Paraneoplastic Syndrome Presenting As Giant Porokeratosis in A Patient with Nasopharyngeal Cancer

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Abstract: Giant porokeratosis is a rare condition in which the hyperkeratotic plaques of porokeratosis reach up to 20 cm in diameter. Porokeratosis is characterized clinically by hyperkeratotic papules or plaques with a thread-like elevated border. Although rare, porokeratosis has been reported in conjunction with malignancies suggesting a paraneoplastic nature. Associated malignancies reported were hematopoietic, hepatocellular, and cholangiocarcinoma. We report a case of giant porokeratosis in a patient with nasopharyngeal cancer responding to removal of the primary cancer by chemoradiotherapy.

1 INTRODUCTION

Porokeratosis is a chronic progressive disorder of keratinization, characterized by hyperkeratotic papules or plaques surrounded by a thread-like elevated border corresponds to a typical histologic hallmark, the cornoid lamella . O regan, 2012) There are at least six clinical variants of porokeratosis recognized with known genetic disorder.[1] Some clinical variant of porokeratosis has been reported in the setting of immunosuppressive conditions, organ transplantation, use of systemic corticosteroids, and infections, suggesting that impaired immunity may be permissive in gentically predisposed individuals (O regan, 2012; Cannavo, 2008) .

Porokeratosis has also been reported in conjunction with malignancies, such as hematopoietic, hepatocellular, and cholangiocarcinoma (Torres, 2010; Wang,2017). Association of porokeratosis and solid organ tumor is rare, with only few cases have been reported in the literature and none was reported in conjunction with nasopharyngeal cancer. About 30% individuals with eruptive disseminated porokeratosis had a recently diagnosed malignancy, with mean of onset of 2.7 months preceding or following the diagnosis of malignancy (Shoimer, 2014). Porokeratosis associated with malignancy tended to improve or regress completely after the treatment of malignancy, suggestive of paraneoplastic syndrome.

2 CASE

Mr. SS, 68-year-old, was referred for evaluation of pruritic, slightly erythematous plaques with raised, hyperpigmented border of one and a half year duration on the extensor surface of both legs. The lesions shown minimal response to potent topical corticosteroids and phototherapy given during the last 8 months in another hospital. None of family members had malignancies nor similar condition.

Past medical history was notable for nonkeratinizing undifferentiated nasopharyngeal carcinoma diagnosed in November 2016. While staged for the extent of his carcinoma, topical treatment and phototherapy was discontinued. Secondly, he also had yellowish thickened palm and soles since birth and later on, onychogryphosis developed. Histopathology examination performed 20 years ago from the palm only revealed chronic dermatitis. Interestingly, similar condition was also present in his father, brothers, and son.

We sent the patient for biopsy just before he started chemotherapy. Histopathology examination revealed massive orthokeratosis, focal columnar parakeratosis (cornoid lamella) with perivascular

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lymphocytes infiltrate. He then underwent external radiation dosing 70 gray in 33 fraction and accompanied with 150 mg carboplatin for 4 cycles.

One month after radiochemotherapy completion, improvement of the lesions over limbs was noted, and full resolution was achieved the following month. However, the lesions over the palms and soles did not change although treated by moisturizer and keratolytic agent.

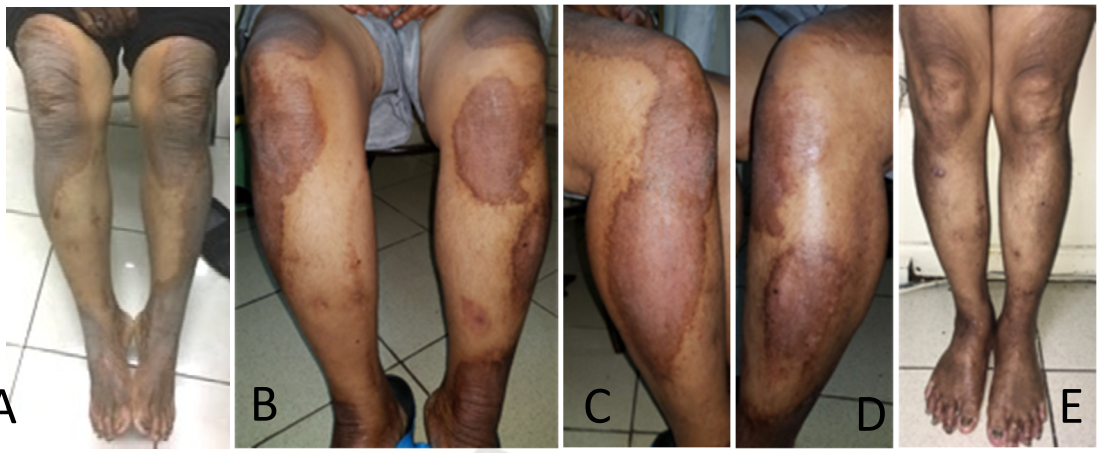

Figure 1. Plaques with elevated borders in November 2016 (A), during radiotherapy in May 2016 (B, C, D), and after patient had completed chemoradiotherapy in August 2017 (E)

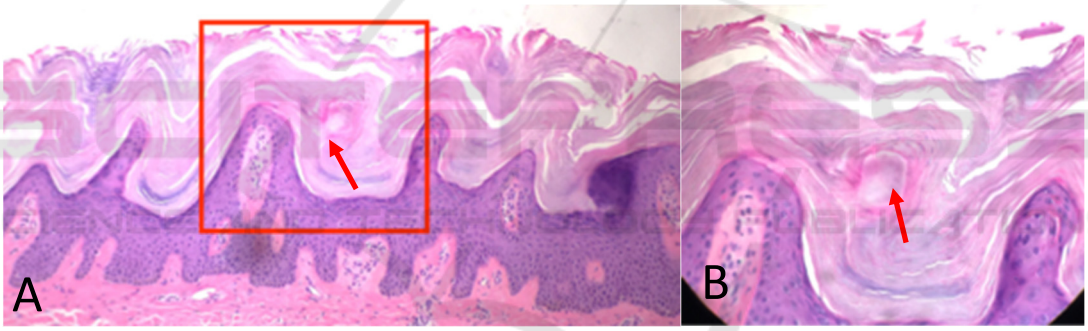

Figure 2. Massive orthokeratosis with column of parakeratosis, 100x (A), 400x (B) (hematoxyllin-eosin)

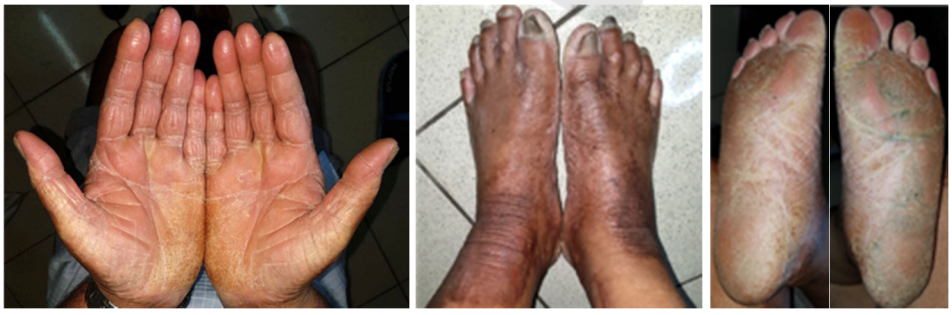

Figure 3. Yellowish hyperkeratotic plaques on both palms and soles with onychogryphosis

3 DISCUSSION

Paraneoplastic dermatoses are skin changes caused by a malignancy but without intrinsically neoplastic nature. Cutaneous manifestations of internal malignancy is a diagnostic enigma both in determining if it is paraneoplastic in nature and from which organ the process originates. Once established, the diagnosis lead to intiate a series of efforts to locate the presence of the tumor, thereby allowing prompt intervention. Diagnosis is more difficult in cases of uncommon dermatosis which only occasionally reported associated with malignancy. (Owen,2012) According to Curth's postulates established an association between a skin disease and malignancy, there are correlation between onset of cutaneous disease and internal malignancy, parallel course of both skin condition and malignancy, specific type malignancy associated with skin disease, statistical evidence of associated malignancy in specific skin disease compared to matched controls, and genetic link between a syndrome with skin manifestations and internal malignancy.(Shoimer,2014; Owen,2012)

The histopathologic patterns of porokeratosis consists of hyperkeratotic epidermis, with a thin column of poorly staining parakeratotic cells (cornoid lamella), edematous underlying keratinocytes and striking dermal lymphocytic pattern. A cornoid lamella is characterized by vertical column of parakeratosis, marked diminution of granular layer at the point where the parakeratin touches epidermal surface, and dyskeratosis and/or vacuolization of the underlying cells of stratum spinosum.(O Regan 2012). The epidermis in the central portion of porokeratosis may be normal, hyperplastic, or atrophic.[1] Cornoid lamella is not pathognomonic for porokeratosis and may also be found in other conditions such as viral warts, seborrheic keratosis, solar keratosis, squamous cell carcinoma in situ, lichen planus, and nevus sebaceous. (O Regan 2012, Biswas, 2015). In our case, we found hyperkeratotic epidermis, with a vertical column of parakeratotic cells, cornoid lamella. Granular layers underlying the vertical column of parakeratosis were not diminished and dykeratotic cells and edematous keratinocytes were not found. Although not typical, clinical appearance along with histopathological finding of cornoid lamella support the diagnosis of porokeratosis.

Molecularly, the tumor suppressor proteins p53 and pRb are overexpressed in keratinocytes immediately beneath and adjacent to the cornoid lamella, although p53 mutations have not been identified in porokeratosis. .(O Regan 2012) Other reported cases of porokeratosis in conjunction with solid tumor malignancies, share a common characteristic of p53 protein in their carcinogenesis (hepatocellular carcinoma, cholangiocarcinoma, ovarian adenocarcinoma).(Cannavo, 2008) Study by Lei et al in nasopharyngeal carcinoma stated expression of tumor suppressor genes p16, p21 and p53 with positive expression rate of 64.7%, 45.7%, and 90.5%, respectively.(Lei X, 1999) Similar study conducted in Istanbul also revealed similar result of 85.4% positive staining for p53 protein in nasopharyngeal carcinoma patients.[9] There might be correlation between malignancy and porokeratosis in terms of p53 pathway, but more studies need to be done. .(Shoimer, 2014)

In our case, the onset of skin disease preceeded the finding of nasopharyngeal cancer for seven to eight months prior. At time he developed skin manifestations, he only complained of having a flu followed by bloody runny nose around two or three months after. It should be taken into account that cancer might be clinically subtle before detection but there was good clinical response to chemoradiotherapy and full resolution of skin manifestation, two months after he was cleared from cancer. The patient was informed that reappearance of skin manifestation could be a hint whether the primary cancer strikes back and he should came for reguler checkup to the otolaryngologist.

4 CONCLUSION

To our knowledge, there are no previous reports associationg porokeratosis with nasopharyngeal carcinoma. In our case, the clinical appearance, size, and to some degree, the histopathological feature, was not highly typical, making diagnosis difficult. The skin eruption and malignancy ran a parallel course and good clinical response was achieved after removal of primary cancer thus we conclude our case was a paraneoplastic syndrome.

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