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CASE REPORT

Basal cell carcinoma arising on two variants of epidermal nevus: a case series

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ABSTRACT

INTRODUCTION Epidermal nevi are hamartomas of the epidermis and papillary dermis that are usually present during the first years of life. Rarely, malignant transformations develop in association with epidermal nevi. Few cases have been reported worldwide, however the lifetime risk and incidence are unknown.

CASE REPORT This is a case series about basal cell carcinoma arising on epidermal nevus.

The first patient is a 42-year-old Filipino female, who presented with a verrucous plaque at birth on the left temple which then developed multiple, discrete to confluent, grayish, papules and nodules on the surface. Histological examination revealed nevus sebaceus and basal cell carcinoma, pigmented type.

The second patient is a 53-year-old Filipino male, who presented with a papillomatous plaque on the left temple since the first year of life which then increased in size along with the presence of a solitary bluish-black macule noted by dermoscopic examination. Histologic examination showed verrucous epidermal nevus and basal cell carcinoma, pigmented type.

CONCLUSION Two rare cases of basal cell carcinoma arising on epidermal nevus are reported. Despite the rarity of malignant transformation on epidermal nevus, any suspicious growth warrants a biopsy. Knowledge of these cases is important for probing suspicious growth over an epidermal nevus that would prompt early treatment before these lesions progress in size making it harder to manage.

KEYWORDS epidermal nevus, nevus sebaceus, verrucous epidermal nevus, basal cell carcinoma, malignant transformation

INTRODUCTION

Epidermal nevi (EN) are congenital lesions that affect about 1 in 1,000 people. They appear shortly after birth as localized epidermal thickening that follow the lines of Blaschko, suggesting that they result from post-zygotic somatic mutations in the skin.[1] EN have been classified historically as non-organoid or organoid. Non-organoid EN are purely keratinocytic in composition, while organoid EN are composed of keratinocytes, sebaceous glands, hair follicles, apocrine or eccrine glands, and smooth muscle cells.[3] In this report, the first patient presents with the organoid type of epidermal nevus (nevus sebaceus [NS]), while the second patient has the non-organoid type of epidermal nevus (verrucous epidermal nevus [VEN]).

The incidence of malignant transformation on EN varies among different reports with few data available worldwide. While malignant transformations of NS are uncommon, basal cell carcinoma (BCC) is the most frequently occurring type. According to Cribier in 2000, recent studies indicate that the rate of BCC development is less than 1%.[4] In 2016, a retrospective study by Hsu et al. about secondary neoplasms arising from NS have shown that BCC represented 0.9% of the secondary neoplasms, being the most frequent malignant tumor to arise from a NS.[5]

Malignant transformation of VEN has been rarely reported.[6] A study of Hafner, et al. in 2008 cited that approximately 10 cases of BCC associated with non-organoid EN have been reported.[7] As described in various journals, BCC on top of VEN typically develops after puberty and is most common in middle-aged or elderly individuals.[2,6]

In the local setting, there are no reported cases of BCC arising on top of VEN. In the case of BCC arising on nevus sebaceous, there was only one (1) published case in 1989 of a 9-year-old Filipino girl.[8]

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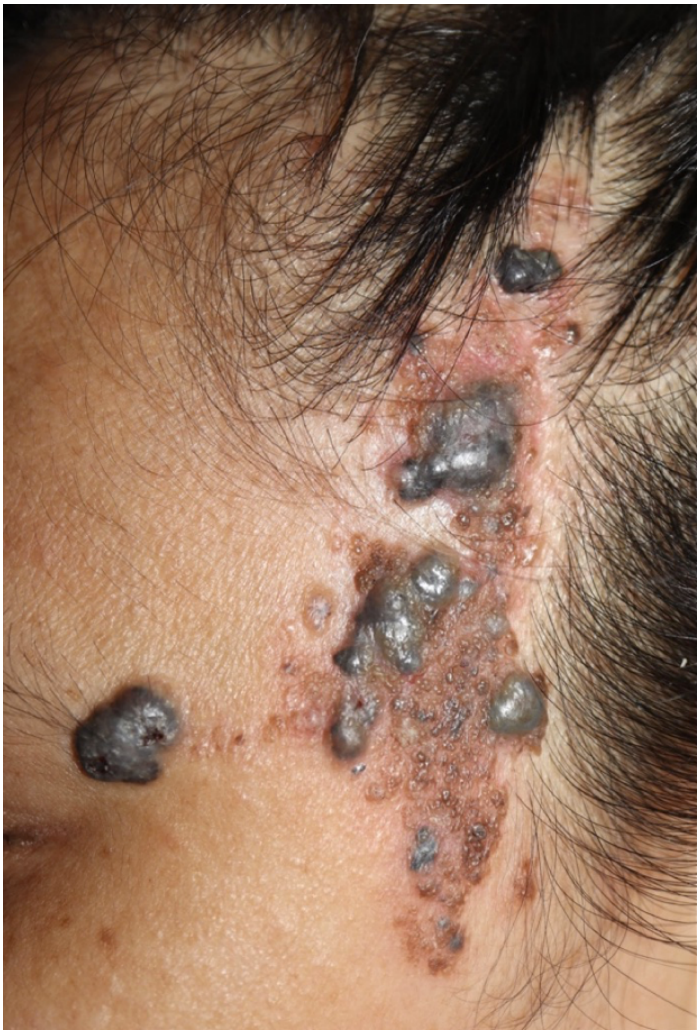

Figure 1. Clinical photo of the 42-year-old Filipino female patient. A yellowish to pinkish verrucous plaque in linear configuration measuring 8.1 x 3.0cm interspersed with multiple, grayish, transluscent, papules, and nodules.

This is a case series about BCC arising on two (2) types of EN. Both manifested with EN on the left temple at birth which had been asymptomatic until a few years prior when changes in the size of the nevus, coupled with the appearance of overlying nodules, prompted consultation.

CASE SUMMARY

PATIENT 1

A 42-year-old Filipino, female, nail technician presented with a verrucous plaque on the left temple at birth. The tumor had grown proportionately with her age and started to manifest with pruritus since puberty. Three (3) years prior to consultation, grayish nodules that are associated with bleeding on trauma appeared over the plaque. She had no personal history of extensive sunburn nor a family history of cutaneous malignancy, or the presence of similar lesions among family members. There was no known significant exposure to chemical carcinogens and ionizing radiation. She had no other comorbidities and review of system was unremarkable.

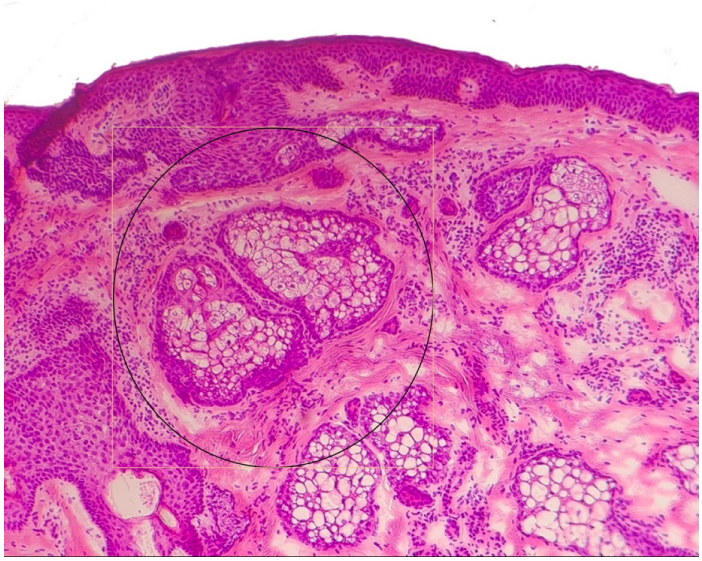

Figure 2. Histopathologic examination of the verrucous plaque of the 42-year-old Filipino female. The tumor shows epidermal hyperplasia, acanthosis, interconnecting rete ridges and proliferation of follicular papilla with presence of sebaceous glands (hematoxylin and eosin, x100).

On physical examination, there was a yellowish to pinkish verrucous plaque in linear configuration measuring 8.1 x 3.0 cm interspersed with multiple, round to irregularly-shaped, grayish, translucent, papules and nodules with smooth surface on the left temporal region and lateral aspect of the left eye 0.5-2.0 cm (Figure 1). Dermoscopy findings of the nodules showed blue-gray blotches, telangiectasia, and ulceration.

Skin punch biopsy specimens were taken from a representative area of the verrucous plaque and the grayish nodule. Histopathological examination of the plaque showed epidermal hyperplasia, acanthosis, interconnecting rete ridges, and proliferation of follicular papilla with presence of sebaceous glands. These findings were consistent with NS (Figure 2).

Histopathology of the nodule showed orthokeratosis, irregular acanthosis, tumor islands of basaloid cells showing hyperchromatic nuclei with peripheral palisading arrangement, focally containing melanin pigments, and embedded in a mucinous stroma. These findings were consistent with BCC, pigmented type.

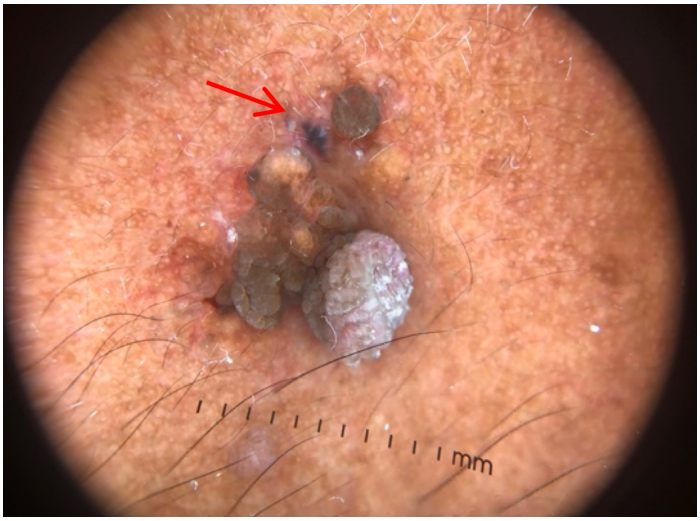

Figure 3. Dermoscopic findings of the verrucous growth of the 53-year-old Filipino male patient. A solitary blue ovoid nest (red arrow) interspersed along the homogenous, brown, globular, cobblestone structures.

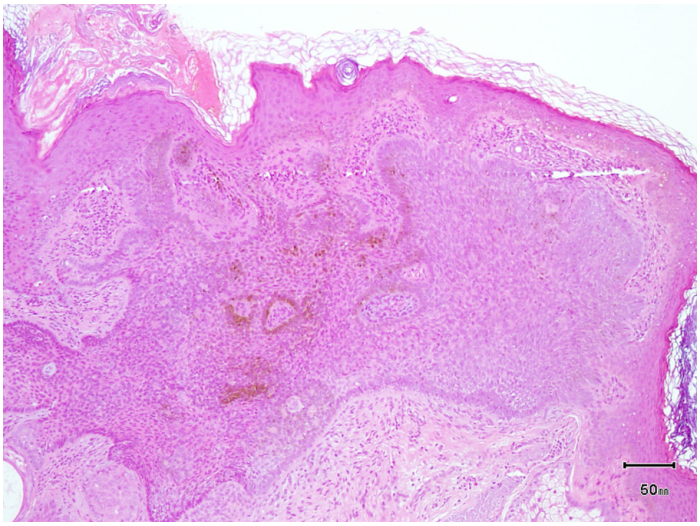

Figure 4. Histopathologic findings of the blue ovoid nest. The tumor shows tumor islands of basaloid cells with hyperchromatic nuclei showing peripheral palisading arrangement focally containing melanin pigments and embedded in a mucinous stroma (hematoxylin and eosin, x100)

The patient was then referred to another institution for Mohs micrographic surgery. On follow-up after five (5) months, there was no noted appearance of new lesions on the post-operative site.

PATIENT 2

A 53-year-old Filipino male, geothermal engineer presented during the first year of life with a solitary, skin-colored to brown papule on the left temple. The lesion was stable until four (4) years prior to consult, when it was noted to gradually increase in size forming a papillomatous plaque. This was not associated with bleeding or fragility. The patient claimed to have significant sun exposure given his job as a geothermal engineer. He had no known significant exposure to chemical carcinogens and ionizing radiation. He had no personal or a family history of malignancy nor presence of similar lesions among family members. He had no other comorbidities and the review of systems was unremarkable.

On physical examination, there was a papillomatous, skin-colored plaque on the left temple measuring 1.1 x 1.2 cm interspersed with a 0.1 cm bluish-black macule. Dermoscopic features of the verrucous growth show homogenous, brown, globular, cobblestone appearance with a solitary blue ovoid nest (Figure 3).

Shave excision biopsy of the verrucous growth showed hyperkeratosis, irregular acanthosis, mild spongiosis, dilated upper dermal blood vessels, and moderate, superficial, perivascular lymphohistiocytic cell infiltrates admixed with extravasated red blood cells. These findings were consistent with VEN.

Histologic features of the solitary bluish-black macule revealed tumor islands of basaloid cells with hyperchromatic nuclei showing peripheral palisading arrangement and embedded in a mucinous stroma. The tumor cells are seen extending from the epidermis to the mid reticular dermis. The biopsy was signed out as BCC, pigmented type (Figure 4).

The remaining lesions were electrocauterized with no noted appearance of new lesions on the post-operative site on follow-up after three (3) months.

DISCUSSION

NS is a hamartoma of the epidermis, hair follicles, sebaceous and apocrine glands usually occurring on the scalp, followed by the face. Clinically, it presents at birth as yellow-orange to pink, finely papillomatous alopecic plaque that is often oval or linear. It generally grows proportionately with age and during puberty, and has a tendency to become more verrucous, raised and greasy by the effects of the androgen hormones.[4] Studies on the molecular basis for the development of BCC has shown that the genetic defect involves the human homologue of Drosophila patched (PTCH) on chromosome 9q22.3. A study by Xin et al. in 1999 provided the first evidence of the involvement of the tumor suppressor gene PTCH

in NS. The results of analysis showed that BCC and NS share 9q22.3 deletions and are therefore likely to be pathogenetically related.[9] Therefore, such findings could explain the development of BCC overlying a NS.

VEN are congenital cutaneous hamartomas composed of keratinocytes. While malignant transformation is observed in NS, this is even rarer in VEN.[6] The link between VEN and BCC has not been fully elucidated. It remains elusive whether these skin tumors are derived directly from epidermal nevus cells, and therefore clonally related, or these secondary tumors could have arisen from other cells, such as hair follicle keratinocytes, accompanying the epidermal nevus.[7] Malignant transformation of VEN commonly happens post-puberty. The oldest patient reported was a 79-year-old male.[10] Furthermore, a study by Hafner in 2008 on a biopsy containing both BCC and VEN described the possible clonal relationship between both lesions based on molecular genetic findings. The study was based on the premise of mosaicism of FGFR3 and PIK3CA mutations being involved in the pathogenesis of epidermal nevus and having oncogenic potential. The hotspot PIK3CA mutation E545K was found in a biopsy containing both EN and BCC. The study concluded that both lesions may still share a common but unknown molecular genetic alteration, and that the PIK3CA mutation may then have occurred during the tumorigenesis of the BCC in terms of subclonal divergence.[7] These studies provide an underlying mechanism by which VEN can theoretically give rise to BCC.

However, the question of the pathogenesis of BCC arising from an EN still remains inconclusive and is subject for further study. Nevertheless, their coexistence is significant, because both may arise from the same pluripotent cells in the embryonic ectoderm. Patients with EN should be closely monitored and any changes suspicious of an evolving tumor should be sampled for pathology. In early stages, total surgical excision remains a matter of debate. Some authors suggest early period prophylactic excision for prevention of malignant development while others find this unnecessary.[5] According to Viana et al., the prophylactic excision of all VEN is not recommended, given the low number of BCC and other malignancies arising from this type of nevus.[6]

In conclusion, two (2) rare cases of BCC arising on two (2) different variants of EN are reported. Both patients presented with an epidermal growth on the left temporal aspect of the face since birth, which manifested with new suspicious lesions on their post-pubertal years. Risk factors such as trauma and sun exposure as demonstrated in the cases could be contributory to the malignant transformation of a pre-existing nevus. Further studies could be done to explore the influence of these risk factors and relate to the molecular studies described above. Despite the rarity of malignant transformation on EN, any suspicious growth warrants a biopsy. Knowledge of these cases is important for probing suspicious growth over a pre-existing epidermal nevus that would prompt early treatment before these lesions progress in size and number making it more complicated to manage.

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