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WOLF-HIRSCHHORN SYNDROME: REPORT OF TWO CASES DEMONSTRATED BY CYTOGENETIC STUDY FROM WESTERN INDIA

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ABSTRACT
We present two cases with Wolf-Hirschhorn Syndrome (4p16 deletion) evidenced by GTG-banding chromosome study. Phenotypic features were not so prominent of classical Wolf-hirschhorn Syndrome during clinical examination.

KEYWORDS: Wolf-Hirschhorn syndrome, GTG-banding, Karyotyping, 4p16.3, deletion.

INTRODUCTION

The Wolf-Hirschhorn Syndrome (WHS) is well known rare chromosomal disorder associated with multiple malformation. The WHS affects 1:50,000 live births and interestingly with 2:1 female to male ratio.[1,2] WHS caused by deletion of Wolf-Hirschhorn Syndrome critical region (WHSCR) within 4p16.3. About 55% have pure deletion; 40 – 45% have unbalanced translocation and remaining have other complex chromosomal rearrangements.[3]

WHS has variety of clinical features such as "Greek warrior helmet" appearance, high forehead, fish like mouth, mild to severe mental retardation, hypotonia, low set ears. Some of these individuals do not show consistent clinical features of WHS and others have overlap to WHS.[4]

CASE REPORT

Case-1: The proband was second child of non-consanguineous parents. A 10 month- old girl presented with dismorphic features and mental retardation. She had low set ears, high forehead, hypotonia and hypertelorism (Fig – 1), The girl was born with low birth weight of 1.6 kg. The father was 32 and mother was 29 at the time of delivery.

Cytogenetic analysis of peripheral blood lymphocytes culture showed the proband had a terminal deletion of chromosome 4 at p16 (4p16) which was detected by GTG-banding technique.[5] The karyotyped revealed 46,XX,del(4) (p16) (Fig – 2).

Case – 2: A nine month old boy presented with dinstinctive facial features such as microcephaly, hypertelorism, prominent globella, broad nose, micrognathia and ambigious genetalia. The boy was born with normal birth weight. The father was 30 and mother was 28 at time of delivery. The proband was second child of non-consanguineous parents.

Cytogenetic analysis revealed a terminal deletiom of chromosome 4 at p16 (4p16) was detected by GTG-banding technique. The karyotyped revealed 46,XY,del(4)(p16) (Fig. – 3).

DISCUSSION

The WHS is a chromosome deletion syndrome with a well delineated phenotype. The majority of cases are the results of hemizygosity of 4p16.3 and a 165 Kb critical region was delineated in 1997, based on children with overlapping deletion [1]. WHS is a contiguous gene syndrome where phenotype depends on the deletion of several different genes present in the homologuous chromosome. Conventional G-banding detect a deletion in distal region of short arm of chromosome 4p16 in approximately 50 to 60% [2] . WHS children have pre- and post-natal growth retardation, feeding difficulties and development delay congenital anomalies include congenital heart disease, renal and ophthalmic anomalies.[6]

Several early studies stated that there was no relationship between the severity of phenotype and deletion size. This would suggest that mortality should be independent. The variability of WHS persentation has been attributed to the size of deletions. For instance, Zollino et al.[7] define a patient with deletion between 5 – 18 mb as "classic WHS" which presents major malformations.

Conclusively, WHS presents a borad spectrum possible phenotypic abnormalities followed by developmental

delay. Therefore it requires prenatal chromosomal analysis.

Also postnatal recognition of WHS requires genetic counseling and testing of parents.

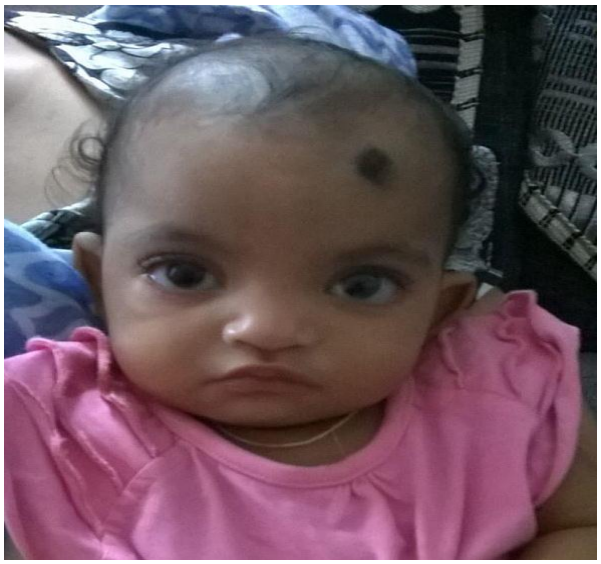

Figure 1. Characteristic dysmorphic features of Case -1.

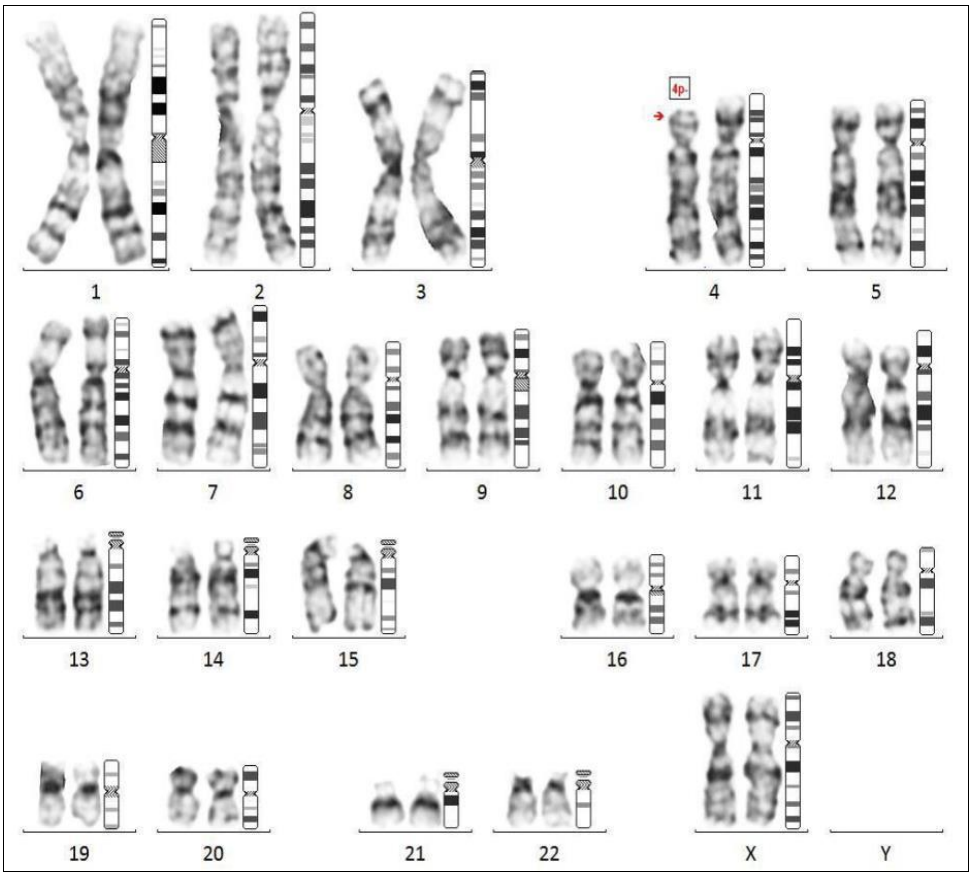

Fig. 2 G-banded karyotyped of Case -1 showing 46,XX,del(4)(p16) chromosome complement.

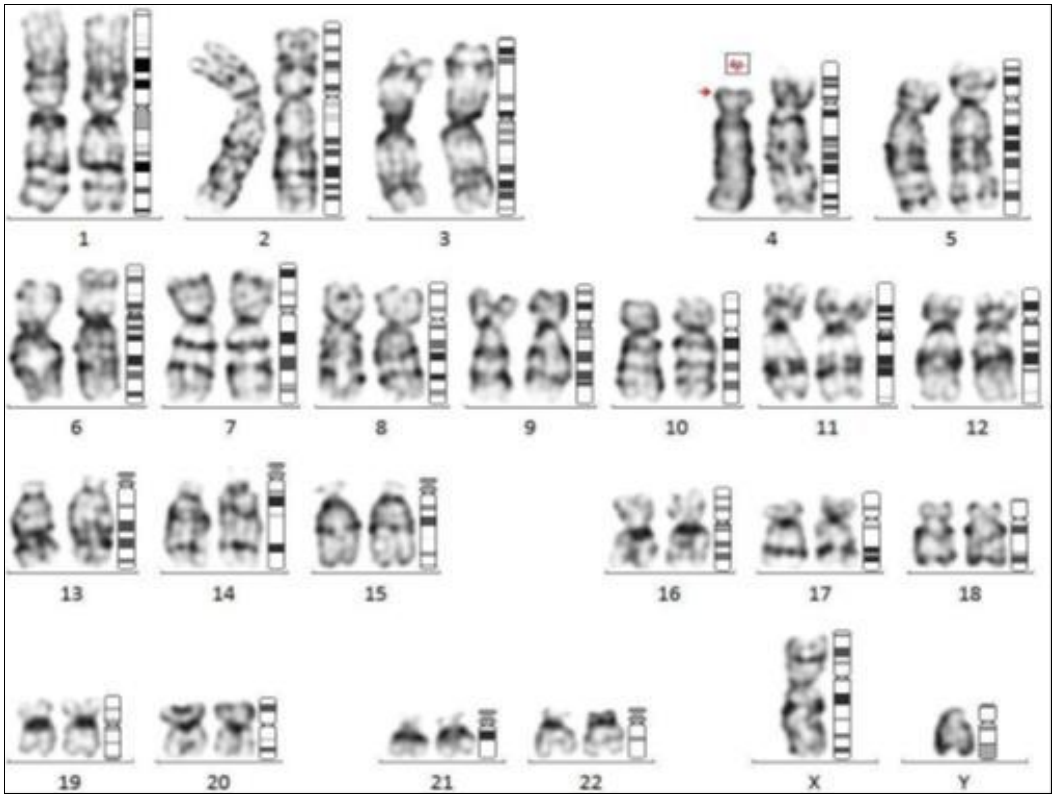

Fig. 3. G-banded karyotyped of Case -2 showing 46,XY,del(4)(p16) chromosome complement.

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