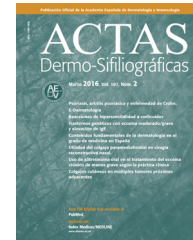




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REVIEW

Epidermal Nevi and Related Syndromes — Part 1: Keratinocytic Nevi[☆]

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PALABRAS CLAVE

Nevus epidérmico;
Nevus
queratinocítico;
Papular Epidermal
Nevus with Skyline
basal cell layer
(PENS)

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 first part of this review article, we will look at nevi derived specifically from the epidermis and associated syndromes.

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Nevus epidérmicos y síndromes relacionados. Parte 1: nevus queratinocíticos

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 primera parte revisaremos los nevus derivados de la epidermis y los síndromes que se han descrito asociados a ellos.

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Introduction

A hamartoma is a tumor-like malformation, usually congenital, arising due to an abnormal mixture in the distribution or proportions of mature, constitutive tissue elements. It is not a neoplasm because the tissues do not undergo autonomous growth. Skin hamartomas are called nevi. There is a

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Table 1 Epidermal Nevi Classified According to Morphological Criteria and Genes Implicated in Development.

		Gene involved	Locus		
Keratinocytic nevi	Common keratinocytic nevus	FGFR3	4p16.3		
		PIK3CA	3q26.32		
		HRAS	11p15.5		
		NRAS	1p13.2		
		KRAS	12p12.1		
		FGFR2	10q26.13		
		Unknown	Unknown		
		Unknown	Unknown		
		Unknown	Unknown		
		Unknown	Unknown		
		Unknown	Unknown		
		Unknown	Unknown		
		Unknown	Unknown		
Nevi derived from adnexal structures	Nevus sebaceous	HRAS	11p15.5		
		NRAS	1p13.2		
		KRAS	12p12.1		
		FGFR2 ^a	10q26.13		
		Unknown	Unknown		
		Follicular nevi	Hair follicle nevus (congenital vellus hamartoma)	Unknown	Unknown
				Unknown	Unknown
				Unknown	Unknown
				Unknown	Unknown
		Apocrine nevi	Apocrine nevus	Unknown	Unknown
				Unknown	Unknown
				Unknown	Unknown
		Eccrine nevi	Eccrine nevus	Unknown	Unknown
Unknown	Unknown				
Unknown	Unknown				
Becker nevus	Porokeratotic adnexal ostial nevus	GJB2	13q12.11		
		ACTB	7p22.1		

Abbreviations: HILD, congenital hemidysplasia, ichthyosiform erythroderma and limb defects; ILVEN, inflammatory linear verrucous epidermal nevus; PENS, papular epidermal nevus with skyline basal cell layer; PTEN, in this context, papillomatous, thick, epidermal, nonorganoid nevus.

^a Association of mutations of the *FGFR2* gene with sebaceous nevus has been debated (see text).

certain degree of confusion regarding the definition of the term *epidermal nevus*. Most articles in the scientific literature consider epidermal nevi to refer to lesions derived from the epidermis or from adnexal epithelial cells. Some texts on skin pathology, however, define epidermal nevi as those lesions derived from epidermal keratinocytes (herein denoted keratinocytic nevi) excluding nevi derived from adnexal structures.^{1,2} In this article, we will refer to both nevi derived from the epidermis and those derived from adnexal structures. The review will be divided into 2 parts. **Table 1** summarizes and classifies the nevi that will be reviewed both in part 1 (keratinocytic nevi) and in part 2 (nevi derived from adnexal structures) and can be used as a table of contents.

Epidermal nevi often exhibit so-called organocity. This concept, in pathology, defines the simultaneous growth of several cell components in the same hamartoma. This phenomenon is often observed in hamartomas derived from adnexal structures and should not be confused with the concept, more often used in medicine, to define a

symptom originating from organic and physical abnormality (as opposed to a psychological cause). Some texts classify epidermal nevi as organoid and nonorganoid (in practice, keratinocytic). Adnexal structures, for their part, can be the cause of certain lesions defined in some skin pathology text books as hamartomas,³ but which are, however, not considered nevi in most text books on clinical dermatology (for example, steatocystoma, fibrofolliculoma, and trichofolliculoma). We will not cover these lesions in the present review.

Pathophysiological Basis

The appearance of these lesions is due to genetic mutations or epigenetic changes that impact the expression of a cell clone during embryo development, leading to mosaicism, that is, the presence of 2 or more genetically distinct cell populations in the same individual.⁴ Four genetic mechanisms have been described that explain most cases of mosaicism in the skin:

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