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Özet

İlk olarak 1958 yılında Cantrell, Haller ve Ravitch tarafından tanımlanan Cantrell sendromu, ektopia kordis ile birlikte diyafragma, orta hat karın duvarı ve perikardı etkileyen nadir görülen bir anomalidir. Cantrell sendromu sıklıkla intrakardiyak defektler ile birliktelik göstermektedir. Kompleks kardiyak anomali prognozu belirlemede önemli bir role sahiptir. Çeşitli derecelerde birçok sistemi etkileyen bu sendromun tedavi süreci fetal tanı başlamaktadır. Bu aşama itibarıyla, farklı disiplinlerden tarafından paylaşılan görüş ve deneyimler hasta yönetimini planlamasında önemlidir. Ancak, tüm bu çabalara rağmen, tedavi şansı bu sendromun ağır formları için düşüktür.

Anahtar Kelimeler

Cantrell Pentalojisi; Ektopia Kordis; Perikardial Defekt

Abstract

First described in 1958 by Cantrell, Haller and Ravitch, Cantrell's Syndrome is a rare anomaly which affects the ectopia cordis together with the diaphragm, the midline abdominal wall and the pericardium. Cantrell's Syndrome is often associated with intracardiac defects. Concomitant complex cardiac anomalies have an important role in determining the prognosis. The diagnosis of this syndrome, which affects numerous systems to varying extent, begins with fetal diagnosis. Starting from this stage, the views and experiences shared by different disciplines are important for the planning of disease management. However, despite the best efforts, the chance of effective treatment for the more severe forms of this disease is fairly low.

Keywords

Pentalogy of Cantrell; Ectopia Cordis; Pericardial Defect

History and Definition

Cantrell's Syndrome was first defined by Cantrell, Haller, and Ravitch in 1958. The components of Cantrell's Syndrome are defined as: external herniation of the heart, pericardial diaphragmatic defects, lower sternal defects, anterior diaphragmatic defects, intracardiac defects, and malrotation of the heart [1]. The pathognomonic characteristic of this syndrome is the coexistence of omphalocele and ectopia cordis [2]. Identification of all components of the syndrome is rare in the patients [3].

Incidence and Typology

Cantrell's Syndrome has an incidence of 5.5-7.9 per 1 million live births [4]. The etiologic factor is not well established and familial occurrence of both isolated ectopia cordis and pentalogy of Cantrell has been reported. [5]. There is male dominance with a male to female ratio of 2.7:1 [6]. There are no publications indicating recurrence in the literature. Cases with Trisomy 13 and 18 are reported to have an increased incidence [7,8].

Ectopia cordis has cervical, cervicothoracic, thoracic, thoracoabdominal, and abdominal types. The most common form is the thoracic or thoracoabdominal type [9,10]. The abdominal wall defects include omphalocele, diastasis recti, umbilical hernia, or a combination of these defects. However, the most common form is the omphalocele [11]. In case an omphalocele is identified in the fetus, a detailed ultrasonographic examination should be performed, and the possibility of a Cantrell pentalogy it should be kept in mind [12].

Toyama et al. classified the Pentalogy of Cantrell in three separate classes. According to this classification, Class 1: definite diagnosis with all five defects present; Class 2: with four defects including intracardiac and ventral abdominal wall abnormalities present; and Class 3: incomplete expression with various combinations of defects present (but always including a sternal abnormality) [13].

Embryology

During the embryonic development; the sternum, abdominal wall, pericardium and part of the diaphragm arise from somatic mesoderm, while the myocardium arises from the splanchnic mesoderm.

The abnormal development of the septum transversum results in pericardial and diaphragmatic anomalies, while defects relating to the migration of mesodermal structures represents the possible cause of abdominal wall and sternum anomalies [5]. While the specific pathogenesis of the disease has not yet been elucidated, it is known that the differentiation occurs at a time between the 14th and 18th day after conception. It has been suggested that, during this period, the lateral mesodermal folds' failure to migrate towards the midline results in abdominal and sternal defects, while problems relating to the development of the septum transversum results in pericardial and anterior diaphragm defects [14]. Cantrell's Syndrome patients without intracardiac defects can be explained by the teratogenicity developed after the differentiation of splanchnic mesoderm [1].

It is believed that the ventricular diverticulum arises from the abnormal fusion of cardiac loop to the yolk sac in the embryonic development. Therefore, the patients with diverticulum detected should be investigated for the other components of Cantrell's Syndrome [15].

Pathology

The malrotation of the heart is the failure to complete the levorotation due to the impaired differentiation and the heart being remained in the dextraposition. Cardiac herniation results from the absence of lower sternum, the absence of abdominal supra-umbilical structures, and the absence of a pericardial diaphragm [1].

The vast majority of the patients with Cantrell's Syndrome have intracardiac defects. The complicated cardiac anomaly has a significant role in the prognosis. There is a wide spectrum of intracardiac defects. The most common form is the ventricular septal defect (VSD), followed by atrial septal defect (ASD) [16]. The cases in the literature were reported to be associated with the left or right ventricular diverticulum, Tetralogy of Fallot (TOF), pulmonary stenosis or atresia, transposition of the great arteries (TGA), tricuspid atresia, truncus arteriosus, anomalous pulmonary venous return, and double outlet right ventricle [17]. The most common forms of the sternal malformations are the absence of the lower third portion, bifid sternum, absence of xiphoid process and short sternum. The most common forms of the pericardial and diaphragmatic abnormalities are the absence of pericardium and the absence of the anterior part of the diaphragm. The absent pericardium establishes the differential diagnosis of Cantrell's Syndrome with ectopia cordis [1]. The Pentalogy of Cantrell may be associated with various organ and system abnormalities [18]. The cases in the literature were reported to have many abnormalities involving various systems such as frontonasal dysplasia, cleft lip and palate, hydrocephalus, exencephalia, neural tube defect, polysplenia and gallbladder agenesis, imperforate anus, cystic hygroma, agenesis of tibia-radius, foot drop, hypodactylia and calcaneovalgus abnormalities [5,18].

The diagnosis of the Pentalogy of Cantrell may be established by fetal ultrasonography scheduled for the first trimester of the pregnancy. Attempts should be made exclude this syndrome in patients with omphalocele, diaphragmatic hernia, and pericardial defect accompanied by pericardial effusion detected in the prenatal assessment [19]. Fetal echocardiography and MRI will provide more detailed assessments as well as a more comprehensive examination of the cardiac structure, which is important for the pediatricians and surgeons providing care and treatment to the infant following delivery

[20,21]. Three-dimensional sonography, in particular, is being increasingly preferred and used by physicians for these patients. We have observed that this method does indeed provide more detailed assessments and information for such cases [19]. Ectopia cordis is not considered an indication for cesarean sections in the literature, and the patients are followed-up under normal obstetric indications. It is reported that there is not any prognostic difference between normal delivery and cesarean section in patients with ectopia cordis. However, some authors highlight the significance of sterility for the postpartum surgery and prefer cesarean section [21].

The team to plan the follow-up and treatment of the patient in the prenatal and neonatal periods should include a gynecologist, neonatologist, pediatric cardiologist, geneticist, pediatric surgeon, and congenital heart surgeon, and every intervention should be planned in a multidisciplinary approach.

Surgical Treatment

The treatment and the prognosis of the patients will depend on their type of EC, the size of their abdominal defect, and their

concomitant defects and disorders [5]. The surgical repair for the syndrome requires a complicated and generally a stepwise surgical intervention [22]. The surgical plan can be made as stepwise or a single operation depending on the patient clinical data, hemodynamic compatibility, thoracic cavity compatibility and the type of intracardiac defect. The primary objectives of the surgical treatment are to cover the heart with tissue, to place the heart into the thoracic cavity, to repair the intracardiac defects and the sternal-thoracic reconstruction [23].

The first choice for covering the heart with tissue should be the primary approximation [1,17]. The primary approximation is a good barrier for infections; however, it may cause a hemodynamic disturbance. A skin autograft, skin allograft, or a prosthetic material can be used for secondary closure. The advantage of using a skin autograft is the presence of a good barrier and the potential of the graft to grow with the patient [1,23,24]. The placement of the heart into the thoracic cavity generally results in low cardiac output and hypotension. The reasons of the low cardiac output include small thoracic cavity, folding of the great vessels, myocardial compression, and the disorientation of the apex. There have been several attempts to overcome these issues. These include opening and freeing both pleurae, separating the costae from the sternal connection (costal shift maneuver), orienting the apex to the left or if dextracardiac, to the right thorax by placing a traction suture on the apex and freeing and lowering the diaphragm [1,24,25].

The timing of the surgical repair for omphalocele depends on the sac content, width and the surface epithelialization. An urgent surgical intervention may not be required for the omphalocele if lined by epithelium well. However, the repair should be scheduled in a short time considering that a rupture will make the surgery difficult and complications may occur such as peritonitis and mediastinitis [26].

Sternal reconstruction may lead to hemodynamic instability and the repair may require tissues or prostheses. For this purpose, periosteal flap, pectoralis muscle flap, rectus abdominis muscle flap, and rib segment dissected from the separate sternum may be used [9,23].

The ventricular diverticulum may cause fatal complications such as cardiac rupture, tamponade, sudden death, endocarditis, embolism, cardiac failure and arrhythmia, and therefore, surgical resection is required even though the diverticulum is asymptomatic [26].

Cantrell's Syndrome has a poor prognosis. There is no consensus on the prognosis. Some authors consider the type of intracardiac defect as the most important factor determining the prognosis; whereas some authors argue that the class of the syndrome determines the prognosis [17].

Mainly due to complications such as bradycardia, tachyarrhythmias, diverticulum rupture, heart failure and low blood pressure, only a few children are able to survive following surgical repair [5,27]. However, it is known that a certain number of children whose thoracoabdominal defects are limited are able to survive into their adult years [28].

EC is associated with high mortality for children, with a survival rate of less than 5% [26]. When the very mild or incomplete forms of the Pentalogy of Cantrell are included in the series, the survival rate is reported to be lower than 40% [13,29]. Most of the patients with a surgical success achieved are the cases without cardiac anomalies and with partial anterior wall defects [22,23,27].

The treatment process of this syndrome affecting many sys-

tems to the various extents starts from the fetal diagnosis. As of this stage, it is important to plan the patient management through the opinions and experiences shared by different multiple disciplines. However, despite all these efforts, the chance of treatment is low for the severe forms of this syndrome.

Competing interests

The authors declare that they have no competing interests.

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