A Case Study of Mosaic Trisomy Chromosome 9 Syndrome

Lidia Perenc[1,3,A,B,C,D,F] **Joanna Bielak**[3,B,C,D,E] **Wiesław Guz**[2,4,B,C,E]

ORCID: 0000-0001-8378-2340 ORCID: 0009-0007-6595-5464 ORCID: 0000-0002-1309-5374

[1] **Institute of Health Sciences, University of Rzeszów,**
[2] **Institute of Medical Sciences, University of Rzeszów,**
[3] **Department of Pediatric Neurology and Pediatrics, Clinical Provincial Hospital No. 2. Saint Jadwiga Queen in Rzeszów,**
[4] **Clinical Department of Radiology and Imaging Diagnostics, Clinical Provincial Hospital No. 2 Saint Jadwiga Queen in Rzeszów**

A – research concept and design, B – collection andassembly of data, C – data analysis and interpretation, D – writing the article, E – critical revision ofthe article, F – final approval of article

DOI: 10.26399/rmp.v29.3.2023.10/l.perenc/j.bielak/w.guz

ABSTRACT

A Case Study of Mosaic Trisomy Chromosome 9 Syndrome

Perenc L.[1], Bielak J.[3], Guz W.[2,4]

[1] Institute of Health Sciences, University of Rzeszów, [2] Institute of Medical Sciences, University of Rzeszów, [3] Department of Pediatric Neurology and Pediatrics, Clinical Provincial Hospital No. 2. Saint Jadwiga Queen in Rzeszów, [4] Clinical Department of Radiology and Imaging Diagnostics, Clinical Provincial Hospital No. 2 Saint Jadwiga Queen in Rzeszów

The article discusses a clinical case of mosaic trisomy of chromosome 9 in a male infant. The discussed syndrome is characterized by the presence of low birth weight, dysmorphic features in the structure of face, hands and feet, defects of organs and various medical problems appearing in the postnatal period. The above-mentioned symptoms occurred in the clinical case discussed. In some cases, skin lesions occur - pigment mosaic skin lesions along the Blaschko lines, which rather indicates the phenomenon of genetic mosaicism. To make a diagnosis, the data obtained on the basis of the interview, physical examination and additional tests should be properly organized and an appropriate genetic test should be performed. It is worth comparing the clinical picture and patient's medical history with data presented in the literature to confirm the existence of a cause-and-effect relationship.

Keywords: *congenital defect syndrome, mosaic trisomy of chromosome 9*

STRESZCZENIE

Studium przypadku zespołu mozaikowej trisomii chromosomu 9

Perenc L.[1], Bielak J.[3], Guz W.[2,4]

[1] Instytut Nauk o Zdrowiu, Uniwersytet Rzeszowski, [2] Instytut Nauk Medycznych, Uniwersytet Rzeszowski, [3] Klinika Neurologii Dziecięcej i Pediatrii, Kliniczny Szpital Wojewódzki Nr 2 im. Św. Jadwigi Królowej w Rzeszowie, [4] Kliniczny Zakład Radiologii i Diagnostyki Obrazowej, Kliniczny Szpital Wojewódzki nr 2 im. Św. Jadwigi Królowej w Rzeszowie

W artykule omówiono przypadek kliniczny mozaikowej trisomii chromosomu 9 u niemowlęcia płci męskiej. Omawiany zespół charakteryzuje się występowaniem: niskiej urodzeniowej masy ciała, cech dysmorficznych w budowie twarzy, dłoni, stóp, wad narządowych: mózgowia, serca, narządów moczowo-płciowych, szkieletu, wad narządów zmysłu: oka i ucha oraz różnych problemów medycznych ujawniających się w okresie pourodzeniowym. Wyżej wymienione objawy występowały w omawianym przypadku klinicznym. W niektórych przypadkach dodatkowo występują zmiany skórne – mozaika barwnikowa wzdłuż linii Blaschki, co wskazuje na zjawisko mozaikowatości genetycznej. Aby dokonać rozpoznania należy uporządkować w odpowiedni sposób dane uzyskane na podstawie zebranego wywiadu, badania fizykalnego, wykonanych badań dodatkowych oraz wykonać odpowiednie badanie genetyczne. Warto porównać obraz kliniczny i historię choroby pacjenta z danymi przedstawionymi w piśmiennictwie, aby utwierdzić się o występowaniu związku przyczynowo-skutkowego.

Słowa kluczowe: *zespół wad wrodzonych, mozaikowa trisomia chromosomu 9*

Introduction

Mosaic trisomy of chromosome 9 is an example of genetic mosaicism [1]. Mosaicism is the presence of at least two cell lines with different genotypes in one organism. In this case, an additional chromosome 9 is present in the karyotype, but not in all cells of the body. The remaining cells of the body have a normal karyotype. Mosaic trisomy is caused by abnormal mitosis of embryonic cells at the blastula or gastrula stage. Excess genetic material changes the course of ontogenetic development. Mosaic trisomy of chromosome 9 has a better prognosis in terms of survival and life expectancy compared to simple trisomy of chro-

mosome 9 [2]. It is possible that there is a correlation between phenotypic variability and the percentage of cells with trisomy 9 [1].

Mosaic trisomy of chromosome 9 has a variable phenotype [9]. It is characterized by the occurrence of:

1. low birth weight [1,3],
2. dysmorphic features in the structure of the face [1-5], hands, and feet [1,4-7],
3. organ defects: brain [1-3], heart [1-3,5-7], urogenital organs [1-2,4,6-7], skeleton [1-4], sense organs: eye [1,2] and ear [1,4],
4. medical problems: intellectual [1,2] and motor disabilities [2], convulsions [4,6], respiratory and circulatory problems [4,8], complications during intubation and general anesthesia [8], gastroesophageal reflux [4-5], feeding difficulties [3], obesity [8], progressive skeletal deformations [8] and others [1,2],
5. in some cases of skin changes - pigmentary mosaic skin lesions along the Blaschko lines [9] - the presence of such skin lesions indicates the phenomenon of genetic mosaicism [10] rather than the syndrome of mosaic trisomy of chromosome 9 [9].

The diagnostic method for determining the genetic mosaicism and the type of aneuploidy, including mosaic trisomy of 9 chromosome, is chromosome microarray analysis [3]. It has a higher diagnostic rate compared to conventional karyotype analysis [3]. In order to determine the degree of mosaicism of trisomy 9, metaphase or interphase fluorescent in situ hybridization [7] or cytogenetic analysis with G banding [2] can be used.

Clinical case presentation

The first stage in the diagnostic procedure was to organize numerous data collected on the basis of an interview, repeated physical examination conducted by various specialists and numerous additional tests collected during the patient's long-term hospitalization at the Clinical Provincial Hospital No. 2. Saint Jadwiga Queen in Rzeszów.

The patient we presented came from the third pregnancy, third delivery, was born by cesarean section (condition after cesarean section, gestational diabetes), in the 38th week of pregnancy. The postnatal Apgar score was 9. The mother's age at conception was 39 years. Prenatal ultrasound revealed only intrauterine hypotrophy. The patient was diagnosed with:

1. low birth weight - the birth weight was 2485 g,
2. dysmorphic face: hypoplasia of the right half of the face, on the right side, the following were found: type II microtia, small palpebral fissure, the lower jaw is set back, the palate is a gothic form and dysmorphic (calcaneovalgus) feet,
3. organ defects: hypotrophy of both frontal lobes of the brain (Table 1A), enlarged lateral ventricles of the brain with rounded frontal horns, Evans index - 0.33, persistent foramen ovale, bilateral inguinal cryptorchidism, obliteration of the right coronary suture, residual ribs at the first lumbar vertebra - the thirteenth pair of ribs divergent strabismus (Table 1B), microphthalmia (Table 1C,D,E), bilateral hypoplasia of the external and middle ear with a predominance on the right side (Table 1F),
4. medical problems: delayed psychomotor development, hypoacusia, apnea, complications during intubation, gastroesophageal reflux, feeding difficulties, disharmonious somatic development, asymmetrical body positioning which may predispose to progressive skeletal deformations and others.

After analyzing and compiling the collected data, it was established that there were grounds for genetic diagnosis. The blood sample was sent to the Cytogenetics Laboratory, Department of Medical Genetics, Institute of Mother and Child in Warsaw. Based on the result of the diagnostic test performed by comparative genomic hybridization using a whole-genome oligonucleotide microarray - a male karyotype was found, and genome imbalance in mosaic form of trisomy 9. In order to determine the degree of mosaicism of trisomy of the 9 pair, it was recommended to perform karyotype testing or fluorescent in situ hybridization. This study has not been carried out yet. Similarly, no genetic testing of the parents was performed, which constitutes a diagnostic limitation.

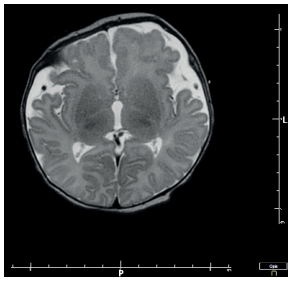
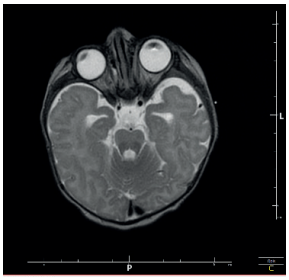
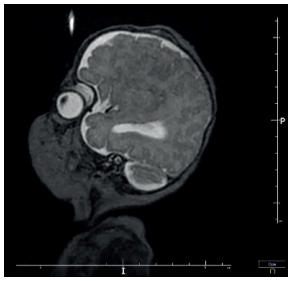
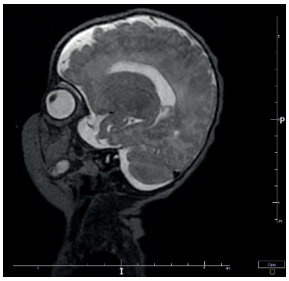
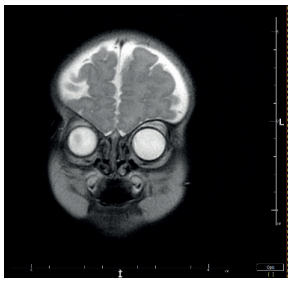
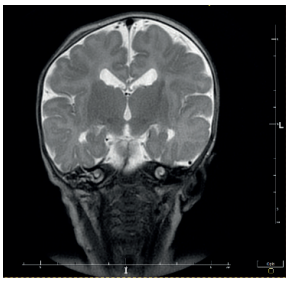
In the discussed case, compared to cases presented in the literature, low birth weight and phenotypic changes, such as dysmorphic features in the structure of the face and feet, organ defects and medical problems, were similar, but there were no dysmorphic features in the structure of the hands and pigmentary mosaic skin lesions along the Blaschko lines. So far, premature closure of the cranial suture has not been described in mosaic trisomy of chromosome 9.

The patient has been under intensive multidisciplinary care since birth, which will be maintained in the future. Surgical treatment of premature closure of the cranial suture and hearing aids are planned in the near future. It requires improvement measures (early development support). Also, it should mentioned that a child with mosaic trisomy of chromosome 9 will need the help of an experienced medical team: a surgeon, a neurosurgeon, an orthopedist, a cardiologist, a neurologist, an ophthalmologist, an audiologist, an otolaryngologist, a dietician, a neurologist, a physiotherapist and a nurse.

Conclusions

In order to make a diagnosis, the data obtained on the basis of the interview, physical examination and additional tests should be properly organized. If an abnormal genotype is suspected as the etiological factor, appropriate genetic testing should be performed. It is worth comparing the clinical picture and patient's medical history with data presented in the literature to confirm the cause-and-effect relationship.

Table 1. Non-contrast enhanced magnetic resonance imaging performed at 8 weeks of age

	A. Asymmetry of the braincase with flattening of the right part of the scales of the frontal bone and the right parietal bone, hypotrophy of both frontal lobes, more severe on the right side, widened paracerebral fluid spaces		B. Divergent positioning of the eyeballs
	C. Changed structure of the roof of the right orbit, a depression in the place where the right coronary suture is obliterating		D. For comparison, the left side
	E. The right eyeball is smaller compared to the left one		F. There is no properly developed auricle on the right side

References

1. Tarani L., Colloridi F., Raguso G. et al.: Trisomy 9 mosaicism syndrome. A case report and review of the literature. Ann Genet 1994; 37(1): 14–20.
2. Miryounesi M., Dianatpour M., Shadmani Z. et al.: Report of a Case with Trisomy 9 Mosaicism. Iran J Med Sci 2016; 41(3): 249–252.
3. Li M., Glass J., Du X. et al.: Trisomy 9 mosaic syndrome: Sixteen additional patients with new and/or less commonly reported features, literature review, and suggested clinical guidelines. Am J Med Genet A 2021; 185(8): 2374–2383.
4. 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(3): 258–264.
5. Stoll C., Chognot D., Halb A. et al.: Trisomy 9 mosaicism in two girls with multiple congenital malformations and mental retardation. J Med Genet 1993; 30(5): 433–435.
6. Pejcic L., Stankovic T., Ratkovic-Jankovic M. et al.: Clinical manifestations in trisomy 9 mosaicism. Turk J Pediatr 2018; 60(6): 729–734.
7. Solomon B.D., Turner C.E., Klugman D. et al.: Trisomy 9 mosaicism and XX sex reversal. Am J Med Genet A 2007; 143A(22): 2688–2691.
8. Riley C.J., Moore T., Eagelston L. et al.: Cardiac Failure in a Trisomy 9 Patient Undergoing Anesthesia: A Case Report. Anesth Prog 2017; 64(1): 29–32.
9. Wang C., Chen Y., Zhao J. et al.: Prenatal diagnosis and genetic counseling of low-level trisomy 9 mosaicism with a favorable outcome. Taiwan J Obstet Gynecol 2020; 59(5): 786–787.
10. Cohen J. 3rd, Shahrokh K., Cohen B.: Analysis of 36 cases of Blaschkoid dyspigmentation: reading between the lines of Blaschko. Pediatr Dermatol 2014; 31(4): 471–476.

No potential conflict of interest was reported by the authors.

Address for correspondence:

Lidia Perenc
Institute of Health Sciences University of Rzeszów
35–310 Rzeszów, St. Warzywna 1a,
Bldg. G5, FL.1. RM. 105
tel. +48697510252
e-mail: lperenc@ur.edu.pl