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REVIEW

# Epidermal Nevi and Related Syndromes —Part 2: Nevi Derived from Adnexal Structures☆

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Porokeratotic adnexal ostial nevus;
Becker nevus

**Abstract** Epidermal nevi are hamartomatous lesions derived from the epidermis and/or adnexal structures of the skin; they have traditionally been classified according to their morphology. New variants have been described in recent years and advances in genetics have contributed to better characterization of these lesions and an improved understanding of their relationship with certain extracutaneous manifestations. In the second part of this review article, we will look at nevi derived from the adnexal structures of the skin and associated syndromes.


**PALABRAS CLAVE**
Nevus sebáceo;
Genes RAS;
Rasopatía;
Síndrome de Schimmelpenning;
Nevus foliculares;
Siringocistoadenoma papilífero;
Nevus ostial anexial poroqueratósico;
Nevus de Becker

## Nevus epidérmicos y síndromes relacionados. Parte 2: Nevus derivados de estructuras anexiales

**Resumen** Los nevus epidérmicos son hamartomas originados en la epidermis y/o en las estructuras anexiales de la piel que se han clasificado clásicamente partiendo de la morfología. En los últimos años se han descrito variantes nuevas y se han producido avances en el campo de la genética que han permitido caracterizar mejor estas lesiones y comprender su relación con algunas de las manifestaciones extracutáneas a las que se han asociado. En esta segunda parte revisaremos los nevus derivados de estructuras anexiales de la piel y los síndromes que se asocian.


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## Introduction

In this second part, we will review hamartomas derived from sebaceous glands, hair follicles, and apoccrine and eccrine sweat glands. Finally, we will discuss Becker nevus. Table 1 summarizes the best characterized syndromes to date associated with these adnexal nevi.

## Sebaceous Nevus

These are organoid lesions that contain epidermal, follicular, sebaceous, apocrine, and eccrine components. They have a prevalence of 0.3% and some familial forms exist.[1,2] They arise as a result of postzygotic somatic mutations in *HRAS* (95%) and *KRAS* (5%).[3,4] More recently, *NRAS* mutations have also been described in a case of nevus sebaceus with extracutaneous manifestations.[5] Some authors refer to a group denoted *mosaic RASopathies* that includes sebaceous nevi and also some keratinocytic nevi, melanocytic nevi, and associated syndromic forms.[6,7]

More than half the lesions are found on the scalp, a third develop on the face, while they are rarely seen on the neck and only exceptionally on the trunk or limbs.[8,9] The lesions are congenital in most cases, although onset may occur in the first years of life. Characteristically, they are distributed along the Blaschko lines, adopting an ovulated or comma form. The clinical aspect varies with age, probably due to the increased number of androgen receptors in components that are stimulated during puberty.[10] In children, the disease is manifest as small yellowish-orange alopecic plaques that can be mistaken for aplasia cutis congenita or a scar. From adolescence onwards, the lesion takes on a more verrucous appearance with a more yellowish color (Fig. 1).

Histological changes also vary with the age of the patient.[8,9] In pediatric patients, mild epidermal acanthosis is usually observed along with presence of small poorly formed hair follicles. From puberty onwards, acanthosis becomes more evident and the number and size of the sebaceous glands increase and these are found higher in the reticular dermis or even in the papillary dermis (Fig. 2). Hair dysgenesis persists into adulthood. Generally, the presence of well-formed terminal hair marks the limits of the lesion.

An epidermal change that is observed fairly often in adults is follicular induction. This is a reactive phenomenon that can be seen in multiple processes and that is thought to

**Table 1** Some of the Best Characterized Syndromes Associated with Nevi Derived From Adnexal Structures (Organoid).

| Syndrome | Type of Nevus | Other Manifestations | Gene Involved (Transmission) | Reference |
|---|---|---|---|---|
| Schimmelpenning syndrome | Sebaceous nevus (possibly also keratinocytic) | Mental retardation, epilepsy, osteopenia, kyphoscoliosis, short stature, abnormalities of fingers and/or toes, eyelid lipodermoid, coloboma, and other abnormalities | *HRAS*, *KRAS* and *NRAS* (sporadic) | 3-5, 32, 34 |
| Phacomatosis pigmentokeratotica | Nevus sebaceus and nevus spilus | Mental retardation, epilepsy, hemiparesis, local abnormalities associated with nevus spilus: hyperhidrosis, dysesthesia, muscle weakness, and sensory and motor neuropathy. | *HRAS* (sporadic) | 35, 36 |
| Hypophosphatemia cutaneous-skeletal syndrome | Keratinocytic nevus and nevus sebaceus | Hypophosphatemia, bone dysplasia and osteomalacia, cerebral, cardiac, and ophthalmological manifestations of the nevus sebaceus or phacomatosis pigmentokeratotica syndrome | *HRAS*, *NRAS* (sporadic) | 37, 41, 42 |
| Didymosis aplasticosebacea and SCALP syndrome[a] | Nevus sebaceus, aplasia cutis congenita | Limbal dermoid, large or giant congenital melanocytic nevus, and neurological abnormalities similar to Schimmelpenning syndrome. | Unknown (sporadic) | 46-48 |
| Nevus comedonicus syndrome | Nevus comedonicus | Ipsilateral cataract, microcephaly, mental retardation, epilepsy, vertebral abnormalities, syndactyly, clinodactyly, polydactyly, and oligodontia | Possibly *FGFR2* in mosaic form of the Apert syndrome in some cases (sporadic) | 56, 61 |
| Becker nevus syndrome | Becker Nevus | Ipsilateral mammary hypoplasia, hypoplasia of the underlying muscles, lipoatrophy, and skeletal abnormalities | *ACTB* (sporadic) | 98, 99 |

[a] Sebaceous nevus, central nervous system malformations, aplasia cutis congenita, limbal dermoid and pigmented nevus.