JCEI /
Journal of Clinical and Experimental Investigations

2012; 3 (3): 412-414
doi: 10.5799/ahinjs.01.2012.03.0191

CASE REPORT

# Epidermolysis bullosa dystrophica inversa: A case report

## *Epidermolizis bülloza distrofika inversa: Olgu sunumu*

**Enver Turan[1], Mehmet Salih Gürel[2], Aslı Turgut Erdemir[2], Burcu Işık[3], Nurdan Yurt[4]**

**ABSTRACT**

Epidermolysis bullosa (EB) is a heterogeneous group of genetically determined, mechanobullous disorders characterized by blister formation in response to mechanical trauma. Three major subgroups, simplex, junctional, and dystrophic EB, contain more than 20 genetically and clinically distinct subtypes. Epidermolysis bullosa dystrophica inversa (DEB-I), which is a rarely seen form of epidermolysis bullosa, shows autosomal recessive inheritance and it is characterized by bulla formation and erosions on flexural areas, frequently affecting the oral and esophageal mucosa. Blistering rash occurs in the newborn period, which in early childhood heals with atrophic scars. DEB-I is rarely seen in adults period, with only a few case reports in the literature. In the present case, we described a patient diagnosed with epidermolysis bullosa dystrophica inversa due to presence of typical clinical features and histopathological and immunofluorescence findings. *J Clin Exp Invest 2012; 3 (3): 412-414*

**Key words:** Blistering disorders, mechanobullous, epidermolysis bullosa

**ÖZET**

Epidermolizis bülloza (EB) mekanik travma sonrası bül gelişimi ile karakterize mekanobüllöz heterojen bir hastalık grubudur. 20'nin üzerinde alt grup barındıran simpleks, jonksiyonel ve distrofik tip olmak üzere üç büyük alt gruba ayrılmaktadır. Epidermolizis bülloza distrofika inversa, epidermolizis büllozanın otozomal resesif geçişli fleksural alanlar, oral ve özofajiyal mukozada bül ve erozyonlarla karakterize nadir görülen bir tipidir. Bül ve erozyonlar sıklıkla yenidoğan döneminde görülür ve erken çocukluk döneminde atrofik skar bırakarak iyileşme gösterir. DEB-I erişkin dönemde nadiren görülür ve literatürde az sayıda olgu bildirimi mevcuttur. Bu makalede tipik klinik ve histopatolojik özellikleriyle epidermolizis bülloza distrofika inversa tanısı konmuş bir erişkin olgu sunulmaktadır.

**Anahtar kelimeler:** Büllü hastalıklar, mekanobüllöz, epidermolizis bülloza

## INTRODUCTION

Epidermolysis bullosa (EB) describes a group of genetic diseases with impaired dermo-epidermal integrity and blistering and erosions of skin and mucous membranes after minimal trauma.[1,2] Dystrophic EB represents a subgroup with dermolytic blistering and scarring. The recessive group contains four clinical subtypes: generalized mutilating, generalized nonmutilating, inversa, and localized. The inverse form of recessive dystrophic epidermolysis bullosa is a rare genodermatosis characterized by autosomal recessive inheritance that causes blistering and erosions involving primarily the flexural areas of the body occurring in early infancy.[3] The typical clinical features are severe blistering and scarring in the inverse regions (i.e., axillary, submammary groove, and inguinal folds), neck, and gluteal region. Ultrastructural analysis revealed dermolytic blistering and absent or rudimentary anchoring fibrils. Immunoreactivity for type VII collagen, however, is preserved.[4] In this report we describe a patient whose clinical and histological features were consistent with epidermolysis bullosa dystrophica inversa.

## CASE REPORT

A 43-years old female patient was admitted to our out-patient clinic with the complaint of symmetrical erosive lesions on the armpits, groin and inframammary grooves. Had a history of spontaneous

*[1] Department of Dermatology, Harran University, Faculty of Medicine Şanlıurfa, Turkey*
*[2] Department of Dermatology, Istanbul Education and Research Hospital, İstanbul, Turkey*
*[3] Ministry of Health, Ordu University, Education And Research Hospital, Dermatology Clinic, Ordu, Turkey*
*[4] Gümüşhane Government Hospital, Dermatology clinic, Gümüşhane, Turkey*

**Correspondence:** Enver Turan,
Harran University, Faculty of Medicine, Department of Dermatology Şanlıurfa, Turkey Email: enverturan@gmail.com

Received: 25.03.2012, Accepted: 13.07.2012

or trauma induced blistering and erosions on the scalp, mouth, flexural areas and nail folds shortly after birth. When she was 27 years old, lesions appeared mainly on the mucosal sites and flexural areas. Dermatological examination revealed bullous and eroded lesions with residues of bulla on both axillary sites and inframammary grooves (Figures1, 2, 3), postlesional hypo- and hyperpigmented atrophic areas on the abdominal, sacral and pubic regions, dystrophic changes on all nails of hands and feet and cicatricial alopecia sites on parietal and temporal regions of the haired skin.

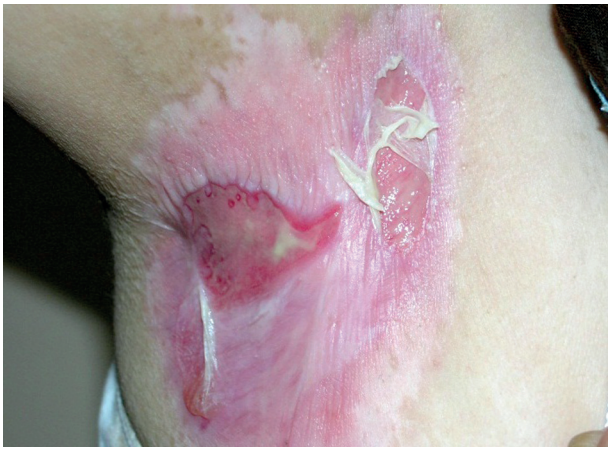

**Figure 1.** Blisters and erosions observed on the axilla

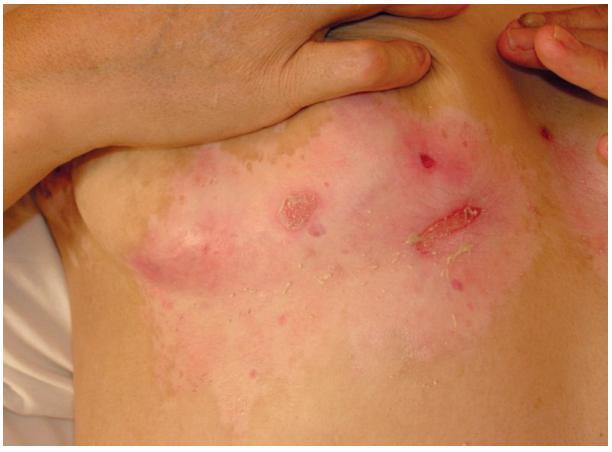

**Figure 2.** Large atrophic plaque and erosions inframammary groove

Upon examination of the oral mucosa, eroded lesions on oral mucosa and tongue were observed (Fig. 4). Her brother also had postlesional hypo- and hyperpigmented atrophic areas on similar locations due to healed bullous lesions. No pathologic findings were identified in laboratory tests. Histopathologic examinations identified formation of subepidermal blister, findings of regeneration in the keratinocytes of the blister roof, rare dyskeratotic cells, exudate of blister lumen containing fibrin, polymorphonuclear neutrophils and nuclear fragmentation, increase in fibroblastic activity on upper dermis and eosinophils, neutrophils and mononuclear cell infiltration spreading to blood vessels. Direct immunofluorescence assay revealed no accumulation of IgG, IgA, IgM, C3 or fibrinogen in epidermis or dermis. The patient was diagnosed with epidermolysis bullosa dystrophica inversa due to her clinic and histopathologic findings, absence of specific immune accumulation, and family history that her brother also developing similar lesions on similar locations.

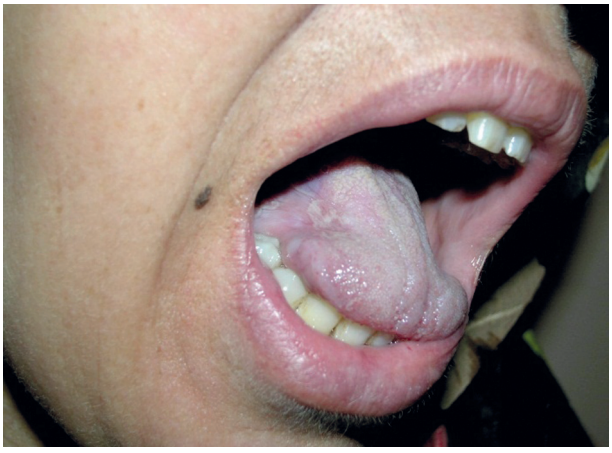

**Figure 3.** Erosion on the tongue

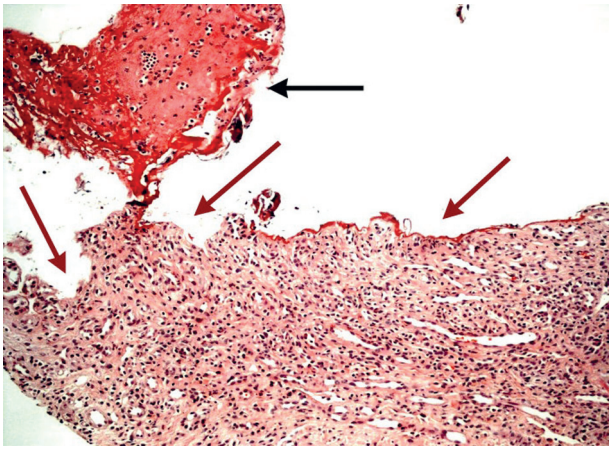

**Figure 4.** Subepidermal blister formation (red arrows), blister lumen contains fibrin, neutrophils, and exudate consisting nuclear fragments of polymorphonuclear neutrophils (black arrows) [Hematoxylin and eosin stain (H&E); original magnification X100].

## DISCUSSION

Dystrophic epidermolysis bullosa is a clinically heterogeneous skin disease in the forms of dominant and recessive inheritance.[1-4] Dystrophic epidermolysis bullosa -1 which was identified by Gedde

and Dahl for the first time in 1971.[2] DEB-I is a rarely observed form of epidermolysis bullosa starting immediately after birth or at early infancy characterized by blister formation and erosions in flexural areas, frequently affecting the mucous membranes as well. Identification of this subtype has special importance because it is different from other epidermolysis bullosa types in terms of prognosis.[3,4] Lesions heal frequently leaving behind skin atrophy or cicatrices. Oral, esophageal and genital mucosa involvement, dental caries and nail dystrophy can be seen.[5,6] Our patient had hypo- and hyperpigmented atrophic scars in the abdominal, sacral and glueteal regions. Oral mucosa was affected but no involvement was observed in esophageal, conjunctival or genital mucosa.

Despite the fact that there have been only a few number of reported cases in the literature, many of these developed generalized bullae in the newborn and early childhood periods, remained limited to flexural areas and mucosal involvement was seen in the adulthood. Involvement of the hands and feet are distinctive in the infancy while it becomes rare in the adulthood. It is very difficult to distinguish it from other epidermolysis bullosa types in the early childhood. However, in the adulthood it can be differentiated from other subtypes by typical localization sites as mucous membranes. Severe mucosal involvement worsens prognosis and requires special care and nutrition. Severe oral lesions may cause microstomia and prevent nutrition. In the case of an esophageal involvement, mechanical dilation is frequently required at regular intervals.[3,7] The dystrophic nature of the disease and the separation of the lamina densa were first identified by Hashimato and colleagues in 1976.[3,4]

There are mutations in the COL7A1 gene, encoding type-VII collagen which is the major component of anchoring fibrils in this recessive type of epidermolysis bullosa.[4,5,8] In a study carried out on two cases, the authors manifested that there was an abnormal structuring in type-VII collagen in DEB-I and this abnormal structure prevented the organizational structuring of anchoring fibrils.[5] Literature reports another case that immunofluorescence assay was made using associated anchoring fibrils protein GDA-J/F3 antibodies of the basement membrane zone, and interestingly the result was negative. This result does not exactly account for whether there is any mutation or not in the GDA-J/F3 gene locus.[7]

In our case the disease started in the infancy with generalized lesions, but was limited to flexural areas and oral mucosa. There were post-inflammatory hypo- and hyperpigmentation and atrophic cicatrices in the both axillary and inguinal regions. Neither any esophegeal or genetial mucosa involvement nor any dental caries or nail distrophy was identified.

The patient was diagnosed with epidermolysis bullosa dystrophica inversa due to presence of lesions that started from the early age and healed by leaving cicatrices behind, history of similar lesions in her brother, histopathologic findings of subepidermal blister formation and immunofluorescence assay revealing absence of specific immune accumulation. There is no effective treatment for epidermolysis bullosa, only palliative care is given. In case of severe oral lesions, nutritional support must be provided. Autologous skin grafting can be performed on non-healing skin lesions.[8-10]

## REFERENCES

1. Leverkus M, Ambach A, Hoefeld-Fegeler M, et al. Late-onset inversa recessive dystrophic epidermolysis bullosa caused by glycine substitutions in collagen type VII. Br J Dermatol 2011 164(5):1104-6.
2. van den Akker PC, Mellerio JE, Martinez AE, et al: The inversa type of recessive dystrophic epidermolysis bullosa is caused by specific arginine and glycine substitutions in type VII collagen. J Med Genet 2011 48(3):160-7.
3. Hashimoto I, Anton-Lamprecht I, Hofbauer M: [Epidermolysis bullosa dystrophica inversa: report on 2 sisters]. Hautarzt 1976, 27(11):532-537.
4. Hashimoto I, Schnyder UW, Anton-Lamprecht I, Gedde-Dahl T, Jr., Ward S: Ultrastructural studies in epidermolysis bullosa hereditaria. III. Recessive dystrophic types with dermolytic blistering (Hallopeau-Siemens types and inverse type). Arch Dermatol Res 1976, 256(2):137-50.
5. Kahofer P, Bruckner-Tuderman L, Metze D, Lemmink H, Scheffer H, Smolle J. Dystrophic epidermolysis bullosa inversa with COL7A1 mutations and absence of GDA-J/F3 protein. Pediatr Dermatol 2003, 20(3):243-8.
6. Gardella R, Castiglia D, Posteraro P, et al. Genotype-phenotype correlation in italian patients with dystrophic epidermolysis bullosa. J Invest Dermatol 2002, 119(6):1456-62.
7. Lin AN, Smith LT, Fine JD. Dystrophic epidermolysis bullosa inversa: report of two cases with further correlation between electron microscopic and immunofluorescence studies. J Am Acad Dermatol 1995;33(2 Pt 2):361-5.
8. Breit R: [Epidermolysis bullosa dystrophica inversa, a review and case report]. Hautarzt 1979;30(9):471-7.
9. Wright JT, Fine JD, Johnson LB, Steinmetz TT. Oral involvement of recessive dystrophic epidermolysis bullosa inversa. Am J Med Genet 1993;47(8):1184-8.
10. Gache Y, Pin D, Gagnoux-Palacios L, Carozzo C, Meneguzzi G. Correction of dog dystrophic epidermolysis bullosa by transplantation of genetically modified epidermal autografts. J Invest Dermatol 2011;12(3):312-5.