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Diagnostics and Treatment of Congenital Epidermolysis Bullosa

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ABSTRACT
Clinical and genetic analysis of 274 patients with various forms of congenital epidermolysis bullosa was carried out. Certain associations of genes with the predominant clinical course of genodermatosis in the Uzbek population have been established.
KEY WORDS:congenital epidermolysis bullosa, clinical forms, genetics, prognosis.

INTRODUCTION

Congenital epidermolysis bullosa (CBE) belongs to the group of hereditary skin diseases and is characterized by clinical polymorphism, and the main manifestations of dermatosis are blisters formed at the sites of skin trauma and long-term non-healing erosion [1,2]. The term "epidermolysis bullosa" was proposed as early as 1886 by G. Kebner [3]. It should be noted that many countries have compiled National registries of epidermolysis bullosa patients, which made it possible to study not only the statistics of the disease, but also to systematically monitor the condition of patients and predict the further course of dermatosis [7].

Purpose of the study. To study the clinical polymorphism of EB and to assess the significance of genetic studies in the formulation of an appropriate diagnosis.

MATERIALS AND METHODS

We used the materials of the National Register of CBE Patients, which numbers 287 patients of the Uzbek population. Genetic studies were carried out by the method of multiplex molecular genetic diagnostics using the target regions of 24 genes by the method of mass parallel sequencing with further validation of the identified genome variants by the method of bidirectional sequencing according to Sanger.

RESULTS

According to the National Register, the following main forms of EB were identified: simple - in 192 (66.9%) patients, borderline - in 12 (4.2%), dystrophic - in 82 (28.6%) and Kindler's syndrome - in 1 (0.3%) of the patient. With simple epidermolysis bullosa, there were blisters and erosion, located mainly on the skin of the hands and feet, subsequently superficial atrophy of the skin developed in these places. In some cases, in patients with a simple form of CBE, callus-like formations were detected on the skin of the palms and soles, which were regarded as palmar-plantar keratoderma, and of a confluent nature. These manifestations were mainly detected in late childhood or early adolescence. With the variant of common simple CBE, blistering can occur on any part of the skin. In the case of borderline CBE, a pathognomic clinical sign is the proliferation of granulation tissue in the form of moist and red plaques prone to bleeding. The favorite localization of these formations is the skin of the face, around the natural openings, armpits, proximal nail folds and the lumbosacral region.

From secondary morphological elements in various forms of CBE, atrophies, scarring, impaired skin pigmentation and fusion of fingers (pseudosyndactyly) are distinguished. Atrophies

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are characteristic of borderline and dystrophic forms of CBE, as well as scarring, and the scars are preceded by skin atrophy. In the case of dystrophic CBE, especially in generalized variants, hypertrophic scars were detected. In CBE, not only fusion of the fingers and toes (pseudosyndactyly) was observed, but also of large skin folds, for example, in the armpits, which we observed in the borderline form of the Herlitz subtype and the recessive dystrophic epidermolysis bullosa Allopo-Siemens subtype.

With CBE, extracutaneous complications are quite often observed, which are mainly found in its dystrophic form and the most noticeable complication is pseudosyndactyly, the final stage of which is often referred to as a "mitten" deformity. Most often in our sample of patients, this complication occurred in the autosomal recessive form of EB, the cause of which is the constant formation of blisters on the hands and feet. Beginning as a partial fusion of one or more interdigital spaces, in severe forms of dermatosis, a complete fusion of all fingers occurs, followed by the conclusion of the limb in a kind of keratinized "cocoon-like shell" [9]. Progressive deformity of the limbs significantly alters their function, atrophy of the muscles of the fingers occurs, and the skeletal system undergoes partial resorption [17]. It should be noted that the described complications were rare in autosomal dominant dystrophic, borderline and generalized simple forms of CBE.

Almost all patients had itching or soreness in the lesions, leading to discomfort and a decrease in the quality of life [12,13,15,16]. With CBE, acute pain may appear, which is associated not only with the presence of blisters or erosions, but also with extracutaneous manifestations of genodermatosis, such as dental caries, esophageal stenosis, etc., then already with a dystrophic form, these manifestations were recorded in 100% of patients. Along with painful sensations, CBE patients are worried about itching of the skin in varying degrees of severity, which is considered as one of the physiological defense mechanisms, helping to protect the skin from harmful external factors [13]. The presence of itching of the skin was recorded in 210 of 287 (73.2%) patients, which was associated with a constant healing process, dry skin and minor inflammation in the lesions [14]. It should be emphasized that the presence of itching leads to the appearance of secondary morphological elements (erosion, crusting, etc.), accompanied by the release of inflammatory mediators, which, in turn, increase the itching of the skin. In this regard, even the pruriginous subtype of dystrophic CBE was identified [19].

With simple CBE, the largest number of genes was detected (TGM5, PKP1, DSP, JUP, CHST8, CDSN, KRT5 / KRT14, DST, EXPH5, ITGA5, ITGB4, PLEC), slightly fewer genes were found in the borderline form (LAMA3 / LAMB3 / LAMC2, ITGA6 / ITGB4, ITGA3, COL17A1, CD151), with dystrophic form - COLK7A1, with Kindler's syndrome - FERMT1.

DISCUSSION

CBE is a group of diseases, the common feature of which is the formation of blisters and increased vulnerability of the skin, its sensitivity to any mechanical stress [4,5,6]. It should be noted that genotypic and phenotypic factors cause the emergence of various forms and subtypes of congenital epidermolysis bullosa [6,7]. Depending on the place of blistering (in the epidermis, in the light lamina of the basement membrane or in the upper part of the papillary layer of the dermis, immediately below the dermoepidermal junction), simple, borderline and dystrophic forms of epidermolysis bullosa are distinguished [6]. Most subtypes of simple CBE are inherited in an autosomal dominant manner. The most common of these is the localized subtype (Weber-Cockayne), the manifestations of which are located on the skin of the palms and soles. A simple form of CBE can also manifest itself in the form of generalized forms (subtypes of Kebner and

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Dowling-Meara). The first signs of the disease are observed already at birth, but the skin of the palms and soles is not affected. With the Dowling-Meara subtype, rashes often have a herpetiform nature, palmar-plantar hyperkeratosis, nail dystrophy, atrophic scars, milia and mucosal lesions develop. In our sample of patients, there was one case of simple CBE, accompanied by muscular dystrophy, which developed in a patient at the age of 12. This form of the disease is associated with a mutation that leads to the formation of a premature termination codon in the PLEC1 gene, which encodes plectin (a structural protein of hemidesmosomes and the Z line in muscle cells. Borderline CBE is subdivided into two main subtypes, which are transmitted in an autosomal recessive manner. The form of CBE is called the Herlitz subtype, which is often fatal. The second form is benign and is called the non-Herlitz subtype.Dystrophic CBE is caused by mutations in the COL7A gene, which encodes type VII collagen. It should be noted that dystrophic CBE is inherited in two ways: autosomal dominant and autosomal recessive, and in the latter, the subtype of Allopo-Siemens (severe) and non-Allopo-Siemens (light) is distinguished [8]. on the fingers and toes, as well as the phenomenon of nihodystrophy (absence of nails). It is with this form of CBE that extracutaneous complications were most often recorded, mainly in the form of atresia of the esophagus and rectum, anemia and growth retardation [9,10]. Among 287 CBE patients, one case (0.35%) of squamous cell skin cancer (histologically confirmed) was registered in a 34-year-old patient in the area of the right ankle who underwent surgery. One of the reasons for the development of squamous cell skin cancer in a patient with CBE was irrational external therapy [20]. With epidermolysis bullosa, there are practically no medical methods of therapy [18]. In this regard, with this genodermatosis, it is important to assess their nutritional status, which is directly related to the severity of the clinical manifestations of the disease [21,22].

CONCLUSION

The clinical picture of EB is characterized by pronounced polymorphism, due to the presence of cutaneous and extracutaneous manifestations of genodermatosis. Some ethnic characteristics of the population are noted that can influence the development of CBE, and, therefore, it becomes possible to carry out preventive measures. Currently, there are no cardinal methods of treating patients with EB, and therefore much attention is paid to methods of external therapy using innovative technologies of dressings, which are atraumatic and contribute to the rapid epithelization of erosive foci of the disease [11].

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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