Case report/Kazuistyka

The incomplete pentalogy of Cantrell – A case report

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ABSTRACT

We report a case of a female neonate with an incomplete (Class II) pentalogy of Cantrell (PC) presenting: omphalocele, thoracoabdominal type of partial ectopia cordis with ventricular septal defect and valvular pulmonary stenosis. The patient underwent a successful complete operation. We discuss associated anomalies that might occur with PC and the general overall prognosis for patients with PC. This report describes a very rare case of a patient with PC and coexisting partial ectopia cordis who survived.

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Introduction

Pentalogy of Cantrell (PC) is an extremely rare multiple congenital malformation syndrome and was first described in 1958 by James R. Cantrell et al. [1]. It comprises of the following five characteristics: (1) midline, upper abdominal wall disorder (e.g. omphalocele, gastrochisis), (2) defect of the lower sternum (i.e. cleft sternum or absent sternum), (3) anterior diaphragmatic defect (i.e. hypoplastic diaphragm, anterior diaphragmatic hernia), (4) pericardial abnormality (e.g. ectopia cordis) and (5) congenital abnormalities of the heart (e.g. tetralogy of Fallot, ventricular septal defect, atrial septal defect). The full pentalogy is very rare with a frequency of approximately 1 incidence per 65 000–100 000 live births and because of its different variants, there are also less severe cases described in the literature.

Pentalogy of Cantrell has a very high mortality rate despite significant improvements in neonatal surgery. The prognosis for patients depends mostly on the severity of cardiac malformation with up to 95% mortality when ectopia cordis is present.

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Case presentation

A female Caucasian baby was born by cesarean section at 39 weeks of gestation to a 22-year-old gravida 1, para 1 mother. The birth weight was 3650 g. No family history was known of any congenital diseases. There was no evidence of exposure to teratogens during pregnancy nor any history of consanguineous marriage. Cesarean section was performed because of acute life-threatening symptoms (centralization of blood circulation and circulatory failure were present) and generalized edema of the fetus diagnosed previously during prenatal ultrasound examination. Partial ectopia cordis and omphalocele were not detected prenatally due to fetus generalized edema which prevented full visualization of both thoracic and abdominal wall.

Apgar score was 1, 6 and 9 at 1st, 3rd and 5th minute respectively. Resuscitation was established with Neopuff device immediately after delivery. pH obtained from umbilical cord blood was normal: 7.35 (BE – 0.1 mmol/L) and 7.34 (BE – 1.8 mmol/L).

After birth, physical examination revealed upper abdominal wall defect in the midline with omphalocele and pulsative mass situated above omphalocele. This was apex cordis located outside the thoracic cavity with no pericardium protection – recognized as a partial, thoracoabdominal type of ectopia cordis (EC) – a severe condition, sometimes associated with PC. Both of which are shown below (Fig. 1). A diagnosis of an incompleteentaly of Cantrell was established.

General edema and ascites were present, therefore peritoneal cavity puncture was done immediately after birth with decompression of 80 ml of exudative fluid. It is believed that fetal edema was due to cardiac failure.

The patient was admitted to Neonatal Intensive Care Unit, where additional volume of 270 ml of fluid was evacuated from peritoneal cavity within five hours. Drainage of peritoneal cavity was maintained for the next 13 days.

At 9th hour of life, respiratory difficulties appeared with tachypnea, grunting and retractions – the baby was supported with non-invasive ventilation and FiO2 25%. Heart rhythm and blood pressure were found to be normal. Diagnostic approach to rule out infection was performed (CRP, complete blood count, blood smear and blood culture). Because chest X-ray showed inflammatory changes and CRP was above the normal range – antibiotic therapy was introduced. Blood culture was negative. The chromosome study showed a normal female karyotype (46,XX).

The consulting cardiologist found in echocardiographic study (ECHO) as follows: ventricular septal defect (1.0 cm) and foramen ovale (0.35 cm). The baby underwent surgery on 2nd day of life (DOL), that was a simultaneous operation including apex cordis relocation into thoracic cavity, pericardium closure and plastic surgery of omphalocele and upper abdominal wall. During surgery baby was intubated and ventilated with SIMV mode. The postoperative treatment was not complicated with gradual respiratory improvement and extubation occurred on 6th DOL. The follow up ECHO study showed (apart from VSD) severe tricuspid insufficiency and severe mitral insufficiency. Diuretic therapy was started and continued (spironolacton and furosemide). Baby was on total parenteral nutrition for the first 12 days of life and initial trophic feeding was started on 13th DOL. At 18th DOL total enteral feeding was achieved. The patient was discharged from the hospital on 35 DOL.

The first cardiac follow up visit was at the end of 2nd month of age. Echocardiography study revealed perimembranous ventricular septal defect with bidirectional shunt, moderate pulmonary regurgitation, moderate mitral regurgitation and severe tricuspid regurgitation, the systolic pressure in the right ventricle calculated from tricuspid regurgitation was 100 mmHg. Due to the suspicion of pulmonary hypertension cardiac catheterization was performed. The study had a mean pulmonary arterial pressure 28 mmHg, Qp:Qs = 3.57, PVRI = 2.69 WU/m². The child was qualified to radical repair of congenital heart disease and 2 weeks later underwent cardiac surgery during which ventricular septal defect was closed with Dacron patch. The postoperative course was complicated by respiratory failure with pulmonary hypertension. There for sternum closing was postponed and the child required inhaled nitric oxide supply for 4 weeks. 8 weeks after surgery tracheostomy was carried out due to persistent respiratory failure. 9 weeks after cardiac surgery the child was removed from mechanical ventilation.

Cardiology follow up visits in the first year of life showed a small volume of the right ventricle, small atrial septal defect with right-to-left shunt, moderate tricuspid regurgitation and systolic blood pressure in the right ventricle calculated from tricuspid regurgitation 27–33 mmHg. Originally Glenn operation was planned. However, due to the gradual improvement of the child’s cardiovascular endurance and increase of the right ventricle’s volume, this surgery was not performed. Currently, at the age of 19 months, the child is waiting for surgery to close tracheostomy.

Fig. 1 – The picture was taken immediately after the birth. Arrow 1: Indicates partial ectopia cordis; Arrow 2: Indicates upper abdominal wall defect with omphalocele.
Discussion

Because not every case of PC has all five originally described defects and the pentalogy of Cantrell might have different variants with various degrees of severity, Toyama [2] suggested a classification scheme for PC in which there are three classes: Class I – certain diagnosis – includes cases with all five defects present; Class II – probable diagnosis – includes cases with four defects (with the presence of intracardiac and abdominal wall defects); Class III – incomplete diagnosis – includes cases with various combinations of defects (but with the presence of sternal defect).

The exact cause of PC remains still unknown, but the syndrome is considered to be of heterogenous origin, caused by multiple factors such as gene mutation, chromosomal abnormalities, physical and chemical teratogens. The widely accepted hypothesis suggests that there is a failure in migration of the primordial mesodermic structures of the chest and abdomen during embryologic development at gestational age of 14–18 days [1]. The cardiac abnormalities are the result of developmental disorders of epimyocardium. Pericardial and diaphragmatic defects are due to developmental failure of the transverse septum.

In some families recessive transmission of a single gene mutations on the chromosome X were reported [3, 4, 8]. However that kind of study was not done in our patient.

Smigiel et al. [18, 19] describes a female neonate with coexistence of Goltz-Gorlin syndrome (GGS), known also as focal dermal hypoplasia (FDH) and pentalogy of Cantrell. GGS is a very rare and highly variable disorder affecting tissues of mesodermal and ectodermal origin. Its major manifestations are: (quote from [18]) “…atrophy or hypoplastic linear skin lesion fat herniation, papillomas around orifices, microphthalmia and ocular coloboma, hypodontia, hearing loss and extremely variable limb malformations”. Presented female patient had classical GGS with the following symptoms: (quote from [18]) “…sparse hair, anophtalmia, clefting, bifid nose, irregular vermilion of both lips, asymmetrical limb malformations, caudal appendage, linear aplastic skin defects, unilateral hearing loss”. In addition there were four typical characteristics of PC: ectopia cordis, omphalocele, anterior diaphragmatic hernia and absent lower sternum. Genetic studies were performed revealing a normal female karyotype (46,XX) and mutation in X-linked PORCN gene, which is pathognomonic manifestation of GGS. Due to coexistence of PC it is highly probable that PORCN gene mutations might lead to PC and therefore PORCN gene analysis should be taken into account in patients with PC. But that kind of genetic study was not performed in our patient.

Steiner et al. [5] performed a chromosomal microarray analysis in a patient born with PC and obtained duplication of the ALDH1A2 gene (on chromosome 15q21.3), which encodes the enzyme retinaldehyde dehydrogenase type 2. That enzyme converts vitamin A into retinoic acid, which in turn is a powerful morphogen, important during cardiac development and diaphragm formation in the first two to three weeks of gestation. So, there is a reasonable linking between ALDH1A2 gene duplication and etiology of PC.

Pentalogy of Cantrell is often associated with ectopia cordis (EC) which is also in itself an extremely rare congenital heart defect characterized by complete or partial displacement of the heart outside the thoracic cavity. According to the heart location, there are four types of EC: cervical, cervicothoracic, thoracic and thoracoabdominal types.

Intracardiac anomalies associated with the PC include: ventricular septal defect (100% of cases), atrial septal defect (around 53% of cases), tetralogy of Fallot (around 20% of cases), valvar or infundibular pulmonary stenosis (around 33% of cases), and ventricular diverticulum (around 20% of cases) [6]. Yuan et al. [7] describes an incomplete pentalogy of Cantrell (absence of sternum, an epigastric hernia and asymmetric kidneys) with two ventricular septal defects, atrial septal defect, tricuspid atresia and transposition of great arteries. Double outlet right ventricle with PC was reported by Takaya et al. [12]. Louis [16] describes PC associated with hypoplastic left heart syndrome and herniation of a single ventricle into the abdominal cavity.

There are also other anomalies that may be present alongside PC, these include the following: (1) asplenia described by Ludwig et al. [9]; (2) tetralogy of Fallout, gallbladder agenesis and polysplenia – described by Bittmann et al. [10]; (3) trisomy 18 – described by Hou et al. [11]; (4) central nervous system anomalies like craniorachischisis – described by Polat et al. [13]; (5) bilateral cleft lip and palate – described by Jafarian et al. [14].

As it was mentioned above, the pentalogy of Cantrell has a very high mortality ratio. Prognosis depends on the severity of both cardiac and extracardiac defects and other associated anomalies as well, if present. Treatment of PC is always surgical and there is a general agreement that PC is lethal without surgery, therefore it should not be delayed, unless it is a cardiac surgery of heart defect(s) which can be postponed to a later period of time.

Both palliative and corrective operations can be successful but the outcome is very poor with mortality rate as high as 95% when ectopia cordis, as the most severe malformation, is present. Figueroa et al. [17] presented a retrospective, observational study of 21 patients diagnosed with PC, of whom four had ectopia cordis. Seventeen patients died. Among them, there were four with EC and only four patients survived.

After birth, surgical repair of omphalocele was done as soon as possible and might be associated with the repair of pericardial, sternal and diaphragmatic defects at the same time.

Jia et al. [15] described successful surgical treatment of a patient with abdominal ectopia cordis and complex heart defect (which included: complete atrioventricular anomaly, total transposition of great arteries, pulmonic valvular stenosis, double outlet right ventricle, atrial septal defect, stenosis of superior vena cava); and another patient with thoracic-abdominal ectopia cordis and tetralogy of Fallot [15]. Both these patients were well at 24- and 29-month follow-up respectively.

It is important to remember that medical treatment of patients with pentalogy of Cantrell should be multidisciplinary and started without delay in medical centers with the highest degree of experience and referentiality.
Authors' contributions/Wkład autorów

TM – study design, data collection and interpretation, statistical analysis, acceptance of final manuscript version, literature search. AM, BM, MS – statistical analysis, data interpretation, acceptance of final manuscript version.

Conflict of interest/Konflikt interesu

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Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

REFERENCES/PiŚMIENNICTWO