Wolf–Hirschhorn syndrome: A case demonstrated by a cytogenetic study

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We present a case with a 4p terminal deletion, evidenced in GTG-banded chromosome study. Phenotypic signs described in the classical Wolf–Hirschhorn syndrome were found on clinical examination of our patient.

Key words: Chromosomes, chromosome deletion, karyotyping, 4p, micrognathia, Wolf–Hirschhorn syndrome

Introduction

The Wolf–Hirschhorn syndrome (WHS) is a rare chromosomal disorder associated with a partial deletion of the short arm of chromosome 4. The syndrome is named after K. Hirschhorn and German U. Wolf who independently found the 4p-chromosome abnormality in the 1960s[1] and was first independently published in 1965 by Wolf et al. and Hirschhorn et al.[2]

Wolf–Hirschhorn syndrome is a condition that affects many parts of the body. The major features of this disorder include a characteristic facial appearance such as a high forehead, highly arched eyebrows, epicanthal folds, fish-like mouth, low set ears, micrognathia (a small chin), congenital hypotonia, low birth weight, dental problems including missing teeth, and cleft lip or cleft palate.[3]

Case Report

The proband was the third child of non-consanguineous parents. The proband was born at term by normal delivery. He did not cry immediately after birth. Unfortunately proband died after 3 days of birth. He presented with distinctive facial features: he had low set ears, cleft palate (an opening in the roof of the mouth), and micrognathia (a small chin). Genitalia was observed male, but the infant had un-descended testes with no regular or well-developed scrotal sac. Examination shows foot deformity.[4,5]

Ultrasound examination of abdomen was reported to show a small kidney measuring 2 × 2 cm. According to Ballard gestational score, he corresponds to 32 weeks of gestation.

Cytogenetic analysis from peripheral blood lymphocyte culture showed the proband having a terminal deletion of chromosome 4 at p14 region large enough to be detected using standard GTG-banding method. The karyotype revealed 46,XY,del(4)(p14)] [Figure 1].

Discussion

Wolf–Hirschhorn syndrome is a malformation syndrome associated with a terminal deletion of chromosome 4. This chromosomal change is also reported as 4p-. The size of the deletion varies among affected individuals; studies suggest that larger deletions...
tend to result in more severe intellectual disability and physical abnormalities than smaller deletions.

WHS is a contiguous gene syndrome, in which the phenotype depends on the deletion of several different genes present in the homologous chromosome regions. Conventional G-banded cytogenetic studies detect a deletion in the distal portion of the short arm of one chromosome 4 involving band 4p14 in approximately 50%–60% of individuals with WHS.\(^6\)

The prevalence of WHS is estimated at approximately 1:50,000 births. Wolf–Hirschhorn syndrome is more common in females than in males, with a male-to-female ratio of 1:2.\(^2\) Usually, the condition is detected in the newborn period because of dysmorphic features.

The proband having a terminal 4p deletion large enough to be detected using standard GTG-banding method.

Cytogenetic investigation of both the parents was done. Paternal karyotype was normal but maternal karyotype was found to be abnormal 46,XX,inv(4)(p14;q35) [Figure 2].

Structural chromosomal rearrangements can have various reproductive outcomes ranging from infertility to a fetus with a normal karyotype or a fetus with unbalanced chromosomal rearrangements resulting in monosomy or trisomy of the these chromosomes or fetus can also inherit the apparently balanced rearranged chromosome of mother.\(^6\) Structural chromosomal aberrations can lead to a wide variety of serious clinical manifestations, including mental retardation (MR) and congenital malformations.

Chromosomal microarray technology as well as FISH (Fluorescence in situ hybridization) and/or G-banded cytogenetic studies may be necessary for complete characterization of the chromosome rearrangement associated with WHS.\(^6\) The genetic counseling, prenatal diagnosis can be offered to determine the chromosomal status of subsequent pregnancies along with monitoring for fetal anomaly scan in all viable future pregnancy.

References


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