

Case Report

A case report on Wolf-Hirschhorn syndrome

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ABSTRACT

Wolf-Hirschhorn syndrome is a genetic condition that affects many systems of the human body. It is caused by a deletion of the band 4p16.3 and this deletion may be sub microscopic. Individuals affected by the syndrome have a special phenotype: wide bridge of the nose, widely spaced eyes, micrognathia, microcephaly, growth retardation, cryptorchidism, heart defects, hearing loss and severe intellectual disability. A familial translocation is seen in 5-13% of the patients. Other patients have de novo deletions, usually on the paternal chromosome 4, or de novo translocations in 1.6%. Prenatal diagnosis is possible. We are hereby reporting a case of 9 months old infant who showed delayed physical and neurocognitive development and a characteristic appearance, which led to the diagnosis of this genetic disease.

Keywords: Wolf-Hirschhorn syndrome, Microcephaly, Micrognathia

INTRODUCTION

The Wolf-Hirschhorn syndrome (WHS) is a rare chromosomal disorder associated with a partial deletion of the short arm of chromosome 4. This syndrome was named after K. Hirschhorn and German U. Wolf who independently found the 4p-chromosome abnormality in the 1960s.¹ It was first independently published in 1965 by Wolf and Hirschhorn et al.² It is seen in 1/50,000-1/20,000 births, with a female predilection of 2:1.³ The most common facial characteristics are the “Greek warrior helmet” like facies, such as a broad, flat nasal bridge and a high forehead. Midline defects in the brain, heart, palate and genitalia are also seen.^{4,5} It is associated with distinct craniofacial phenotype (microcephaly, micrognathia, ocular hypertelorism, prominent glabella, dysplastic ears and periauricular tags) growth and mental retardation, delayed psychomotor development, difficulty in ambulation with ataxic gait, muscle hypotonia and congenital heart defects. Other less common features include hypospadias, colobomata of the iris, renal anomalies, and deafness. Another characteristic feature is seizures where approximately 90% of individuals with

WHS are affected.⁶ Different mechanisms have been reported to cause WHS, such as de novo deletions, familial translocations, and de novo translocations.⁷ Nearly 35% of the patients die in 1st year of life due to congenital heart disease.⁸

CASE REPORT

A 9-month-old female infant presented with 2 episodes of unprovoked generalized tonic clonic seizures (GTCS). She had global development delay. She was born at 35 weeks of gestation and was resuscitated with bag and mask ventilation at birth. Her birth weight was 1.5 kg (SFD). Her follow up neuro-sonogram showed periventricular leukomalacia, stage-2. Her family history was non-contributory.

On examination, she had failure to thrive, had microcephaly, hypertelorism, low set ears, frontal prominence, flat nasal bridge, short philtrum, micrognathia and clinodactyly. She had development delay, development age was corresponding to 4 months,

with generalized hypotonia. Rest of the examination was unremarkable (Figure 1).



Figure 1: Wolf-Hirschhorn syndrome child.

Her laboratory investigations revealed normal blood counts, normal renal function and liver functions tests. She had normal serum electrolytes. MRI brain was also normal. 2-D echocardiography showed ASD (ostium secundum). Ophthalmic evaluation showed hypertelorism with canthal index of 42.8, interpupillary distance of 45 mm and no evidence of papilledema. Her karyotyping showed 46 XX,4 p deletion.

On the basis of clinical features and karyotyping diagnosis of Wolf-Hirschhorn syndrome was made. The child was initiated on oral sodium valproate (20 mg/kg/day) and she did not have seizures on follow up.

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.⁹

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.⁹

Microdeletion involves WHSC1, LETM1 and MSX1 genes. It is believed that loss of the WHSC2 gene is associated with many of the characteristic facial features of Wolf-Hirschhorn syndrome and developmental delay.

Apart from 5-13% of patients showing a translocation responsible for the syndrome, the rest is *de novo* deletions, usually on the paternal chromosome 4, or *de novo* translocations in 1.6%. Recurrence risk is low in *de novo* deletions and translocations, but is remarkably increased in familial translocations. Prenatal diagnosis is possible again by FISH. Early diagnosis by identification of facial features will help in managing the learning difficulties.⁸

CONCLUSION

Genetic anomalies remain one of the biggest problems of modern paediatrics worldwide. There are no distinct etiological and pathogenic mechanisms we could influence to prevent a variety of chromosomal abnormalities. A wide range of laboratory-instrumental methods of diagnosis are now available, and the latest developments in treatment are used to improve the quality of life for patients with different genetic abnormalities, and help them to sufficiently adapt to society, even if long-term prognosis is unfavourable.

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