CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 44 (2018) 114–117

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Bilateral split hand foot malformation in siblings: Case series

Mohammed Ashi[a,*], Rehab Assur[b], Basim Awan[c], Hattan Aljaaly[c]

[a] King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia
[b] College of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia
[c] Division of Plastic and Reconstructive Surgery, Department of Surgery, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

ARTICLE INFO

Article history:
Received 21 November 2017
Accepted 15 December 2017
Available online 27 December 2017

Keywords:
Congenital anomalies
Split hand/foot malformation
Genetics
Chemical exposure

ABSTRACT

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

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-

* Corresponding author at: College of Medicine – Jeddah, King Saud Bin Abdulaziz University for Health Sciences, King Abdulaziz Medical City,' National Guard Health Affairs,' Mail Code 6660', P.O. Box 9515, Jeddah, 21423, Saudi Arabia.
E-mail address: mhmmd.ashi93@gmail.com (M. Ashi).

https://doi.org/10.1016/j.ijscr.2017.12.030

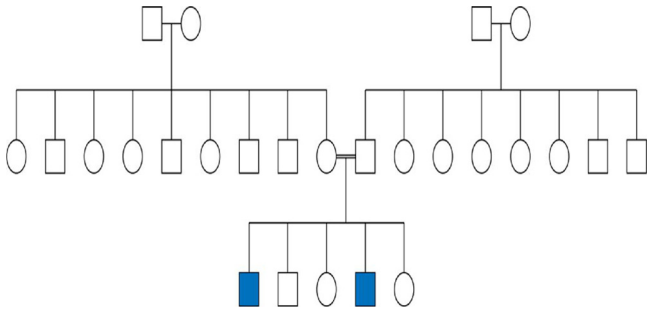

Fig. 1. Family pedigree.

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.

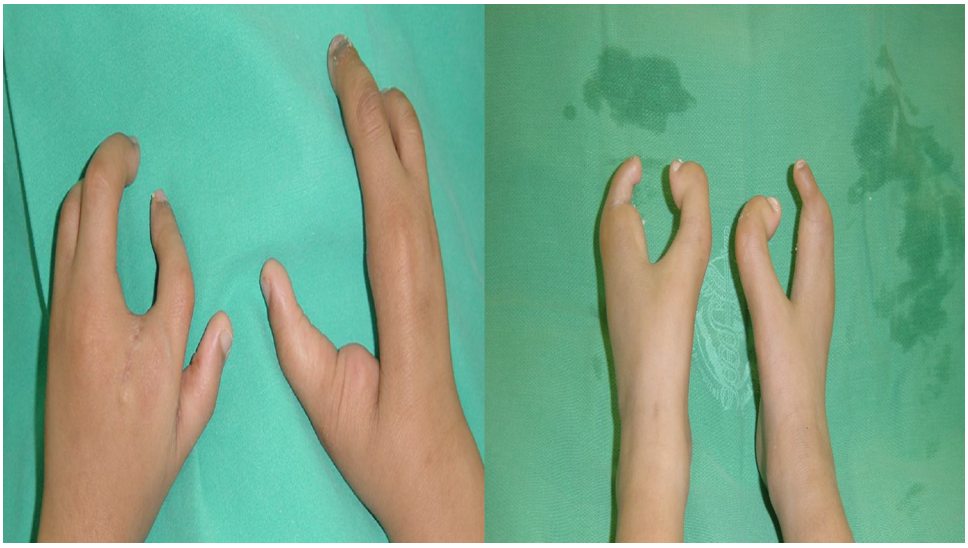

Fig. 2. Deformities of the hands and feet.

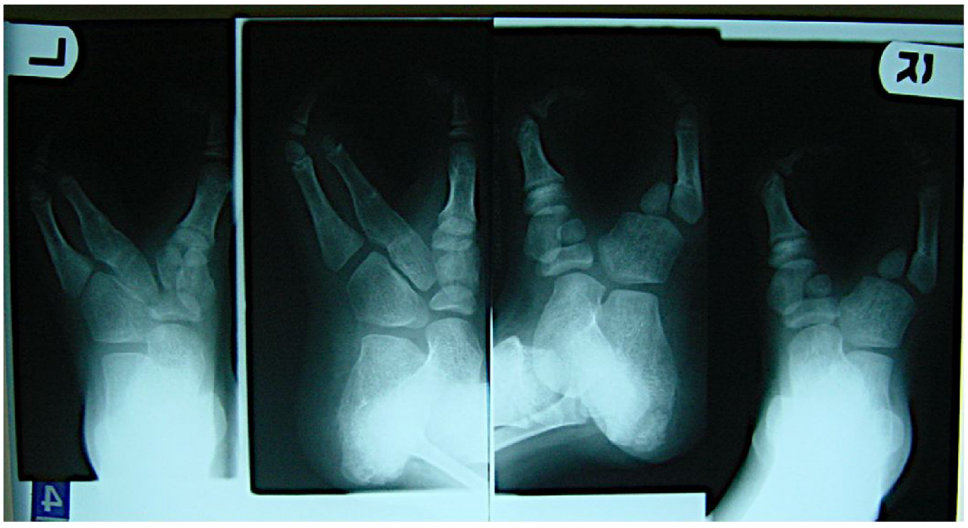

Fig. 3. Both feet show aplasia of the central rays.

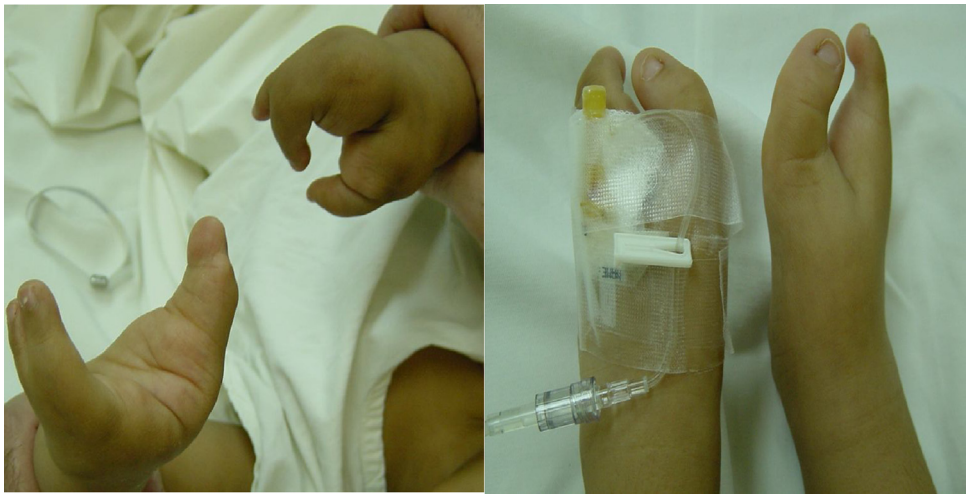

Fig. 4. Anomalies of the hands and feet.

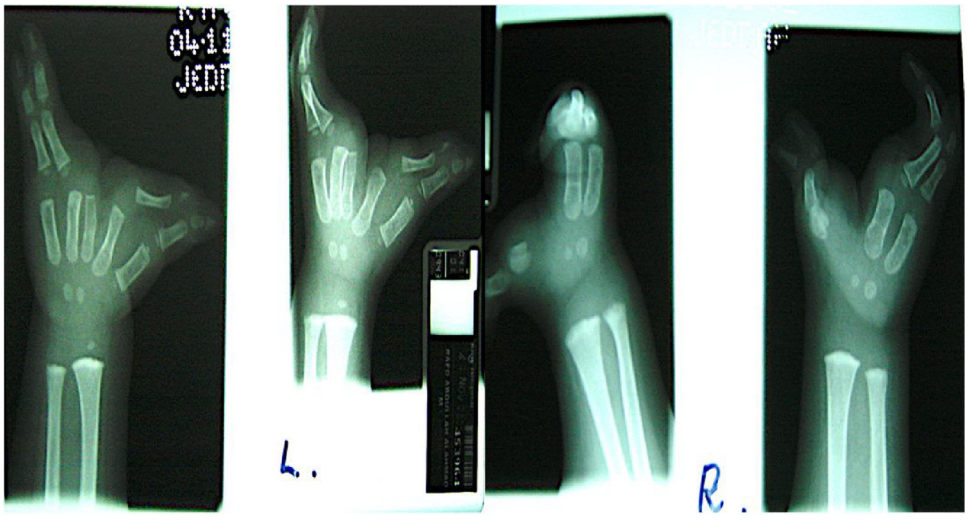

Fig. 5. X-rays of the hands showing deformities.

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.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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.

References

[1] A. Elliott, J. Evans, A. Chudley, Split hand foot malformation (SHFM), Clin. Genet. 68 (6) (2005) 501–505.
[2] A.M. Elliott, M.H. Reed, A.E. Chudley, B.N. Chodirker, J.A. Evans, Clinical and epidemiological findings in patients with central ray deficiency: split hand foot malformation (SHFM) in Manitoba, Canada, Am. J. Med. Genet. 140A (2006) 1428–1439, http://dx.doi.org/10.1002/ajmg.a.31245.
[3] L. Dai, Y.H. Li, Y. Deng, J. Zhu, Y.P. Wang, J. Liang, Y.W. Zhang, Z.Y. Liu, Prevalence of congenital split hand/split foot malformation in Chinese population, Sichuan Da Xue Xue Bao Yi Xue Ban 41 (2) (2010) 320–323.
[4] H.E. Shamseldin, M.A. Faden, W. Alashram, F.S. Alkuraya, Identification of a novel DLX5 mutation in a family with autosomal recessive split hand and foot malformation, J. Med. Genet. 49 (1) (2012) 16–20.
[5] M. Faiyaz ul Haque, S. Uhlhaas, M. Knapp, H. Schüler, W. Friedl, M. Ahmad, P. Propping, Mapping of the gene for X-chromosomal split-hand/split-foot anomaly to Xq26-q26.1, Hum. Genet. 91 (1) (1993) 17–19.
[6] R.A. Agha, A.J. Fowler, S. Rammohan, I. Barai, D.P. Orgill, the PROCESS Group, The PROCESS statement: preferred reporting of case series in surgery, Int. J. Surg. 36 (Pt. A) (2016) 319–323.
[7] A. Sowińska-Seidler, M. Socha, A. Jamsheer, Split-hand/foot malformation – molecular cause and implications in genetic counseling, J. Appl. Genet. 55 (1) (2014) 105–115, http://dx.doi.org/10.1007/s13353-013-0178-5.
[8] A.K. Ray, Another case of split foot mutation in two sibs, J. Hered. 61 (1970) 169.
[9] A. Freire-Maia, A recessive form of ectrodactyly, and its implications in genetic counselling, J. Hered. 62 (1971) 53.
[10] I.C. Verma, R. Joseph, S. Bhargava, S. Mehta, Split-hand and split foot deformity inherited as an autosomal recessive trait, Clin. Genet. 9 (1976) 8–14.
[11] M. Mufti, S. Wood, Ectrodactyly in sisters and half sisters, J. Med. Genet. 24 (4) (1987) 220–224.
[12] A. Al-Jobair, A. Al-Saleem, Possible association between acetazolamide administration during pregnancy and multiple congenital malformations, Drug Des. Dev. Ther. (2016) 1471.
[13] Han Kang, et al., Pregnancy outcomes among U.S. Gulf war veterans: a population-based survey of 30,000 veterans, Obstet. Gynecol. Surv. 57 (3) (2002) 144–145, Web.
[14] David N. Cowan, et al., The risk of birth defects among children of Persian Gulf war veterans, Obstet. Gynecol. Surv. 52 (11) (1997) 672–673, Web.
[15] K. Leung, N. MacLachlan, W. Sepulveda, Prenatal diagnosis of ectrodactyly: the 'lobster claw' anomaly, Ultrasound Obstet. Gynecol. 6 (6) (1995) 443–446.
[16] B. Rochelson, M. Blitz, Prenatal diagnosis of ectrodactyly in the first trimester by three-dimensional ultrasonography, Am. J. Perinatol. Rep. 06 (01) (2016) e142–e144.