IJMS
Vol 41, No 3, May 2016

Case Report

Report of a Case with Trisomy 9 Mosaicism

Mohammad Miryounesi[1], MD, PhD;
Mehdi Dianatpour[2], PhD;
Zahra Shadmani[3], BSc;
Soudeh Ghafouri-Fard[4], MD, PhD

[1]Genomic Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran;
[2]Department of Medical Genetics, Shiraz University of Medical Sciences, Shiraz, Iran;
[3]Vali-Asr Hospital, Fasa University of Medical Sciences, Fasa, Iran;
[4]Department of Medical Genetics, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Correspondence:
Soudeh Ghafouri-Fard, MD, PhD;
Department of Medical Genetics, Shahid Beheshti University of Medical Sciences, Velenjak St, Chamran Highway, Tehran, Iran
Tel\Fax: +98 21 23872572
Email: ghafourifard@razi.tums.ac.ir
Received: 13 September 2014
Revised: 02 November 2014
Accepted: 28 December 2014

Abstract

Trisomy 9 is a rare chromosome disorder with high neonatal mortality. It is often seen in mosaic form. Most patients who survive are severely mentally retarded. The main features of this syndrome are "bulbous" nose, microphthalmia, dislocated limbs, and other anomalies of skeletal, cardiac, genitourinary, and central nervous system. Most patients have developmental and cognitive impairment. Patients with mosaicism survive longer than non-mosaics, but it was believed that the degree of mosaicism in lymphocytes or fibroblasts does not associate with survival or degree of impairment. In this report, we present a 2.5-year-old male case of mosaic trisomy 9, to show the wide range of clinical findings in this chromosome disorder. The patient had cardiac anomalies, inguinal hernia, and undescendent testes. He had low-set slightly malformed ears, deeply-set malformed eyes, small palpebral fissures, micrognathia, developmental delay and unilateral optic hypoplasia. The most prominent facial anomaly in this patient was eye anomalies. Cytogenetic analysis with G banding showed karyotype 47XY,+9 in 44% of peripheral lymphocytes examined (47XY,+9[22], 46XY[28]). His parents' karyotypes were normal. Moderate developmental delay, which was detected in this patient shows that the range of motor and cognitive impairment in this chromosomal disorder is quite broad. This fact should be considered in genetic counseling as well as prenatal diagnosis of this chromosomal disorder.

Please cite this article as: Miryounesi M, Dianatpour M, Shadmani Z, Ghafouri-Fard S. Report of a Case with Trisomy 9 Mosaicism. Iran J Med Sci. 2016;41(3):249-252.

Keywords ● Mosaicism ● Chromosome 9 ● Trisomy ● Cytogenetic analysis

What's Known

- Trisomy 9, often seen in a mosaic form, is a rare chromosome disorder with high neonatal mortality.
- Most patients who survive are severely mentally retarded.

What's New

- We describe a 2.5-year-old male case of mosaic trisomy 9 with a moderate developmental delay.
- The range of motor and cognitive impairment in this chromosomal disorder is quite broad, which should be considered in genetic counselling and prenatal diagnosis of this chromosomal disorder.

Introduction

Trisomy 9 is an uncommon chromosome disorder with high neonatal mortality. It is generally seen in the mosaic state. Most patients who survive are severely mentally retarded. In a case diagnosed as complete trisomy 9 by conventional cytogenetic techniques, fluorescence in situ hybridization (FISH) studies of metaphase and interphase blood cells and skin fibroblasts could identify the presence of euploid and trisomy 9 cells. Therefore, it has been suggested that trisomy 9 may be viable only in the mosaic state, which might be remained undetected in cases diagnosed by conventional chromosome analysis of a few metaphase cells or only one tissue type.[1] The main features of trisomy 9 syndrome are "bulbous" nose, microphthalmia, dislocated limbs and other anomalies of skeletal, cardiac, genitourinary, and central nervous system (CNS). Skeletal malformations

reported in this disorder, include congenital hip dislocation, calcaneovalgus deformity, joint hyperflexation, punctate mineralization, scoliosis and kyphosis. Patients with mosaicism survive longer than non-mosaics, but it had been believed that the degree of mosaicism in lymphocytes or fibroblasts does not associate with survival or degree of impairment.[2] Atypical signs reported in trisomy 9 patients include hemivertebra,[3] holoprosencephaly,[4] sex reversal,[5] an unexpectedly normal psychomotor development,[6] no evident external or internal congenital anomalies and congenital leukemia.[7] Partial trisomy 9p cases have been also reported with dysmorphic features, congenital anomalies, severe mental retardation and gross delay in speech.[8]

In this report, we present a male case of mosaic trisomy 9 with higher survival than the mean survival mentioned for this chromosome disorder and no CNS structural abnormality, which shows the wide range of clinical manifestation of this disorder.

Case Presentation

The patient is a 2.5-year-old boy, the first child to a normal non-consanguineous parent. He was born spontaneously to a 32-year-old, G1P1A0 Iranian mother. He was delivered by cesarean section at 36 weeks of gestation because of fetal intermittent bradycardia and intra-uterine growth retardation. At the time of birth, his head circumference was 35 cm. At the age of 3 months, his chest radiograph showed an enlarged heart with prominent pulmonary vasculature. Atrial and ventral septal defects were confirmed in his echocardiogram afterwards. In addition, he had inguinal hernia and undescendent testes. Other signs include low-set slightly malformed ears, deeply-set malformed eyes, small palpebral fissures, micrognathia, developmental delay and unilateral optic hypoplasia (figure 1a and 1b). No other anomaly was detected in the brain magnetic resonance imaging (MRI). No skeletal anomaly was detected in his physical examination. He had no history of seizures. No hearing problem was detected in audiometry tests. His weight and length were below the 10th percentile. Although he had neck control at the age of 5 months, he was noted to be developing slowly afterwards, particularly in fine and gross motor skills. At the age of 2 years, he started sitting with support. He could not walk and speak until now.

Cytogenetic Studies

Cytogenetic studies were performed on peripheral blood lymphocytes of the child and both of his parents. Informed consent for the case report was obtained from the parents. Fifty metaphases were analyzed and karyograms were prepared using the Cytovision computer-assisted karyotyping system version 4.1 (Applied Imaging, Newcastle Upon Tyne, UK). The karyotypes were described according to the International System for Human Cytogenetics Nomenclature. Cytogenetic analysis with G banding showed karyotype 47XY,+9 in 44% of peripheral lymphocytes examined (47XY,+9[22], 46XY[28]) (figure 2). His parent's karyotypes were normal.

Discussion

Trisomy 9 is a rare chromosome disorder in liveborn infants, but accounts for 2.4% of spontaneous abortions.[9] Despite the difference in survival between mosaic and complete trisomic patients, the incidence of anomalies in

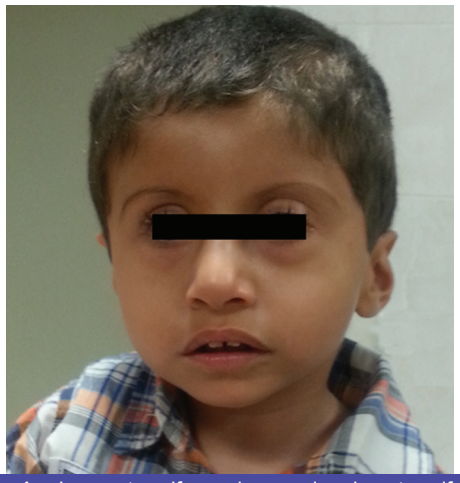

Figure 1a: Low-set malformed ears, deeply-set malformed eyes, small palpebral fissures and micrognathia are seen in patient's face.

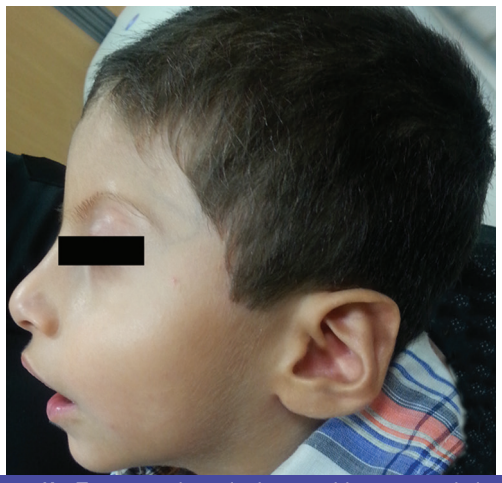

Figure 1b: Ear anomaly and micrognathia are seen in lateral view.

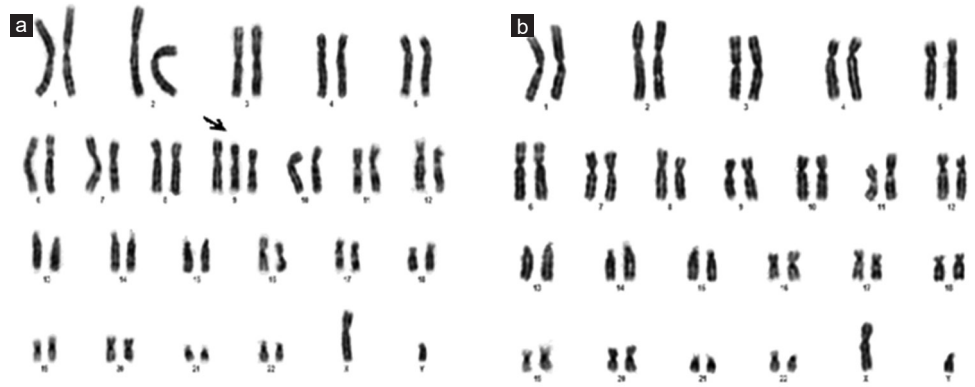

Figure 2: Chromosome analysis shows both of the mosaic karyotypes, 47XY,+9 (a) and 46XY (b).

multiple body systems is not different between them.[1] Previous reports demonstrated ocular manifestations of trisomy 9 patients as deeply-set eyes, small palpebral fissures, telecanthus, keratolenticular adhesion and marked iris hypoplasia. These manifestations are similar to Peters' anomaly, ocular lesions associated with aplasia of the optic nerve and Lowe's and Potter's syndrome.[10] In the patient presented here, the most prominent facial characteristic was his eye anomaly. No other prominent facial dismorphic feature was seen. In addition, unlike most cases of trisomy 9, no skeletal anomaly was detected in our patient. Our patient survival is greater than what is usually described in the literature. The mean survival of trisomy 9 patients is 20 days.[11] However, patients with mosaicism may survive beyond the first year of life.[12] A few cases of mosaic trisomy 9, albeit with a low proportion of trisomic cells in lymphocytes, have been reported who survive until late childhood.[13] Although most of patients had severe mental impairment, only in one third of them gross CNS structural abnormalities have been detected. Similar to most of trisomy 9 patients, no CNS structural anomaly was detected in our patient. The most common reported malformation has been Dandy-Walker malformation, which is only found in complete trisomy 9 patients. Other CNS malformations, included dilated ventricles, structural abnormalities of the lobes, and altered cellular structure.[14] An important issue raised in PND is the variation in the percentage of trisomic cells in different tissues. In such cases, ultrasound findings would help karyotyping results to achieve accurate diagnoses.[15]

Conclusion

Similar to some other cases reported in the literature, moderate developmental delay was seen in our patient, which implies that the range of motor and cognitive impairment in this chromosomal disorder is quite broad. This fact would complicate decision making in PND of this chromosomal disorder.

Acknowledgment

We thank the patient's family for participation in this study.

Conflict of Interest: None declared.

References

1. Cantu ES, Eicher DJ, Pai GS, Donahue CJ, Harley RA. Mosaic vs. nonmosaic trisomy 9: report of a liveborn infant evaluated by fluorescence in situ hybridization and review of the literature. Am J Med Genet. 1996;62:330-5. doi: 10.1002/(SICI)1096-8628(19960424)62:4<330:AID-AJMG1>3.0.CO;2-V. PubMed PMID: 8723059.
2. Arnold GL, Kirby RS, Stern TP, Sawyer JR. Trisomy 9: review and report of two new cases. Am J Med Genet. 1995;56:252-7. doi: 10.1002/ajmg.1320560303. PubMed PMID: 7778584.
3. Tarani L, Colloridi F, Raguso G, Rizzuti A, Bruni L, Tozzi MC, et al. Trisomy 9 mosaicism syndrome. A case report and review of the literature. Ann Genet. 1994;37:14-20. PubMed PMID: 8010707.
4. Gerard-Blanluet M, Danan C, Sinico M, Lelong F, Borghi E, Dassieu G, et al. Mosaic trisomy 9 and lobar holoprosencephaly. Am J Med Genet. 2002;111:295-300. doi: 10.1002/ajmg.10481. PubMed PMID: 12210326.
5. Solomon BD, Turner CE, Klugman D, Sparks SE. Trisomy 9 mosaicism and XX sex reversal. Am J Med Genet A. 2007;143A:2688-91. doi: 10.1002/ajmg.a.31996. PubMed PMID: 17935231.

6. Frydman M, Shabtal F, Halbrecht I, Elian E. Normal psychomotor development in a child with mosaic trisomy and pericentric inversion of chromosome 9. J Med Genet. 1981;18:390-2. doi: 10.1136/jmg.18.5.390. PubMed PMID: 7328619; PubMed Central PMCID: PMC1048764.
7. Djernes BW, Soukup SW, Bove KE, Wong KY. Congenital leukemia associated with mosaic trisomy 9. J Pediatr. 1976;88:596-7. doi: 10.1016/S0022-3476(76)80015-7. PubMed PMID: 1062544.
8. Shetty D, Desai K, Dave U. Trisomy 9p Syndrome in a Mentally Retarded Female Inherited from Maternal Reciprocal Translocation. Int J Hum Genet. 2006;6:203.
9. Stoll C, Chognot D, Halb A, Luckel JC. Trisomy 9 mosaicism in two girls with multiple congenital malformations and mental retardation. J Med Genet. 1993;30:433-5. doi: 10.1136/jmg.30.5.433. PubMed PMID: 8320712; PubMed Central PMCID: PMC1016387.
10. Ginsberg J, Soukup S, Ballard ET. Pathologic features of the eye in trisomy 9. J Pediatr Ophthalmol Strabismus. 1982;19:37-41. PubMed PMID: 6809924.
11. Wooldridge J, Zunich J. Trisomy 9 syndrome: report of a case with Crohn disease and review of the literature. Am J Med Genet. 1995;56:258-64. doi: 10.1002/ajmg.1320560304. PubMed PMID: 7778585.
12. Zen PR, Rosa RF, Rosa RC, Graziadio C, Paskulin GA. New report of two patients with mosaic trisomy 9 presenting unusual features and longer survival. Sao Paulo Med J. 2011;129:428-32. doi: 10.1590/S1516-31802011000600010. PubMed PMID: 22249800.
13. Okumura A, Hayakawa F, Kato T, Kuno K, Watanabe K. Two patients with trisomy 9 mosaicism. Pediatr Int. 2000;42:89-91. doi: 10.1046/j.1442-200x.2000.01159.x. PubMed PMID: 10703244.
14. Saneto RP, Applegate KE, Frankel DG. Atypical manifestations of two cases of trisomy 9 syndrome: rethinking development delay. Am J Med Genet. 1998;80:42-5. doi: 10.1002/(SICI)1096-8628(19981102)80:1%3C42:AID-AJMG7%3E3.0.CO;2-S. PubMed PMID: 9800910.
15. Saura R, Traore W, Taine L, Wen ZQ, Roux D, Maugey-Laulom B, et al. Prenatal diagnosis of trisomy 9. Six cases and a review of the literature. Prenat Diagn. 1995;15:609-14. doi: 10.1002/pd.1970150704. PubMed PMID: 8532619.