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Case Report

Goldenhar Syndrome and Pericentric Inversion of Chromosome 9

F. Ashrafzadeh, M. Faraji[1]

Abstract
Oculo-auriculovertebral dysplasia (Goldenhar) is a congenital syndrome. Its phenotype differs from craniofacial anomalies to cardiac, vertebral or central nervous system defects. This syndrome is rare and its etiology is not apparent yet. Pericentric inversion of chromosome 9 is one of the most common structural balanced chromosomal aberrations with its incidences 15% to 25%. Herein we present a case of Goldenhar syndrome in a one-yr-old girl with pericentric inversion of chromosome 9. We used the patient's peripheral blood and studied 30 metaphase spreads on the basis of G-bands by trypsin using Giemsa (GTG) technique at 400 band resolution that revealed a pericentric inversion of chromosome 9 with break points at p11 and q13.
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Keywords ● Goldenhar syndrome ● chromosome 9 ● pericentric inversion

Introduction

Oculo-auriculo-vertebral dysplasia (Goldenhar syndrome) is a rare inherited disease and its incidence is 1/5600.[1] It has multifactor etiology that include nutritional and environmental issues and it can result in disturbances of blastogenesis involving the first and the second bronchial arches.[2] Several terms are used to describe this condition such as oculo-auriculo-vertebral (OAV) dysplasia, Goldenhar syndrome and hemifacial microsomia (HFM). Goldenhar syndrome is manifested a combination of several anomalies such as dermal epibulbar tumors, peri-auricular appendices and malformations of the ears.[3]

Some studies have suggested a disturbance of the neural crest cells as the cause of the disease.[3] Vascular abnormalities, particularly hemorrhage and expanding hematoma formation in the region of the stapedial artery have been implicated as possible environmental factors.[2] The use of some drugs such as cocaine, thalidomide, retinoic acid, and tamoxifen during pregnancy and maternal diabetes were also suspected.[2-3]

Pericentric inversions (PI) have been observed in all chromosomes except chromosome 20.[4] Scientists have tried to make an association between different clinical conditions and PI chromosome 9.[5,6] In particular, psychiatric disturbances such as schizophrenia-like syndromes,[7] personality disorders,[8] central nervous system involvements such as mental retardation, seizures, Walker-Walburg syndrome, double cortex syndrome, cerebral cysts are reported as carriers of this chromosomal rearrangement.[9,10] Herein, we present a case of Goldenhar syndrome with PI of chromosome 9.

Departments of Pediatric Neurology and Neurosurgery[1],
Ghaem Hospital,
Mashhad University of Medical Sciences,
Mashhad, Iran.

Correspondence:
Farah Ashrafzadeh MD,
Department of Pediatric Neurology,
Ghaem Hospital,
Mashhad University of Medical Sciences,
Mashhad, Iran.
Tel: +98 511 8424834
Fax: +98 5118425878
E-mail: fashrafzadeh@yahoo.com

Case report

A one-yr-old girl was referred to pediatrics division of Ghaem Hospital of Mashhad University of Medical Sciences, for seizure attacks that had started since her neonatal age. She was born with normal term vaginal delivery and normal phonotype. Her parents were not consanguineous with negative family history and their second child was healthy. Mild prenatal asphyxia was reported with seven and eight APDAR score at one and five minutes respectively. Her birth weight and head circumference were normal but psychomotor developmental milestones were slightly delayed. The patient presented facial asymmetry, hypoplasia of the mandible but no mental problems were detected at the time of the examination except Goldenhar syndrome. She had some hearing impairment and soft cleft palate deformity (Fig 1).

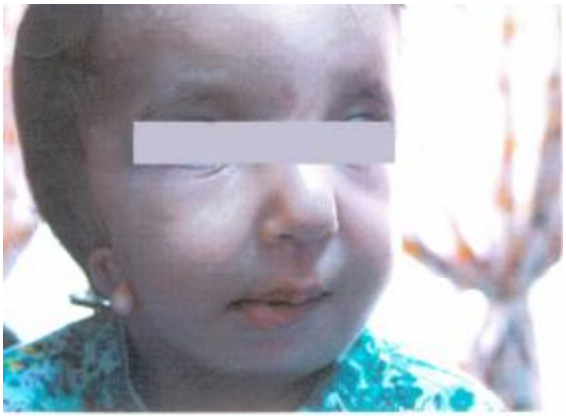

Fig 1: Facial asymmetry, microtia, Hypoplastic mandibule.

Evaluation of her orthopantomographic X-ray revealed vertebral column abnormalities in cervicothoracic spine, hypoplasia of the mandible on the left side, absence of the coronoid process and hypoplasia of the mandibular condoyle without dental hypoplasia. She had short stature, 3% below the average, and neurological examination revealed normal with the exception of facial palsy with normal brain CT-Scan. EEG showed scattered epileptiform discharges for seizures. Cytogenetic examination of the peripheral lymphocytes showed a pericentric inversion of chromosome 9 [46 XY inv 9 (p11; q13)].

Discussion

The diagnosis of Goldenhar syndrome is mainly based on the clinical aspects associated with both systemic conditions and radiological findings. Our patient had anomalies of the ear (microtia) with several periauricular tags, like what is reported by Barbosa et al.[3] Besides having facial palsy in the left side, the patient had hearing loss the same as what was reported by Sata et al.[10]

Imaging tests used for the diagnosis of the anomalies of the skeletal or facial bones are needed to reveal the macroscopic deficiency of the zygomatic bones and development symmetry.[10] Our patient had hyoplasia of mandible and agenesis of the coronoid process with lack of fusion of the zygomatic arch and agenesis of the palatine bones in the left side. Ophthalmologic and otorinolaryngologic examination is also important for the final diagnosis.[3] Epibulbar dermoid tumor is reported in some patients but was not observed in our patient. Our patient also had kidney anomalies and unilateral renal agenesis inconjunction with malformations of the ears although the last anomalies are said to uncommon.[2-10]

Goldenhar syndrome is a complex disorder, and in some cases major genetic determinants in some cases is reported. Most affected individuals are cytogenetically normal; however, a number of chromosome abnormalities have been reported to be associated with HFM.[12] We have studied 30 metaphase spreads on the basis of GTG technique at 400 band resolution of the patient's peripheral blood with the outcome of a pericentric inversion of chromosome 9 with break points at p11 and q13.[18]

The results of studies on the mouse support a genetic involvement in HFM. The recessive lethal mutation in mouse may cause hemifacial maxillary malformation in heterozygotes.[2,13] Familial cases are the best evidence which support the possibility of major effect of a single gene mutation. In these cases the condition appears to segregate in a dominant manner, albeit with variable penetrance and phenotypic expression within and between families.[1,2]

The pericentric region of 9 chromosome is highly fragile(breakage-prone)both in vivo and in vitro.[13] Several subjects carrying these apparently balanced genetic alterations showed phenotypic abnormalities without any specific picture. Psychiatric and/or neurological disorders were also often described, our case was normal in view of developmental, her CT scan was normal too, but she had seizure, while took antiepileptic drug became seizure free.[13] Delparado and Barid reported a case of cephalothoracopagus syncephalus and genitourinary tract malformations associated with PI of chromosome 9.[14,15] Miyazaki M et al also suggested the association between congenital myotonic dystrophy and PI of chromosome 9.[14] Chronic myelomonocytic leukemia has been described in a patient with an inversion 9 constitutional karyotype,[16,17] whereas, these problems were not existed in our patient.

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