A boy with recessive type dystrophic epidermolysis bullosa presented by the manifestations of dilated cardiomyopathy

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Summary

Background: Dystrophic epidermolysis bullosa (EB) comprises a heterogeneous group of inherited mechano-bullous disorders characterized by trauma-induced blistering, scarring associated with milia formation, and nail dystrophy.

Case Report: A 13-year-old boy was admitted to our intensive care unit, with dyspnea on exertion, weakness and orthopnea. He complained of generalized abdominal pain, pallor, distress and tachypnea. A gallop rhythm was heard on auscultation, and heart failure was diagnosed. He received packed cells, antibiotics, dobutamine, dopamine, diuretics and ¾ maintenance IV fluid. He was discharged with the diagnosis of recessive dystrophic epidermolysis bullosa and dilated cardiomyopathy.

Conclusions: Chronic anemia can lead to dilated cardiomyopathy.

key words: recessive dystrophic epidermolysis bullosa (RDEB) • dilated cardiomyopathy (DCMP)

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**Background**

Dystrophic epidermolysis bullosa (EB) comprises a heterogeneous group of inherited mechanobullous disorders characterized by trauma-induced blistering, scarring associated with milia formation, and nail dystrophy. Both recessive and dominant forms of dystrophic EB are caused by mutations in the \( \text{COL7A1} \) gene, which encodes type VII collagen, the major component of anchoring fibrils at the dermal-epidermal junction, and results in impaired anchoring fibril formation/function. Ultrastructurally, there is blister formation at the sublamina densa level, and quantitative or qualitative changes in the anchoring fibrils at dermal-epidermal junction. However, phenotypic variations occur in affected individuals, and at least 10 distinct clinical variants of dystrophic EB have thus far been recognized [1].

Dilated cardiomyopathy (DCMP) has been reported in severe epidermolysis bullosa (EB) subtypes. Poor nutritional status, low carnitine levels, selenium deficiency, chronic iron overload, drugs and viral etiology have been proposed as potential contributors [2].

Besides skin and the musculoskeletal system, a variety of other organs may be involved in patients with DEB, especially those with recessive forms of DEB. Apart from blistering, other skin disorders like cutaneous neoplasms, eczema, atopic dermatitis and hayfever have been proposed as potential contributors [2].

Mean age at diagnosis of DCMP was 12.18±4.99 years. This study substantiates the association between DCMP and EB, but currently there is no single risk factor identified in EB patients that leads to DCMP [3].

The most common gastrointestinal manifestations include dysphagia, esophageal stricture or stenosis, pyloric stenosis, anal stricture, chronic constipation and fecal impaction and laryngeal stenosis or obstruction [6]. This presents special problems for the anesthesiologist because the equipment used to deliver anesthesia and monitor vital signs may cause serious mechanical complications [7].

Chronic anemia was diagnosed in 86.7% of patients; 60% of them had prior red blood cell transfusions. Mean age at diagnosis of DCMP was 12.18±4.99 years. This study substantiates the association between DCMP and EB, but currently there is no single risk factor identified in EB patients that leads to DCMP [3].

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Figure 1A–F. Showing skin lesions of RDEB & the sparse hair.

There are previous reports of dilated cardiomyopathy in recessive dystrophic epidermolysis bullosa (RDEB). A 6-year-old

**Figure 1A–F.** Showing skin lesions of RDEB & the sparse hair.
girl with RDEB who died of DCM was reported by Taibjee et al in Birmingham, UK in 2005. Attention is drawn to the possible role of 2 potentially cardiotoxic drugs – amitriptyline and cisapride – where amitriptyline, used for chronic pain in epidermolysis bullosa [14].

Marti et al. reported 2 patients with DCM listed for cardiac transplantation showing recovery of cardiac function after withdrawal of tricyclics [15].

CASE REPORT

A 13-year-old boy was admitted to our intensive care unit, complaining of dyspnea on exertion, weakness and orthopnea. He had generalized abdominal pain and anorexia, but had no cough, nausea, vomiting or diarrhea. On physical examination he was ill, pale, acyanotic, severely dehydrated with dry mucosa and had tachypnea, and had respiratory distress with diffuse skin lesions. The temperature, heart rate and respiratory rate were 36.5°C, 110 bpm and 60/min, respectively. Due to skin lesions, BP was not able to be detected. The skin lesions included diffuse vesicles, ulcerations and hyperkeratotic wounds, widely spread throughout the limbs and trunk. The face was scarred, and the hair was sparse (Figure 1A–F). No conjunctivitis was present, but the sclera was severely pale and anicteric. There was a large quantity of pus in the nasal discharge and the teeth were extremely decayed (Figure 2). The chest expansion was symmetric, and crackles and a gallop rhythm were heard in the lungs and heart, respectively. The jugular venous pressure was prominent. The abdomen was slightly distended, and hepatomegaly was detected. The genitalia were normal and male. Muscular atrophy and scarring of the limbs were the reasons for the fusion of the fingers, simulating amputation (Figure 3A–C). On chest X-ray, cardiomegaly was evident (Figure 4). The echocardiography showed low ejection fraction (50%), dilated ventricles, mitral and tricuspid regurgitations (Figures 5, 6). The hemoglobin was 2.3, and so the congestive heart failure was considered secondary to anemia. The patient received 4 units of packed cells, fractionally, limited serum, dobutamine, dopamine, furosemide and ceftriaxone. He stayed in the ICU for 2 days, then was moved to a ward and was finally discharged with a relatively good condition, with digoxin, furosemide, captopril, Q-10 and carnitine.

DISCUSSION

The cause of DCM in RDEB is uncertain. Micronutrient deficiency has been implicated, particularly selenium and carnitine [16,17]. Sidwell et al reported mean baseline carnitine levels significantly lower in RDEB patients with DCM than in other RDEB patients attending Great Ormond Street Hospital [3]. However, there was considerable overlap between the 2 groups, and baseline selenium levels and overall mean carnitine and selenium concentrations did not differ significantly. The authors also conceded that correction of carnitine and selenium deficiency via gastrostomy replacement did not improve cardiac function. Nutritional deficiency also seems an unlikely cause of DCM in RDEB given the apparent excess of cases of DCM in patients at Great Ormond Street Hospital despite close nutritional supervision, contrasting with the absence of reports of DCM in 15 years of cumulative data on 3280 EB patients enrolled in the US National EB Registry [18].
Conclusions

In our case the most probable cause of RDEB was severe chronic anemia. Although the nutritional status of the patient was not acceptable, we had no reliable reason to suspect any kind of special nutritional deficiency. After blood transfusion, the status of our patient improved, and after receiving iron at the dose of 4 mg/kg/day accompanied by traditional treatment for DCMP, he felt much better at follow-up.

Chronic anemia might be a significant reason for DCMP in patients with RDEB, or at least be a predisposing factor for aggravating a relatively compensated status of heart failure. This requires more investigations and a more comprehensive study.

References:


Figure 5. M-mode echocardiography showing low EF.

Figure 6. Four chamber view demonstrating dilated ventricles.