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Nevus Sebaceous with Multiple Basal Cell Carcinomas and Extracutaneous Abnormalities: Genetic Origin or Coincidence?

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ABSTRACT The association of cutaneous and extracutaneous abnormalities is a common phenomenon, widely described in a variety of genetic syndromes. Nevertheless, yet undescribed syndromic combinations may still exist. Herein we present a case report of a patient who was admitted to the Dermatology Department due to multiple basal cell carcinomas arising from nevus sebaceous. In addition to the cutaneous malignancies, the patient presented with palmoplantar keratoderma, prurigo nodularis, hypothyroidism, multiple lumbar abnormalities, uterine myoma, an ovarian cyst, and highly dysplastic colon adenoma. Such a combination of multiple disorders may indicate a genetic origin of the diseases.

KEY WORDS: basal cell carcinoma, malignancy, syndrome, nevus sebaceous

INTRODUCTION

Medicine knows countless exceptional cases that are steadfast evidence of how much remains to be researched and explained. In our article, we would like to present an extremely rare case of multiple basal cell carcinomas arising within a nevus sebaceous of Jadassohn. Moreover, our patient is an example of a coexistence of numerous cutaneous and extracutaneous abnormalities. They may suggest an unknown genetic predisposition or even rise suspicion of a syndrome. However, to the best of our knowledge, such an association has not been reported in the literature until now.

CASE REPORT

A 65-year-old Caucasian women was referred to the dermatosurgery unit for diagnosis and treatment of a lesion which developed from a congenital nevus (Figure 1, A). On admission, physical examination revealed a large (5×2 cm) linear yellow-orange plaque localized on the patient's left temporal area. Three nodules and multiple erythematous and pigmented papules were visible within the lesion. The lesion was surgically removed. On histological examination, nests of basaloid cells with peripheral palisading associated with a fibromyxoid stroma were observed, confirming the diagnosis of three basal cell

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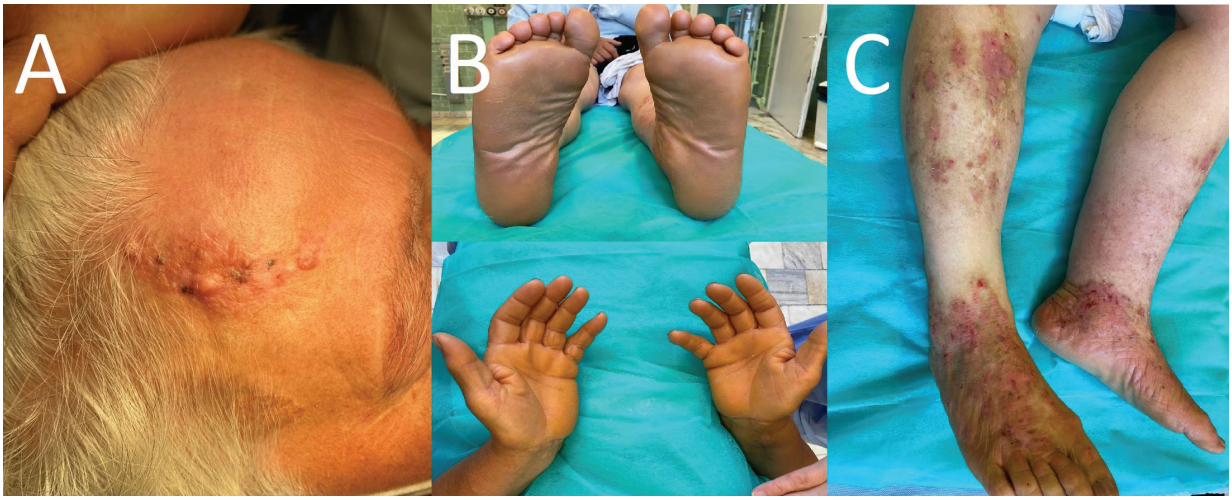

Figure 1. (A) Basal cell carcinoma on a congenital nevus before surgery. (B) Palmoplantar keratoderma; (C) Nodular prurigo.

carcinomas (BCCs) arising within nevus sebaceous (Figure 2, A and B). Interestingly, the woman had an extensive dermatological history and had suffered from palmoplantar keratoderma (Figure 1, B) since teenagerhood, as well as from prurigo nodularis since her forties (Figure 1, C). Furthermore, the patient presented many extracutaneous abnormalities such as multilevel lumbar discopathy and compression fracture of the L_2 vertebral body, hypothyroidism resulting in bilateral carpal tunnel syndrome, uterine myoma, an ovarian cyst, and highly dysplastic colon adenoma.

DISCUSSION

Nevus sebaceous of Jadassohn (NS), also referred to as an organoid nevus, is a congenital hamartomatous lesion derived from epithelium and adnexal structures that predominantly occurs on the head and neck. It is usually described as a solitary, alopecic, yellowish patch or plaque of variable size (1-3). NS is present in approximately 0.3%, births with equal incidence in male and female newborns. All races and ethnicities may be affected (4). NS is not an inherited dermatosis. However, a postzygotic somatic mutation of the Ras protein family, not only in the nevus itself but also in skin tambours arising from NS, has been reported (4). The lesions usually appear at birth or shortly afterward as a hairless yellowish plaque usually located on the face or scalp, associated with partial or total alopecia (4,5). Initially, it is characterized by immature and abnormally formed pilosebaceous units. Clinical and microscopical enlargement is subsequently observed due to hormonal disturbances during puberty. Moreover, the epidermis takes on a verrucous or mamillated appearance and pilloma-

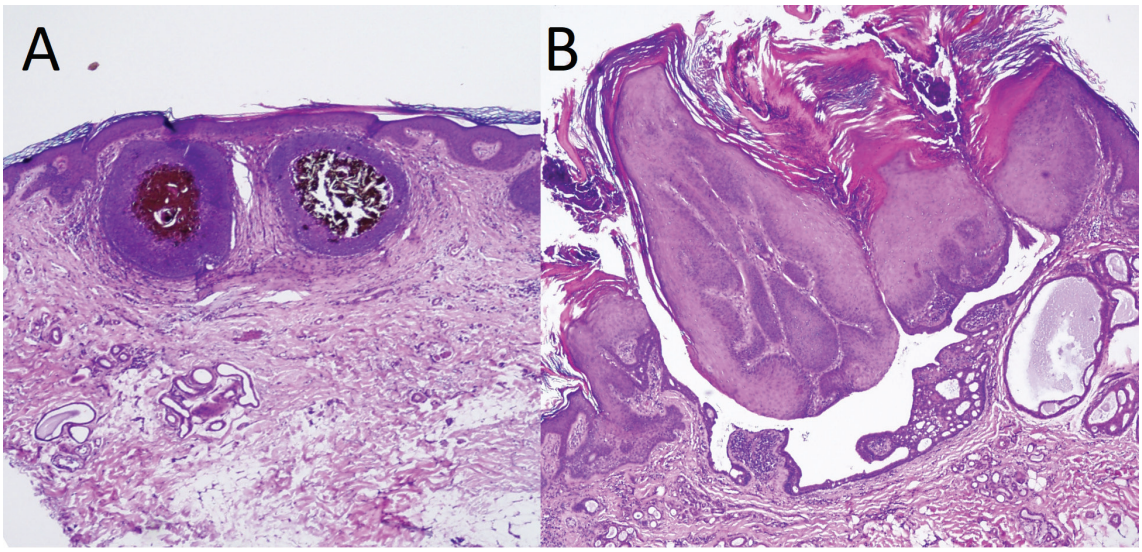

Figure 2. Histopathological image of pigmented basaloid nests (A) and irregular acanthosis, hyperkeratosis with signs of superficial basal cell carcinoma (B).

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tous character (2,4). Authors emphasize that multiple lesions may arise along the lines of Blaschko (4,6,7).

According to the available literature, a significant number of benign and malignant neoplastic transformation may arise within NS. More than 90% of those transformations are benign (5). The most frequent ones include trichoblastoma, syringocystadenoma papilliferum, and viral warts (5). It is important to emphasize that the true lifetime risk of malignancy in NS is difficult to estimate, as the majority of lesions are removed in childhood or adolescence (1,8). Moreover, recent studies highlight significant overestimation of the risk, caused by misinterpretation of benign trichoblastomas as basal cell carcinomas (BCCs) (9). BCC is generally considered the most frequent malignant tumor associated with NS; however, it is still a rare occurence. The actual prevalence of BCC secondary to NS is debatable, and some authors estimate it at around 0.8% (3,4,9). Moreover, multiple BCCs arising on NS are even more unusual and, to the best of our knowledge, the present case is the second one described so far (3). Regarding excision, there is no agreement on the matter of its necessity and timing. Some authors suggest prophylactic surgery before puberty, while others recommend monitoring the lesion and maintaining oncological vigilance (1,6). Excision may be justified not only to avoid malignant transformation, but also for cosmetic reasons. Due to typical head or neck localization and its association with alopecia, NS may significantly affect the quality of life (10). Moreover, patients should be advised that they have to report to a clinician in case of any changes in color, texture, size, or presence of accompanying symptoms (11,12).

According to current knowledge, extracutaneous findings associated with NS are extremely rare. Therefore, their existence strongly suggests a syndromic form of NS, as it could indicate a genetic basis of the diseases (6,7). The literature outlines the group of epidermal nevus syndromes (ENS). Originally, the term was used to define a syndrome that was actually several different disorders erroneously grouped together. It seems that ENS does not represent one entity, and epidermal nevi are not simply variants of each other. Well defined ENS include: phacomatosis pigmentokeratotica, nevus comedonicus syndrome, angora hair nevus syndrome, Becker nevus syndrome, and Schimmelpenning syndrome (6). The first syndrome, phacomatosis pigmentosa, is defined by the coexistence of nevus sebaceous and papular nevus spilus. The phenotype represents an example of didymosis (twin spotting). The combination of nevus comedonicus and ipsilateral ocular, skeletal, or neurologic defects is essential to diagnose nevus comedonicus syndrome (6,7). In the second of the above ENS, angora hair nevus syndrome, a linear epidermal nevus is covered by long smooth white hair resembling angora hair and growing out from follicular pores (6,7). The third, Becker nevus syndrome, is characterized by the presence of a Becker nevus in association with other cutaneous anomalies and muscular or skeletal defects. Cutaneous features include ipsilateral breast hypoplasia, patchy hypoplasia of extramammary fatty tissue, supernumerary nipples, sparse hair of ipsilateral axilla, or accessory scrotum. Among skeletal anomalies, authors mention scoliosis, fused or accessory cervical ribs, pectus excavatum, pectus carinatum, asymmetry of scapulae or short limbs, and muscular anomalies include hypoplasia or absence of ipsilateral muscles of the shoulder girdle (6,7). The last abovementioned ENS, also called Schimmelpenning-Feuerstein-Mims syndrome, is characterized by coexistence of NS with cerebral disorders such as mental deficiency and seizures, with skeletal defects such as spinal malformations, craniofacial defects, arm or leg deformities, and also with ocular abnormalities such as coloboma or corneal opacity (6,7). As in the case of our patient, the association of NS with many cutaneous and extracutaneous abnormalities is particularly noteworthy. Currently, it is not possible to diagnose any of the well-defined ENS in our patient, as she did not present the characteristic symptoms. Nevertheless, simultaneous occurrence of numerous dermatoses and extracutaneous abnormalities strongly suggests a genetic background. In case of additional extracutaneous findings, it is necessary to perform ophthalmic, orthopedic, and neurological consultations (4, 6).

As mentioned above, our patient also suffered from palmoplantar keratoderma (PPK) since teenagerhood. PPKs are a diverse group of diseases marked by thickening of the skin on the palms and soles (13). Inherited and acquired PPKs should be distinguished. Early onset and positive family history suggest a genetic cause. Hereditary forms may also be associated with ectodermal abnormalities such as scaling, nails thickening or absence, hypotrichosis, woolly hair, or even extracutaneous manifestation involving changes in the teeth, ears, heart, or eyes (12,14). Because of many possible underlying causes for acquired PPKs, some authors categorize them as: keratoderma climactericum, drug related, malnutrition associated, chemically induced, systemic disease related, malignancy associated, dermatoses related, infectious, and idiopathic (13). A number of systemic diseases including hypothyroidism, also present in our case, myxedema, chronic lymphedema, and other circulatory abnormalities, may be associated with acquired

PKK (11). Isolated nonspecific keratoderma has been described as a paraneoplastic marker for internal malignancy (13,15). Additionally, many reactive and inflammatory dermatoses including psoriasis, keratoderma blennorrhagica, pityriasis rubra pilaris, eczema, chronic hand dermatitis, lichen planus, lichen nitidus, lupus erythematosus, and aquagenic keratoderma are associated with PKK (13). However, the relationship between PPK and the occurrence of NS or nodular prurigo, as in our patient, has not been described so far.

In conclusion, according to the current literature, tumor formation from NS is an uncommon phenomenon. Moreover, the occurrence of three or more BCCs arising on NS is extremely rare and, to the best of our knowledge, our case is the second one ever described. It is important for clinicians to consider the possibility of malignancy arising from NS. At the same time, the coexistence of several dermatoses and extracutaneous disorders may indicate genetic or syndromic origin of NS and may require extensive medical investigation.

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