

Epidermolysis Bullosa Acquisita in a Newborn – Case Report

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Abstract

Epidermolysis bullosa (EB) is a group of inherited conditions characterized by mechanical fragility of skin and epithelial-lined tissues. EB should be suspected in individuals with a history of recurrent blistering or erosions following mild trauma and in neonates presenting with blisters and erosions without other plausible etiology, especially if family history is positive for similar manifestations. Treatment options for EB are cumbersome as data are limited and rely largely on the case series published in the literature. We report a case of newborn presenting with Epidermolysis Bullosa Acquisita, a rare subtype of EB confronted in childhood.

Keywords: Epidermolysis Bullosa; Epidermolysis Bullosa Acquisita; Case Report; Genetic Therapy

Introduction

Epidermolysis bullosa (EB) is a rare inherited condition characterized by mechanical fragility of skin and epithelial tissue associated with blisters and erosions [1]. Autoimmunity to type VII collagen within anchoring fibril structures located at the dermal epidermal junction is the underlying pathology of this disease. There are four main types and more than thirty subtypes of EB. Genetic heterogeneity, epigenetic factors and environmental factors contribute to variable phenotypes of EB [2,3]. Genetic mutations of around 20 different structural skin proteins leading to EB are identified to date [4]. The same mutations that cause skin blistering is also the reason for many of the extracutaneous complications of EB occurring within the eyes, GI and GU tracts, and upper respiratory tract [5,6].

According to a study published in 2016 based on 16 years of data collection in the United States, the overall incidence and prevalence of inherited EB were 19.57 per 1 million live births and 11.07 per million populations [7]. The only known risk factor for EB is family history [8]. Unlike the genetic forms of epidermolysis bullosa, epidermolysis bullosa acquisita (EBA) is considered as acquired. Few reports suggest genetic component may be involved, but the condition is not thought to be due to any specific gene [9]. Although the incidence of EBA is still obscure, it is estimated to be rare. EBA prevalence in Germany is determined to be 2.8 cases per million [10].

The diagnosis is challenging as it shares common features with other blistering disorders hence differential diagnosis is important. Histology and direct immunofluorescence (DIF) of skin biopsies, salt-split skin DIF, indirect immunofluorescence (IIF) of patient's serum, salt-split skin IIF, immunoblotting of patient serum against type VII collagen, detection of anti-type VII collagen autoantibodies by ELISA and/or immune-electron microscopy of a skin biopsy are the various diagnostic methods. There is no specific treatment for this condition and hence largely supportive. Modern treatment depends on non-specific immunosuppression. Novel treatment options are urgently needed. As exacerbations and remissions are expected in EBA, the goal of therapy is to obtain control of the disease followed by complete remission. Experts disclose the prognosis of EBA depends on its severity at the time of diagnosis and the treatment offered accordingly. Generally, these findings highlight the need for an early diagnosis, multidisciplinary care by experienced practitioners and prompt implementation of appropriate treatment to improve the prognosis of EBA.

EBA in neonates without a positive family history is few and far between. Newborns suspicious of EB should be given ultimate care. We report a case of a newborn diagnosed with Epidermolysis Bullosa Acquisita (EBA) who had no family history of bullous disorder.

Case Report

A male term baby was born as a third child to a nonconsanguineous couple by normal vaginal delivery with birth weight 3.04 kg, and Apgar score 9/10 at one minute. Antenatal period was uneventful. He had no family history of any blistering skin diseases. Mother was 26 years old without any significant medical problems. Baby was noticed to have large skin erosions at different sites of the body such as knee, elbows, ankles, feet, base of umbilicus and penis. No lesions were seen in oral cavity and eyes at birth. Nails were dystrophic. No lesion was seen in scalp, and hair was normal. Baby was hemodynamically stable; his systemic examination was normal. He was admitted in NICU and septic work up was done. He was given with strict wound care, intravenous fluids, intravenous antibiotics and other supportive care. Paracetamol was administered for pain control. Septic screen including blood culture, skin swab culture was negative.

During hospital stay the baby developed multiple bullous lesion of variable sizes at different parts of the body. He had few oral lesions too. Nikolsky sign was positive. Multidisciplinary consultations were sought. Skin biopsy showed large subepidermal bullae with focal subepidermal clefts. Dermis showed no significant increase in inflammation except for a mild increase in perivascular lymphocytes. Direct immunofluorescence showed IgG/IgM/C3-linear deposits +++ along the basement membrane zone of blister and epidermis with a dermal pattern in salt split skin. IgA was negative. Morphology and DIF pattern were consistent with Epidermolysis Bullosa Acquisita (EBA), a classic variant. The baby was discharged after mother was given counselling and training about baby care, breast feeding, wound care and vaccination. He is under follow up (Figures 1 & 2).



Figure 1: Skin Erosions Soon After Birth



Figure 2: Blister and Skin Erosion on Right Upper Limb

Discussion

EB is a rare disease among children [11-15]. It is an enduring disease characterized by fragile cum blistering skin. Severity of this disease ranges from mild to life threatening forms. Besides many subtypes there are four major categories of EB; Epidermolysis bullosa simplex, Junctional epidermolysis bullosa, Dystrophic epidermolysis bullosa and Kindler syndrome [16,17]. Depending on the type, EB may be inherited either as an autosomal dominant or autosomal recessive pattern. Blisters in this disease can be seen anywhere including skin, oral cavity, eyes, respiratory, gastrointestinal and genitourinary tract. The pathology lies in genetically mediated defects in epithelial adhesion proteins resulting in fragility and blistering of skin and mucous membrane.

Epidermolysis bullosa acquisita (EBA), a classic variant of EB, is an orphan autoimmune disease. It is considered as an acquired sporadic disease. EBA can be clinically classified into classical and non-classical depending on the type of bullous. Nevertheless, patients present with cutaneous mucous fragility regardless of the clinical form. Presentation of the skin signs varies according to the EB subtype. Crohn's disease, systemic lupus erythematosus, amyloidosis, and multiple myeloma are some of the common diseases seen with it. EB at birth or during early infancy is diagnosed by the presence of mechanical fragility of skin with recurrent blisters and erosions and poorly healing wounds, usually noticed when children starting to crawl and walk. There is no sex or ethnic prediction for EB. The major complications are infection, septicemia, poor wound healing, dehydration, nutritional deficiency, and growth failure. The severity can be assessed by Brimingham EB severity score, comprising eleven items including area of damaged skin, involvement of nails, mouth, eyes, larynx and esophagus, scarring of hands, skin cancer, chronic wounds alopecia and nutritional compromises. Most children who survive the first 12 to 24 months of life will live into at least adulthood if aggressive medical care is provided [18].

Meticulous wound care has greatly reduced the risk of death from sepsis. A case report published in Clinical Neonatology in 2014 has described the mortality of baby due to septicemia [19]. A retrospective study encounters frequent and severe mucosal involvement in children [12]. It is proposed antibody against type VII collagen, one of the major components of anchoring fibrils in the basement membrane zones of skin and mucosa, is the pathology behind epidermolysis bullosa acquisita. Most severe subtypes own risk of premature death including death from metastatic squamous cell carcinoma, and complications like renal failure, upper airway occlusion, or sepsis [8]. Claudia et.al reports the incidence of diabetes mellitus along with EB in 2018 [20]. Secondary abnormalities contribute to abnormal wound healing [21].

There is no cure or specific treatment for epidermolysis bullosa. Treatment is largely supportive and individualized. The early management of affected neonates should be undertaken in neonatal unit. Management includes wound care, prevention of infection and dehydration, treatment of infection, nutritional support and, indeed prevention and treatment of complications. Extra cutaneous manifestations must be treated accordingly. Do not keep neonates in incubator as heat and humidity can exacerbate blistering. It is better to use a ligature to secure umbilical cord. They should be placed on a thick foam pad and the pad should be used for transporting them. Of course, pain control is an important aspect of management. Open wounds are to be covered with non-adherent dressing such as petroleum impregnated gauze, silicon dressings, foam dressings that absorb exudates and non-adherent silicon-based tape. Breast feeding is recommended [22].

Patients with EB also require regular monitoring for complications and sequelae. Genetic counselling should be advised. Prenatal counselling as well as prenatal diagnosis is important for future pregnancies. Gene therapy, protein replacements therapies, stem cell transplantation, cell therapies are under research for better management and outcome of EB [23-26]. A case report had elucidated the success story of an infant with EB treated with tissue engineered skin in 1999 [27]. In short, epidermolysis bullosa acquisita in new-born is a rare condition. It usually occurs in adults; children are rarely affected. This chronic, auto immune bullous lesion occurs mostly by IgG, sometimes by IgA antibodies, against the non-collagenous terminus of the alpha chain of type VII collagen. These antibodies compromise the strength of the basement membrane zone of skin resulting in blistering and erosions. Newborns are usually affected by the vertical transfer of maternal auto antibodies. It has a genetic susceptibility. However, in our case, the mother was healthy without any history of bullous disorder.

As we mentioned earlier, both phenotypes of EB, inflammatory and non-inflammatory types, can be diagnosed by skin biopsy, direct and indirect immunofluorescence studies, ELISA and immunoblot analysis. Skin biopsy and direct immunofluorescence were our diagnostic approaches. ELISA test and genetic tests were not done due to financial constraints and refusal by parents. The treatment of this condition includes corticosteroids, anti-inflammatory agents along with supportive treatment. Malnutrition causes refractory anemia, hypoalbuminemia, failure to thrive, and delayed puberty with secondary hypogonadism. Chronic loss of blood, proteins as well as nutrients from the lesioned skin and intestinal tract results in anemia cum growth retardation. Our patient was given with strict wound care, intravenous fluids, intravenous antibiotics and other supportive care. The baby was also well breastfed. As circulating autoantibodies are supposed to decline over time, newborn symptoms are expected to be self-limited.

Conclusion

Epidermolysis bullosa is a rare inherited blistering disease which can have a devastating impact on patients and their families. Epidermolysis bullosa acquisita, rare sub type of EB, occurs in newborn usually by the vertical transfer of maternal autoantibodies. Properly diagnosing EB is often a challenge. EB at birth or during early infancy is identified by the presence of mechanical fragility of the skin, recurrent blisters and erosions, and poorly healing wounds. Skin biopsy, immunofluorescence studies, and ELISA help to diagnose EB. Genetic diagnostics is recommended as it is important for predicting prognosis, management planning, genetic counseling, and prenatal diagnosis. The only preventive action for couples known to be silent carriers of this disease is prenatal or preimplantation diagnosis. Unfortunately, there are no tests available today to screen an asymptomatic population for EB carrier states.

Treatments of EB, especially newborns, present a unique challenge because of its rareness, and lack of randomized controlled trails. Management requires a multidisciplinary approach not only to treat the cutaneous and extra cutaneous manifestations, but also to promote adequate growth and prevent complications. Nutritional support is essential in severe forms of EB. Epidermolysis bullosa acquisita may be self-limited due to declining of maternal autoantibodies, but regular follow up is recommended.

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