

Presentation of pleural effusion and dilated cardiomyopathy in a case of dystrophic epidermolysis bullosa

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Abstract

Epidermolysis Bullosa (EB), a genetic disorder of the skin that presents with eruptive lesions accompanied by blistering has multiple types. We present a case of dystrophic and epidermolysis bullosa (DEB), a rare variant of the disease with the underlying pathophysiology involving a mutation of type VII collagen that serves as an anchoring protein for basement membrane to the dermis. The patient presented with palmoplantar hyperkeratosis with blistering extending on multiple sites of the body, bilateral pleural effusion and an ejection fraction of 23% with moderate mitral regurgitation. The patient was treated symptomatically with diuretics and inotropic medication for the dilated heart, along with draining of pleural spaces. No case of DEB with pleural effusion has been reported prior to this one. We believe this is the first case that presented with both pleural effusion and dilated cardiomyopathy.

Keywords: Epidermolysis Bullosa Dystrophica, Pleural Effusion, Dilated Cardiomyopathy.

DOI:<https://doi.org/10.5455/JPMA.49858>

Introduction

Epidermolysis Bullosa (EB) is a genetic condition that affects the skin, making it friable with blistering. The eruptive lesion can occur as a result of a minor trauma or abrasion. The pathology involves structural and functional modifications of proteins involved in maintaining the integrity of dermo-epidermal junction. Epidermolysis Bullosa is classified into four major types based on the distinct pattern of tissue separation. EB simplex is present in 92% of the cases where tissue

separation is seen in epidermis. Dystrophic EB is present in 5% of the cases with splitting occurring just underneath the lamina densa. Junctional EB is present in 1% of the cases with splitting taking place at the level of lamina lucida. The fourth type of EB is the Kindler syndrome that is characterised by splitting involving multiple layers of the skin.¹

EB is a clinically and genetically heterogeneous group of inherited blistering diseases that affects approximately 500,000 people worldwide.² The mutation causing Dystrophic EB (DEB) involves the COL7A1 gene that encodes the type VII collagen which forms the main component of the anchoring fibrils. These fibrils adhere the epidermal basement membrane to the underlying dermis that is the major component of anchoring fibril adhesion structures which link the epidermal basement membrane to the subjacent dermis.^{3,4}

Here we present a rare case of DEB that presented with pleural effusion and dilated cardiomyopathy. To the best of our knowledge, no case of DEB with pleural effusion and dilated cardiomyopathy has been reported previously.

Case Report

A six-year-old boy, who was a known case of DEB since birth, presented in March 2019 in the emergency department of Fatima Memorial Hospital, Lahore with an intermittent fever of 101°F, rhinorrhoea and cough for the last 10 days. He had an episode of vomiting three days ago followed by a lethargic state. The patient had noisy breathing since the previous day. The antenatal and natal birth history was normal but in postnatal period the child remained in the ICU for one month due to DEB. The developmental history was normal except that the child could not walk or crawl due to the contractures in the ankles and knees. Feeding history showed that the child had been bottle-fed since birth. The vaccinations were complete.

The patient was pale, irritable and uncomfortably lying on

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Figure-1: (a) The hands of the child show mitten deformity that is seen in DEB. (b,c) Multiple erosions can be seen on both the limbs. (d) The first Chest X-Ray shows the initial presentation with bronchopneumonia. (e,f) subsequent X-Rays showing the response to treatment.

Table-1: Pleural fluid analysis.

Physical Examination	
Volume	9 ml
Colour	Yellowish
Transparency	Turbid
pH	8.0
Specific	1.016
Microscopic Examination	
Physical Examination	
WBC	370/cumm
RBC	860/cumm
Neutrophils	07%
Lymphocytes	93%
Biochemistry	
Glucose	84mg/dl
Protein	0.88g/dl
Albumin	0.24g/dl
LDH	76U/L
Amylase	06U/L
Comments	Exudative Fluid present

LDH: Lactate Dehydrogenase.

the bed with obvious respiratory distress. Growth parameters were below the 5th percentile. Vital signs revealed a respiratory rate of 37/min, pulse of 150 bpm, BP: 90/60mmHg, body temperature of 100° F and SpO2 of 98%. On skin examination, there were multiple erosions of different sizes coalescing to form large denuded areas with glistening and shiny atrophic skin predominantly

involving both the upper and lower limbs with no flexor or extensor predilection. There was a mitten glove deformity of both hands and fixed contractures in both the upper and lower limbs. Nails and hair were not properly developed.

The severe pallor was positive with no cyanosis, jaundice, clubbing, lymphadenopathy and dependent oedema. Suprasternal, intercostal and subcostal recessions were present with flaring of the ala nasi. A thorough systemic examination revealed harsh vesicular breathing, bilateral crepitations and rhonchi. The apex beat was displaced with soft S1 and normal S2 with a Grade 3/6 ejection systolic murmur at mitral area radiating to the axilla. The patient had soft, non-tender abdomen with hepatomegaly. A differential diagnosis of DEB with bronchopneumonia, severe anaemia and dilated cardiomyopathy (DCM) was made. Dilated cardiomyopathy in this patient could have been primary dilated cardiomyopathy or secondary due to chronic anaemia.

Chest X-ray showed bilateral bronchopneumonia. The patient was severely anaemic with haemoglobin count of 2.6gm/dl (14-18), RBC count of 1.59(4.5-5.3), MCV 64.8(77-91), MCHC of 25.2(32-36) and a serum ferritin of 9.58 (21.81-274.66) showing a hypochromic and microcytic picture indicating iron deficiency anaemia. The pH of the patient was 7.092(7.35-7.45), pCO2 13.7(32-45) and H2CO3 4.1(22-30) showing metabolic acidosis due to

infection and sepsis. The APTT was 48.6(control=28) and PT was 21.4(control=11) indicating a disseminated intravascular coagulation (DIC).

Blood cultures showed gram positive cocci in clusters that were coagulase negative staphylococcus species which were the probable cause of sepsis. Chest X-ray was repeated to see the progress of treatment which showed bilateral pleural effusion. Ultrasound of the chest reported a gross bilateral effusion which was more evident in the right lung. There was bilateral atelectasis of the lungs. An ultrasound guided fine needle aspiration was performed, using a 10cc syringe, 10 ml straw coloured fluid was aspirated from the right side by a consultant radiologist. The pleural fluid was clear with no debris. Pleural fluid analysis was evaluated for acid fast bacilli (AFB) and ZN (Ziehl-Neelsen) staining, which showed negative results. Pleural fluid was exudative and the results of pleural fluid analysis are shown in Table-1.

Echocardiographic imaging of the patient showed dilated cardiomyopathy with dilated left ventricle with decreased ejection fraction of 23% and moderate mitral regurgitation. In anaemia, cardiac output is usually more than normal but in DCM it is usually below normal which was present in this case.⁵

To drain bilateral pleural effusion, a bilateral chest intubation was done. For pleural effusion, nebulisation, oxygen via cannula, and intravenous (IV) Cilipenem and Linezolid was given. For severe iron deficiency anaemia, packed cell volume was transfused with 1ml Furosemide before and after the transfusion and IV iron sucrose (Venofir) was given. For DIC, fresh frozen plasma was given. For heart failure, the patient was given IV Dobutamine and IV Dopamine with IV amino plasma and IV albumin. Body fluids were maintained by dextrose water and half normal saline with potassium chloride and calcium gluconate. Paracetamol was given for fever. Despite all the treatment, the O2 saturation started falling and the baby expired due to bilateral bronchopneumonia with multi-organ failure, sepsis and DIC.

Discussion

In this report we present different complications that occurred and their management in a patient of DEB. Our patient had developed pleural effusion secondary to bronchopneumonia that has not been reported in literature before. Previously, one case with pulmonary amyloidosis was reported by Csikos et al in which type AA amyloid deposits were found in the lung and renal glomeruli.⁶ The presence of amyloid deposits in the lung indicated the presence of remarkably severe pulmonary infections. Death from pneumonia has been seen in

recessive DEB- non-Hallopeau-Siemens with cumulative risk of 0.4% by the age of one year and that increases to 1.1% by the age of 15 years. However, death from Recessive DEB-Hallopeau-Siemens has not been seen until the age of 10 years with the cumulative risk rising upto 1.8% by the age of 15 years.⁷ In our case, the patient died due to pneumonia in spite of the use of IV antibiotics. The patient initially responded to the treatment and improved but later on his condition started deteriorating and he expired due to bilateral pneumonia with multi-organ failure, sepsis and DIC.

Mixed anaemias are seen in EB patients due to iron deficiency and chronic inflammation that is common in patients with epidermolysis bullosa.⁸ Peripheral smear of the patient showed anistocytosis, microcytosis, hypochromia in RBCs that presented the picture of iron deficiency anaemia. The serum ferritin was very low and the reticulocyte count was higher than normal.

Dilated cardiomyopathy is a complication of DEB and may be associated with other aetiologies, such as chronic anaemia, iron overload by repeated transfusions or viral myocarditis.⁹ The exact mechanism of DCM is not known although Sidwell et al reported that micronutrient deficiency such as carnitine deficiency play a significant role in its pathophysiology.¹⁰ In our patient, DCM was found on echocardiography of the heart with dilated left ventricle having poor function with an ejection fraction of 23% with moderate mitral regurgitation.

Conclusion

DCM is a rare complication of DEB whereas pleural effusion secondary to bronchopneumonia has not been previously reported. More research is required to know the presentations and symptomatology of the disease.

Disclaimer: None to declare.

Conflict of Interest: There are no competing interests of any author.

Funding Disclosure: There was no source of funding except self-funding by the researchers.

Consent: Written informed consent was taken from the child's parents before being included in the study.

References

1. SoroL, Bartus C, Purcell S. Recessive dystrophic epidermolysis bullosa: a review of disease pathogenesis and update on future therapies. *J Clin Aesthet Dermatol*. 2015; 8:41-6.
2. Rashidghamat E, McGrath JA. Novel and emerging therapies in the treatment of recessive dystrophic epidermolysis bullosa. *Intractable Rare Dis Res*. 2017; 6:6-20.
3. Shimizu H, McGrath JA, Christiano AM, Nishikawa T, Uitto J. Molecular basis of recessive dystrophic epidermolysis bullosa:

- genotype/phenotype correlation in a case of moderate clinical severity. *J Invest Dermatol.* 1996; 106:119-24.
4. Dang N, Murrell DF. Mutation analysis and characterization of COL7A1 mutations in dystrophic epidermolysis bullosa. *Exp Dermatol.* 2008; 17:553-68.
 5. Bozkurt S, Safak KK. Evaluating the hemodynamical response of a cardiovascular system under support of a continuous flow left ventricular assist device via numerical modeling and simulations. *Comput Math Methods Med.* 2013;2013:986430.
 6. Csikos M, Orosz Z, Bottlik G, Szocs H, Szalai Z, Rozgonyi Z, et al. Dystrophic epidermolysis bullosa complicated by cutaneous squamous cell carcinoma and pulmonary and renal amyloidosis. *Clin Exp Dermatol.* 2003; 28:163-6.
 7. Fine JD, Johnson LB, Weiner M, Suchindran C. Cause-specific risks of childhood death in inherited epidermolysis bullosa. *J Pediatr.* 2008; 152:276-80.
 8. Li AW, Prindaville B. Inpatient management of children with recessive dystrophic epidermolysis bullosa: *Pediatr Dermatol.* 2017; 34:647-55.
 9. Lara-Corrales I, Mellerio JE, Martinez AE, Green A, Lucky AW, Azizkhan RG, et al. Dilated cardiomyopathy in epidermolysis bullosa: a retrospective, multicenter study. *Pediatr Dermatol.* 2010; 27:238-43.
 10. Sidwell RU, Yates R, Atherton D. Dilated cardiomyopathy in dystrophic epidermolysis bullosa. *Arch Dis Child.* 2000; 83:59-63.
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