CASE REPORT

Wolf–Hirschhorn Syndrome

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ABSTRACT

Chromosomal abnormalities are important cause of mental retardation and congenital anomalies. We report a case of a rare chromosomal disorder, Wolf-Hirschhorn syndrome, caused by deletion of short arm of chromosome 4. It was characterized by well-described facial appearance, seizures, microcephaly and midline closure defects along with growth and mental retardation.

Key words: Dysmorphism. Seizures. Midline defects. Wolf-Hirschhorn syndrome.

INTRODUCTION

Wolf-Hirschhorn syndrome is a well-known contiguous gene syndrome resulting from a deletion in the terminal band of the short arm of chromosome 4 (4p 16.3).¹ The cause in 87% of cases is a de novo interstitial deletion of preferentially paternal origin, while the remaining 13% are due to unbalanced product of a parental chromosomal rearrangement, usually a reciprocal translocation, which can be demonstrated by FISH (Fluorescence in situ hybridization) technique in cytogenetically normal parents of affected offspring.²

It occurs more frequently in females with a male to female ratio being 1:2, manifesting as severe growth retardation, mental retardation, seizures, multiple congenital anomalies and characteristic dysmorphic features including prominent glabella, hypertelorism, broad beaked nose, collectively described as “Greek Warrior Helmet” faces.³ Ocular abnormalities can occur in the form of downward palpebral slants, epicanthic folds, strabismus, ptosis, cataract, congenital nystagmus and coloboma.⁴ Short philtrum, cleft lip or palate, bifid uvula, micrognathia and ear anomalies may be observed in some patients. Sensorineural hearing loss, brain malformations, complex cardiac defects, gut and genitourinary abnormalities have also been seen along with abnormal dermatoglyphics, skeletal deformities and a variety of other manifestations (Table I).

The most common method to detect this disorder is G-banded cytogenetic analysis, both conventional and high-resolution, giving positive yields in about 60-70% cases, while FISH technique allows detection of very small deletions and subtle translocations, difficult to analyze with other methods.⁵ Since no treatment exists for the underlying genetic disorder, a multidisciplinary approach is required along with symptomatic management.

The present report describes a case of this rare syndrome.

CASE REPORT

A 4 years old boy presented in the outpatient department with concern of failure to thrive. He was born to consanguineous parents with unremarkable family history, all other siblings being healthy. He was a developmentally delayed child with history of low birth weight, though, antenatal and perinatal events were insignificant. Parents noticed failure to thrive and delayed motor milestones including absence of speech with productive language limited to monosyllables till now, but his comprehension and interaction with environment was fairly good. He could walk unsupported, but needed assistance in feeding and dressing/undressing himself, although he had a lively and social behaviour. Seizures had begun at 3 years of age, which were generalized and tonic-clonic in nature. Physical examination revealed an obviously short-statured, malnourished boy with a height of 92cm

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Table I: Clinical spectrum of Wolf-Hirschhorn syndrome.

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<th>Minimal diagnostic criteria</th>
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<tr>
<td>Distinctive facial features</td>
<td>Feeding difficulties</td>
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<td>Mental retardation</td>
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<td>Midline closure defects</td>
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<td>Eye/optic nerve defects</td>
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<td></td>
<td>Cleft lip/palate</td>
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<td>Genitourinary tract defects</td>
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<td>Structural brain anomalies</td>
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As the clinical features included developmental delay, seizures, distinct facial appearance and midline closure defects, a genetic testing was performed for suspected chromosomal abnormalities in the form of conventional cytogenetic studies of the child as well as both the parents. The karyotyping revealed a structural defect in one of the “G” chromosomes of the patient, while study of both the parents was normal. High-resolution cytogenetics and FISH technique were not performed due to non-availability of facilities.

The initial evaluation of the child also revealed disturbed background on electroencephalography with epileptic findings. Renal dysplasia was found in the right kidney on abdominal ultrasound with mild dilatation of calyceal system of the left kidney, while Te99 DTPA (Diethylene Triamine Penta Acetate) scintigraphy showed absent/non-functioning right kidney. Other imaging studies performed were VCUG (voiding cystourethrogram), echocardiography and CT scan of brain, which were all normal. Audiometry, otological evaluation and the fundoscopic examination were also unremarkable.

The patient is on regular follow-up and taking anticonvulsant therapy since the diagnosis of seizure disorder. He has not undergone surgery (palatoplasty) for cleft palate yet but is visiting the speech therapy clinic with a good compliance. There are regular visits in dental and ENT outpatient departments as well for detection of teeth abnormalities and otitis media respectively, which are common complications in patients with cleft palate. The nature of the condition was discussed with the parents and the developmental assessment planned for future visits including speech therapy with referral to early intervention and appropriate school placement.

REFERENCES


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