

## Case Report

# Does there exist a steroid responsive inflammatory variant of dystrophic epidermolysis bullosa? – a case report

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**Abstract** A six-year-old girl presented with extensive blisters, erosions and scarring over trauma prone areas which started soon after birth. The lesions were refractory to conservative treatment with antibiotics and dressings. Peripheral blood count showed eosinophilia and raised ESR. Histopathology showed subepidermal bulla with prominent eosinophilic and lymphocytic infiltrate in dermis. Direct and indirect immunofluorescence tests were negative proving our clinical diagnosis of dystrophic epidermolysis bullosa. We gave a trial of oral corticosteroid and patient's condition improved dramatically. She once again started developing new lesions once we tapered the drug. We propose an existence of steroid responsive inflammatory variant of epidermolysis bullosa; an observation which is supported by many earlier published evidences.

### **Key words**

Dystrophic epidermolysis bullosa, steroid, eosinophil.

## **Introduction**

Three major inherited forms of epidermolysis bullosa (EB) are EB simplex (EBS), junctional EB (JEB) and dystrophic EB (DEB); all are characterized by varying degrees of skin fragility and blistering. Despite major advances in understanding of the genetic pathogenesis for these disorders, the scientific basis and evaluation of treatment interventions remain unclear. Many interventions were described for these diseases including wound care, infection control, antibiotics, vitamin E, systemic steroids, phenytoin, chloroquine, cyproheptadine and retinoids; but it remains unclear which one is actually beneficial. Some treatments are directed at wound care, whereas others purport to reduce

skin fragility through systemic effects. Langan *et al.* reviewed randomized controlled trials of treatments for inherited forms of EB and concluded that there is no reliable evidence for interventions in inherited EB.<sup>1</sup> In future, gene therapy may become the treatment of choice.<sup>2</sup>

Role of corticosteroid has been controversial. Though there are many isolated case reports claiming varying degree of success by treatment with steroids, modern understanding of pathogenesis of EB casts a huge doubt in any possible role of steroids. Here, we present a case of DEB which showed dramatic response to oral corticosteroids.

## **Case report**

A 6-year-old female patient, born of second degree consanguineous marriage, presented to our hospital with a few tense blisters and extensive erosions and crusting mostly in trauma

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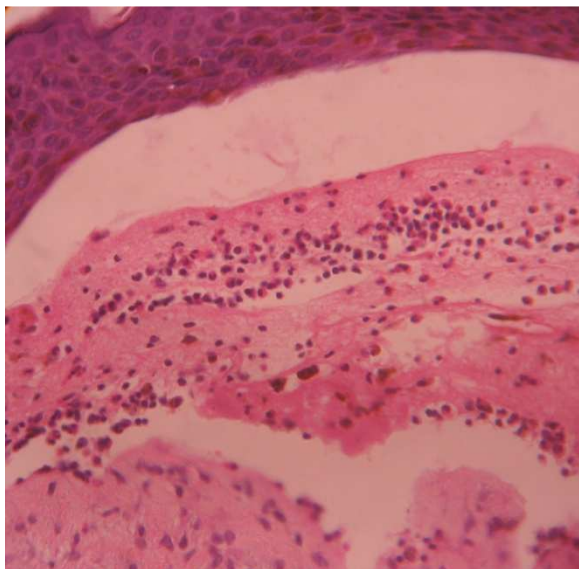
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**Figure 1** Multiple erosions and crusting on front of trunk.



**Figure 2** Multiple erosions and hemorrhagic crusting on back.



**Figure 3** Subepidermal blister and prominent dermal infiltration of eosinophils and lymphocytes.

prone areas of back, elbow, forearm, thigh and legs (**Figures 1 and 2**). The lesions started appearing soon after birth usually arising after a minor trauma. Blisters ruptured spontaneously forming erosions which healed slowly with extensive scarring and pigmentary changes. Nail plates of all fingers showed diffuse thickening and dystrophic changes. Patient had no mucosal involvement. None of her family members had similar complaints. All routine investigations including the blood counts were within normal limit except for a mild elevation of total count and ESR. Absolute eosinophils count was

540/ml. Tzanck smear revealed eosinophils in blister fluids. Biopsy for histopathology showed a subepidermal blister and prominent dermal infiltration of eosinophils and lymphocytes (**Figure 3**). At this stage, a clinical diagnosis of dystrophic epidermolysis bullosa was considered; however the presence of intense inflammatory infiltrates on histopathology made us consider the possibility of early onset autoimmune bullous disease, including juvenile variety of bullous pemphigoid and chronic bullous disease of childhood. A rare incidence of epidermolysis bullosa acquisita occurring in infancy was also kept in mind.<sup>3</sup> Hence, a direct immunofluorescence from perilesional skin was done and it was negative for IgA, IgG, IgM, C3 and fibrin. Similarly patient's serum was negative on indirect immunofluorescence studies confirming our diagnosis of epidermal bullous dystrophica and ruling out immunobullous diseases.

Patient's parents were explained about the nature of the disease and the prognosis; and treatment was commenced with oral and topical antibiotics. At two weeks follow up, her condition worsened with the appearance of fresh crops of blisters. At this stage we started a trial course of oral prednisolone at 1 mg/kg body weight keeping in mind the inflammatory nature of the condition and a few reported cases of EB responding to oral steroid. To our astonishment, patient responded dramatically and all her lesions started healing in two to three weeks with scarring and pigmentary change (**Figure 4** and **5**). We gradually tapered the dose of steroid in three months and her condition could be well maintained with a very low dose of steroid. However about two weeks after stoppage of steroids fresh crops of bulla appeared. We again started the patient on steroids with prompt response. The patient is now in our follow up



**Figure 4** Healing of lesions on trunk after 2-week prednisolone therapy.



**Figure 5** Healing of lesions on back after 2-week prednisolone therapy.

and her condition is well controlled over last two months with prednisolone 10mg per day.

## Discussion

Dystrophic epidermolysis bullosa is a genetic disorder mostly associated with collagen VII gene mutation. Histologically, EB usually shows subepidermal bullae with minimal inflammatory cells infiltrate. No effective treatment is available for EB except topical non-steroidal ointment and avoidance of the use of physical force in daily life because complex pathomechanisms induce skin fragility resulting in blister formation. Rarely, EB was reported to be associated with eosinophil infiltration of the skin lesions. Previous reports hypothesize that bone marrow, relatively rich in myelocytic elements in the first week of life; some nonspecific injury to the skin can lead to eosinophil infiltration of dermis during this period.<sup>4,6</sup> However, in these studies they did not conduct any clinical trials of the use of oral steroids to control the disease.

Though rationality of using topical or systemic corticosteroid has been questioned by the modern understanding of the disease pathogenesis, there had been several trials of steroids in EB claiming to be helpful. Moynahan was able to arrest blister formation in a severely affected 14-year-old boy with 300mg. of cortisone acetate daily.<sup>7</sup> Severin and Farber described the successful treatment of EB in children with 0.2% fluocinolone acetonide cream and occlusion, which again suggests the efficacy of corticosteroids in the treatment of this disorder.<sup>8</sup> Shenefelt *et al.* successfully treated an albopapuloid EB (Pasini's variant) with pulse topical corticosteroid therapy.<sup>9</sup>

More recently Mabuchi *et al.* reported a case of non-Herlitz JEB with COL17A1 mutation who

responded well to oral corticosteroid. As a reason of this surprising finding they hypothesize that this abnormal protein of type XVII collagen might be secreted and released from the cell and possibly cause an immune reaction to raise eosinophil infiltration as in the case of BP.<sup>10</sup>

However, definitely not all cases of EB are responsive to topical or oral steroids.<sup>11</sup> Our case was an unusual case of DEB which showed remarkable improvement with oral steroid and relapse on withdrawal of it. In conclusion, we suggest the existence of an inflammatory variant of EB with tissue and peripheral blood eosinophilia, which shows good response to oral corticosteroids. The authors suggest that in this subset of disease the initial mutation alone may not be sufficient to produce full blown manifestation of the disease. The inflammatory response of the body which treats the mutated antigen as 'foreign' could be the major pathogenic factor; thus allowing steroid to play a preventive and therapeutic role. However, further studies are required to find out the exact etiopathogenesis of this form of EB which may give us an insight to this unusual phenomenon.

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