation in BSC. It was suggested that BSC originates as a BCC and undergoes partial differentiation into SCC through the accumulation of ARID1A mutations and activation of the RAS/MAPK pathway.[10]

There are very few case reports of development of squamous cell carcinoma in vitiligo and basal cell carcinoma in vitiligo.[11-18] Development of concurrent squamous cell carcinoma and basal cell carcinoma has been reported in literature once, and it was concluded to be due to chronic sun exposure.[19]

Our patient, an elderly male with Vitiligo, without history of PUVA, developed synchronous non-melanotic malignancies. The development of carcinogenesis in this case may be attributed to both genetic mutations and epigenetic modifications affecting gene expression and cellular regulation.

4. Conclusion

Our case highlights the importance of recognizing the potential for synchronous non-melanotic malignancies in patients with vitiligo. Given this association, such patients should be kept under regular clinical follow-up. Further studies are warranted to elucidate the underlying genetic, epigenetic, and environmental factors contributing to the development of non-melanotic malignancies in vitiligo.

5. Source of Funding

None.

6. Conflict of Interest

None.

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