

## CASE REPORT

### DARRIERS DISEASE WITH BASAL CELL CARCINOMA: A CASE REPORT

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**ABSTRACT:** Darriers disease (Keratosis follicularis) is an autosomal dominantly inherited, acantholytic disorder due to mutation in ATP2A2 gene located on chromosome 12. Darriers disease can be localised to a segment due to postzygotic mutations where it is called as segmental darriers. Clinical features of DD include greasy, warty papules and plaques on seborrheic areas, dystrophic nails, palmo-plantar pits and papules on the dorsum of the hands and feet. There is increased predisposition to non-melanoma cutaneous malignancies in darriers disease. We report a rare case of darriers disease with basal cell carcinoma A, with rapid progression over 4 months into ulcer penetrans with destruction of eye ball.

**KEYWORDS:** Darriers Disease, Basal Cell Carcinoma.

**INTRODUCTION:** Darier's disease (DD), also known as Keratosis Follicularis or Darier-White disease, is a rare disorder of keratinization. The disease is caused by a loss-of-function mutation in the ATP2A2 gene on chromosome 12q23-24 that encodes the sarco/endoplasmic reticulum calcium ATPase (SERCA2). This loss of function leads to a disruption of Ca<sup>2+</sup> homeostasis within the keratinocytes, specifically depletion of Ca<sup>2+</sup> stores in endoplasmic reticulum. Ultimately, the mutation leads to impaired cell-to-cell adhesion with the common histological findings of suprabasal acantholysis and dyskeratosis of cells in the epidermis.<sup>[1]</sup> DD can present as a generalized autosomal dominant condition as well as a localized or segmental postzygotic condition.<sup>[2]</sup> Clinical features of DD include greasy, warty papules and plaques on seborrheic areas, dystrophic nails, palmo-plantar pits, and papules on the dorsum of the hands and feet.

**CASE REPORT:** A 55 years old female presented with multiple papular lesions all over the body since childhood and ulcer over the right temple extending to eye ball with loss of vision since 4 months. There is family history of similar papular leions in her father. Lesions started over dorsum of hands and feet and gradullay progressed to involve entire body. papular lesion over the right temple gradually ulcerated . Initially started as small lesion gradually increased and extended to the eyeball, painless, with loss of vision. There was no history of weight loss.

Past history is not significant except for multiple papular lesions. She did not seek any medical treatment as the lesions were asymptomatic with a slight discomfort.<sup>3</sup>

On examination her general condition was normal and cutaneous examination showed multiple hyperpigmented greasy papular lesions all over the body mainly distributed over the seborreic areas. Warty papules as well as larger verrucous papules and plaques were noted on the dorsum of hands, shins and feet (Fig 1, 2, 3).

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**Fig. 1:** Warty, yellowish brown papules over upper and lower limbs.

**Fig. 2:** Warty yellowish brown papules over back.

**Fig. 3:** Popular lesions over face, upper limbs and lower limbs and right temple.



**Fig. 1 2 3**



**Fig. 4: Palmar pits**



**Fig. 5: Distal nicking of nail plate**

Several fingernails demonstrated distal nicking of the nail plate (fig 4). Palms had pits (fig 5).

Large ulcer was present over right temple extending to right eye ball, the ulcer had crusting and characteristic rolled out edge ulcer extended to right eye with complete destruction of right eyeball (Ulcus penetrens) (Fig 6, 7)

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**Fig. 6 & 7:** Large ulcer over right temple extending to eye ball destruction of eyelids, characteristic rolled out everted edges.



**Fig. 6**



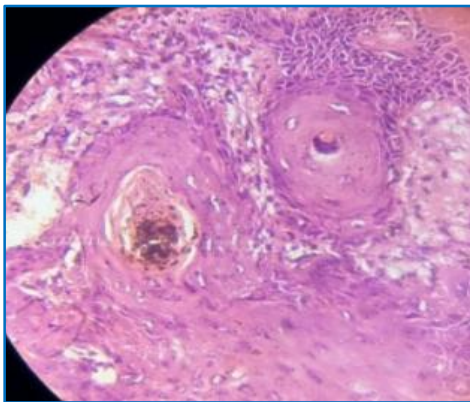
**Fig. 7**

Biopsy from ulcer edge shows histological features of basisquamoid type of BCC. (Fig. 8)

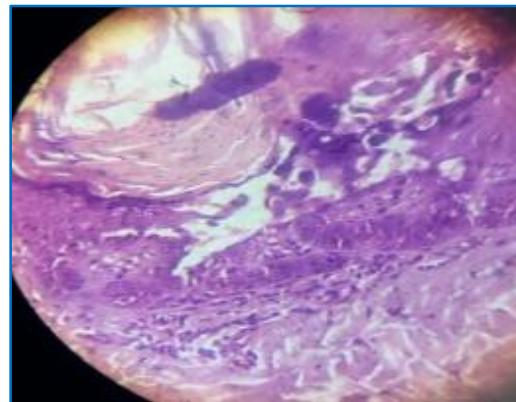
Biopsy from warty papule shows characteristic suprabasal acantholysis and dyskeratosis seen in DD. Fig. 9

**Fig. 8:** Palisading pattern of cells in dermis with keratin pearls in center with squamous differentiation.

**Fig. 9:** Suprabasal cleft with dyskeratotic keratinocytes.



**Fig. 8**



**Fig. 9**

Ophthalmological evaluation there is total loss of right eyeball and part of right upper and lower eye lid.

MRI brain showed no intracranial extension.

The case was diagnosed as DARIERS DISEASE WITH BASAL CELL CARCINOMA rapidly progressing destructing eyeball -variant ULCUS PENETRANS.

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**DISCUSSION:** Darier's disease<sup>1</sup> is caused by a loss-of-function mutation in the ATP2A2 that leads to a disruption of Ca<sup>2+</sup> homeostasis within the keratinocytes.<sup>2</sup> A decreased SERCA activity leads to an up regulation of the transient receptor potential canonical 1 Ca channel that increases cell proliferation and resistance to apoptosis. The imbalance of cellular survival and apoptosis due to the DD mutation or other genodermatosis may contribute to the presentation. DD have reduced expression of the antiapoptotic proteins Bcl-2 and Bcl-XL which may activate apoptosis and lead to increased cell turnover<sup>3</sup>. Further, alteration of ATP2A2 gene has been reported in the development of various other human carcinomas including colon and lung cancers.<sup>4,5</sup>

Present case had multiple papular lesions since childhood and father had similar lesions suggesting autosomal dominant pattern of inheritance. On examination lesions were mainly distributed over seborrheic areas, greasy in nature, yellowish brown. And lesions were also present over dorsum of hands and feet. Distal nicking of nail plate and palmar pits were present. Biopsy from papular lesions showed suprabasal acantholysis, acantholytic and dyskeratotic cells.

Patient developed painless ulcerated plaque over the right temple 4 months ago. The lesion extended to eye ball with loss of part of eyelids and loss of vision in right eye. Ophthalmological examination revealed destruction of eyeball, and only tumour mass in orbit. Biopsy from ulcer edge squamoid type of basal cell carcinoma

Darriers disease may increase the risk for BCC, due decreased apoptosis and increased proliferation.<sup>6,7</sup> This case is being presented for its rarity.

Although the literature is scarce and our understanding of the relationship between carcinomas and DD is developing, the case presented illustrates a possible association between DD and BCC.

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