



## Dental Management of a Child With Trisomy 9 Mosaicism: A Case Report

Moti Moskovitz, DMD, PhD<sup>1</sup> Dan Brener, DMD, MSc<sup>2</sup> Raas-Rothschild Annick, MD<sup>3</sup>

### Abstract

This case report presents the dental management of a 13-year-old girl with mosaic trisomy 9. She had: (1) severe psychomotor retardation; (2) short stature; (3) progressive microcephaly; (4) flat feet; (5) genu valgum; and (6) severe kyphoscoliosis. Dysmorphic facial features included: (1) maxillary prognathism; (2) narrow high-arched palate; (3) short philtrum; (4) small low posterior dysplastic ears; and (5) down slanting palpebral fissures with right eye ptosis. The case report describes initial treatment under general anesthesia and further treatments using conscious sedation. Emphasis was placed on the need to adjust the treatment to patient's skeletal malformations and respiratory problems by adjusting her ability to sit in the dental chair in an upright position. Supernumerary premolars and opalescent changes of the maxillary incisors might be part of the clinical features related to trisomy 9 mosaic syndrome. (*Pediatr Dent* 2006;28:265-268)

**KEYWORDS:** TRISOMY 9, GENETIC DISEASE, MULTIPLE CONGENITAL ANOMALIES, MOSAICISM

*Received September 29, 2005 Revision Accepted February 21, 2006*

Trisomy 9 syndrome was first reported in 1973.<sup>1</sup> Over 50 cases have been reported since then. Of these case reports, only 5 patients reported until 1995 were older than 1.<sup>2</sup> Trisomy 9 has a mosaic or nonmosaic karyotype. Using fluorescence in situ hybridization (FISH) studies of metaphase and interphase blood cells and skin fibroblasts, Cantu et al detected the presence of euploid and trisomy 9 cells in an infant who had been diagnosed as full trisomy 9 by conventional cytogenetic studies. They suggested that earlier reports of trisomy 9 might, in fact, be mosaic trisomy 9 and that trisomy 9 may be viable only in the mosaic state.<sup>3</sup> Mosaicism for trisomy 9 predicted longer survival than non mosaic trisomy 9, while the degree of mosaicism in lymphocytes or fibroblasts did not predict the degree of impairment nor the survival.<sup>4</sup>

Individuals with trisomy 9 have 3 copies of chromosome 9 due to paternal or maternal meiosis nondisjunction or nondisjunction during mitosis (somatic cells). The majority of nondisjunction events are due to maternal meiotic nondisjunction, and incidence of trisomies like trisomy 21 are linked to advanced maternal age. Advanced maternal age remains a risk factor for maternal meiotic nondisjunction, but the understandings regarding the mechanisms behind the maternal age effect are not well understood.<sup>5-8</sup>

Trisomy 9 mosaicism is a rare chromosomal disorder in which, in addition to the aforementioned, there is also a nondisjunction error with a loss of an extra chromosome 9 in some of the cells early during the mitosis. The term "mosaic" indicates that some of the cells contain the extra chromosome 9, while others have the normal chromosomal pair.<sup>9</sup>

A major chromosomal abnormality is detected in less than 1% of live births.<sup>10</sup> The description of trisomy 9 syndrome manifestations is based on the study of more than 50 case reports—most of them in the mosaic form.<sup>11</sup> Characteristic cardiac, skeletal, craniofacial, and central nervous system malformations are the most frequent abnormalities found in the ultrasound of fetuses with trisomy 9. Intrauterine growth retardation and single umbilical artery are prevalent nonspecific findings in both nonmosaic and mosaic trisomy 9.<sup>12</sup>

Mosaic trisomy 9 is a clinically distinct syndrome. Affected patients present with: (1) congenital heart disease; (2) skeletal and genitor-urinary anomalies; (3) abnormal palmar creases; (4) failure to thrive; (5) hypotonia; and (6) mental retardation. The facial and oral manifestations include: (1) upward-slanted eyes; (2) small palpebral fissures; (3) enophthalmos or microphthalmos; (4) broad base and prominent tip of the nose; (5) low-set malformed ears; (6) microcephaly; (7) micrognathia or mandibular retrognathia; (8) protruding upper lip; (9) "pouched" cheeks; (10) cleft lip or palate; (11) narrow high-arched palate; (12) small mouth; and (13) down-turned mouth.<sup>13,14</sup>

<sup>1</sup>Dr. Moskovitz is clinical lecturer and <sup>2</sup>Dr. Brener is postgraduate student, Department of Pediatric Dentistry, School of Dental Medicine, and <sup>3</sup>Dr. Annick is senior lecturer, Department of Human Genetics, Hadassah - Hebrew University Medical Center, Jerusalem, Israel. Correspond with Dr. Moskovitz at [motimo@md.hu](mailto:motimo@md.hu)



Figure 1. Anterior view demonstrating severe anterior open bite and an increase in overjet. Notice the heavy accumulation of plaque and increased saliva secretion.

The purpose of this case report was to present the dental findings and treatment of a patient with trisomy 9 mosaicism and a description of the intraoral anomalies are presented.

### Case report

A 13-year-old girl was in the follow-up program of the Department of Pediatric Dentistry, Faculty of Dental Medicine, Hassadah – Hebrew University Medical Center, Jerusalem, Israel. Two years earlier, she was treated under general anesthesia (GA) in the department.



Figure 3. Maxillary occlusal view demonstrating a narrow high-arched palate. Maxillary central incisors demonstrate an opalescent change. The intrinsic change in color has a white appearance on the labial surface of the tooth and a yellowish color in the incisal edge.



Figure 2. Lateral view of right side in occlusion, demonstrating the micrognathia or mandibular retrognathia, protruding upper lip, anterior open bite, and an increase in overjet.

She was born following an uncomplicated pregnancy of 37 weeks to Ashkenazi Jewish parents with no family history of genetic diseases who have 4 other healthy children. Her apgar score was 7 at 1 minute and 9 after 5 minutes. At the age of 2 weeks, her mother reported that the child did not follow with her eyes and that she had an abnormal cry.

The child was examined in the genetic clinic of the Ha-dassah Medical Center at the age of 13. She presented with severe psychomotor retardation, short stature (height=129 cm, 4 standard deviations below the mean; weight=25.5 kg, 3 standard deviations below the mean). Her palm length was 8.5 cm (3%) and her third finger length was 3 cm (3 standard deviations below the mean). She had a progressive microcephaly (head circumference=50 cm, 2.2 standard deviations below the mean), flat feet, genu valgum, and severe kyphoscoliosis.

Facial dysmorphic features included maxillary prognathism (Figures 1 and 2), narrow high-arched palate (Figure 3), short philtrum, small low posterior dysplastic ears, and down slanting palpebral fissures with right eyes ptosis. The results of the chromosomal analysis were: 46 XX (17 metaphases)/47 XX +9 (7 metaphases). This karyotype was compatible with the diagnosis of trisomy 9 mosaicism.

At 11 years of age, dental treatment under GA included:

1. root canal filling of the permanent anterior right central incisor because it was necrotic with a radiographic periapical lesion;
2. amalgam and composite resin restorations;
3. fissure sealants; and
4. root extraction of left permanent first upper molar.

A supernumerary tooth was found near the apex of the permanent mandibular right second premolar and was left for observation (Figure 4).

Another dental finding was an opalescent change in both first anterior maxillary incisors. The intrinsic change in color had a white appearance on the tooth's labial surface and a yellowish color in the incisal edge (Figure 3).

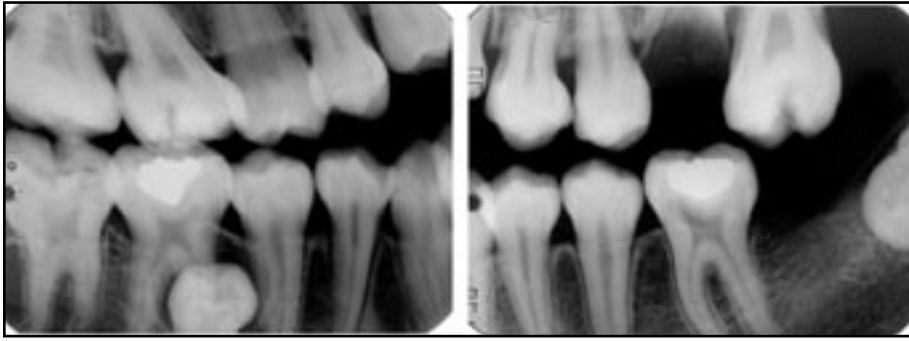


Figure 4. Bitewing radiographs at age 11 years showing severe destruction of the upper first left permanent molar's crown. A supernumerary tooth is visible near the mesial root of the right first permanent molar (arrow).

After the procedure, the parents were instructed to brush her teeth at least twice a day using tongue blade sticks taped together to maintain mouth opening during brushing. Recall appointments were carried out every 3 months for fluoride application, scaling, and plaque control. No use of mouthrinses was prescribed, due to lack of cooperation and the hazard of possibly swallowing the rinse.

During the follow-up, new additional carious lesions were diagnosed. Although maintaining oral hygiene was difficult for the parents, they were reluctant to attempt additional dental treatment under GA in order to avoid complications. Treatments were performed using 10 mg benzodiazepine (Valium) with 50% N<sub>2</sub>O/O<sub>2</sub> sedation, and the patient was monitored using a pulse oximeter during the procedure. Protective stabilization was required at the initial appointment due to lack of cooperation. Her cooperation improved during the following appointments. Because of the massive crown destruction in the lower anterior permanent teeth, pediatric strip crowns were performed. A stainless steel crown was prepared for the permanent mandibular left first molar. Other restorations were performed using amalgam and composite materials. Treatments also included fissure sealants, scaling, and, at the end of each appointment, fluoride varnish (Duraphat, Colgate, Inc) was applied.

## Discussion

There is only one case report in the literature on dental treatment of a child with trisomy 9 mosaicism.<sup>15</sup> The present case report describes the dental findings in a 13-year-old girl with trisomy 9 mosaicism.

Short stature, kyphoscoliosis, and leg deformities, as in this case, are reported in 84% of the patients with trisomy 9.<sup>2</sup> Cardiac malformations are reported in 65% of individuals with trisomy 9,<sup>2</sup> although the patient reported here had no cardiac malformations.

Due to the patient's mental retardation, treatment could only be performed under sedation in the dental chair or under GA. Her parents were ready to be present and assist with treatment to spare their child a second GA in less than 2 years. The parents' presence throughout the treatment sessions and the fact that only a small amount of dental treatment was needed allowed the authors to perform the

treatments using oral and inhalation sedation.

An emphasis was placed on the patient's skeletal malformations—particularly her kyphoscoliosis, leg deformities, and respiratory problems—and treatment was adjusted to enable the patient to sit in the dental chair in an upright position. Her tendencies to vomit and secrete saliva were another reason to adapt the facilities and use the saliva ejector underneath the rubber dam.

According to Butler et al, clinical findings that may complicate sedation or anesthesia in trisomy 9 patients include: (1) micrognathia; (2) cleft lip/palate; (3) joint contractures; (4) kyphoscoliosis; (5) narrow chest; (6) diaphragmatic hernia; (7) gastroesophageal reflux; and (8) cardiac, central nervous system, liver, vertebral, rib, and renal defects. Their recommendations for presedation evaluation are:

1. radiographic assessment for vertebral, rib, joint, and diaphragm anomalies;
2. estimation of upper airway obstruction or defects;
3. evaluation of cardiac, liver, and renal function; and
4. diagnosis of gastroesophageal reflux.<sup>16</sup>

Interestingly, the patient reported here had a supernumerary tooth in the premolar region, as described by Lopez.<sup>15</sup> Supernumerary premolars and an opalescent change in the maxillary central incisors should be added to the dental findings in trisomy 9 mosaic syndrome. No known environmental etiology could explain the opalescent appearance in the central incisors alone. Additionally, no known trauma curbed the development of these teeth and no fluoride dentifrice was used, as they are typically not recommended at an early age. Furthermore, there was no use of antibiotics or other medications that can cause enamel changes and the patient did not suffer any long high fever episodes during tooth germ development. It is especially hard to explain why the opalescent area appears merely on the central incisors, covering only part of the buccal surface. This dental finding was not previously mentioned in the literature. Dental clinical findings should be systematically examined in children with malformation syndromes.

## Summary

To avoid complication during inhalation sedation or general anesthesia in trisomy 9 patients, presedation evaluation should include:

1. radiographic assessment for vertebral, rib, joint, and diaphragm anomalies;
2. estimation of upper airway obstruction or defects;
3. evaluation of cardiac, liver, and renal function; and
4. diagnosis of gastroesophageal reflux.

During dental treatment, adjusting the treatment to the patient's special condition, namely skeletal malformations and respiratory problems, should be done by modifying

the patient's ability to sit in the dental chair in an upright position. Tendencies to vomit and to secrete saliva should be addressed by adapting the facilities and using a saliva ejector underneath the rubber dam.

Supernumerary premolars and an opalescent change in the maxillary central incisors might be part of the dental findings in trisomy 9 mosaic syndrome.

### Acknowledgements

The authors would like to thank Dr. Eliezer Eidelman for his enlightening remarks and Dr. Ziva Luria for her invaluable help.

### References

1. Feingold M, Atkins L. A case of trisomy 9. *J Med Genet* 1973;10:184-187.
2. Wooldridge J, Zunich J. Trisomy 9 syndrome: Report of a case with Crohn's disease and review of the literature. *Am J Med Genet* 1995;56:258-264.
3. Cantu ES, Eicher DJ, Pal GS, Donahue CJ, Harley RA. Mosaic vs nonmosaic trisomy 9: Report of a live-born infant evaluated by fluorescence in situ hybridization and review of the literature. *Am J Med Genet* 1996;62:330-335.
4. Schinzel A. Trisomy 8 and trisomy 9 are distinctly different clinical entities [letter; comment]. *Am J Med Genet* 1993;46:603.
5. Pellestor F, Andreo B, Arnal F, Humeau C, Demaille J. Maternal aging and chromosomal abnormalities: New data drawn from in vitro unfertilized human oocytes. *Hum Genet* 2003;112:195-203.
6. Hawley RS. Human meiosis: Model organisms address the maternal age effect. *Curr Biol* 2003;13:R305-307.
7. Petersen MB, Mikkelsen M. Nondisjunction in trisomy 21: Origin and mechanisms. *Cytogenet Cell Genet* 2000;91:199-203.
8. Wolstenholme J, Angell RR. Maternal age and trisomy—a unifying mechanism of formation. *Chromosoma* 2000;109:435-438.
9. Mange EJ, Mange AP. *Basic Human Genetics*. Sunderland, Mass: Sinauer Associates; 1994:212-213.
10. 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;30:433-435.
11. Gerard-Blanluet M, Danan C, Sinico M, et al. Mosaic trisomy 9 and lobar holoprosencephaly. *Am J Med Genet* 2002;15:111:295-300.
12. Stipoljev F, Kos M, Kos M, Miskovi B, Matijevic R, Hafner T, Kurjak A. Antenatal detection of mosaic trisomy 9 by ultrasound: A case report and literature review. *J Matern Fetal Neonatal Med* 2003;14:65-69.
13. Arnold GL, Kirby RS, Stern TP, Sawyer JR. Trisomy 9: Review and report of two new cases. *Am J Med Genet* 1995;56:252-257.
14. Qazi QH, Nasakawa A, Madahar C, Ehrlich R. Trisomy 9 syndrome. *Clin Genet* 1977;12:221-226.
15. Lopez Jimenez J, Romero Dominguez A, Gimenez Prats MJ, Chimenos Kutsner E. Characteristics and dental treatment of partial trisomy 9. *Med Oral* 2001;6:290-295.
16. Butler MG, Hayes BG, Hathaway MM, Begleiter ML. Specific genetic diseases at risk for sedation/anesthesia complications. *Anesth Analg* 2000;91:837-855.
17. Lurie IW, Lazjuk GI, Gurevich DB, Usoev SS. Genetics of the 9p+ syndrome. *Hum Genet* 1976;32:23-33.
18. Centerwall WR, Beatty-DeSana JW. The trisomy 9p syndrome. *Pediatrics* 1975;56:748-755.
19. Milunsky A, ed. *Genetic Disorders and the Fetus*. 4th ed. Baltimore, Md: The Johns Hopkins University Press; 1998:179.
20. Tarani L, Colloridi F, Raguso G, Rizzuti A, Bruni L, Tozzi MC, Palermo D, Panero A, Vignetti P. Trisomy 9 mosaicism syndrome. A case report and review of the literature. *Ann Genet*. 1994;37:14-20.
21. Hacıhanefioglu S, Guven GS, Deviren A, Silaharoglu AN, Yosunvkaya Fenerci E, Ozkilic A, Yuksel A. Trisomy 9p syndrome in two brothers: With new clinical findings and review of the literature. *Genet Couns* 2002;13:41-48.
22. Sherer DM, Wang N, Thompson HO, Peterson JC, Miller ME, Metlay LA, Abramowicz JS. An infant with trisomy 9 mosaicism presenting as a complete trisomy 9 by amniocentesis. *Prenat Diagn* 1992;12:31-37.