Epidermodysplasia Verruciformis in a Girl Born to a Xeroderma Pigmentosum Mother: An Unusual Presentation

Zainab Qadir[1], Najia Ahmed[1], Ammara Hameed[2] and Tariq Mahmood Malik[1]

[1]*Department of Dermatology, PNS Shifa Hospital, Karachi, Pakistan*
[2]*Department of Paediatrics, Bahria University of Health and Sciences, Karachi, Pakistan*

ABSTRACT

Epidermodysplasia verruciformis (EV) and xeroderma pigmentosum (XP) both are examples of genodermatoses. Although no association is identified between XP and EV in the literature, both are genetic disorders with cutaneous manifestations and related to mutations in DNA repair genes. We describe a case of a 6-month female, diagnosed with EV, born to her mother, who has been diagnosed with XP. The child presented with multiple hypopigmented lesions on the body. Verrucous warts were observed on the scalp and plain warts on the forehead. Clinical presentation and supporting histopathology led to the diagnosis of EV. The mother had multiple lentigines and hypopigmented macules on photo-exposed areas. Family history was significant as well. Based on clinical findings and supporting histopathology, she was diagnosed as XP. It is interesting to see the genetic clustering of different genetically inherited disorders in the same family. No such case has been reported before to the best of the authors' knowledge.

Key Words: *Epidermodysplasia verruciformis, Genodermatoses, Warts, Xeroderma pigmentosum.*

How to cite this article: Qadir Z, Ahmed N, Hameed A, Malik TM. Epidermodysplasia Verruciformis in a Girl Born to a Xeroderma Pigmentosum Mother: An Unusual Presentation. *JCPSP Case Rep* 2024; **2**:93-95.

INTRODUCTION

Epidermodysplasia verruciformis (EV) and xeroderma pigmentosum (XP) both are examples of genodermatoses. Both disorders have different presentations. EV is a rare genetic disorder in which the patient is immunologically unable to defend and eradicate certain types of human papillomaviruses (HPVs).[1] It is inherited in an autosomal recessive manner. XP is transmitted in an autosomal recessive mode caused by an inability to repair DNA after damage caused by sunlight exposure.[2] It is well-established that inherited genetic disparity within families is undoubtedly related directly or indirectly to the pathogenesis of the disease.[3] Both Mendelian and multifactorial genetic patterns explain the genetic susceptibility to various diseases. Whether the presence of one genetic disorder increases the susceptibility to other genetic disorders is still uncertain. No association has been reported between EV and XP in the literature. Both diseases are genetic disorders with cutaneous manifestations and pathology related to the mutations in the DNA repair mechanism, but the genes for both diseases lie on different chromosomes.

Correspondence to: Dr. Ammara Hameed, Department of Paediatrics, Bahria University of Health and Sciences, Karachi, Pakistan
E-mail: ammarahameed@hotmail.com
Received: September 06, 2023; Revised: January 31, 2024; Accepted: March 07, 2024
DOI: https://doi.org/10.29271/jcpspcr.2024.93

Environmental factors are known to affect the expression of various genetic disorders, but whether the presence of one mutation can result in another genetic defect is still uncertain. Taking this into account, we present a case of a 6-month female, diagnosed with EV, born to a mother, who was a case of XP.

CASE REPORT

A 6-month baby girl presented with complaints of multiple hypopigmented lesions on the trunk for the past 3 months (Figure 1 a and b). The lesions were 0.5 to 1 cm in diameter and started on the trunk and gradually spread to involve the lower extremities and forearms. A few slightly raised brownish lesions were also noted on the scalp. Moreover, small, skin-coloured plaque-like lesions were noticed on the forehead. Family history was insignificant for any similar findings among any other family members. Parents were cousins and there was a history of intermarriages for many generations in the family.

On examination, hypopigmented lesions on the trunk appeared like pityriasis-versicolor. The lower half of the body was relatively spared with fewer lesions. Verrucous warts were noted on the scalp. Plane warts were noticed on the forehead. No lesions were noted on palms and soles, mucous membranes, hair, and nails. There was no other associated illness. The clinical picture suggested EV. Histopathology of the lesion showed numerous koilocytes in the upper epidermis characteristic of warts (Figure 1 c and d). The findings were consistent with the clinical diagnosis of EV.

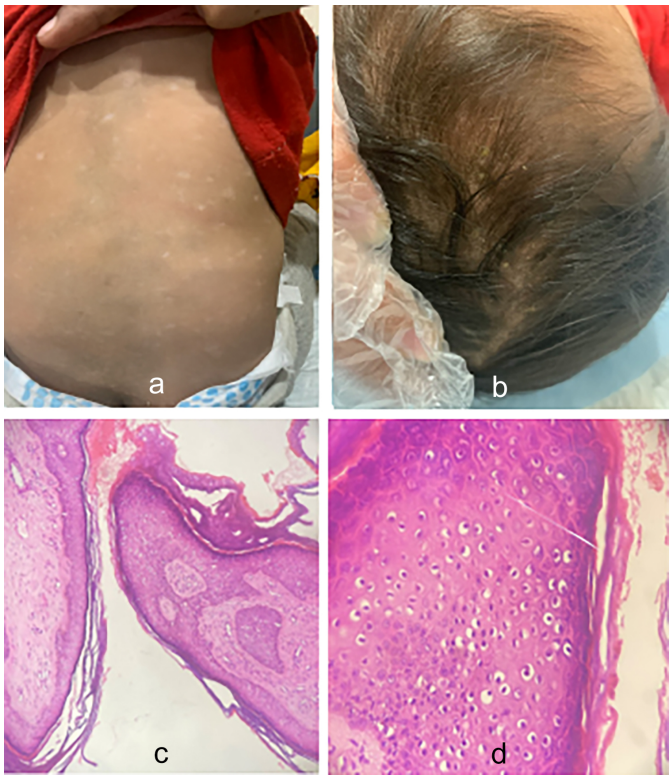

Figure 1: (a) Maculo papular lesions on back: coalescent, discrete and polymorphi; (b) Verrucous warts on the scalp of the 6-month baby girl with epidermodysplasia verruciformis; (c) Histopathology of verrucous wart on the forehead; (d) Epidermis showing numerous koilocytes.

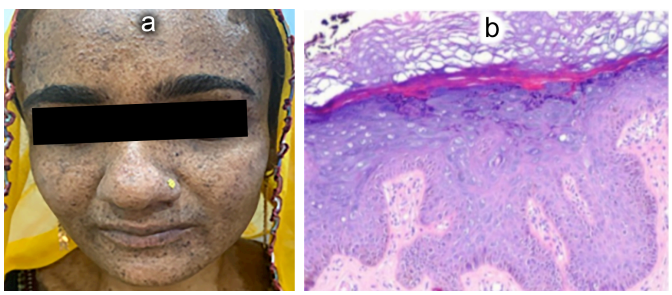

Figure 2: (a) Multiple dense lentigines and hypopigmented macules distributed on photo-exposed areas; (b) Skin biopsy showing hyperkeratosis, parakeratosis, acanthosis, and vacuolated enlarged keratinocytes.

Mother was noticed to have multiple dense lentigines and hypopigmented macules on the photo-exposed parts (Figure 2a). Baseline laboratory investigations were normal. A skin biopsy was performed to rule out suspicious lesions. Biopsy showed hyperkeratosis, parakeratosis, acanthosis, and vacuolated enlarged keratinocytes with occasional enlarged, hyperchromatic, nuclei, and perinuclear halos in the granular and spinous layers (Figure 2b). These features were consistent with actinic keratosis (AK). XP is mainly diagnosed on clinical findings and presentation. For confirmation, genetic testing is required. Unfortunately, the facility of genetic testing for XP is not available in Pakistan. So, based on the clinical presentation and supporting histopathology, the case was diagnosed as XP. This patient had skin features only. No eye or neurological findings were observed. The family history of the mother revealed that among her 5 siblings, 1 brother and 2 sisters had similar lesions. The family never acquired any medical advice for this reason.

DISCUSSION

Studying the genetic causes of various inherited disorders has been a subject of interest for many decades. Many studies have been carried out on the subject of genetic transmission of various diseases.[4] Single gene disorders, chromosomal imbalances, and epigenetics have been researched extensively. However, whether the presence of one kind of genetic disorder can lead to another unrelated genetic disorder or not is still a grey area. Not much research has been carried out on this subject. EV is a rare genetic disorder inherited in autosomal recessive mode, in which the patient is immunologically unable to defend and eradicate certain types of HPV, which leads to persistent infection, and also the patient is exposed to increased risk of developing malignancy and skin dysplasia. EV is caused by alterations in genes, including EVER1 and EVER2 located on chromosome 17q25 that regulate immune function and DNA repair processes.[5] XP is inherited in an autosomal recessive manner; the mutation is in the XPA gene located on chromosome 9q34.[6] In XP, affected patients cannot repair the DNA damage caused by UV radiations.[7] Interestingly, both diseases result in faulty DNA repair and lead to increased risks of developing malignant skin cancers, most commonly squamous cell carcinomas. However causative agent is HPV in EV and sunlight leading to DNA damage in XP. Also, the defective genes are located on different chromosomes. So, the hypothesis that the presence of one defective gene can result in another defective gene is an area that needs more research. A literature search shows no correlation between the two disorders and no such case has been reported previously. Consanguineous marriages lead to an increased tendency to inherit genetic disorders.[8] Pakistan is among the countries with the highest percentage of cousin marriages globally, with reported cousin marriages to be 65%.[9] So, an increased risk of genetic disorders in the population can be anticipated. Unfortunately, in Pakistan, there is a lack of the latest genetic testing technologies, necessary for the diagnosis of various genetic disorders, as in this XP patient. So, we only rely on the clinical presentation for diagnosing these diseases.

Whether XP in the mother could have led to EV in the offspring is an area that is still unexplored and needs more research. Also, more research is required to establish the clustering of various genetic disorders in the same family.

PATIENT'S CONSENT:

Informed consent was obtained from the patient's parents.

COMPETING INTEREST:

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

ZQ, AH: Conception and design of the work.
NA: Reviewing the work critically for important intellectual content.
TMM: Final review and approval.

All authors approved the final version of the manuscript to be published.

REFERENCES

1. Myers DJ, Kwan E, Fillman EP. Epidermodysplasia Verruciformis. [Updated 2023 Jan 29]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023s. Available from: http://www.ncbi.nlm.nih.gov/books/NBK534198.
2. Mareddy S, Reddy J, Babu S, Balan P. Xeroderma pigmentosum: Man deprived of his right to light. *Scientific World J* 2013; **2013**:534752. doi: 10.1155/2013/534752.
3. Hernan-dez LM, Blazer DG. Genes, behavior, and the social environment: Moving beyond the nature/nurture debate. Washington (DC): National Academies Press (US); 2006. doi: 10.17226/11693.
4. Jackson M, Marks L, May GHW, Wilson JB. The genetic basis of disease. *Essays Biochem* 2018; **62(5)**:643-23. doi: 10.1042/EBC20170053.
5. Emsen IM, Kabalar ME. Epidermodysplasia verruciformis: An early and unusual presentation. *Can J Plast Surg* 2010 Spring; **18(1)**:21-4.
6. Takahashi Y, Endo Y, Sugiyama Y, Inoue S, Iijima M, Tomita Y, *et al*. XPA gene mutations resulting in subtle truncation of protein in xeroderma pigmentosum group a patients with mild skin symptoms. *J Invest Dermatol* 2010; **130(10)**: 2481-8. doi:10.1038/jid.2010.137.
7. Sethi M, Haque S, Fawcett H, Wing JF, Chandler N, Mohammed S, *et al*. A distinct genotype of xp complementation group A: Surprisingly mild phenotype highly prevalent in Northern India/Pakistan/Afghanistan. *J Invest Dermatol* 2016; **136(4)**:869-72. doi: 10.1016/j.jid.2015.12.031.
8. Hamamy H. Consanguineous marriages: Preconception consultation in primary health care settings. *J Community Genet* 2012; **3(3)**:185-92. doi: 10.1007/s12687-011-0072-y.
9. Oniya O, Neves K, Ahmed B, Konje JC. A review of the reproductive consequences of consanguinity. *Eur J Obstet Gynecol Reprod Biol* 2019; **232**:87-96. doi: 10.1016/j.ejogrb.2018.10.042.