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Case Report

Case Report: Junctional Epidermolysis Bullosa in Newborn

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Abstract

Junctional epidermolysis bullosa is a rare, autosomal recessive bullous genetic disease characterized by propensity to erosion and blister after having a trauma or in a spontaneous way. It is characterized by cleavage in the lucida blade zone due to mutations of certain genes, resulting in the absence or reduction of the 332 laminin, XVII collagen, α6β4 orα3-integrins. We report in here a full-term Caucasian male newborn case with cutaneous exulcerations in trauma zones such as the face, upper limbs, buttocks, back, lower limbs, cervical region and umbilical region, as well as strained blisters of hyaline content on the hands. We carried out a skin biopsy for indirect immunofluorescence with a panel of antibodies which was compatible with junctional epidermolysis bullosa. We emphasize the importance of quick transfer to reference centers in order to facilitate early diagnosis and the future complications prevention.

Keywords: Early Diagnosis; Junctional Epidermolysis Bullosa; Newborn

Introduction

Epidermolysis Bullosa (BE) is within a blistery genetic sickness group characterized by a certain skin and/or mucous connectives frailty with a large phenotypic variation. Blisters or erosions that take place at the birth period or any further are typically seen in certain propitious trauma zones such as the face, the members and the cervical region. The severity and the EB's course rely on the genes mutations that modify the proteins entangling within the basal membrane zone. It might be classified within four subtypes: simplex, junctional, dystrophic and Kindler syndrome [1,2]. In this study, we report the clinic case of a junctional Epidermolysis Bullosa Newborn (EBJ) that led into death and we highlight the importance of having an early diagnosis and of the neonatal caring.

Clinic Case

A full-term masculine newborn, Caucasian, normal delivery, weighing at his birth 3,235g. He was transferred to the Pedro Ernesto University Hospital, as he was born with cutaneous exulcerations within trauma zones such as on face, the cervical region, the upper limbs region (Figure 1), the back-buttocks region (Figure 2), the lower members region (Figure 3), as well as having been noticed to have tense blisters with hyaline content in his hands (Figure 4). He also presented nail dystrophy at the first and at the third chirodactile of the left hand and anonychia at the fourth right chirodactile.

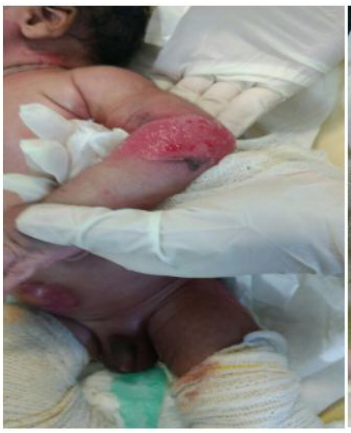

Figure 1: The upper limbs region.

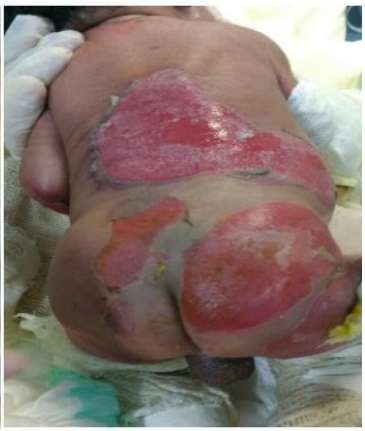

Figure 2: The back-buttocks Rgion.

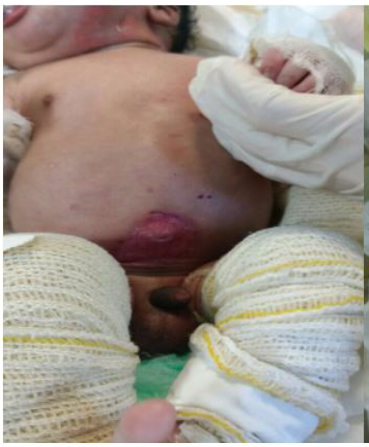

Figure 3: Tense blisters with hyaline content in his hands.

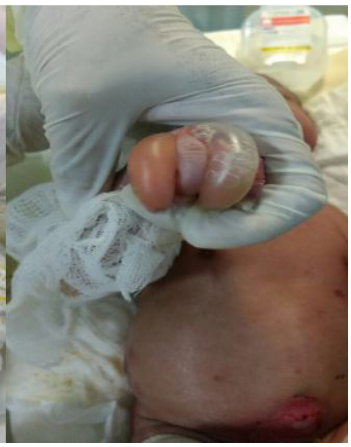

Figure 4: Nail dystrophy.

During the course of the first life fortnight, it was noticed the aggravation of his clinical condition with new lesions emergence, fever and prostration. Hemoculture isolated Pseudomonas aeruginosa. It was set up a large spectrum antibiotic therapy through intravenous route. The clinical diagnosis was confirmed by the mapping examination through antigenic immunofluorescence from the skin fragment after erythema induction with distal end of the chirodactile in the dorse (healthy skin adjacent to the exulceration). The realization of the molecular test was not possible, due to the fact that the newborn was led to death by sepsis having lived for 20 days, three days after being welcomed at the aforementioned hospital, despite all the due neonatal care. In the family, the parents had no knowledge about similar cases and refused further investigations.

The indirect immunofluorescence with the antibodies panel to IV, VII collagen, laminin and antigen of the bullous pemphigoid (AgPB), proteins of dermal-epidermal junctions, revealed fluorescence in the dermic side of the cleavage to the three first ones and in the epidermal side to the last one, being compatible with EBJ.

Discussion

The hereditary EB may be divided within four categories: simplex, junctional (EBJ), dystrophic and the Kindler syndrome - multiple levels cleavage. In the first one, the cleavage occurs in the basal epidermis layer (intraepidermal), in the second one, in the dermoepidermal junction (basal membrane zone - lamina lucida) and, within the third one, the cleavage occurs in the basal membrane zone in the sub-lamina densa [3].

The EBJ is a rare Genodermatosis, autosomal recessive, characterized by mutations in the LAMA3, LAMB3 or LAMC2 genes, resulting in the absence or reduction of the 332 laminin. Rare EBJ subtypes have mutations in the COL17A1, ITGB4, ITGA6 or ITGA3 genes, leading up to a dysfunction or to a reduction of the XVII collagen, α6β4 and α3 integrins. Blisters, oral lesions and nail dystrophies might be seen, as well as the in the gastrointestinal, respiratory and genitourinary systems, having the possibility of being early mortality causes [2].

The EBJ may be generalized as severe, often lethal in the very first two lifetime years, old Herlitz (EBJ - H) characterized by the absence or strong reduction of the 332 laminin and intermediary generalized, old non-Herlitz (EBJ - nH), characterized by the reduction of the 332 laminin, XVII collagen, α6β4 or α3 integrin [4,5]. The different junctional epidermolysis bullosa may be indistinguishable in the neonatal period [5]. Mutations in the COL17A1 gene that originates the XVII collagen are predominant in the EBJNH and lead up to the absence of the protein synthesis (frameshift or nonsense), or more rarely, in the production of an anomalous protein (missense), [3,5] although mutations in the genes that codify the 332 laminin may also take place [2,3]. Patients with the absence of the XVII collagen are clinically characterized with cutaneous frailty, with large blisters on the skin and mucous, atrophic scar, alopecia universalis, dystrophy and nail loss and dentary abnormalities [3,6]. In these cases, the extracutaneous impairment is rare (with the exception of the esophagus stenosis) and the prognostic is better, opposed to the EBJH [7].

The diagnosis of the EBJ may be given through the Indirect Immunofluorescence (IFI) with an antigenic mapping or by an Electronic Microscopy (EM) (gold pattern) to classify the cleavage zone and to molecular mutations research. These methods do not serve as for the prognostic. The EM advantages are the following: it enables the researcher to visualize ultrastructural abnormalities and the basal membrane zone deficits that may be particularly useful in the mild forms, as well as in the superposition form (Kindler syndrome). The disadvantages entangle the fact of the exam being such a high complexity, a costly and an operator-dependent one. The IFI is more sensible and specific, accessible, done under easy transportation, with a quicker result, being possible to be stored for more than 28 days and detect in the first gestation trimester severe forms of EB by biopsy of the chorionic villi.

The biopsy must be done preferentially with lamina, after the asepsis and anesthesia, within an adjacent integral skin zone to a blister zone with a recent appearing (less than a 12-hour-duration-period), so that half of the fragment might be constituted by the blister and the other half by healthy skin, in order to avoid the proteolytic degradation of the antigen or the blister superior reepithelialization which might generate artifacts and difficult in this way the correct definition of the cleavage zone. The blister might be induced by friction with downward pressure and with a 180-cotton swab rotation, a rubber glove finger or with a pencil having an eraser at its end. The amount of friction required to induce a subclinic blister might vary from person to person, being the development of erythema in the zone a good indicator that the cleavage was obtained. In newborns or young children, it is normally sufficient to rub the selected zone about 20 times. In patients with less frailty in their skin, it may be necessary up to two minutes of friction to induce the blister formation. The biopsy must be

administered after 5 minutes of the formation of the erythema, in order to guarantee the due time period to the microscopy blister formation. To the realization of the indirect immunofluorescence, one 3 to 4 mm sample is enough and the transportation must be done in Michel's solution right away.

Besides the EM and the IFI, it is important the realization of a molecular study through the blood collection of the newborn and of his/her parents, as for detecting genetic mutations. The exam based in the search of fetal DNA mutations might be executed from the 10th gestation week. The protein level mutations consequence knowledge is also important to define the methodology of the genic therapy to be used, in order to restore the expression of the mutated gene, introducing a copy of the normal gene within epidermal cells [8]. The molecular identification of the illness in this family allows to determine the risk of recurrence and to offer to the couple the possibility of a prenatal diagnosis within the subsequent gestations. 5

The newborn differential diagnosis with a blistery disease must be: infectious diseases, such as herpes, impetigo, Scald Staphylococcic Skin Syndrome (SSSS) or Ritter von Rittershain sickness; heritable ones, such as bullous congenital ichthyosiform erythroderma, besides bullous mastocytosis and immunological disorders (for instance, dermatosis by linear IgA) [2,5,9,10-12].

The neonatal cares made by a multidisciplinary team are pivotal to prevent the cutaneous lesions development and secondary infections, to control the pain and avoid complications. The EB treatment is palliative, being generally recommended: avoid friction or mucocutaneous abrasion, constriction, overheating; water mattress, the use soft fabrics and clothes, well-adjusted diapers and proper skin lubrication will help to limit the friction and the trauma; gloves (to minimize the self-induced trauma); comfortable shoes, better with the larger ones to allow the placement of dressings; maintain the palms and the soles dry in order to minimize the appearing of blisters, especially during the hot weather. It might be necessary previous analgesics to place the dressings and ruptures of blisters with a sterilized needle with maintenance of its skin surface in order to act as a biological dressing [5].

Daily baths and the application of topic products in the erosion zones (Vaseline or essential fatty acid or hydrogel) are necessary. Protective bandage (gauze impregnated with petrolatum, Telfa, Mepilex, Mepilex Transfer, Mepitel, Restore) that do not adhere to the wounds must be done in the affected zones in an aseptic way to promote the cicatrization and avoid additional erosions when the dressings are changed. In children, the bandage must be placed between the fingers as for minimizing the risks of pseudosyndactyly. Nutritional supplementation of iron, D3 vitamin, zinc and proteins is necessary, since the mortality rates due to malnutrition are high (20.5%). Dental hygiene with gauze and chlorhexidine should be regular in order to avoid the appearing of dental cavity [13]. Moreover, studies of reverse mosaicism have been carried out and aim at the development of cellular therapies in which the patient's own corrected cells are used as a source for cutaneous transplantation [5]. However, there is still a lack of studies to better manage the disease and guarantee life quality for these patients.

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