CASE STUDY

INHERITED EPIDERMOLYSIS BULLOSA IN NEWBORN (CASE STUDY)

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ABSTRACT

Inherited epidermolysis bullosa (IEB) is a group of genetically and clinically heterogeneous diseases characterized by the formation on the skin and mucous membranes blisters and erosion due to injury. Different forms of IEB can be accompanied by various extracutaneous complications, such as blisters and erosion on the cornea and mucous membranes, stenoses and strictures of the respiratory system, gastrointestinal tract, urinary system, muscle dystrophy, and malignant tumors. Therefore diagnosis and prescribing appropriate treatment and follow-up care is an important task for neonatologists and pediatric dermatologists. Because the manifestations of IEB are numerous, a specialized center is required for optimal care, where multidisciplinary care will be provided (neonatologists, pediatric surgeons, pediatric dermatologists, etc.). The purpose of this case report is to pay attention of specialists to a disease that is rare, to present clinical case of IEB in newborn who was admitted to the intensive care unit of newborns of Vinnitsa Regional Children's Clinical Hospital.

KEY WORDS: inherited epidermolysis bullosa, newborns

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INTRODUCTION

Inherited epidermolysis bullosa (IEB) is a group of genetically and clinically heterogeneous diseases characterized by the formation of blisters on the skin and mucous membranes and erosions due to injury. Different forms of IEB can be accompanied by various extradermal complications, namely the formation of blisters and erosions on the cornea and mucous membranes, stenosis and strictures of the respiratory system, gastrointestinal tract, urinary system, muscle dystrophy and malignant tumors. The term "epidermolysis bullosa" was introduced in 1886 by Kebner. IEB is divided into three types depending on the level of blistering: simplex, junctional and dystrophic. There is a stratification of the epidermis due to cytolysis of keratinocytes in simplex IEB. Blisters are formed on the border of the epidermis and dermis due to splitting of the light plate of the basement membrane (lamina lucida) in junctional IEB type. There is blisters formation under the dense plate of the basal membrane in dystrophic IEB. Nowadays we know more than 30 subtypes of IEB [1, 2], main of them are present in table I.

Currently, mutations have been identified in more than 10 genes encoding the structural proteins of keratinocytes and the basal membrane of the skin and mucous membranes. A common feature of these proteins is their involvement in the formation of strong bonds between the epithelium and the basement membrane. The nature of the mutations and their localization determine the severity of the clinical manifestations of IEB. Mutation information is a prerequisite for effective medical and genetic counseling, prenatal and pre-implantation DNA diagnosis.

Most variants of simplex IEB are inherited autosomal dominantly. The most common – localized – is known as the Weber-Cockayne subtype. The disease manifests itself in the neonatal period, extradermal manifestations in the form of blisters on the oral mucosa. The most difficult variant is the autosomal dominant generalized BE, the Dowling-Meara subtype.

Junctional IEB is inherited autosomal recessively. Severe generalized form, Herlitz subtype is called lethal IEB due to the high risk of premature death. The cause of death is considered to be sepsis, pneumonia, obstruction of the larynx and trachea.

Dystrophic IEB can be inherited autosomally dominantly and autosomally recessively. This form is characterized by generalized blisters, erosions, scars, contractures of the hands, feet, elbows and knees. Typical are damage to the gastrointestinal tract, urinary system, eyes, chronic anemia, developmental delay, high risk of squamous cell skin cancer.

The frequency of IEB is unknown. Mild variants are registered with a frequency of 1 in 50,000 births, heavy – 1 in 500,000. The incidence does not depend on gender. Examination of a child with suspected IEB should include a study of the pedigree. Importantly, individual cases may be due to spontaneous mutation or incomplete penetration of the autosomal dominant gene.

The main treatment is skin care. All forms of IEB are characterized by skin damage, respectively, wound healing is central to treatment. Due to the formation of blisters, constant inflammatory process, polymicrobial colonization with

infectious complications, poor nutritional status and trophic disorders, skin damage turns into chronic wounds. They cause severe pain, and changing bandages makes it worse.

Delicacy and a minimum of touches are important in care. Preventing overheating and lubricating the skin to reduce friction can limit blistering. Auxiliary is the use of a special water or air mattress. The child should not be taken under the armpits, it is taken in the arms, holding the neck and buttocks. Clothing should be made of soft material, simple cut. It is not advisable to use diapers, it is better to keep the crotch open.

Wound healing occurs in four stages: inflammation, reepithelialization, tissue formation and renewal. The ideal bandage should provide a sufficient level of moisture, not stick, be atraumatic, protect against infection, reduce pain, and have the appropriate size. Soft silicone bandages meet these requirements. Hydrogel dressings are recommended for dry wounds. Absorbent dressings are used for wet wounds. Bacterial colonization and infection inhibit wound healing. Local antiseptics should be used for a short period of time. When healing does not occur due to the above actions, use the biological equivalents of the skin – xenografts.

Severe forms of IEB are accompanied by a deep protein-energy deficiency. [3, 4] Eating disorders are caused by the following reasons: increased catabolism on the background of chronic inflammation – open wounds with loss of blood and serous fluid, increased protein breakdown, heat loss, infection, and complications from the mouth, esophagus and other gastric departments. -intestinal tract limit food intake and disrupt the absorption of nutrients. Therefore, the main objectives of therapeutic nutrition are as follows: to prevent nutrient deficiencies, reduce stress during feeding, maintain normal body fat, normalize intestinal function and immune status.

The daily energy requirement of babies with IEB is from 130 to 180 kcal / kg, and in some cases up to 225 kcal / kg. The need for protein is 2.5-4 g / kg, the liquid is 150-200 ml / kg. It is necessary to support breastfeeding, applying Vaseline on the lips and nipple reduces friction. When breastfeeding is not possible, use expressed breast milk with fortifiers. Severely ill children with IEB need a subsidy for all vitamins, especially vitamin C, which plays an important role in iron absorption and collagen synthesis.

Constant loss of blood from the wound surface leads to chronic anemia, so it requires correction with iron supplements. Zinc is a cofactor of more than 200 enzymes, so due to its antioxidant properties it plays an important role in the processes of growth, wound healing, immune protection, membrane stabilization. [5,6] Recommended liquid dosage forms in the form of zinc sulfate (30 mg in 5 ml). In all children with impaired nutritional status, it is recommended to monitor the level of selenium and carnitine, which is used as a solution at a rate of 50-100 mg / kg / day. In children with IEB, bone metabolism is impaired due to increased concentrations of cytokines on the background of chronic inflammation, as well as impaired calcium absorption due to gastrointestinal complications. Therefore, such children are offered a combination of calcium and vitamin D.

Thus, bullous epidermolysis is a severe disabling disease that adversely affects the quality and life expectancy of patients. Patients die between the ages of 3 and 30, depending on the form of the disease.

THE AIM

The purpose of this case report is to draw the attention of specialists to a disease that is rare, to share their own experience of managing patients with IEB of newborns.

CASE STUDY

Child L., born from the first normal pregnancy, first physiological delivery, Apgar score 7 and 9 points. Mother is 23 years old, father 28 years old, no inherited diseases in both families. Child's body weight is 2930 g, length is 49 cm.

The general condition of a child was severe; the child is routinely anesthetized with IV paracetamol. Unaffected areas of the skin were without impaired microcirculation. Self-breathing, RR – 48 per minute. Hemodynamic was not disturbed, HR – 128 per min, blood pressure – average 60 mm Hg. Swollen, holds through a probe 80 ml of breast milk. Diuresis 760 ml per day, bowel movements 6 times was not disturbed.

The presence of skin aplasia at birth (both lower extremities from the fingers to the lower third of the thighs, lesions of the mucous membranes of the mouth, the presence of blisters on the skin 0.5-1 cm serous-hemorrhagic content on the skin of the forehead.

Wounds on the skin of the cheeks, elbows, palms, knees, legs, feet are closed by xenoskin, single erosions are open, there are cracks on the legs in areas of exfoliation of xenoskin. New damage occurs due to friction.

Additional examination which was performed during hospitalisation:

- CBC (leukocytosis, mild anemia);
- Measuring level of proteins (normal), bilirubin (normal), ALT and AST (normal), thymol test (normal), urea and creatinine(normal);
- CRP – 14 mg/l;
- ASLO (normal),
- *electrolyte* imbalance;
- normal serum level of zinc and low amount of serum $25(OH)D_3$;
- thyroid hormones (T4, TSH, ATPO) were in normal ranges;
- General urine analyses was performed 2 times a week (normal);
- ECG / EchoCG (sinus arrhythmia, patent foramen ovale);
- ultrasound of the thyroid gland and kidneys hadn't show anomalies;
- bacterial investigation of the wounds content and sensitivity to antibacterial drugs.

Diagnosis: Inherited epidermolysis bullosa, dystrophic type.

Treatment we used included daily skin care, management of infected and non-infected wounds, management of the oral mucosa membranes and rehabilitation. It was per-

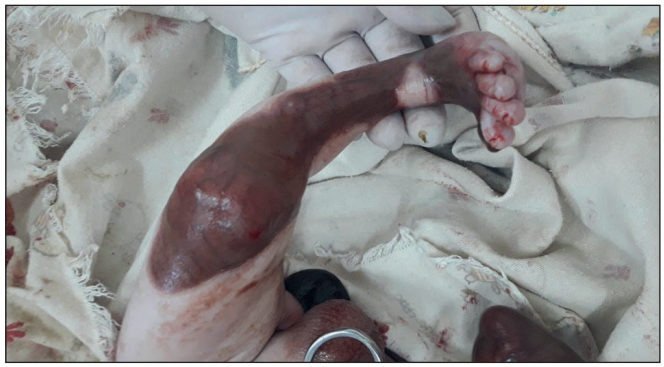

Fig. 1. Skin aplasia of the left leg

Fig. 2. Skin aplasia of the right leg

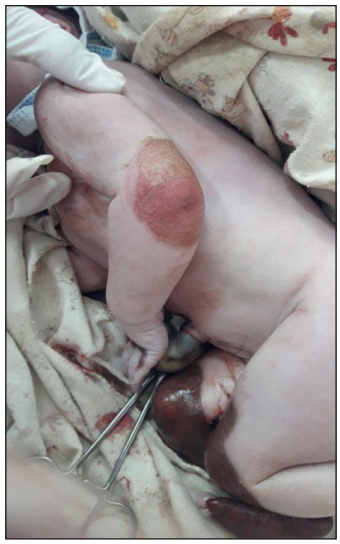

Fig. 3. Skin aplasia of the elbow

Fig. 4. Damage of the skin closed with xenoskin

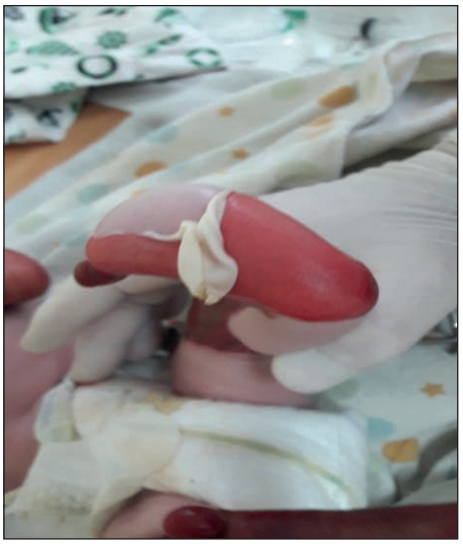

Fig. 5. Damage of the foot skin closed with xenoskin

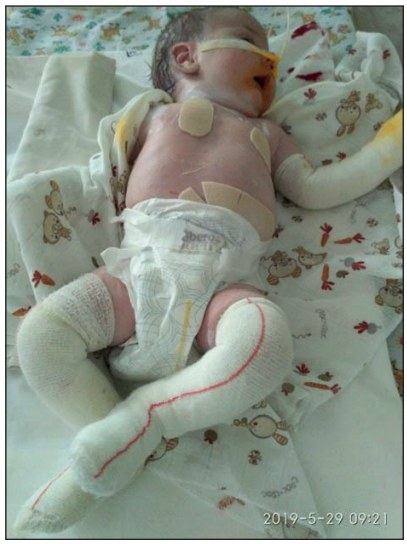

Fig. 6. Damage of the skin closed with xenoskin during treatment

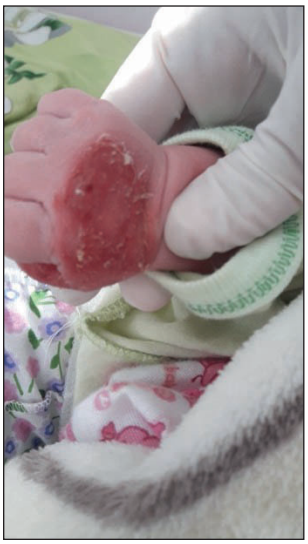

Fig. 7. Child with IBE during treatment

formed according to the "Adapted evidence-based clinical guidelines. Bullous epidermolysis"[7].

Management of skin folds (neck, ears, elbows, thighs and knees) is carried out daily 1-2 times a day with special liquids gently. Management of dry elements and those that are at the stage of epithelialization is carried out with ointment 2-5 times a day. Wounds in the perineum were treated as needed after using the toilet.

Care for blisters and wounds included bathing (0.9% salt solution: hypo (less than 90 g) or 90 g per 10 liters

Table I. Classification of the main types and subtypes of inherited epidermolysis bullosa

Main type	Subtypes	Proteins in whose genes occur mutations
Simplex IEB	Simplex Weber-Cockayne IEB	Keratin 5, 14
	Simplex Koebner IEB	Keratin 5, 14
	Simplex Dowling-Meara IEB	Keratin 5, 14
	Simplex IEB with muscle dystrophy	Plectin
Junctional IEB	Junctional Herlitz IEB	Laminin 332
	Junctional Non-Herlitz IEB	Laminin 332, Collagen 17 type
Dystrophic IEB	Dominant dystrophic IEB	Collagen 7 type
	Recessive dystrophic Hallopeau-Siemens IEB	Collagen 7 type
	Recessive dystrophic non-Hallopeau-Siemens IEB	Collagen 7 type

of water for clean wounds); in case of wound infection, octenidine dihydrochloride/chlorhexidini bigluconas/povidone-iodine solution 1:20 in the bath, combine solution (hexamidine diisothionate 100 mg, chlorhexidine bigluconate solution 20% 0.5 ml, chlorocresol 300 mg) as a detergent (requires rinsing).

Care of the infected wounds included using of creams or ointment with bandages which are listed above:

– argosulfan (silver sulfathiazole 20 mg, cetostearyl alcohol (cetyl alcohol 60%, stearyl alcohol 40%) 84.125 mg, liquid paraffin – 20 mg, white vaseline – 75.9 mg, glycerol – 53.3 mg, sodium lauryl sulfate – 10 mg, methyl parahydroxybenzoate – 0.66 mg, propyl 0.33 mg, potassium dihydrogen phosphate – 1.178 mg, sodium hydrogen phosphate – 13.052 mg, water d/i – up to 1 g.)

or

– Tyrosur gel (1 g of gel contains 1 mg of thyrotricin; cetylpyridinium chloride, propylene glycol, ethanol 96%, carbomer, trometamol, purified water)

or

– Bactroban (mupirocin 2.2 g, macrogol 400 – 58.7 g, macrogol 3350 – 39.1 g)

or

– Octenilin (100 ml of solution contain: 0.050% octenidine dihydrochloride, 9.90% propylene glycol, 2.50% hydroxyethylcellulose, 87.55% distilled water)

or

– Levomikol (chloramphenicol 7.5 mg, dioxomethyltetrahydropyrimidine (methyluracil) 40 mg, macrogol 1500 – 190.5 mg, macrogol 400 – 762 mg).

There were performed steps describing below in case of formation of "fresh" elements:

– evacuation of the vesicular element contents without removing the epidermal film;
– wound care (description below);
– applying a bandage the size of the wound or slightly larger than it (description below).

Puncture of blisters in 2 points or the lower point with a sterile Microlance G18-G19 needle or sterile scissors with liquid evacuation and preservation of a tire with the following processing:

– Creams containing zinc oxide 15.25%, benzyl benzoate 1.01%, benzyl alcohol 0.39%, benzyl cinnamate 0.15% in combination with dexpanthenol and/or miramistin;
+ Antibacterial sponge bandage with silver
+ Absorbent wipes and tampons
+ Ointment bandage (Peruvian balm, white vaseline, cetomacragol 1000, glycerol monostearate 40–50%, hydrogenated fat, medium triglycerides).
+ Fixation with lightweight elastic tubular bandage that stretches in radial and longitudinal directions

Treatment of the oral mucosa membranes included oral antiseptic for 7 days such as:

– Benzydamine hydrochloride 0.255 mg 0.15 g (with ethanol 96% – 10 ml, glycerol – 5 g, methyl parahydroxybenzoate – 0.1 g, menthol flavor (flavoring) – 0.03 g, saccharin – 0.024 g, sodium bicarbonate – 0.011 g, polysorbate 20 – 0.005 g, purified water – qs up to 100 ml)

or

– Solkoseril (deproteinized dialysate from the blood of healthy dairy calves (in terms of dry matter) 4.15 mg, methyl parahydroxybenzoate, propyl parahydroxybenzoate, sodium carmellose, propylene glycol, calcium lactate pentahydrate, water d/i)

or

– Octenidine dihydrochloride, water-based.

During hospitalization specialists of the multidisciplinary team trained parents how to provide daily care of the child's skin and make correct rehabilitation. It included information about how to

rehabilitate the body and wounds carefully, avoiding significant pressure and pulling movements; avoid "erasing" movements when handling/cleaning the body with wipes, to change them for "wetting" movements; making correct bandages.

It was recommended to provide after discharge:

– continuous care of the child's skin
– social assistance as a child with a disability
– supervision by a dermatologist and pediatrician/family doctor;
– consultation of a dentist, surgeon, ophthalmologist, psychologist, nutritionist after 6 months.

CONCLUSIONS

Inherited epidermolysis bullosa requires the patient to fight the disease throughout his life, which is associated not only with the severity of the disease, but also with the development of secondary complications, such as deformity of the musculoskeletal system or eating problems. Despite the fact that patients with IEB need special living conditions, they try to live a normal life with its ups and downs, successes and failures, desires and dreams, overcoming daily difficulties. Dissemination and clarification of information about the disease and the difficulties caused by it, in most cases, help to understand the problems of the patient, evoking respect for him and help to form the attitude to him that he really deserves.

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