ANNQUEST NOVEMBER 2017
ISSN: 2321-3043
www.stannsannquest.com

Epidermolysis Bullosa Simplex: A Case Report with two Affected Sibs in a Family

Dr V Venugopal Rao
Head of the Department of Genetics,
St.Ann's College for Women,
Mehdipatnam, Hyderabad.
rao5749@gmail.com

P Brinda
Student,
St.Ann's College for Women,
Mehdipatnam, Hyderabad.
brindapalliyana@gmail.com

Abstract—Epidermolysis Bullosa Simplex (EBS), a rare autosomal dominantly inherited skin disorder, is characterised by the formation of intraepidermal skin blisters. Among the three EBS subtypes found, the Dowling Meara subtype is the most severe form with extensive herpetiform arrangement of blisters all over the body sometimes leading to scarring. During a survey on genetic inheritance of blood pressure, a case of two patients with EBS-Dowling Meara type born to same unaffected parents was identified. No history of this disease in the past four generations of the family was identified. Since the unaffected parents and the maternal grandparents of affected individuals are into a consanguineous marriage, this consanguinity may be considered as one of the possibilities for sudden occurrence of this disease as the alleles of the genes expressing this condition might have been transmitted to the affected individuals in a dominant fashion with reduced penetrance, making them homozygous dominant to this severe form of disease. The other possibility might be the mutations induced in the germinal epithelium of the father due to exposure to chemical composition of building materials, who is employed in a building construction company. Since the mother of the affected individuals was identified with Gestational Diabetes mellitus and was under constant medication during gestational period, the chemical composition of the medicines might have simulated the effect of a mutation of such type resulting in a phenocopy. However, further investigations are necessary to support the above findings.

Key words**:** Blister formation, Herpetiform cluster, Consanguinity

I. Introduction

Epidermolysis bullosa (EB) comprises of disorders which are inherited and are primarily recognized by formation of blisters and fragility of skin (Y. Kitajima et al. 1989; Stephens et al. 1993). Based on the various levels of cleavage at the dermal-epidermal junction, EB is further classified into three main types. They are Epidermolysis Bullosa simplex (EBS), Junctional EB and Dystrophic EB. In EBS, as a result of basal cell cytolosis, the formation of blisters is seen in the zone above the basement membrane (lamina lucida and lamina densa). In Junctional EB, formation of blisters is seen within the lamina lucida in the zone of basement membrane. In Dystrophic EB, the blister formation occurs below the lamina densa in the superficial dermis of the basement membrane zone (Y. Kitajima et al. 1989).

Epidermolysis bullosa simplex (EBS) is a rare group of skin disorder inherited predominantly in an autosomal dominant manner (Stephens et al.1993; Sorensen et al.1999; Smith et al. 2004). This genetic heterogenous group of skin diseases is characterized by intraepidermal blister formation due to cytolysis of basal keratinocytes by mechanically induced stress (Chan et al. 1996; Smith et al. 2004). Clinically, EBS is again reported to be divided into three major subtypes like the EBS Dowling Meara type (EBS-DM), EBS Weber-Cockayne type (EBS-WC) and EBS-Koebner type

(EBS-K) (Sorensen et al. 1999; Smith et al. 2004). Among the above three subtypes reported, the Dowling-Meara form of Epidermolysis bullosa simplex (EBS-DM) is the most severe form which is characterized by severe widespread blister formation in a herpetiform cluster or arrangement seen all over the body and even in the oral mucosa. It is even reported that an abnormal clumping of Keratin intermediate filaments in the basal keratinocytes is a characteristic of EBS-DM type (Ishida-Yamamoto et al.1991; Chan et al. 1996; Sorensen et al. 1999; Smith et al. 2004). During a survey on the genetic inheritance of the blood pressure, two patients with EBS-Dowling Meara type were identified. In this study, we are reporting a case of these two affected individuals with EBS Dowling Meara type born to same unaffected parents.

II. Case report

This case concerns a 13-year old boy and a 16 months old female infant who are born to the same unaffected parents of consanguineous marriage. The boy and the female infant were born with severe blistering and erosions all over their body. The boy, who is born in the year 2004, is identified with numerous bullous grouped in a herpetiform fashion on the face, trunk, limbs, palms, soles and even on the tongue. The blisters appear spontaneously owing to any mechanical stress or injury. The nails showed mild deformity which eventually shed off and re grew at a slow rate without any deformity (Figure 1). When the boy was born, the Doctors who attended the boy and his mother could not diagnose the health issue and kept him in the intensive care unit for a period of one month for observation and detection of the disease. Then the boy's father was advised to consult a Dermatologist who attended the boy in his clinic and explained the family about the disease (EBS-DM) he is suffering. The family was made to understand in detail about the boy's health condition which has no cure.

The female infant, born in the year 2015, is also identified with the same disease like her sibling. During the second gestation period, the parents have consulted more than a couple of Gynaecologists, Physicians and Genetic counsellors to ascertain the non-recurrence of the disease in their second child as they learnt that EBS is a genetic disease. The tests and the scannings performed during the whole of gestation period showed no signs of this disease in the baby in the mother's womb. Hence the parents were assured that the child will be born normal

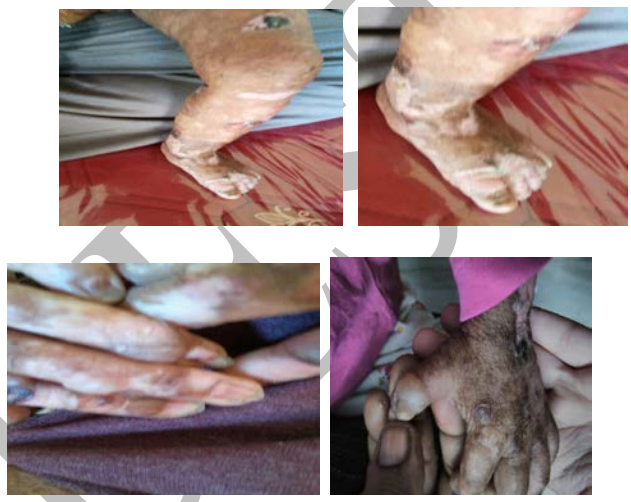

Figure 1*. (a), (b) and (c) shows the blister formation, leading to scarring and deformity of nails in the boy. (d) Shows the blister formation and scarring in the infant.*

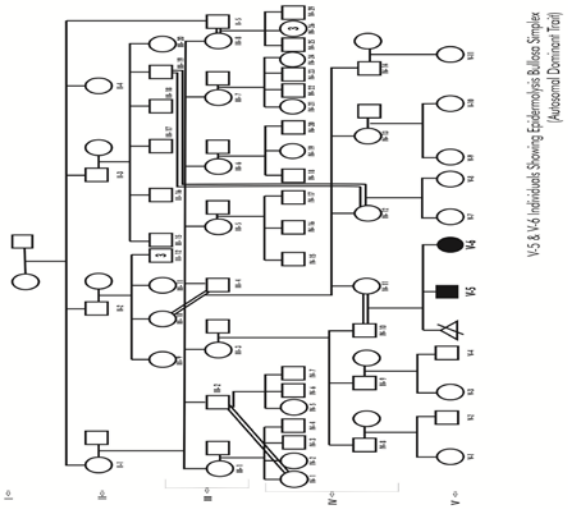

Figure 2 *Pedigree showing the five generations of the family of the affected patients*

The mother of the patients had a history of termination of pregnancy in the second trimester (seventh month) of her first child due to the deformity of the brain and head of the baby. The mother of the patients reported that she had gestational diabetes mellitus during her second (13-

year old boy) and third (16 months old female infant) gestational periods. Both the affected children were born by caesarean section.

The patients' parents reported that they usually puncture the blisters formed using a fine needle to drain out the fluid and apply antibiotic ointments like T-Bact or Fucidine to prevent infections and also to reduce pain and itching in that part of the skin. Later the skin becomes fragile and falls off which may even lead to scarring. The hair growth of the patients is very minimal. The decaying of the teeth is also observed. Due to the blister formation on the tongue, the patients are restricted from any hard food intakes. Hence, they are underweight and are having irregularities in metabolism. The boy has been identified with Myopia. The patients are active and the intelligent quotient is normal as compared to other children of their age. Their outer physical condition makes them insecure psychologically.

III. Discussion

In this case, the patients with EBS-DM type were identified to be the individuals of the fifth generation of the family. No history of this disease is identified in the past four generations of the family (Figure 2). The reason for the sudden occurrence of this disease is not studied in this particular case but few possibilities can be proposed. The penetrance of the disease causing gene might be one of the reasons of the non occurrence of this disease in earlier generations of the family. The unaffected parents of the patients were into a consanguineous marriage. Not only the parents but also the maternal grandparents of the patients were into a consanguineous marriage. So the alleles of the genes expressing this condition might have been transmitted from their ancestors to the affected individuals in a dominant fashion making them homozygous dominant which might lead to this severe form of the disease. Since there is no history of this disease in the previous generations, the occurrence of this disease might be due to incomplete penetrance but the figures are unknown. The other possibility may be the mutations induced in the germinal epithelium of the father. As the father of the patients is reported to be employed in a building construction company, the germinal epithelium of the father might be mutated due to exposure to the chemical composition of the building materials which might have further triggered mutations in the genes causing this disease. It is previously reported that a clumping of Tonofilaments (TF) or the keratin intermediate filament bundles in the basal epidermal cells is typical of this disease and is characterized mainly due to the abnormality in keratins K5 and K14 gene products due to mutations leading to the formation of blisters (Ishida-Yamamoto et al. 1991; Y. Kitajima et al. 1992; Chan et al. 1996; Sorensen et al. 1999).

The mother of the affected individuals was identified with gestational Diabetes mellitus during the gestational periods of both the children and was under medication. The chemical composition of the medicines might have interfered with embryo development, a teratogenic effect leading to phenocopies of the disease. It is observed that the condition of the boy has shown little improvement as compared to his early years. There is no specific treatment or cure found out till date. The gene therapy treatment trials are being carried out by researchers in order to find a cure for this genetic disease. However, further investigations are necessary to support our findings.

IV Acknowledgment

We would like to thank the family of the patients for their valuable time and co-operation in willingly giving the complete information for the case study. Also, we would like to thank the Department of Genetics, St. Ann's College for Women, Mehdipatnam, Hyderabad for its support.

References

1. Y. Kitajima, S. Inoue, and H. Yaoita. (1989). Abnormal organization of keratin intermediate filaments in cultured

2. keratinocytes of Epidermolysis bullosa simplex. Archives of Dermatological Research 281: 5-10.
3. Markku Ryynanen, Robert G. Knowlton, and Jouni Uitto. (1991). Mapping of Epidermolysis Bullosa Simplex Mutation to Chromosome 12. American Journal of Human Genetics 49: 978-984.
4. Akemi Ishida-Yamamoto, John A. McGrath, Stephen J. Chapman, Irene M. Leigh, E. Birgitte Lane, and Robin A. J. Eady. (1991). Epidermolysis Bullosa Simplex (Dowling-Meara Type) Is a Genetic Disease Characterized by an Abnormal Keratin-Filament Network Involving Keratins K5 and K14. The Journal of Investigative Dermatology 97: 959-968.
5. Y. Kitajima, Y. Jokura and H. Yaoita. (1993). Epidermolysis bullosa simplex, Dowling-Meara type. A report of two cases with different types of tonofilament clumping. British Journal of Dermatology 128: 79-85.
6. Karen Stephens, Virginia P. Sybert, Ellen M. Wijsman, Pamela Ehrlich, and Anne Spencer. (1993). A Keratin 14 Mutational Hot Spot for Epidermolysis Bullosa Simplex, Dowling-Meara: Implications for
7. Diagnosis. The Journal of Investigative Dermatology 101: 240-243.
8. Yiu-Mo Chan, Jian Cheng, Tobias Gedde-Dahl Jr., Kirsti-Maria Niemi, and Elaine Fuchs. (1996). Genetic Analysis of a Severe Case of Dowling-Meara Epidermolysis Bullosa Simplex. The Journal of Investigative Dermatology 106: 327-334.
9. Charlotte B. Sorensen, Anne-Sofie Ladekjaer-Mikkelsen, Brage S. Andresen, Flemming Brandrup, Niels K. Veien, Sanne K. Buus, Ingrun Anton-Lamprecht, Torben A. Kruse, Peter K.A. Jensen, Hans Eiberg, Lars Bolund, and Niels Gregersen. (1999). Identification of Novel and Known Mutations in the Genes for Keratin 5 and 14 in Danish Patients with Epidermolysis Bullosa Simplex: Correlation between Genotype and Phenotype. The Journal of Investigative Dermatology 112: 184-190.
10. Frances J.D. Smith, Susan M.Morley, and W. H. Irwin McLean. (2004). Novel Mechanism of Revertant Mosaicism in Dowling-Meara Epidermolysis Bullosa Simplex. The Journal of Investigative Dermatology 122:73-77.