IJN
Iranian Journal of Neonatology
http://ijn.mums.ac.ir

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Case Report

Congenital Hereditary Endothelial Dystrophy with Valvular Heart Disease: A Case Report

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ABSTRACT

***Background*:** Congenital hereditary endothelial dystrophy (CHED) is a rare disease of the corneal endothelium. It is a nonprogressive clouding of the corneal, presenting at birth in most cases or shortly after it. This disease is categorized as an autosomal recessive disorder, which manifests with diffuse corneal edema, Descemet membrane thickening, and lack of endothelial cells. The primary abnormality in CHED is a degeneration of endothelial cells during or after the fifth month of gestation. The literature review has shown that CHED can occur with progressive, postlingual sensorineural hearing loss in Harboyan syndrome; however, it is not associated with any systemic abnormality.

Case report: Our study reports a case of CHED and valvular heart disease in a neonate. To the best of our knowledge, no research has been performed to investigate the relationship between CHED and valvular heart disease. In addition, the patient's mother had vaginal discharge in the fifth month of gestation, which was, as stated in the previous studies, the period during which the abnormality occurs in CHED. The two aforementioned issues highlight the need for performing the present study.

Conclusion: Occurrence of CHED and heart disease has not been reported, there is a need for more research into this subject.

Keywords: Congenital hereditary endothelial dystrophy, Corneal, Valvular heart disease

Introduction

Congenital hereditary endothelial dystrophy (CHED) is a form of corneal endothelial dystrophy, which is a rare disease characterized by diffuse bilateral clouding of the corneal. The prevalence of this disease is unknown (1), and most cases occur in children having consanguineous parents (2). This disease was first described in 1960 by Edward Maumenee (3). Congenital hereditary endothelial dystrophy, affecting the Descemet's membrane and the corneal endothelial layer (4), is present at birth without developing over time (5).

In a normal corneal, the endothelium is a single layer of polygonal cells that function as a fluid pump to ensure dry stroma resulting in a clear corneal. The endothelial cells work by Na^+/K^+-ATPase ion pump to transport water from the corneal to the aqueous humor. The presence of fluid can disrupt the organized lamellar collagen matrix and lead to cloudy corneal (6). In CHED, the degeneration of endothelial cells results in corneal edema due to fluid build-up in the corneal stroma. Although the etiology of this disease is unknown, its genetic, metabolic, developmental, and idiopathic factors have been discussed in the pathophysiology (7).

Congenital hereditary endothelial dystrophy exhibits autosomal recessive inheritance, with the majority of the cases linked to mutations in the *SLC4A11* gene on chromosome 20p13 (2, 8). *SLC4A11* gene code for transmembrane protein, working as a pump, is found in the stromal of the endothelial cells (9). The affected transmembrane protein fails to glycosylate and never reaches the cell surface (10). Therefore, it becomes unable to

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Please cite this paper as:
Ogundele T, Francis Akinkunmi B, Adebola Oladipo R, Fajimi O. Congenital Hereditary Endothelial Dystrophy with Valvular Heart Disease: A Case Report. Iranian Journal of Neonatology. 2021 Jan: 12(1). DOI: 10.22038/ijn.2020.50303.1883

keep the corneal dehydrated and clear. *SLC4A11* gene is not only expressed in the corneal endothelial cells but also in fibrocytes and stria vascularis of the inner ear, indicative of a common origin of these cell families in the neural crest (10). It has been speculated that the primary abnormality in CHED can be endothelial cells degeneration during or after the fifth month of gestation (11). Congenital hereditary endothelial dystrophy has not been reported to be associated with any systemic abnormality (11). We report one case of CHED with valvular heart disease.

Case report

A term female neonate was admitted at birth on account of fast breathing and evidence of respiratory distress. The Apgar score was recorded as 6^{1}, 7^{5}, 9^{10}. The birth weight was 2,000 g. The patient was delivered by a 31-year-old, booked, Nigerian, Para 2+0 (i.e., 2 alive) female, who received antenatal care in our facility. She had offensive vaginal discharge in the fifth month of gestation and was treated with antibiotics, such as metronidazole. There was neither a history suggesting the use of herbal medicine or any illicit drugs during pregnancy, nor a history of febrile illness or rash during pregnancy. She delivered by spontaneous vagina delivery with no history of prolonged rupture of membrane.

Considering the demographic information, she was a trader while her husband was an electrician, and both of them had a senior secondary school level of education. They are married in a monogamous setting and no history suggestive of either their consanguineous marriage or of their family members. On physical examination, the patient was a female neonate with features of term, in obvious respiratory distress having bilateral corneal cloudiness. She had a respiratory rate of 66 cycle/min, oxygen saturation of 72%, and heart rate of 152 beats/min. In addition, the first and second heart sounds were heard. Diagnosis of a term, low birth weight neonate in respiratory distress query leads to ruling out aspiration and occurring of bilateral corneal opacity.

An ophthalmologist was invited to examine the patient. The clinical findings were as follows: visual acuity, blink to light on both eyes, normal eyelids, quiet conjunctiva in both eyes, bilateral, diffuse, and uniform corneal cloudiness and thickened pachymetry, rough epithelium and irregular in shape, deep anterior chamber of both eyes, and absence of strabismus or nystagmus. Based on the results of the examination, the subject was diagnosed with CHED. At about the end of the first week, the patient was still in severe respiratory distress and was maintained on continuous positive airway pressure. On routine examination of the cardiovascular system, a murmur was heard; therefore, a chest X-ray was ordered. The result of the chest X-ray was indicative of congenital valvular heart disease. Although echocardiography was required, the patient's parents refused and requested discharge regardless of medical advice.

Discussion

The occurrence of CHED with congenital valvular heart disease is rare, and to the best of our knowledge, no research has been performed to investigate this domain. Various syndromes have been reported, including Harboyan, in which CHED is associated with progressive, postlingual sensorineural hearing loss. None of the syndromes described CHED with valvular heart diseases, suggesting that the spectrum presented by our patient may represent an association to or syndrome of CHED required to be investigated more. In this regard, while genetics can be beneficial in describing this incidence, few genetic studies have targeted this domain.

The clinical identification of neonates with cornea opacity may not be difficult; however, its association with valvular heart disease make the management demanding and complicated since it matches with none of the previously known syndromes or associations. The correct diagnosis of this disease is vitally important concerning the appropriate implementation of the management.

The results of a study revealed that CHED can be the degeneration of endothelial cells during or after the fifth month of gestation (11). In the current study, the subject's mother had a vaginal discharge in the fifth month of pregnancy. There may be some relationships between the cause of the mother's vaginal discharge in the fifth month and the occurrence of CHED in this patient, which was unknown. Therefore, more research is needed to investigate this possible relationship.

It has been found out some genetic factors are associated with CHED, being initially divided into two groups, namely autosomal dominant (CHED 1) and autosomal recessive (CHED 2). However, with the advancements in corneal imaging and genetic analysis, it has been discovered that its mode of inheritance is autosomal recessive. Therefore, the International Classification of Corneal Dystrophies classifies it as CHED, rather than CHED 1 or CHED 2 (4, 5).

Congenital hereditary endothelial dystrophy is associated with sensorineural hearing loss in Harboyan syndrome and has been linked to a mutation of the *SLC4A11* gene (12). The *SLC4A11* gene is expressed in the corneal endothelial cells and inner ear's fibrocytes and stria vascularis, indicative of a common origin of these cell families in the neural crest (10). Regarding this patient, the researchers of this study could not perform any genetic analysis to determine the exact cause or the genetic basis of the disease. The patient's parents were incapable of affording the expenses even before the end of the first week; as a result, all other investigation procedures requested, including echocardiography, were not carried out. The patient was discharged on the thirteenth day of life, regardless of medical advice, on account of financial inability. The outcome of such patients would improve provided that there is an extension of the National Health Insurance Scheme to the general populace, especially those with low socioeconomic status in need of being supported. Genetic studies would have facilitated a better investigation of the patient; however, it was not feasible in our research setting.

Conclusion

The incidence of CHED with congenital valvular heart disease is rare. This relationship has not been investigated before, suggesting the need for more research to be conducted in this subject.

Acknowledgments

The authors would like to express their gratitude to the doctors and nurses at the Department of Paediatrics, Newborn Unit, University of Medical Teaching Hospital, Ondo State, Nigeria, who assisted in managing the patient.

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