Bilateral split hand foot malformation in siblings: Case series

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A B S T R A C T

INTRODUCTION: Split Hand-Foot malformation (SHFM) is a congenital limb defect that affects the central rays of the hands and/or feet. It is a rare condition that has genetic and environmental etiologies. It ranges in severity depending on the extent of the malformation. We report on two siblings with severe SHFM affecting all limbs.

METHODS: We described two cases of siblings with SHFM and discuss the possible causes of the condition.

RESULTS: Case 1 is a 7-year-old boy, and case 2 is his 4-year-old brother. They are both medically and surgically free. They had normal growth and development and were products of a consanguineous marriage. They both presented with bilateral deformities of the hands and feet, and had no previous family history of congenital anomalies.

CONCLUSION: SHFM may occur as a result of consanguineous marriage, genetic mutation, and chemical exposure. Genetic counseling and thorough assessment of associated anomalies is mandatory.

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1. Introduction

Split Hand-Foot malformation (SHFM) is a rare congenital affecting the central rays of the limbs characterized by hypoplasia to a complete absence of the fingers or toes with a possible cleft in the hand or foot [1]. The prevalence of SHFM estimated to range from 1 in 6000 to 1 in 20,000 worldwide and three times more common in eastern countries like China [2,3]. Mutations in this malformation may occur sporadically, however, its mode of inheritance is variable and may be either autosomal dominant (AD), autosomal recessive (AR), or X-linked [1,4,5].

The presence of a severe form of SHFM affecting all four limbs in a single family has never been reported before. We present two brothers with a severe form of SHFM affecting four limbs. Also, this case was reported in line with the PROCESS criteria [6].

2. Case presentation

2.1. Case 1

7-year-old male with bilateral hand and foot anomalies. He was the first child for this family with a consanguineous marriage, his pregnancy was with no complications and he was delivered vaginally. He had normal developmental milestones with no previous similar congenital deformities or other deformities in both families. Fig. 1 illustrates the family pedigree.

He had asymmetrical central clefts of the hands and symmetrical central clefts of the feet on exam. The 2nd and 3rd rays were absent on the right hand, the 3rd absent on the left hand, the 2nd to 4th rays were absent on both feet [Fig. 2]. The X-rays correlated well with clinical examination [Fig. 3]. There were no other dysmorphic features or feature of other anomalies. The management was with multiple procedures to close the cleft area and approximate the hand fingers for better function.

2.2. Case 2

4-year-old brother of the previous case was born bilateral anomalies of his hands and feet [Fig. 4]. The deformities were treated surgically via a multiple stages approach and a good functional outcome was attained.

3. Discussion

The development of the limb buds is orchestrated by certain cell groups that produce signaling molecules to guide the rapidly proliferating mesenchymal layer and its ectodermal coverage, resulting in three-dimensional limb growth. These groups are: the apical ectodermal ridge (AER), the progress zone (PZ), and the zone of polarizing activity (ZPA). The AER, which is a thickened layer of ectoderm overlying the limb buds guiding the mesodermal layer differentiation, is responsible for the growth of the proximal to dis-
tal axis of the limb, as well as separation of the webbed hand via interdigital apoptosis [7]. SHFM is a result of degeneration of the AER secondary to genetic mutation or environmental insult.

SHFM may occur as an isolated deformity or in association with other anomalies. Many reports have agreed that consanguineous marriage may result in SHFM in the off spring, predicting and AR pattern as reported by Ray, Freire-Maia, and Verma et al. [8,9,10]. Another report further supported this statement with two patients of SHFM and tibial agenesis where their parents were first cousins [11]. Genetic mutation may result in SHFM, DLX5 mutation has been associated with syndromic SHFM and sensorineural hearing loss [4].

He was the fourth child of the same family. His antenatal history, delivery, and developmental milestones were unremarkable. He had asymmetrical hand anomalies that include absence of the 3rd rays with syndactyly of the two borders digit on the left hand, and absent central rays and syndactyly of the ulnar border digit of the right hand. He had absence of the central three rays of his feet bilaterally. X-rays of the limbs confirmed the findings of the physical examination [Fig. 5].

Prenatal exposure to medication might lead to an increased risk of congenital malformations in general. Exposure to acetazolamide has reported to result in isolated SHFM [12]. Some studies revealed an association between the chemical exposure and the increase of congenital malformations [13,14]. Majority of those have been done on US veterans who served on a war zone. Chemicals could be associated with our reported cases as the parent were living in the eastern province of the Kingdom of Saudi Arabia, which was considered as a war zone during the Gulf war.
Fig. 4. Anomalies of the hands and feet.

Fig. 5. X-rays of the hands showing deformities.

There is a paucity of reports for this anomaly. Most of which have suggested some genetic association or chemical exposure in non-isolated SHFM. This case is the first to describe two cases of bilateral isolated SHFM in siblings. Unfortunately, the association of genetic mutation in our cases could not be ruled out due to parent’s refusal for the test.

Prenatal ultrasonography may aid in the earlier detection, three-dimensional visualization of this condition, and to detect also associated anomalies if present [15,16]. Depending on the severity of the condition, surgery might improve the condition and improves the functional outcome of the condition. Both cases have had good functional hand use, near normal walking and use of normal shoes.

4. Conclusion

SHFM may occur as a result of consanguineous marriage, genetic mutation, and chemical exposure. Genetic counseling and thorough assessment of associated anomalies is mandatory.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Ethical approval

This research did not require ethical approval due to the institute not requiring it for this type of study.

Consent

Informed consent has been taken from the patients’ parents. Anonymity was kept and both the text and images included have no identifying information that could reveal the patients’ identity.

Authors contribution

Mohammed Ashi, data collection and writing of manuscript. Rehab Assur, data collection and writing of manuscript. Basim Awan, writing and revision of manuscript. Hattan aljaaly, writing and revision of manuscript.
Guarantor
Dr. Basim Awan.

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