Congenital Melanocytic Lesions and Neurocrystic Development

Miguel Reyes-Múgica, M.D.
Marjory K. Harmer Endowed Chair in Pediatric Pathology, Chief of Pathology and Head of Laboratories Children's Hospital of Pittsburgh of UPMC, Professor of Pathology University of Pittsburgh School of Medicine

Objectives: At the end of this activity, the participant will be able to:

- Recognize the main clinical and histological features of Large/Giant Congenital Melanocytic proliferations and Neurocutaneous Melanocytosis
- Understand the main complications associated with Large/Giant Congenital Melanocytic Proliferations in Children
- Understand the most frequent genetic abnormalities leading to Congenital Melanocytic Proliferations

Description:

Large and Giant Congenital Melanocytic Nevi (L/GCMN) are least frequent types of congenital melanocytic proliferations involving the skin pigment cells. Their phenotype is highly variable, and although no firm bases to support inheritance exist, a few instances of familial transmission have been reported. The current favored understanding is that a somatic mutation occurs during or early after the first trimester of gestational age melanocyte precursors, in the context of a predisposing genetic background. Although the role of NRAS and BRAF, of the MAP kinase pathway is well established, other genetic pathways converging on transcription factors essential for multipotent precursor maintenance and/or melanocyte differentiation, may predispose cells to inappropriate proliferation in the central nervous system and other sites. These other forms of melanocytic proliferation have a variable presentation, and may lead an individual to clinically favorable or fatal outcomes. A vigorous exploration of the molecular bases of L/GCMN development is leading to new tools for more accurate prognostication in patients afflicted by these conditions.

In this session, we will discuss the main features of L/GCMN at the histological and genetic level, from the viewpoint of Neural Crest development. We will describe new observations and experimental therapeutic approaches alternative to surgery.

References:

Blistering Genodermatosis in Newborns and Infants

Stéphanie Leclerc-Mercier, MD
Praticien Hospitalier, dermatologie et dermatopathologie
Services de Dermatologie du Pr Bodemer et d’Anatomie et Cytologie Pathologiques du Pr Molina
Centre de référence MAGEC
Hôpital Necker Enfants Malades
149 rue de Sèvres 75015, Paris

OBJECTIVES: Following the session, attendees should be able to choose the best location and number of skin biopsies and know their purpose. They should be familiar with routine and specialized techniques, and finally know the histologic aspects leading to the diagnosis of blistering genodermatosis. The role of electron microscopy will also be discussed.

DESCRIPTION: the onset of blisters in a newborn or infant is a common situation and the dermatopathology is the first step in the diagnosis, leading to a rapid and adapted therapy. Inherited epidermolysis bullosa (EB) comprises a highly heterogeneous group of rare diseases characterized by fragility and blistering of skin and mucous membranes. Some of them have a severe prognosis whereas other are mild. Clinical features combined with antigen mapping and sometimes electron microscopy examination of a skin biopsy allow to define the EB type and subtype.

During the session, antigen mapping of EB will be extensively discussed, in view of the latest recommendations on diagnosis and classification of EB (Fine et al 2014).

Epidermolytic ichthyosis can be easily recognized by a standard technique and we will also define the value of immunohistochemistry.

Another part of the session will be dedicated to Incontinentia Pigmenti.

Lastly, the new entity called “genodermatosis leading to skin fragility” will be touched on.

REFERENCES
Cornification Disorders as Markers for Syndromic Diseases

Dieter Metze, MD
Professor of Dermatopathology
Department of Dermatology
Univ- Muenster, von Esmarchstrasse 58
Muenster 48149, Germany

A specific diagnosis of cornification disorders is mandatory to differentiate between syndromic and non-syndromic forms. Some types of palmoplantar keratoderma are associated with lethal cardiomyopathy, hearing impairment and other neurological manifestations, as well as cancer. In syndromic ichthyoses severe growth defects of organs, as well as immunologic and neurologic dysfunctions should be identified for further genetic counselling and management of the patient.

Dermatopathology contributes to early diagnosis by histologic patterns and clues, histochemical and immunohistochemical findings.
What’s New in Genodermatoses?

Sylvie Fraitag-Spinner, MD
Dermatopathologie
Praticien Hospitalier
Département de Pathologie
Hôpital Necker-Enfants Malades
149, rue de Sèvres 75015, Paris

Over the last years several new entities showing multi-organ lesions and notably affecting the skin, have been described thanks to the recognition of new gene mutations. Some of them were already known but not properly classified. Recent and improved understanding of the physiopathology of these disorders has allowed the development of targeted therapies, which are currently being evaluated. This is the case with newly recognized type I interferonopathies, which are a group of Mendelian disorders including Aicardi-Goutières syndrome, familial chilblain lupus, SAVI and others. These diseases present phenotypic overlap including cutaneous features that can be inaugural or present during the first months of life. Proteasome-associated autoinflammatory syndromes include different newly described disorders such as CANDLE syndrome which is probably one of the most intriguing. All these entities have an autosomal recessive transmission and are linked to mutation in PSMB8 gene; they present with roughly the same, often highly recognisable clinically and histologically, cutaneous lesions.

H syndrome is an autosomal recessive disorder first described in 2008 and caused by mutations in the SLC29A3 gene. It is known now that other syndromes are related to these mutations such as Faisalabad histiocytoses, familial Rosai-Dorfman syndrome and other histiocytoses.

All these disorders are first diagnosed by the combination of clinical and histopathological findings. That's why knowledge of the histological characteristics of these diseases is important.

References:
Crow YJ. Ann N Y Acad Sci 2011 ; 1238 : 91-8

*The information contained in the "Cutaneous Markers for Genetic Diseases" handout is not intended as medical advice or consultation, and should not be relied upon as such*. 