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Lesson No. 8

In-depth rare diseases

RAREDUCANDO DIGITAL EDUCATION

Epidermolysis Bullosa

What is it?

Epidermolysis Bullosa is the generic name given to a group of genetic diseases in which the skin and the lining tissues (epithelium) of the mucous membranes meet, spontaneously or as a result of minimal trauma, disconnection and formation of bubbles. Gravity is very variable: there are mild forms that allow an almost normal life and very serious forms, which can be lethal within the first months of life. The first symptoms usually occur in the first hours after birth. Depending on the depth of the lesions, hereditary bodily epidermolysis is divided into three main classes: simple, junctional and dystrophic. In simple forms the epidermis (the most superficial layer of the skin) is involved, while mucous membranes are rarely affected; the bubbles heal almost without scars, and the main complication is the infection of the lesions. In junctional forms, the lesions are deeper (between the epidermis and the dermis), and the bubbles are extensive and often affect the mucous membranes; this group includes lethal bollosa epidermolysis (Herlitz type). In the dystrophic forms, the lesions are very deep and the mucous membranes of the tongue, eyes and oesophagus are often involved; in the most severe forms, there are syndactyly, tooth malformations and hair and nail loss, recurrent bleeding, malnutrition and anaemia. There is also an autoimmune form called acquired bully epidermolysis, which usually occurs in adulthood**.**

Simple bully epidermolysis usually starts at birth or soon after, although in localised forms bodily lesions may appear in late childhood or early adulthood. In addition to bubbles and erosions, in localized or generalized form (in the herpetiform group), the other skin characteristics include nail dystrophy with loss of nails and, rarely, miliary lesions. Often scarring is absent or minimal (little wrinkled atrophy and depigmentation). Other features are congenital skin agenesis and localised or confluent palmoplantar keratoderma. The most common non-skin sign is the formation of bubbles in the oral cavity. Other age-related extracutaneous complications may arise, with the onset and cumulative risk of occurrence depending on the subtype of EB. Many subtypes are classified according to the intraepidermal location of bubbles. In many cases, bubbles arise in the basal layer of the epidermis (However, three subtypes have suprabasal site bubbles (Placophyline Deficit EBS, superficial and lethal acantholytic EB).

How do you transmit bully epidermolysis?

Various genes have been identified that, if altered, are involved in the onset of bully epidermolysis. These genes are codifying for proteins that maintain adhesion between the epidermis and the dermis (the underlying layer), including collagen, laminin, keratins, and integrins. Some forms are inherited with autosomal dominant mode, so a sick parent has a 50 % chance of transmitting the disease to each of their children. Other forms are inherited in autosomal recessive mode: both parents are healthy carriers of the same gene associated with the disease and the probability that they will transmit it to their children is 25 % at each pregnancy.

How does the diagnosis of bully epidermolysis happen?
The first diagnosis is based on clinical observation. Until a few years ago histological analysis was carried out on skin biopsy followed by molecular genetic tests. Thanks to modern diagnostic techniques, it is only possible to take blood from the patient and parents, without having to biopsy. Prenatal diagnosis and preimplantation diagnosis are also possible in pregnancies of couples where the genetic defect underlying the disease has been identified.

What are the possibilities of treatment currently available for blistered epidermolysis?
There is no conclusive treatment; the only available garrison is daily wound treatments with advanced dressings. In 2006, a team of the University of Modena led by Michele De Luca carried out, with the contribution of the Telethon Foundation, the first treatment of a patient suffering from junctional boiled epidermolysis through gene therapy, with extremely promising results, confirmed on a second patient a few years later and on a third in 2015, saved by genetically correct epidermis transplantation on more than 80 % of the body surface.

Very frequent clinical signs:
Clinical signs vary considerably, from the localized formation of bubbles on the hands and feet to the general formation of bubbles on the skin and in the oral cavity, to lesions in the internal organs. Four main types of hereditary EB have been identified: Simple EB (EBS), Junctional EB (JEB), Dystrophic EB (DEB), each with numerous subtypes, and Kindler syndrome. These forms differ not only phenotypically and genotypically, but also, significantly, by the site of rupture or ultrastructural cleavage.
All types of bodily epidermolysis manifest with painful and inappropriate vesicles. The severity of symptoms is related to the seriousness of the formation of blisters and scars and varies from mild to severe. Extensive mucocutaneous epidermolysis of any type can cause intense pain. Widespread skin lesions cause fluid imbalance and protein loss. Skin lesions can become infected, and infections can become systemic. Involvement of mucous membranes can cause malnutrition and growth difficulties, respiratory problems and genito-urinary problems.
Severe junctional bollosa epidermolysis and dystrophic bollosis epidermolysis cause significant mortality below 2 years of age. Severe generalised bodily epidermolysis can also be fatal. Death occurs after complications such as infections, malnutrition and dehydration.
Vesicles tend to decrease with age. Patients with junctional bollosa epidermolysis, dystrophic bollosis epidermolysis and Kindler syndrome may develop squamous cell carcinomas of the skin and mucous membranes in adulthood.
Chronic disease can be debilitating and disabling. However, some serious symptoms may decrease over time, when somatic growth again expands the inner lumen that had been stented by previous scars.

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