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(CASE REPORT)

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Wolf-Hirschhorn syndrome revealed by status epilepticus: A case report

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Abstract

A Wolf-Hirschhorn syndrome is a rare chromosomal anomaly, which results from a deletion of the distal portion of the short arm of chromosome 4 (4p-), the diagnosis is based on a clinical picture, easily recognizable in children, confirmed by molecular cytogenetics. We report the case of baby with wolf-Hirschhorn syndrome revealed by status epilepticus.

Keywords: Wolf-hischorn syndrome; Del (4) p syndrome; Subtelomeric deletion; Cranio-facial dysgenesis; Growth deficiency; Epilepsy

1. Introduction

Wolf-Hirschhorn syndrome (WHS) is defined by a set of basic characteristics, which include severe mental retardation, epilepsy, growth deficiency and cranio-facial dysgenesis. It is a rare and a sporadic syndrome occurring in 1 /20,000-1 /50,000 births [1] with a female predilection [2, 3] caused by subtelomeric deletions of the short arm of chromosome 4 (4p-). We report a five-month-old baby who present wolf-Hirschhorn syndrome revealed by status epilepticus.

2. Case report

A five-month-old baby female, from a non-consanguineous marriage, with a history of: Prenatal onset growth retardation with a birth weight of 1500g, an early neonatal infection and delay in psychomotor acquisition, the patient was admitted to our pediatric department for a generalized tonic-clonic seizure state with a background of fever. The clinical examination on admission finds a hypotonic baby with growth deficiency: which weighs 3200 g (-3SD) with size of 54 cm (-3SD) and cranial perimeter of 37 cm (-3SD), a facial dysmorphia made up of micrognathia, bilateral cleft lip and palate, wide nose, hypertelorism, right unilateral ptosis, left exophthalmos, divergent strabismus, arched eyebrows, and hemmed ears (Figure 1). The malformative assessment objectified a partial agenesis of the corpus callosum in the brain computed tomography, the Echocardiography was normal, we also performed an electroencephalogram which showed ill-defined, diffuse, a typical slow sharp element spike and wave complexes, often occurring in long bursts, activated by slow wave sleep The routine blood laboratory investigations were without anomaly, in front of this clinical picture, we evoked the wolf-hirschhorn syndrome. The diagnosis was confirmed by the karyotype through the high-resolution banding array CGH, which reveals a terminal deletion of the short arm of chromosome 4 at p16.3, with a pericentric inversion of chromosome 9. The karyotype of the parents was normal.

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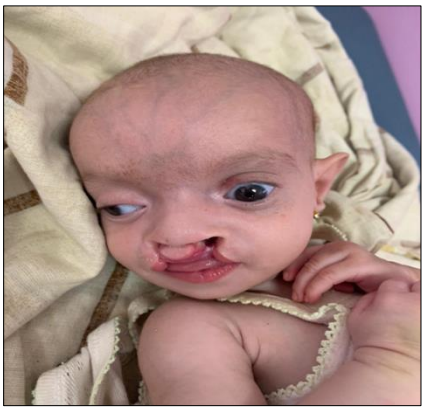

Figure 1 The facial dysmorphia of our patient: prominent glabella, arched eyebrows, hypertelorism, divergent strabismus, bilateral left Ptosis, cleft lip and cleft palate

3. Discussion

Wolf-Hirschhorn syndrome is a rare monosomal syndrome, caused by deletion of the telomeric end of the short arm of chromosome 4, approximately 20% of cases are deletions limited to the 4p16. 3 bands [4]. The critical region was in the WHSCR area that include the candidate genes: WHSC1, WHSC2, NELFA, LETM1, PIGG, CTBP1, FGFRL1 [5-7]. In other cases the deletions are more important can extend up to 4p14 [8, 9] Most cases are De novo deletions, while 20% of cases result of an unbalanced translocation in one or the other of the parents associating a deletion in 4p and a partial trisomy of another arm[10]. A few cases present with other complex rearrangements as a ring chromosome [11]. The clinical presentation correlates with the size of the deletion [3], three phenotypes were described in the literature, the mild phenotype with deletions less than 3.5 MB often undiagnosed, the moderate phenotype with deletions between 5 and 18 MB and the severe type with a very large deletions exceeding 22-25 MB [8]. The cardinal phenotype of WHS is that found in our patient, associated: growth retardation, craniofacial dysmorphia, mental retardation, and epilepsy. Prenatal onset growth retardation is observed in 80% of WHS individuals [3], as well as postnatal delay, many factors aggravate this growth delay: oral facial clefts, difficulty in sucking and gastroesophageal reflux, no hormonal cause has been identified. Typical cranio-faciale apperence has been described as “Greek warrior helmet” easily recognizable in all WHS individuals from birth to childhood, becoming less evident around puberty [11], made up of hypertelorism, prominent glabella, broad and / orbroken nose, low ears implanted at posterior angulation [2].Unilateral cleft lip and cleft palate are reported in approximately one third of patients, 40% have ocular abnormalities (divergent strabismus, foveal hypoplasia, chorioretinal coloboma), can be observed in approximately 50% [12]. Psychomotor retardation is moderate to severe with the presence of microcephaly and often structural abnormalities of the brain (fine corpus callosum). Epilepsy occurs in 95% of children with onset within the first 3 years of life and peak at around 6 to 12 months of age [8, 11], it is often triggered by fever, even of low intensity, as the case of our patient. However, some cases without abnormalities on the electroencephalogram have been reported [13, 14].other malformations are sometimes present including congenital heart defects, reported in 50% of children, a wide variety of skeletal abnormalities (60-70%), urogenital malformations (25%) include hypospadias with uni-bilateral cryptorchidism in males, and clitoral aplasia / hyperplasia, gonadal streaks and absence of uterus / vagina in females [3], a hearing loss can be detected in just over 40% of patients [15]. many cases of metabolic acidosis and malignant hyperthermia are reported in addition to a major risk of gastroesophageal reflux, immune disorder, and hepatic adenomas [16].The differential diagnosis arises with other syndromes associating growth retardation, mental deficiency, and facial dysmorphia: Seckel, CHARGE, Smith-Lemli-Opitz, Opitz G / BBB, Williams, Rett, Angelman and Smith-Magenis. The prognosis is multifactorial; depending on the extent of the deletion[7] the presence of significant chromosomal abnormalities [17], the intensity of the seizures, the presence of associated malformations including cardiac and the extent of mental retardation. The treatment is symptomatic and requires a multidisciplinary approach, including various rehabilitation programs, treatment of epilepsy and nutritional support.

4. Conclusion

A Wolf-Hirschhorn syndrome is a contiguous gene deletion syndrome, its diagnosis is based on the clinical picture, the genetic origin is currently well determined. The treatment requires a multidisciplinary approach in order to avoid chronic complications, to provide rehabilitation programmes and to offer genetic advice to these patients.

Compliance with ethical standards

Acknowledgments

We would like to thank all the residents who took part in the diagnosis of the patient.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest

Statement of informed consent

Written informed consent for participation was obtained from the patient.

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