Prenatal diagnosis of an atrioventricular canal in a foetus with deletion of chromosome 8 (pter→p21).

Diagnostyka prenatalna płodu ze wspólnym kanałem przedsionkowo-komorowym i delecją chromosomu 8 (pter→p21).

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Summary

Congenital heart malformations, detected during a pregnancy, are associated in 20-48% of cases with a chromosomal aberration. In the following study we have reported the deletion of chromosome 8 (pter→p21), diagnosed prenatally at 22 weeks of gestation, because of a visible defect in the upper part of the interventricular septum and a partial defect of the atrial septum.

The atria and the ventricles were joined with a common central valve. The cordocentesis was performed and karyotype: 46, XX ish del(8)(wcp8x2) was detected. Because of the persistent bradycardia of the foetus, indicating a danger of intrauterine asphyxia of the foetus, as well as features of premature placental detachment, the caesarean section was performed at 27 weeks of gestation. The patient gave birth to a daughter weighing 960 g. The child died in the 4th hour of her life. On the basis of the present observation it is safe to say that when an AV-canal defect is diagnosed prenatally, special attention must be paid to the detection of chromosomal abnormalities and amniocentesis or cordocentesis should be performed to assess the state of affairs.

Key words: **atrioventricular canal** / **chromosome – human – pair 8** / **deletion, foetus** /

Streszczenie

Wrodzone wady serca wykrywane podczas ciąży w 20-48% związane są z aberracjami chromosomowymi.

Opisano przypadek płodu z delecją chromosomu 8 (pter→p21) zdiagnozowaną w 22 tygodniu, u którego w badaniu usg stwierdzono ubytek w górnej części przegrody międzykomorowej i częściowy ubytek przegrody międzyprzedsionkowej. Przedsionki i komory łączyła wspólna zastawka centralna.

Wykonano kordocentezę. W badaniu cytogenetycznym określono kariotyp płodu: 46, XX ish del(8)(p21)(wcp8x2)[31] - delecja fragmentu ramion krótkich (p) chromosomu 8 prowadząca do częściowej monosomii chromosomu 8 od prążka p21do pter.

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Ze względu na zaburzenia w tętnie płodu pod postacią utrzymującej się bradykardii płodu do 60 uderzeń/minutę w zapisie kardiotokograficznym, wskazujące na zagrażającą zamartwicę wewnątrzmaciczną płodu oraz cechy przedwczesnego oddzielenia łożyska, ciążę ukończono drogą cięcia cesarskiego w 27 tygodniu. Pacjentka urodziła córkę o masie 960g. Dziecko zmarło w 4 godzinie życia. W przypadku wystąpienia wspólnego kanału przedsionkowo-komorowego u płodu trzeba zwrócić uwagę na możliwość istnienia aberracji chromosomowych i należy wykonać amniopunkcję lub kordocentezę celem oceny kariotypu płodu.

Słowa kluczowe: **wspólny kanał przedsionkowo-komorowy** / **chromosom 8** / **delecja, płód** /

Introduction

Congenital heart malformations detected during pregnancy are associated in 20-48% with a chromosomal aberration. The prenatal diagnosis of a chromosomal aberration and heart defect influences further obstetrical and neonatal management. Prenatally detected foetal heart defects are one of the indications for fetal karyotyping.

In the cases of deletion of chromosome 8 (pter→p21) the following features are observed: pre- and postnatal growth retardation, microcephaly, severe mental retardation, a narrow and receding forehead contrasting with a prominent occiput, high frontal hairline, low-set and dysplastic ears, hypertelorism, epicanthic folds, hypospadias and cryptorchidism in males, single palmar creases, short nose with depressed bridge and bulbous tip, small mandible, short neck, barrel chest with widely spaced nipples [1].

In children with deletion of chromosome 8 other individual additional defects have also been described [1, 2, 3, 4].

Case report

Patient 36 years old, after 2 caesarean sections consulted a gynaecologist in the 5th week of pregnancy. Four subsequent visits took place at the 9, 12, 17 and 24 weeks of gestation.

The first ultrasound examination at 8 weeks of gestation did not reveal any abnormalities. The second ultrasound examination performed at 21 weeks of gestation confirmed one foetus in the pelvic lie – biometry indicated its age as 20 weeks and 4 days. The image of the foetus's heart was abnormal.

There was a visible defect in the upper part of the interventricular septum and a partial defect of the atrial septum. The atria and the ventricles were joined with a common central valve. The heart was not enlarged and was properly situated in the chest. No fluid was observed in the pericardial sac. The FHR was regular. Furthermore, the area around the nape of the foetus's neck revealed features of oedema.

Heart disease was diagnosed in the form of the atrioventricular canal. Because of the most frequent connection between this defect and trisomy of chromosome 21 and because of the age of the patient, diagnostic cordocentesis was suggested in order to assess the karyotype of the foetus.

At 22 weeks of gestation, the patient was admitted to the Department of Obstetrics of the Medical University of Gdańsk for further diagnostics.

The patient was referred to the Department of Children's Cardiology. The following things were confirmed: the pericardial sac was empty; the heart was not enlarged; chambers were of appropriate proportions; atrioventricular valves were situated on the same level; there was a visible defect of the atrioventricular septum, about 4-5mm; the atrioventricular valve was probably singular. The Doppler tests registered a small defective closure of the valve. The exit of the aorta from the left chamber was visible – no features of dysfunction of the aortal valve. It was not possible to see clearly the valve of the pulmonary artery because of the disadvantageous lie of the foetus. Aortic arch was normal. There was a free flow from RA to LA (possibility of ASD II). Conclusion: the tests revealed a balanced common atrioventricular canal.

On the following day, diagnostic cordocentesis was performed. The following results were obtained : Karyotype: 46, XX ish del(8)(wcp8x2); deletion of a fragment of the short (p) arms of chromosome 8 leading to partial monosomy of chromosome 8 from band p21 to pter.

Because of the disturbances in the foetus's pulse in the 27 week of gestation in the form of persistent bradycardia of the foetus indicating the danger of the foetus's intrauterine asphyxia as well as features of premature placental detachment, the caesarean section was performed The patient gave birth to a daughter weighing 960g. The child was in average condition (Apgar 5). She died in the 4th hour of life.

Post-mortem examination confirmed the presence of heart malformation. No other abnormalities were confirmed in the internal organs of the child. External appearance was normal.

Discussion

Deletions taking place in the distal region of chromosome 8 are associated with congenital heart malformations. A high prevalence of AVC in 8p- syndrome is observed and a non-random association of the 2 conditions is suggested [4].

The presence of certain heart malformations is more frequent in association with specific chromosomal aberrations, as for instance supravalvular aortic stenosis in Williams syndrome, conotruncal heart defects in DiGeorge/Velo-cardio-facial syndrome, or coarctation of the aorta in Turner syndrome. Approximately 75% of AV-canal defects occur as in the context of a syndrome and in almost 60% of cases with AVSD trisomy 21 is found [4].

AVSD can be caused even by very small terminal deletions of chromosome 8 (p23.1→pter) and as a result this has lead to the suggestion that this chromosomal region around 8p23.1 possesses a gene crucial in the heart development process [5]. In the case of patients with a deletion 8p, the AV-canal defect is often associated with other cardiac malformations, such as persistence of the left superior caval vene, or pulmonary valve obstruction.

There can also exist other less frequent cardiac malformations including ASD II with PS and tetralogy of Fallot [4, 6].

In eight out of 14 patients with deletion 8 (pter→p21) congenital heart defects were observed and these included tetralogy of Fallot in two cases, and atrioventricular canal in four cases [2, 4, 5, 7].

The children frequently presented adaptation difficulties at birth and feeding difficulties during the first month. Cardiac failure was the cause of death in two described children (between one month and 2 years of age). The oldest child with deletion of chromosome 8 survived 13 years [5].

Devriendt reported a prenatal diagnosis of a terminal deletion of chromosome 8p at 30 weeks of gestation of a del (8) (p21.3→pter) in a growth retarded foetus with a hypoplastic right ventricle and an atrioventricular septal defect (AVSD). Hypospadias grade II was noted. Malposition of the large vessels side to side and double outlet right ventricle was present. Also, an associated pulmonary valve stenosis was observed. The child was delivered at gestational age of 37 weeks [4].

On the basis of this observation, the association of AVSD with terminal deletions of chromosome 8p can be further confirmed. Terminal deletions of chromosome 8p are more frequent than it was previously thought, but it is easy to overlook small terminal deletions. Thus, the observation shows that in the case when an atrioventricular septal defect is diagnosed prenatally, special attention should be paid to distal chromosome 8p [2].

The foetus with deletion of chromosome 8 (pter-p21) and co-exsiting AVC was diagnosed at our Department and is the second case in literature diagnosed prenatally.

Additional structural malformations constitute rare cases in deletion 8p, and thus, the vital prognosis of these children is largely associated with the heart defect.

Judging from the present observation, it can be stated that when an AV-canal defect is diagnosed prenatally, there should be special attention paid to distal chromosome 8p in the cases when no other chromosomal abnormalities are found.

Piśmiennictwo

1. Schnizel A. Catalogue of Unbalanced chromosome aberrations in Man. Second Revised and Expanded Edition. Berlin-New York: *Walter de Gruyter,* 2001, 346-348.
2. Bröcker-Vriends A, Mooij P, van Bel F, [et al.]. Monosomy 8p: an easily overlooked syndrome. *J Med Genet.* 1986, 23, 153-154.
3. Devriendt K, De Mars K, De Cock P, [et al.]. Terminal deletion in chromosme region 8p23.1-8pter in a child with features of velo-cardio-facial syndrome. *Ann Genet.* 1995, 38, 228-230.
4. Devriendt K, Van Schoubroeck D, Eyskens B, [et al.]. Prenatal diagnosis of a terminal short arm deletion of chromosome 8 in a fetus with an atrioventricular septal defect. *Prenat Diagn.* 1998, 18, 65-67.
5. Digilio M, Giannotti A, Marino B, [et al.]. Atrioventricular canal and 8p- syndrome. *Am J Med Genet.* 1993, 47, 437-438.
6. Hutchinson R, Wilson M, Voullaire L. Distal 8p deletion (8p23.1-8pter): a common deletion? *J Med Genet.* 1992, 29, 407-411.
7. Dobyns W, Dewald G, Carlson R, [et al.]. Deficiency of chromosome 8p21.1-8pter: case report and review of the literature. *Am J Med Genet.* 1985, 22, 125-134.