Case Report

Wolf–Hirschhorn syndrome

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Abstract

The Wolf–Hirschhorn syndrome (WHS) is a rare chromosomal disorder associated with a partial deletion of the short arm of chromosome 4. The major features of this disorder include a characteristic facial appearance such as a high forehead, highly arched eyebrows, epicanthal folds,coloboma iris and retina, short philtrum, fish-like mouth, low set ears, micrognathia, delayed growth and delayed developmental milestones, intellectual disability and seizures. We are hereby reporting a case which showed typical phenotypic facial features at birth with cloudy cornea.

Key words: High forehead, Highly arched eyebrows, Epicanthal folds, Fish-like mouth.

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].

WHS is a rare disorder which is misdiagnosed and hence, is underestimated. It is rare in occurrence with frequency ranging from 1 per 20,000 to 1 per 50,000 births [3, 4].

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, delayed growth and delayed developmental milestones, intellectual disability and seizures. It is characterized by congenital hypotonia, low birth weight, dental problems including missing teeth, and cleft lip or cleft palate [5]. Ocular abnormalities are characteristics of this syndrome such as hypertelorism, strabismus, refractive errors, epicanthalfolds, proptosis, downslanting palpebral fissures, microophthalmos, microcornea, iris coloboma, optic nerve coloboma, ocularcysts, ptosis, glaucoma and nystagmus [6]. In a previous case report megalocornea and buphthalmos were observed [7].

Associated heart defects includes Ventricular septal defects and left hypoplastic heart, Abnormalities of brain, genitourinary system, skeletal system can also be associated features in this syndrome.

Case Report

A term female baby born to a 3^0 consangious married couple with birth weight of 2.6 kg was referred to our hospital in view of thick meconium stained amniotic fluid and dysmorphic facial features. On examination vitals and anthropometric measurements were within in normal limits. Head to toe examination revealed low set ears, micrognathia, short philtrum, depressed nasal bridge, downward slanting of palpebral fissures (Fig 2). There was a coloboma in the iris of the right eye at 6^o clock position (Fig 1) and iris of the left eye was normal. Bilaterally cornea and retina were normal. The ocular pressures in both eyes were measured and found to be slightly elevated (22 mmHg and 21mmHg in right and left eyes respectively).

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Systemic examination revealed small Patent Ductus Arteriosus which was confirmed by doing echocardiography. Other systems were found to be normal. Routine blood investigations, USG abdomen and Neurosonogram were within normal limits. Baby had hypotonia and developed recurrent aspiration pneumonia during the neonatal period. Baby expired on day 24 of life due to aspiration of milk.

Antenatal period was unremarkable.

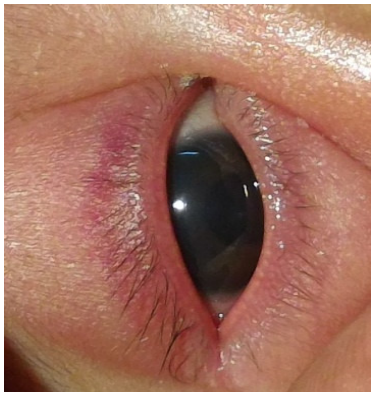

Fig -1: Coloboma of iris

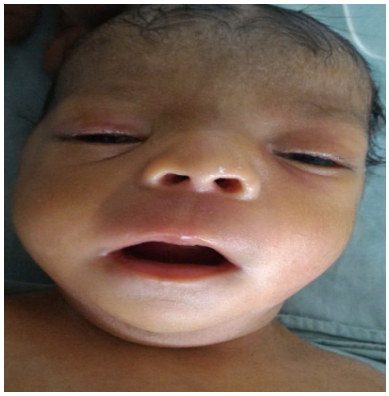

Fig-2: Dysmorphic Face

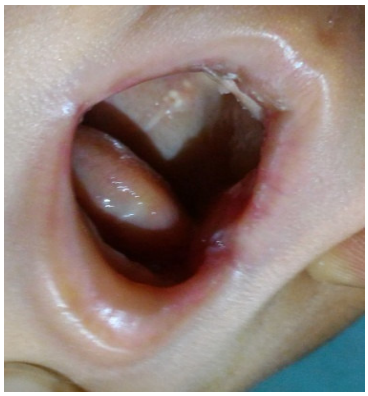

Fig-3: High Arched Palate

Discussion

Our case had many features of Wolf-Hirschhorn syndrome like hyprertelorism, downward slanting palpebral fissure, inferonasal iris coloboma, depressed nasal bridge, short philtrum, fish like mouth. Increased intraocular pressure in newborn stretches the sclera and cornea which explains the, megalocornea rather than a micro cornea usually seen in this syndrome. Our case had a significant rise of intra ocular pressure.

Microdeletion involves WHSC1, LETM1 and MSX1 genes [8]. It is believed that loss of the WHSC2gene in Chromosome 4 associated with many of the characteristic facial features of Wolf-Hirschhorn syndrome and developmental delay.

A microdeletion of band 4p16.3, can be detected only by molecular probes. The presentation and severity of this syndrome depend on the extent of the chromosomal deletion. Band 16.3 on chromosome 4p is an important region for the disorder and its deletion results in full expression of the disorder. Hence, it is also called as a critical region for the disorder. Mild cases occur with deletion of 3- 5 Mb.

Classic symptoms of WHS occur when the deletion is between 5-18 Mb. More than 22Mb deletion is considered severe [9].

To detect the deletion, techniques like micro satellite analysis, fluorescence in situ hybridization (FISH) is indicated. Fluorescence In Situ Hybridisation technique is done to exclude translocations in both the patient and her parents. Recurrence risk is low in de novo deletions and translocations, but is remarkably increased in familial translocations. Prenatal diagnosis is possible againby FISH [8].

Early diagnosis by identification of facial features and ophthalmic evaluation will help in managing the learning difficulties.

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