CONGENITAL ABSENCE OF SKIN ON THE RIGHT LEG AND NAIL ABNORMALITIES-EPIDERMOLYSIS BULLOSA OR BART'S SYNDROM ?

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UROĐENI NEDOSTATAK KOŽE NA DESNOJ NOZI I ABNORMALNOST NOKATNE PLOČE - BULOZNA EPIDERMOLIZA ILI BARTOV SINDROM?

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ABSTRACT

Children born with the epidermolysis bullosa (so-called "butterfly children") can eat only liquid or soft food due to the blisters on their mouth, tongue and esophagus. Due to their inactivity and permanent wounds, their fingers are curved and grown with a fist. Their eyes, anus and genitals are not spared either. The digestion is usually poor, so they often suffer from the constipation, and sometimes the intestine discharge can be performed only surgically. Due to frequent and numerous wounds, infections may develop, which can lead to sepsis. Wounds are caused by any kind of the pressure and re-bandaging of wounds is the most painful. These children can later be susceptible to other diseases, especially the skin cancer. More than 80% of children diagnosed with this disease become disabled in the first years of their lives, and some of them pass away immediately after birth. The average lifespan of the diseased is about 28 years. Here we have presented a rare case of a newborn male infant with a dystrophic epidermolysis bullousa, a congenital skin aplasia on the right leg and a nail dystrophy. Based on a typical clinical presentation, we think that it is Bart's syndrome.

***Keywords**: epidermolysis bullosa, "butterfly children", Bart's syndrome*

SAŽETAK

Deca rođena sa buloznom epidermolizom (takozvana „deca leptiri") mogu da jedu samo tečnu ili kašastu hranu zbog plikova na ustima, jeziku i jednjaku. Zbog neaktivnosti i stalnih rana prsti im se krive i srastaju sa šakom. Nisu pošteđene ni oči, analni otvor i genitalije. Varenje je obično loše, pa često imaju opstipaciju, a ponekad se pražnjenje creva može izvršiti samo hirurški. Usled čestih i mnogobrojnih rana, dolazi do infekcija koje mogu dovesti do sepse. Rane izaziva svaka vrsta pritiska, a najbolnije je previjanje. Ova deca su kasnije podložnija drugim bolestima, a posebno karcinomu kože. Preko 80% obolelih postaju invalidi već u prvim godinama života, a neki od njih umiru neposredno po rođenju. Prosečan životni vek obolelih je 28 godina. U ovom radu smo predstavili redak slučaj muškog novorođenčeta sa distrofičnom bulloznom epidermolizom, urođenom aplazijom kože na desnoj nozi i distrofijom nokta. Na osnovu tipične kliničke prezentacije mislimo da je u pitanju Bartov sindrom.

Ključne reči: *bulozna epidermoliza, „deca leptiri", Bartov sindrom*

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INTRODUCTION

Epidermolysis bullosa (EB) is an inherited mechanobullous disorder characterized by skin fragility and blister formation, following minor trauma or traction on the skin. Children born with the EB are commonly referred to as "butterfly children" due to their skin being so fragile it mimics a butterfly wing. The EB encompasses many clinically distinctive phenotypes: the EB simplex (EBS), the junctional EB (JEB), the dystrophic EB (DEB) and the Kindler syndrome (KS). The EBS was further separated into suprabasal and basal subgroups, based on the histopathologic site of cleavage within the epidermis. (1, 2)

As a correlate, the presence of diagnostically useful skin findings (e.g. exuberant granulation tissue, mottled pigmentation, pseudosyndactyly and other) may permit further subclassification at this level. Each patient then can be further subclassified on the basis of a mode of transmission and, if identifiable, by the specific gene involved, the latter initially determined by means of immunohistochemical techniques (IFM, using EB-pertinent monoclonal antibodies) and later by the mutation analysis. In some clinical settings, some EB investigators prefer to pursue molecular screening without first obtaining of IFM results. The EB can be inherited in the dominant or recessive form, it can also arise as a spontaneous mutation where neither parent carries EB or is physically affected by the condition. The gene mutation occurs spontaneously in the sperm or egg before conception. (1, 3)

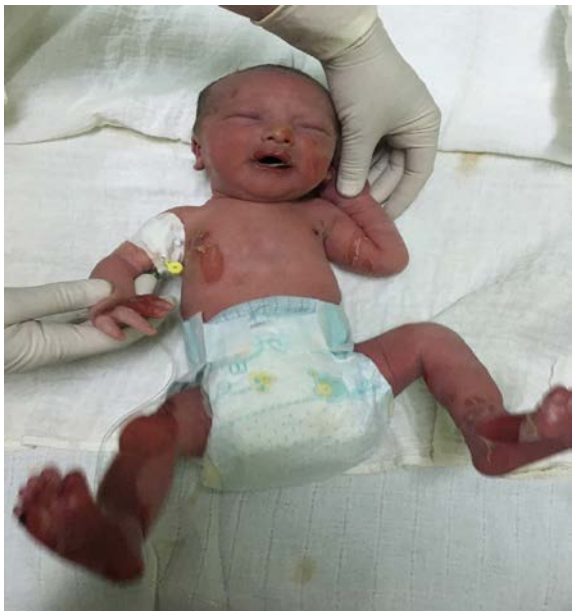
The overall prevalence of EB has been estimated to be about 1 in 100,000 in Italy, 1 in 130,000 in the United States, 1 in 20,000 in Scotland and in Croatia it is 9.6 cases per million live births. The number of the diseased in Serbia is still unknown, but according to the latest data there are about 140. The incidence and prevalence of dominant DEB were found to be 2.12 and 1.49 cases per 1 million live births and recessive DEB were found to be 3.05 and 1.35 cases per 1 million live births. (4, 5)

In our case, the clinical finding of DEB, the Aplasio Cutis Congenital (ACC) and nail dystrophy shows that it is Bart's syndrome, first described by Bruce J. Bart in 1966. Bart's syndrome is usually diagnosed based on the clinical presentation. In some cases, the analysis may require skin biopsy to determine the type of epidermolysis bullosa and genetic study to look for the exact gene mutation that may help to confirm the final diagnosis. (6)

CASE REPORT

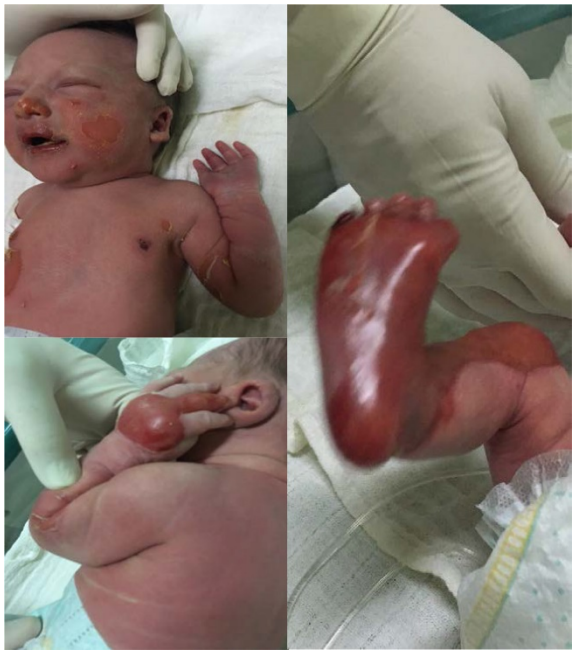
A term newborn male delivered by Caesarean section (C-section) after an uncomplicated pregnancy and spontaneous rupture of membranes approximately 32 hours prior to delivery. Apgar score was 8 at 5 minutes. The baby's weight was 2780 g and the head circumference was 33 cm. Upon initial physical examination, the patient was presented with multiple skin defects: on the anterior side of the lower third of the upper leg, knee, lower leg and whole feet, on the dorsal parts of the fist and fingers, on the head skin frontal and temporal right, in the area of the upper lip and right hemithorax. (Picture1.)

Picture 1. Appearance of the newborn after birth



These defects were dark red color, dry and slightly deeper on the right leg with visible vascularization. Also, there were rarely collapsing blisters. On the front of the right leg, including the knee, foot dorsum, thumb and right-foot sole, the complete absence of the skin, peripheral with the individual haemorrhagic blisters. The nail plate on the right foot is missing. Haemorrhagic blisters were present on some finger nails and toes of the fist and feet. (Picture 2.)

Picture 2. Congenital localized absence of skin, blistering of the skin and absence of nail plate on the right foot



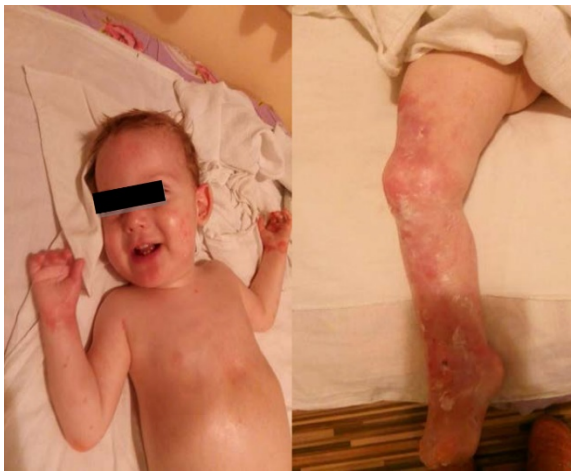
Other physical findings were normal for the age. Baby was transferred to the Neonatal Intensive Care Unit (NICU), on the first day of life.

In the NICU, the intravenous catheter for rehydratation was placed to prevent dehydration from extended evaporation from the skin and for initial dual antibiotic therapy (cefotaxime - Tolycar® and vancomycin) to prevent infection. The inflammation parameters were elevated, the C reactive protein was 23 mg/L, while procalcitonin was 4.450 ng/ml. Blood and urine results were normal for the age. Abdominal and cranial ultrasound imaging, and echocardiography revealed normal findings. Bacteriological analysis of eye swabs, nasal swabs and erosion swabs (axillary region, knees, fists, right upper arm and knee) have shown normal flora. He received phenobarbitone due to sedation and acetaminofene (Paracetamol®) as an analgesic. The skin was treated according to a Dermatologist's advice (bandage once a day, 1% chloramphenicol unguent daily on skin defects). After four days, the patient was transferred to the Clinical Center of Serbia (CCS), Pediatric department, for further treatment and examination. A Dermatologist's physical examination in the CCS has also identified a variety of skin changes and congenital aplasia of the skin on the right leg and foot and nail dystrophy.

Topical treatment for all erosion was 0,1% gentamicin unguent, and than wrapping with sterile gauze (Mepilex® Transfer gauze) and bandaging soaked with vaseline once a day and for eyes 1% chloramphenicol unguent daily. Skin zones with residual changes and without erosion were treated with emollients once a day. For erythema on the face 1% hydrocortison unguent was used twice per day and for erythema in the diaper region miconazole (Dactanol®) gel several times per day. Regarding skin care and daily bathing, oil bath (Lipikar syndet baby®) and nonadhesive re-dressing were prescribed. The substitution of vitamin D 500 IU./mL was recommended once per day. After 3 weeks, the erosion was in the final phase of epithelialization. The zone of congenital skin absence on the right lower leg was in the final phase of epithelialization. The erythema on the face was significantly bleached. (Picture 3.) The general condition was well and the mother was given detailed instructions about handling the baby and continuing with the local wound care. Further therapy was performed by 0,1% gentamicin unguent and emollients and bandage Mepilex® Transfer gauze and separation of fingers by Mepilex®.

In the fourth month of life the child was diagnosed with Dermatitis atopica, the child has the highest number of erosions on the face and ear shells with eczema and itching. After 1% hydrocortison unguent therapy for 7 days, the child had an erythema with white squamous on cheeks. Levocetirizine (Xyzal®) 0,5 mg/ml oral solution was recommended twice a day for 2.5 ml in the case of itching and eczema exacerbation.

Picture 3. After topical treatment in the final phase of epithelialization



DISCUSSION

The EB is a very rare disease, especially in the form of congenital skin aplasia. In previous studies, it has been shown that the EB manifestation is not only limited to the skin. Systemic signs might involve the nose, ear, eye, genitourinary tract and upper gastrointestinal tract. A. Michalak et al. have described in their work that gastrointestinal manifestation of the EB is most commonly reflected by esophageal stenosis due to recurrent esophageal blistering, followed by consequent scarring. (7) Also, in study of nine cases with the Congenital Pyloric Atresia (CPA), M.Kansra et al. had one patient with the CPA (type 3) and the ileal atresia associated with the EB. (8) In our case the EB is in combination with congenital skin aplasia, which is based on the author Frieden, in 6th group and it is called Bart's syndrome. The inheritance pattern of Bart's syndrome appears to be an autosomal dominant. Nevertheless, several sporadic cases have been reported. Bart's syndrome is considered as an exceedingly rare genetic disorder. (9) Our case of Bart's syndrome presented with the classic triad of congenital localized absence of skin over right lower leg, blistering of the skin, and absence of nail plate on the right foot.

When evaluating newborns with plaques and/or erosion, in addition to numerous diagnostic conditions, the EB should be taken into consideration. The differential diagnosis for blisters in a neonate is extensive and includes common acquired etiologies such as sucking blisters or other birth trauma-induced blisters, infection-related blisters such as the herpes simplex, the bullous impetigo, the staphylococcal scalded skin syndrome, the neonatal candidiasis, the neonatal varicella; maternal autoimmune bullous conditions such as the bullous pemphigoid (can also appear de novo), the pemphigoid gestationis or the pemphigus vulgaris; others such as a bullous aplasia cutis congenita, and bullous mastocytosis; and genetic disorders including the incontinentia pigmenti, the ectodermal dysplasia, the epidermolytic hyperkeratosis (bullous congenital ichtyosiform erythroderma), the pachyonychia congenita, the congenital erosive dermatosis with

reticulated supple scarring and the epidermolysis bullosa (all subtypes). (2) Analogous to peeling an onion, Jo-David Fine et al. suggested that the classification and subclassification of patients with the EB begin with their separation into 1 of 4 main EB groups, based on the level (intraepidermal [EBS]; within [JEB] or beneath [DEB] the skin basement membrane zone (BMZ); or mixed pattern [Kindler syndrome]) within which blisters develop. In EB simplex (EBS) suprabasal, the blisters form within the middle/upper epidermal layers, depending on which protein is mutated. In the EBS basal, the cleavage plain is within the basal keratinocytes. In junctional EB (JEB), the separation takes place within the lamina lucida, and in dystrophic EB (DEB), within the sublamina densa region within the uppermost dermis. In the fourth type cleavage it can occur within the basal keratinocytes, at the level of the lamina lucida or below the lamina densa and it is Kindler syndrome [KS], mixed pattern. Further, intraepidermal EBS is divided into two groups: suprabasal and basal EBS. Targeted proteins by the gene mutation in suprabasal EBS are Transglutaminase 5 (TGM5), plakophilin 1 (JUP), desmoplakin (DSP) and plakoglobin (PKP1); in basal EBS are keratins 5 or 14 (KRT5, KRT14), plectin (PLEC), exophilin 5 Slac2-b (EXPH5) and bullous pemphigoid antigen 1 (DST). Changes in JEB are in intralamina lucida and in the generalized form affected proteins are: laminin-332 (LAMA3A), collagen XVII (COL17A1), α6β4 integrin (ITGB4, TGA6), α3 integrin subunit; in localized form: collagen XVII, laminin-332, α6β4 integrin. In DEB only collagen VII (COL7A1) is affected. (1, 10) The next level of subclassification takes into account the clinical phenotypic features present in a given patient, most notably the distribution (localized vs generalized) and the relative severity of cutaneous and extracutaneous disease involvement. Ensuring that the correct treatment plan and dressing regimen are implemented with EB patients is challenging due to painful open wounds and the exceptionally fragile skin.

CONCLUSION

Epidermolysis bullosa is a rare, hereditary, non-contagious, but still incurable disease. The average lifespan of the diseased is shortened, requiring constant care and complete dependence on other people.

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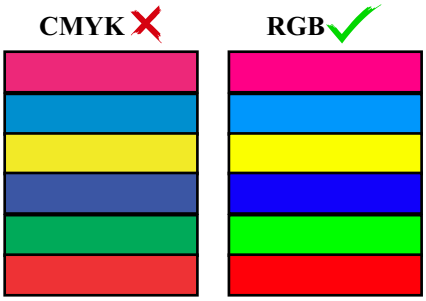

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