Causes of Mutation Article 4:

DNA building mistakes: Ectrodactyly/ SHFM

Genetic mutations leading to disease are often thought to be caused by things outside the human body such as chemicals and radiation, this is a misconception. Many times the human body and the machinery it uses in cell division and DNA replication make mistakes, causing genetic mutations. These genetic mutations can sometimes lead to diseases; below is an example of a diseases caused by these types of mistakes.

Malformed: abnormally formed; misshapen

Syndromatic: concerning a group of symptoms that consistently occur together

Homeobox genes: A large family of genes that direct the formation of body structures during development.

Ectrodactyly/split hand feet malformation

Source:

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Abstract

Split-hand/split-foot malformation is a rare limb malformation with splits in the middle of hands and feet as well as deformed toes and fingers. When this genetic disease happens as an isolated event in a family it is usually inherited as a dominant disease. This study presents a case where the disease is inherited as a recessive trait. The study also discusses prenatal and genetic counseling as well as treatment for the malformation.

Introduction

Split-hand/ split foot malformation (SHFM)/ ectrodactyly, also known as "lobster claw hand," is a limb malformation involving the centers of hands and feet. This malformation presents as fused fingers and toes as well as malformation of the fingers and toes. There is a central split in the hands and feet due to the absence of the middle fingers and toes, giving the appearance of a lobster. [1]

A case of ectrodactyly involving both hands and feet is reported here.

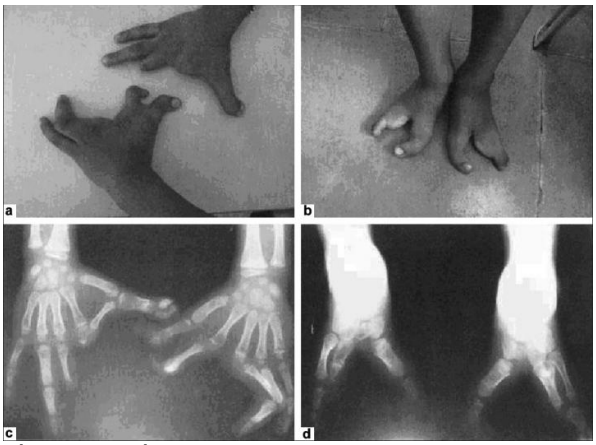

Figure 1a-d
a. Split hands b. Split feet c. X-ray of split hands showing fusion of fingers d. X-ray of split feet showing no middle toes and fusion of toes.

Case Report

A 6 ½-year-old boy presented with deformed hands and feet since birth. There were central splits in both hands. In the left hand the middle and ring finger were fused as well as the thumb and the index finger. In the right hand the index finger and thumb were fused [Figure 1a]. The X-rays of the hands [Figure 1b] showed normal finger in both hands but the absence of the middle and pinky finders in both hands. Both the feel also had a deep cleft down the center [Figure 1c and 1d]. There was fusion of toes and absence of middle toes in both feet.

The child had no other malformed features and the proportions of the body where within normal limits. The physical examination was normal as well. The child did well in school and was developmentally normal for his

age. The child's parents were un-related and he was delivered after a normal length pregnancy with no problems occurring immediately before or after birth.

Discussion

SHFM involved central splits of the hands and feet with associated fusion and malformation of fingers and toes. [1] Its incidence has been reported to be about 1 in 90,000 babies with no bias towards either sex. [2] Two expressions of SHFM occur, one with isolated involvement of the limbs, known as the non-syndromatic form, and the second, the syndromatic form, with associated abnormalities such as malformed legs, mental retardation, skin and skull malformations, cleft palates and deafness. [3] Our case belongs to the non-syndromic type of SHFM as there are no associated abnormalities.

Five different genetic mutations are known to be associated with SHFM. Type I, the most frequent variety, is due to a mutation on chromosome 7 in a region that contains two homeobox genes, DLX5 and DLX6. [1] The syndromic form has a variable degree of expression. The non- syndromal SHFM limited to hands and feet usually follows the pattern of inheritance seen in dominant genes with high penetrance. [4] Howeverm in out case, the probably inheritance pattern is autosomal recessive as only siblings and no other family members were affected.

There have been isolated case reports in the literature of the recessive inheritance pattern of the SHFM non-syndromal type. Verma *et al.* described split-hand and split-foot in two siblings born from two unrelated parents, this indicate that the split-hand and -foot malformation can be inherited as a recessive trait. [5] Ray and Freire-Maia also reported recessive ectrodactyly. [6,7] Klein also reported ectrodactyly in who siblings born from a man and the daughter of his half brother. [8] Zlotogora and Nubani described a family in which four siblings had typical SHFM, this also suggests a recessive form of the disorder. However, a two-locus model has also been suggested as an alternative possibility. In the two-locus model, the dominant mutation leading to the SHFM is controlled by a gene at another locus. A dominant mutation at the controlling locus leads to non-penetrance of the split hand/ foot mutation and the appearance of normal carries. [9]

Ectrodactyly can be treated surgically in order to improve function and appearance. Prosthetics may also be used. [2] Parents should be counseled regarding the possibility of recurrence of the disease in future children and a pre-natal diagnosis by ultrasonography should be offered. [3.10]

References

1. %183600 split-hand/foot malformation 1; SHFM1. Available from:http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?cmd=entryandid=183600 [accessed on 2007 Jun 13]
2. Vadoma. Available from: http://en.wikipedia.org/wiki/Vadoma#column-one#column-one[accessed on 2007 Jun 13]
3. Pinette M, Garcia L, Wax JR, Cartin A, Blackstone J. Familial ectrodactyly. J Ultrasound Med.2006;25:1465–7. [PubMed]
4. Zlotogora J. On the inheritance of the split hand/split foot malformation. Am J Med Genet.1994;53:29–32. [PubMed]
5. Verma IC, Joseph R, Bhargava S, Mehta S. Split-hand and split-foot deformity inherited as an autosomal recessive trait. Clin Genet. 1976;9:8–14. [PubMed]
6. Ray AK. Another case of split foot mutation in sibs. J Hered. 1960;61:169–70. [PubMed]
7. Freire-Maia A. A recessive form of ectrodactyly and its implications in genetic counselling. J Hered. 1971;62:53. [PubMed]
8. Klein IJ. Hereditary ectrodactylism in siblings. Am J Dis Child. 1932;43:136–42.
9. Zlotogora J, Nubani N. Is there an autosomal recessive form of the split hand and split foot malformation? J Med Genet. 1989;26:138–40. [PMC free article] [PubMed]
10. Arbués J, Galindo A, Puente JM, Vega MG, Hernández M, de la Fuente P. Typical isolated ectrodactyly of hands and feet: Early antenatal diagnosis. J Matern Fetal Neonatal Med.2005;17:299–301. [PubMed]