● Case Report

TRISOMY 9 IN PRENATAL DIAGNOSIS - CASE REPORT


Authors:
Małgorzata Soroka[1], Maciej Słodki [1, 2, 3]

1.Department of Obstetrics and Gynecology - Hospital St. Trinity in Plock, 2.Department of Prenatal Cardiology, Polish Mother's Memorial Hospital Research Institute, 3.Institute of Health Sciences. The State School of Higher Professional Education in Płock

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Abstract

Trisomy 9 is a rare chromosomal disorder that often results in significant mortality. We present a case report in a low-risk pregnancy. The prenatal ultrasonography at 12 weeks of gestation showed normal nuchal translucency and the presence of the nasal bone. The anatomy scan performed by an experienced doctor revealed an abnormal four chamber view and abnormal posterior cranial fossa. First trimester biochemical analysis (free βhCG and PAPP-A) showed high risk for trisomy 18. By amniocenthesis (at 16 weeks of gestation) and karyotype evaluation trisomy 9 was diagnosed and at 20 weekstermination was conducted on maternal request.

Key words: *trisomy 9, prenatal ultrasound, Dandy-Walker malformation (DWM), horseshoe kidney, echocardiography*

CASE PRESENTATION

The patient was a healthy 31 year old, gravida 3, with no medical history. Previous pregnancies without complications, vaginal delivery at term. The family with no chromosomal anomalies.

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The woman conceived naturally. She received antenatal care since the sixth week of gestation. At 12 weeks of gestation she underwent first trimester scan according to Fetal Medicine Foundation standards.

The scan revealed a fetus of 65 mm with nuchal translucency of 1.9 mm and presence of the nasal bone. The ductus venosus flow and the tricuspid valve flow were normal.

Using the algorithm provided by the Fetal Medicine Foundation, the background risk of aneuploidy resulting from the age of the mother for trisomy 21, 18, 13 was 1:6135, 1:6901 and <1:20000, respectively.

The anatomy scan revealed an abnormal four chamber view, abnormalities of the posterior fossa, short femora, and suspicion of bilateral cleft lip. The patient was referred for further diagnosis. The first-trimester biochemical analysis were conducted and the results were abnormal (free β-hCG and PAPP-A were 0.131 and 0.472 MoM, respectively). The risk of autosomal trisomy was calculated again. When the markers of aneuploidy were included, the new, adjusted risk of chromosomal aberration for trisomy 18 was 1:146.

Amniocentesis was performed at 16 weeks' of gestation and revealed a complete 47,XY,9+.

Fetal ultrasound during the second trimester confirmed suspected abnormalities of fetal anatomy in first trimester.

In the central nervous system the Dandy-Walker malformation and ventriculomegaly were observed. Cardiac anomalies included an abnormal four chamber view, tricuspid insufficiency, double outlet right ventricle, abnormal three vessel view. Also identified were bilateral cleft lip, horseshoe kidneys with bilateral hydronephrosis, shortened long bones.

After genetic counseling, the pregnancy was terminated at 20 weeks' gestation with prostaglandin E applied to the cervix. After 10 hours from the application of drugs, male fetus with a body weight of 250 g and 23 centimetres long was delivered.

DISCUSSION

Trisomy of chromosome 9 is rare among live-born infants, but common among aborted fetuses. [3]

Trisomy 9 was first described by Murray Feingold and Leonard Atkins in 1973. [1] Fetal trisomy 9 (especially its nonmosaic, complete form) is a rare (3,7:1000000) chromosomal abnormality constituting only 2.7% of all trisomic cases, [2] that can be detected sonographically. [22] Early prenatal diagnosis of trisomy 9 is important to the parental decision-making process, because nonmosaic

Corresponding author: maciejslodki@op.pl

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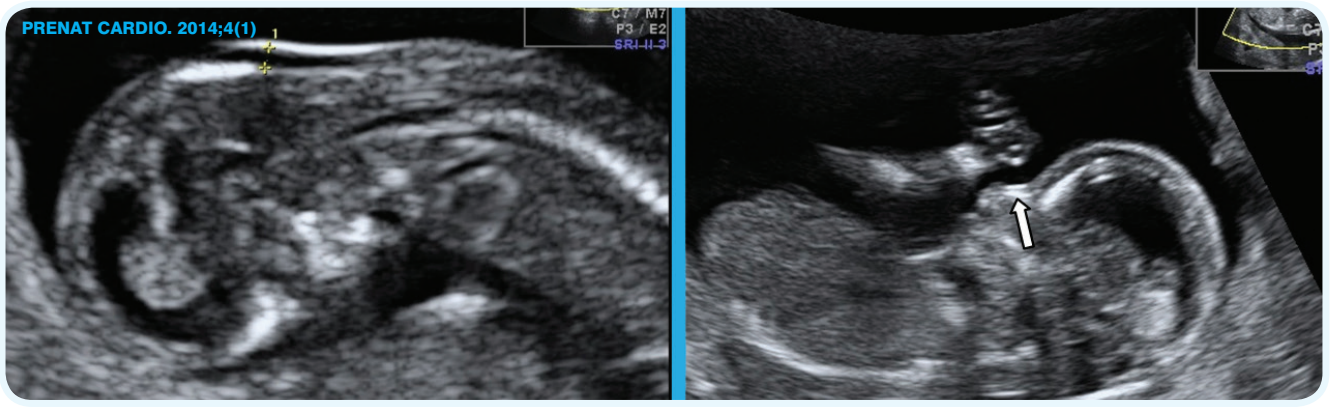


Photo 1. Ultrasonography images at 12 weeks' gestation shows normal nuchal translucency (NT, marked with callipers) and the presence of the nasal bone (arrow).

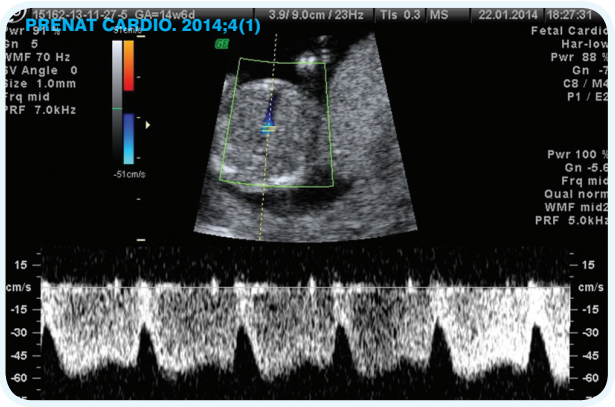


Photo 2. Ductus venosus flow velocity waveform in 14 weeks of pregnancy in the fetus with trisomy 9.

trisomy 9 is universally lethal. [3]

A first-trimester ultrasound diagnosis of trisomy 9 is very rare and was first reported by Pinette in a fetus at 11.7 weeks' gestation in 1998.[4] Most of the fetuses with complete trisomy 9 are spontaneously aborted in the early first trimester, only those individuals that survive to be delivered at term are mosaics. [5,6]

Almost 85% of cases occur in mothers younger than 35 years,[7] mean maternal age was 33 years,[8] which reduces the importance of advanced maternal age as a risk factor of this chromosomal disorder, [9,10,11,12,13] nevertheless Schwendemann presented 6 previously unpublished cases of complete trisomy 9, where maternal age was advanced. [22]

It is noteworthy that screening ultrasonography is recommended especially to patients above 35 years of age, what would lead to chromosome abnormalities being undetected in a significant number of younger patients. This underlines the importance of fetal ultrasonography and echocardiography as a screening method in the low-risk population, what allows the early detection of chromosome abnormalities, including trisomy 9.[5]

Some authors reported a correlation between increased nuchal translucency and elevated maternal serum free-βhCG and pregnancy-associated plasma protein A (PAPP-A). [5,14,16,22]

Interestingly, NT (1.9 mm) and the nasal bone were normal in our case, (Fig. 1) but maternal serum testing showed abnormal results.

Controversy in the diagnosis of trisomy 9 also relates to the biochemical markers.

Previous reports in the literature have described low free-βhcg and low PAPP-A levels in 11-13,6 weeks of gestation[10,15] which suggested trisomy 13 or 18, but in 2 of 9 cases of trisomy 9 presented by Sepulveda maternal serum testing was normal. [16]

Ultrasound evaluation of flow in the ductus venosus in the first trimester of pregnancy is described as a screening test in the diagnosis of aneuploidy. [17]

In our case the flow in the ductus venosus had a characteristic triphasic waveform, which showed no abnormalities. (Fig.2) A similar case report can be noticed in the Bijok[8] publication, although in the literature we can also find descriptions of abnormal reverse ductus venosus flow in fetuses with trisomy 9.[18]

In the presented case, we have observed mainly cardiovascular, musculoskeletal, genitourinary and central nervous system malformations.

Trisomy 9 is strongly associated with central nervous system abnormalities, particularly Dandy-Walker malformation (complete or partial agenesis of the cerebellar vermis, dilatation of the fourth ventricle, enlarged posterior fossa) and agenesis of corpus callosum. [5,14,16,22] First trimester scan, which was performed by an experienced doctor revealed an abnormal posterior cranial fossa, which demonstrated Dandy-Walker malformation with complete agenesis of the cerebellar vermis in second trimester. (Fig. 3)

Cardiac malformations have been reported to occur in 75-80% of cases of trisomy 9. [9,14,22] The most common cardiac manifestations of trisomy 9 are cardiomegaly, [3,11] ASD (atrial septal defect), [14,16,19,22] VSD (ventricular septal defect), [3,9,14,22] DORV (double outlet right ventricle), [3,5,8] aortic stenosis,[11] coarctation of the aorta,[20] overriding aorta,[3,5,8] pulmonary valve stenosis,[3] and tetralogy of Fallot.[3] We observed an abnormal outflow from ventricles

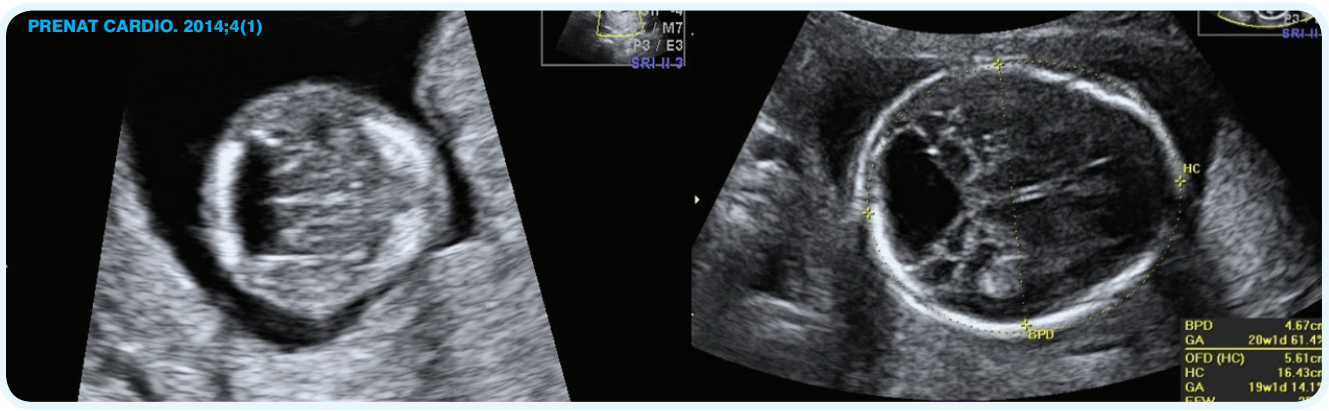
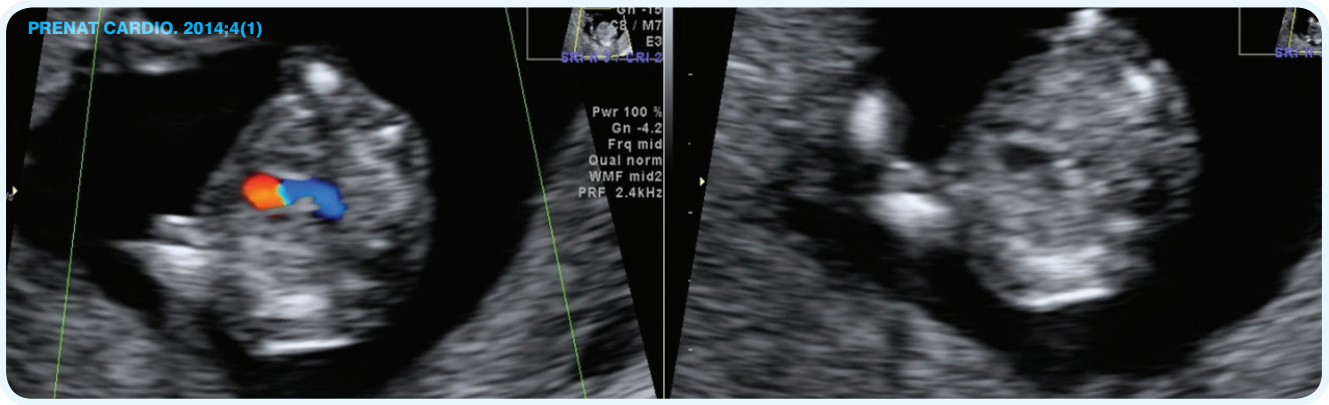


Photo 3. Dandy-Walker malformation at first and second trimester ultrasonography scan in a fetus with trisomy 9.



Phot 4. Three-vessel view of the fetal upper mediastinum in 12 weeks of pregnancy. The enlarged aorta is visible.

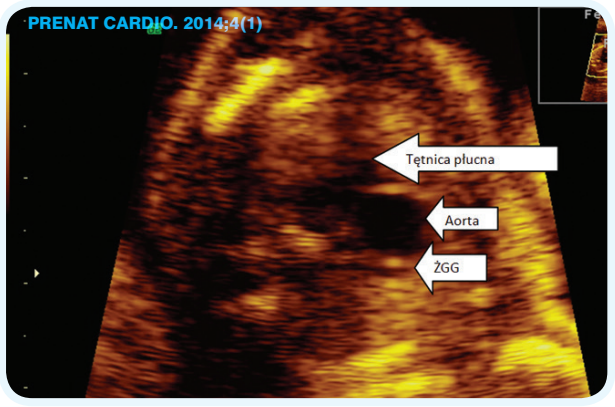


Photo 5. Three-vessel view of the fetal upper mediastinum in 19 weeks of pregnancy. Is it noteworthy ,that the aorta is enlarged and the superior vena cava is compressed [SVC].

and the enlarged aorta in the first echocardiography. (Fig. 4)

A fetal ultrasound at 19 weeks' of gestation identified disproportion of ventricles, common atrium, overriding aorta, tricuspid regurgitation, (Fig. 3) abnormal 3 vessel view showing significantly enlarged aorta and compressed the superior vena cava. (Fig. 5)

In 30% of trisomy 9 cases the two-vessel cord is present,[3,5,16,22] but not observed in the presented case.

The anomalies identified in urinary system were horseshoe kidney,[16,19,20,21] absent bladder,[19] hydronephrosis, [9] and also dysplastic kidneys. [10] Fetal ultrasound during the second trimester identified horseshoe kidneys with bilateral hydronephrosis. (Fig. 7)

Hypoplastic genitalia (micropenis, hypoplastic labia)[3] are very common in cases of complete trisomy 9, which was also presented in our case. (Fig. 8)

The most common facial manifestations described in literature were hypotelorism, [3] low set malformed ears, [3] hypoplastic nose, [3] micrognathia, [5] cleft lip and palate.[3]

Dysmorphic features in the fetal face showed flat profile, small nose, micrognathia, harelip, bilateral cleft lip. (Fig. 9 and 10)

Many of the findings associated with the skeletal system are polydactyly, [22] abnormal ossification, [16] shortened long bones, [10,11] clubfeet, [10] brachycephaly, [3,22] the thirteenth rib and thirteenth thoracic vertebra. [3] At 20 weeks' of gestation femur length was 2.71 cm corresponding to 18.2 weeks of gestation, showing a slight shortening of the femur. (Fig. 11)

The sonographic characteristics of trisomy 9 overlap with those of trisomy 13 and 18, with the most prominent ultrasonographic findings being thickened NT, intrauterine growth restriction, craniofacial dysmorphism, central nervous system defects (Dandy-Walker malformation, absent cerebellar vermis, megacisterna magna), congenital

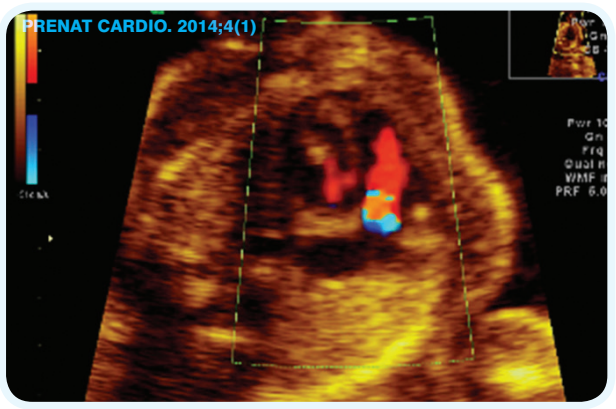


Photo 6. A four chamber view of the fetal heart at the second trimester scan. A fetal ultrasound identified disproportion of ventricles, common atrium, tricuspid regurgitation.

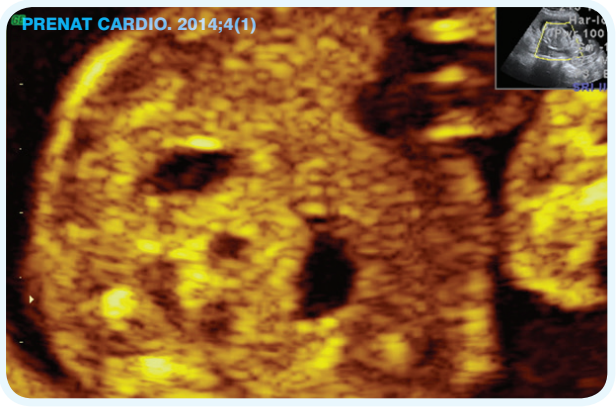


Photo 7. Horseshoe kidneys with bilateral hydronephrosis.

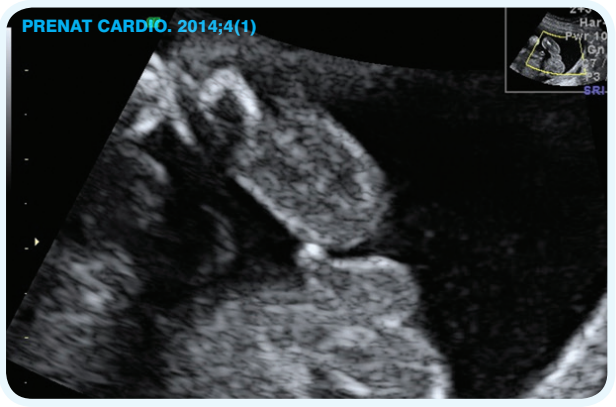


Photo 8. Hypoplastic genitalia – micropenis.

heart defects, genitourinary anomalies and skeletal defects (lumbosacral spina bifida), [5,9,11] but also maternal serum marker trends are similar for trisomies 9, 13 and 18 (-hCG, PAPP-A).

The case described by our team is interesting, because there were no positive markers of fetal aneuploidy - increasing nuchal translucency and the absence of the nasal bone, while echocardiography and detailed assessment of fetal anatomy allowed for the detection of trisomy 9. We compared similar cases of complete trisomy 9 in literature and found only two cases – the first described by Schwedemann in 2009 and the second by Bijok in 2012.

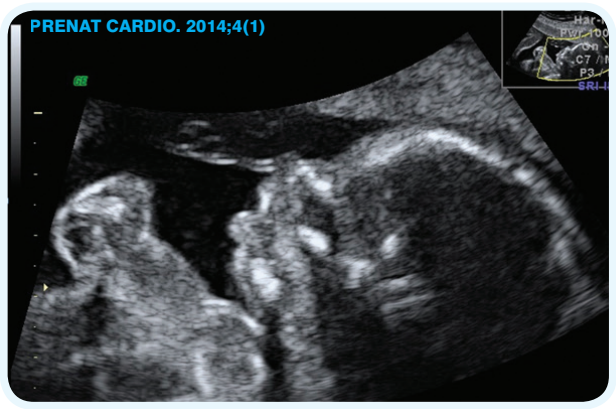


Photo 9. Dysmorphic features in the fetal face showed flat profile, small nose, micrognathia, harelip.

SUMMARY

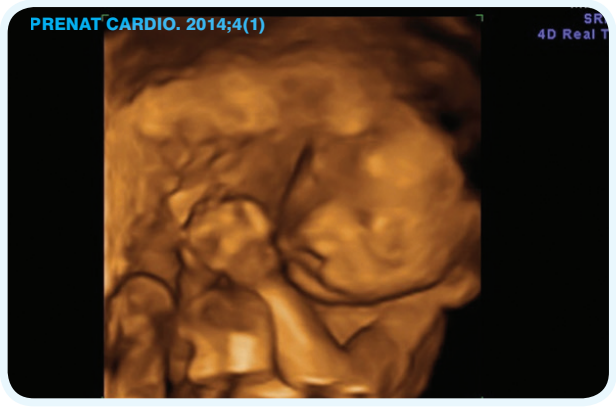


Photo 10. Bilateral cleft lip.

The finding of multiple structural fetal anomalies during the first trimester ultrasonography and echocardiography screening allowed for the diagnosis of a rare chromosomal disorder: trisomy of chromosome 9. This is the second report on this subject in Polish literature.

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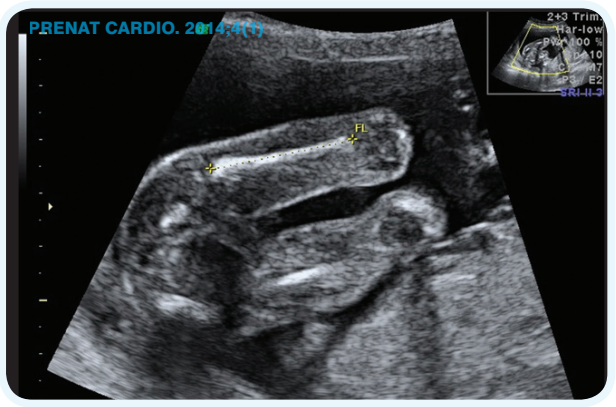

Photo 11. Shortening of the femur.

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