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ISOLATED VENTRICULAR SEPTAL DEFECT IN CHILDREN

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Review

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Abstract

Ventricular septal defect is one of the common acyanotic congenital heart diseases. Although it is generally asymptomatic, it can develop to pulmonary hypertension and Eisenmenger syndrome. Therefore, close monitoring of patients is essential. In case of delayed diagnosis time or inappropriate follow up program, the need for medical or surgical treatment will not be met, VSD complications may occur, and the chance of surgical treatment may be lost after the development of Eisenmenger syndrome. The complication and mortality rates of surgical treatment are low. However, we think that it is important to inform families before surgery, as mortality may also develop due to complications other than cardiac causes such as infection.

Keywords: Congenital heart disease, Ventricular septal defect, Pediatric cardiology

Özet

Ventriküler septal defect sık görülen asiyanotik konjential kalp hastalıklarından birisidir. Genel olarak asemptomatik olsa da pulmoner hipertansiyon ve Eisenmenger sendromuna ilerleyebilir. Bu nedenle hastaların yakın izlemi gerekmektedir. Hastalar zamanında tanı almaz ve takip edilmezlerse medical veya cerrahi tedavi ihtiyacı karşılanmayacağı için VSD

komplikasyonları ortaya çıkabilir ve bir sure sonra Eisenmenger sendromu gelişmesiyle cerrahi tedavi şansı kaybedilebilir. Cerrahi tedavinin komplikasyon ve mortalite oranlarıdüşüktür; ancak enfeksiyon gibi kardiyak neden dışındaki komplikasyonlar nedeniyle de mortalite gelişebileceğinden ailelerin cerrahi öncesinde detaylı bir şekilde bilgilendirilmesinin önemli olduğunu düşünmekteyiz.

Anahtar Kelimeler: Konjenital kalp hastalığı, Ventriküler septal defect, Pediatrik kardiyoloji

1. Introduction

Ventricular septal defect (VSD) is an interruption at the interventricular septum. It can be developmental or embryological. (Anderson et al., 2019) It is the most common congenital heart disease in children with a rate of %30. VSDs can be isolated or associated with tetralogy of Fallot, atrioventricular canal defect, transposition of great arteries (Dakkak&Bhimji, 2020). Meanwhile VSDs can close spontaneously or by surgical method or by catheter (Hollman, 1967). Determining characteristics, treatment, prognosis and complications are important to recognize the patients with isolated ventricular septal defect.

2. Ethology

The exact ethology of VSD is not known yet but associated with genetic and environmental factors (Spicer et al., 2014). Among the genetic factors causing VSD, chromosomal, single gene, and polygenic disorders with a rate of 5% are included. Trisomies (13, 18, 21), DiGeorge syndrome, Turner syndrome, Cornelia de Lange syndrome have been found to be associated with VSD. DNA sequence variants of GATA4, GATA6, CITED2, NKX2-5, HAND1, TBX2, TBX18, SMAD3 can also cause VSD. Although VSD is associated with chromosomal anomalies and syndromes, chromosomal anomalies are not detected in 95% of patients (Penny, 2011). Maternal infections (rubella, influenza, febrile illness), maternal diabetes mellitus, phenylketonuria, smoking, alcohol, cocaine, marijuana, agricultural chemicals, benzene, and certain medications (metronidazole, ibuprofen) are also among the environmental factors (Newman, 1985).

3. Epidemiology

Isolated VSD is the most common congenital heart malformation in adults following bicuspid aortic valve and mitral valve prolapse (MVP). In children, VSD is the most common cardiac anomaly with a rate of 30%. Various studies have been conducted on its frequency; however, these studies have not been generalized to the population as they were conducted on specific patient groups. Generally asymptomatic but more comprehensive information about the frequency of VSD has been obtained after the routine use of Doppler and echocardiography in clinics. It is more common in premature and low birth weight babies. Race, gender, maternal age, birth order, and socioeconomic status are not associated with its incidence. Although prevalence varies among centers, the average is 3 per 1000 live births (Anderson et al., 2019). Approximately 90% of cases close spontaneously within the first year of life. After the age of 10, the rate of spontaneous closure is very low (Pinto et al., 2018). While gender is not associated with incidence, some studies have shown that VSD is more common in girls. In the first year of life, invasive treatment is required in 14-16% of patients (Park, 2020).

4. Anatomy and Classification

There is no complete consensus on how to define and classify VSD. This is due to differing opinions on the structures of the heart's anatomy and authors expressing the same concepts with different terminology. Different classifications have been used by various authors from the past to the present (Anderson et al., 2019). One of the commonly used classifications today is the classification proposed by Soto and colleagues. In this classification, the ventricular septum consists of membranous and muscular parts. The muscular septum comprises the following components: inlet, trabecular, and outlet or infundibular. If the defect is on the membranous septum, it is termed perimembranous; if it is on the muscular septum and adjacent to the great arterial valves, it is called subarterial infundibular defect. Perimembranous defects are found adjacent to the inlet, trabecular, or infundibular septum. Muscular defects are found within these septa. The inlet septum separates the mitral and tricuspid valves and merges with the widest portion, the trabecular septum. The trabecular septum forms the region extending from the apex and crest supraventricularis of the tricuspid valve leaflets. The straight-walled area extending from the crest to the pulmonary valve is the infundibular septum. The portion divided by the septal leaflet of the tricuspid valve is termed the membranous septum (Soto et al., 1980).

According to the Anderson classification, VSDs are divided into four main groups: perimembranous, muscular, doubly committed (juxtaposed to the artery), and juxta-tricuspid (non-perimembranous) defects. This classification serves as a guide in understanding the relationship of the defect with the conducting tissues and valves, thus providing insights into potential complications during follow-up, the likelihood of spontaneous closure, and surgical approach. Since the shape of the defect can appear differently when viewed from different planes, it is classified based on its relationship with the atrioventricular conduction axis (Anderson et al., 2019).

In 2017, the International Society for Pediatric and Congenital Heart Disease (ISNPCHD) proposed a classification system accepted by the World Health Organization (WHO) and the International Classification of Diseases (ICD-11) to unify different approaches, which is used in the International Pediatric and Congenital Cardiac Code (IPCCC). This classification system includes perimembranous, inlet, and trabecular categories (Lopezet al., 2018).

In the classification by Moss and Adams, VSDs are categorized as perimembranous (membranous, infracristal), outlet (supracristal, conal, infundibular, subpulmonary, doubly committedsubarterial), inlet, and muscular (central, mid-muscular, apical, marginal) defects.

4.1. Perimembranous type: It is the most common type, accounting for 70-80% of cases. The membranous septum is a small area located below the aortic valve. The membranous defect includes some muscular tissue adjacent to the membranous septum. Therefore, these defects are defined as perimembranous. Defects seen adjacent to the muscular septum are classified as perimembranous inlet, AV canal type, or perimembranous trabecular (outlet, Tetralogy type).

4.2. Outlet type (infundibular or conal): While it is seen in 5-7% of European countries, it is observed in 30% of Far Eastern countries. The defect is found in the conal septum, with a portion formed by the aortic and pulmonary annuli. The aortic valve prolapses through the VSD, which can lead to aortic insufficiency. Therefore, the defect is termed supracristal, conal, subpulmonary, or subarterial.

4.3. Inlet or AV canal type defects are seen in 5-8% of cases. They are located in the posterior and inferior part of the perimembranous defect, below the septal leaflet of the tricuspid valve.

4.4. Trabecular or muscular defects are seen in 5-20% of cases. They can be seen in multiple locations when viewed from the right side of the heart. Mid-muscular defects are located posterior to the septal band. Apical muscular defects are close to the cardiac apex but are difficult to visualize and repair. Anterior (marginal) defects are generally small, tortuous, and multiple in number. Repairing "Swiss cheese" type VSDs surgically is quite challenging (Park, 2020; Van Praagh et al., 1989).

In the classification by Van Praagh and colleagues, VSDs are named AV canal, muscular, conoventricular, or conal (Van Praaghet al., 1989). In addition to these classifications, a hemodynamic classification is also made. According to this classification, VSDs are divided into small, moderate, and large categories.

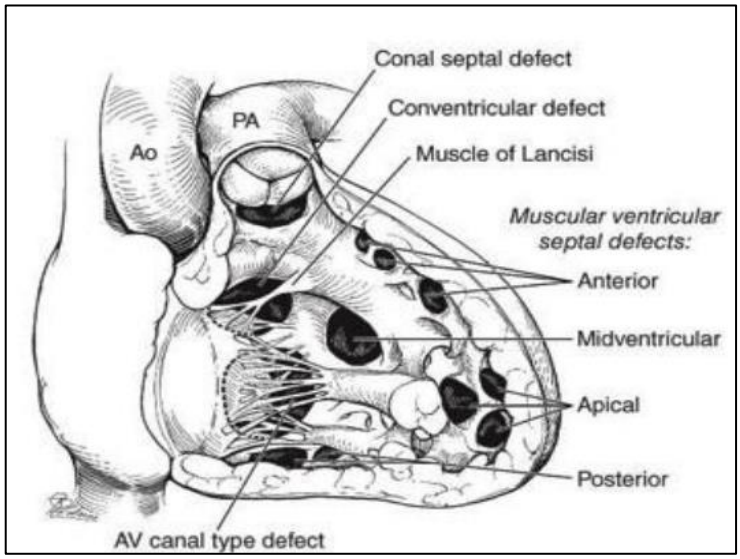

Figure 1. Classification of VSD according to Van Praagh et al.

5. Pathophysiology

In an Asiaticotic VSD, the shunt direction is from left to right. The severity of the shunt depends on the size of the defect and the pulmonary vascular resistance (PVR). Although there is no complete consensus on determining the size of the defect, decisions are made based on hemodynamic evaluation. When the VSD is small, the defect itself creates resistance to flow. This affects the amount of shunting but not the direction. The direction and size of the shunt are

determined by the ratio of PVR to systemic vascular resistance (SVR). Conversely, if the VSD is large, there is a decrease in resistance to flow, and the degree of left-to-right shunting becomes more dependent on PVR. The lower the PVR, the greater the severity of left-to-right shunting. If an isolated VSD is large enough, the pressures in the right and left ventricles equalize during systole (Park, 2020).

In the neonatal period, PVR remains high for the first two weeks and then reaches normal levels. The amount of left-to-right shunt and the amount of blood returning to the left atrium increase. Therefore, the left atrium and ventricle enlarge. In the presence of a large VSD, the decrease in PVR is delayed, so the degree of shunting does not increase significantly for 4-8 weeks; if the degree of shunting increases after this period, congestive heart failure (CHF) develops. If the pulmonary circulation is excessively exposed to pulmonary blood flow and systemic pressure due to the VSD, pulmonary hypertension (PHT) develops. In infancy, PVR may remain mildly elevated. If the increase in pulmonary blood flow persists and the PVR value equals SVR, symptoms of CHF decrease. The direction of the shunt turns from right to left, cyanosis may be observed, and pulmonary vascular obstructive disease (PVOD) and Eisenmenger syndrome develop (Andersonet al., 2019).

6. Clinical Signs and Symptoms

The majority of VSDs are asymptomatic because they are too small to cause a significant shunt, and approximately 75% of them close spontaneously within the first two years. These patients usually receive a diagnosis as a result of murmurs detected during routine examinations. The intensity of the murmur may be related to the size of the defect, the smaller the defect, the louder the murmur. The murmur is typically heard as a 2-3/6 grade, pan-systolic murmur in the left lower sternal border, regardless of the defect's localization. Patients with moderate-sized defects may experience increased pulmonary artery pressure (35-65 mmHg) and an increase in the left-to-right shunt amount (Minette, 2006; Hoffmann, 1965). In infants, failure to thrive, recurrent respiratory infections, wheezing, sweating, fatigue during feeding, inadequate weight gain, and respiratory distress may develop. In patients with large VSDs, signs of congestive heart failure (CHF) may also occur in their first year of life (low body weight, jugular vein distention, tachypnea, tachycardia, hepatomegaly). The characteristics of the murmur are similar in small, moderate, and large VSDs. If pulmonary hypertension (PHT) develops, there may be a stiffening of the S2 sound (Muralidaran&Shen, 2019). With the

progression of PHT, Eisenmenger syndrome may develop. In this condition, the left-to-right shunt decreases (Qp/Qs<2), symptoms regress, the murmur disappears, and signs of CHF disappear. However, the right ventricular impulse becomes accentuated, and in subsequent stages, cyanosis and clubbing of the fingers may develop. If patients reach adulthood, they may experience hemoptysis, exercise intolerance, arrhythmia, right heart failure, dyspnea, fatigue, palpitations, chest pain, headache, dizziness, syncope, and cyanosis (Paytoncu& Saylam, 2008).

7. Evaluation

In the past, the diagnosis of VSD relied on clinical findings, physical examination, electrocardiography (ECG), and chest radiography. Nowadays, echocardiography (ECHO) plays a significant role in diagnosis. In addition to these, cardiac catheterization, cardiac magnetic resonance imaging (MRI), computed tomography (CT), and angiography are also used as diagnostic aids (Spicer DE et al, 2014).

8. Natural History

In the past, the diagnosis of VSD was made based on clinical signs, physical examination, electrocardiography (ECG), and chest radiography. Nowadays, echocardiography (ECHO) plays a significant role in diagnosis. In addition to these, cardiac catheterization, cardiac magnetic resonance imaging (MRI), computed tomography (CT), and angiography are also used as diagnostic tools (Spicer et al., 2014). Fetal echocardiography and pulse oximeter are important techniques to diagnose congenital VSDs (Adan et al., 2021).

With the increased use of echocardiography today, the detection rate of VSD and all congenital heart diseases has increased. Consequently, the rates of spontaneous closure during follow-up have also increased (Gabrielet al., 2002). When the defect is small or does not disrupt hemodynamic, the risk of developing morbidity in the later stages is low. In moderate-sized defects, the natural course may vary depending on the size, anatomical location, and pulmonary artery pressure. While moderate-sized defects may decrease in size, spontaneous closure is rare. Congestive heart failure (CHF) may develop depending on the amount of shunting, but most respond well to medical treatment. In large defects, CHF develops in the early months, and if left untreated, mortality rates are high within the first year. In large defects not closed surgically within the first two years, CHF unresponsive to medical treatment may develop. Eisenmenger syndrome develops in untreated cases; this condition is irreversible and has a high mortality

rate. This condition may occur earlier in patients with Down syndrome; therefore, if the defect is large, surgery should be performed at 3-4 months of age. Moderate and large defects generally have a good prognosis if operated on in the early period. Symptoms that occur during this period regress, and if there is growth retardation, it improves (Robert et al., 2019).

9. Complications

9.1. Pulmonary vascular disease and Eisenmenger syndrome:

Pulmonary vascular disease is the most serious complication of VSD. In patients with large defects where there is excessive left-to-right shunting, there is an increase in pulmonary vascular resistance (PVR), leading to pathological changes in the pulmonary vessels. If the increase in PVR is not prevented, the shunt will reverse from right to left. As a result, hypoxemia and cyanosis develop. In the early stages of Eisenmenger syndrome, there is no shunt, so the symptoms disappear. This condition can be mistaken for spontaneous closure (Mebus et al., 2010).

Pulmonary vascular disease does not develop in patients with small defects. Although some patients with large VSDs have low PVR, an increase is observed within the first two years. In patients with moderate-sized and some large defects, PVR is either normal or mildly elevated in the first decade. Failure of PVR to decrease or only a slight decrease after birth is considered a high risk because these patients may not be noticed until cyanosis develops. Attention should also be paid to irreversible and progressive pulmonary vascular disease before the onset of cyanosis (Landzberg, 2007).

9.2. Infective endocarditis (IE):

Apart from secundum atrial septal defect (ASD), there is a risk of developing infective endocarditis (IE) in patients with congenital heart diseases. The likelihood of occurrence increases in adulthood. The risk is higher in patients with small to moderate defects. After closure of the defect, the risk decreases, but there may be a higher risk in the immediate postoperative period. Other congenital heart diseases accompanying VSD, such as palliative shunts, conduits, prosthetic heart valves, closure of VSD with prosthetic material, detection of residual defects after surgery, and a history of previous IE, increase the risk. In patients with prolonged fever and VSD, the possibility of developing IE should be considered. In cases of

residual defects after surgery, prophylaxis is required if the defect is closed with prosthetic material or a device. Prophylaxis is performed with antibiotics (Goldberg, 2015).

9.3. Aortic regurgitation and aortic valve prolapse:

Aortic regurgitation (AR) can be seen in 1-5% of patients. It is more common in perimembranous type defects after doubly committed and juxta-arterial types. If AR becomes irreversible, it can lead to increased load on the left ventricle. Therefore, some centers consider the presence of AR as a surgical indication even if asymptomatic. AR becomes symptomatic if it is moderate to severe (Wilson et al., 2007).

9.4. Congestive heart failure (CHF) and mortality:

9% of infants with large defects who do not undergo surgical intervention result in death within the first year. This is due to CHF and recurrent lung infections due to pulmonary edema. If mortality is not observed in the first year, these patients are candidates for complications of pulmonary vascular disease and Eisenmenger syndrome until the second decade. Mortality rates are higher in defects with large defects, PDA, aortic coarctation (CoA), and large ASD compared to isolated VSDs. In patients with small defects, the mortality rate is low, but death due to infective endocarditis may occur (Tweddell et al., 2006).

10. Treatment/Management

10.1. Symptomatic management:

Oxygen support can be provided to patients with pulmonary hypertension and Eisenmenger syndrome. Patients with moderate to large defects who exhibit signs of congestive heart failure (CHF) may experience fatigue during feeding and may have reduced oral intake. Therefore, in addition to breast milk, formula can be supplemented, or high-calorie foods can be added to increase daily calorie intake (150 kcal/kg/day). There is no need for fluid restriction. If there is fluid overload, diuretics can be used. Vitamin deficiencies and iron deficiencies may occur due to inadequate oral intake. If there is iron deficiency anemia, supplementation with iron is necessary to increase hematocrit and oxygen-carrying capacity (Galie et al., 2008).

10.2. Medical management:

Patients with small VSDs are generally asymptomatic and do not require treatment. In patients with moderate to large VSDs, if symptomatic CHF develops, there is a need for medical treatment. Depending on the patient's clinical presentation, furosemide, enalapril, and digoxin can be initiated. Furosemide is usually initiated first; if symptoms worsen, the dose of furosemide is increased, and spironolactone may be added. Close monitoring of patients for side effects is necessary when medical treatment is initiated. If symptomatic improvement is not observed despite a reduction in congestion with furosemide and surgery is not considered, digoxin may be initiated. Digoxin provides clinical relief and benefits in hemodynamic parameters in patients. The duration of medical treatment varies depending on the patient. Surgical repair is recommended for patients showing symptoms and growth retardation if there is no response to medical treatment. The duration of medical treatment varies depending on the patient (Montignyet al., 1989).

10.3. Percutaneous device closure:

In selected cases, transcatheter closure can be applied as an alternative to surgical repair. This method is performed by placing a device into the defect through a catheter under transesophageal echocardiography (TEE) and fluoroscopy guidance. The procedure is performed via the left femoral artery and right femoral vein (Santhanam et al., 2018). For this method to be applicable, the sheath inserted into the femoral vein should be easily usable and suitable for the procedure. The localization and type of defect are also important. This method can be applied for appropriate muscular defects and in patients weighing over 5 kilograms (Feltes et al, 2011). In patients weighing less than three kilograms, this method is contraindicated due to sepsis and aspirin use. Supracristal and inlet defects, as well as multiple small muscular defects, are not suitable for this method. The use of this method for perimembranous defects is difficult due to their proximity to the aortic and tricuspid valves, and complete heart block may occur during the procedure. Therefore, close follow-up is required after the procedure. It can also be used to close significant residual defects hemodynamically after surgery (Butera et al., 2007).

10.4. Surgical management:

Open surgical repair with sternotomy is recommended for patients with symptomatic CHF who do not respond to medical treatment within the first six months. Performing surgery before one

year of age can largely prevent the development of pulmonary vascular disease. Surgical repair is generally not needed for small VSDs, but repair is necessary if subacute bacterial endocarditis develops. Patients who reach six months of age without signs of CHF and have small defects are not candidates for surgery. If the pulmonary artery pressure exceeds 50% of the systemic pressure, surgical repair is required by the end of the first year. After the first year, if there is an increase in left-to-right shunt and the Qp/Qs ratio is 2:1, surgical repair is required regardless of pulmonary artery pressure. Larger children with large defects and high PVR should also undergo surgery. Surgical repair is contraindicated if there is pulmonary vascular disease with a right-to-left shunt (Park, 2020). Pulmonary banding is used for palliation in patients with complex cardiac pathologies but is not a preferred method. Most perimembranous and inlet defects are closed through a transatrial approach. Outlet defects are closed by making an incision over the main pulmonary artery. In cases of apical muscular defects, a right ventriculotomy may be necessary (Robert, 2019). Post-pericardiectomy syndrome, cerebral and renal damage, and pulmonary complications may develop in patients after surgery (Hoffmann et al., 1965).

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Conflicts of interest

None

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