VENTRICULAR SEPTAL DEFECTS

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ABSTRACT

Ventricular septal defects (VSD) is a malformation of the heart, most commonly found in infants and children. Failure on interventricular septum formation that began at the end of the fourth week to the seventh week caused by VSD. The disorder can caused by multiple factors, including the interaction between predisposing factors such as hereditary and environment factors, leading to growth factor deficiency and failure of the unification of the components forming the ventricular septum. Mutations in the TBX5 gene, NKX2-5 gene and GATA-4 gene was identified as the cause of the congenital heart malformations. VSD anatomy may arise in the ventricular septum, among others: VSD subartery, perimembranous, atrioventricularis canal and muscular. VSD management with a minor defect is usually asymtomatic and have a good prognosis. Medical treatment is indicated for patients with a defect VSD was great and showed symptoms of congestive heart failure. Surgery is indicated for patients with large defect VSD with severe congestive heart failure and uncontrolled and the presence of recurrent respiratory tract infections. Surgical correction is indicated in moderat to large defect with left to right shunt without pulmonary vascular resistance.Keywords: Heart, Congenital heart malformation, Ventricular septal defect

Background

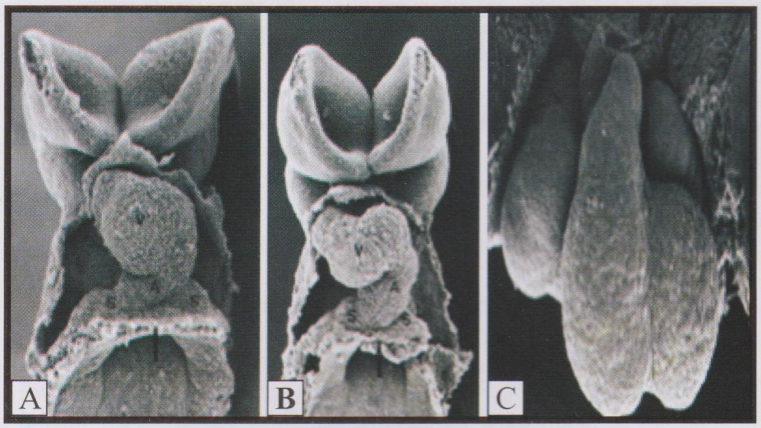
Ventricular septal defect (VSD) is the most common heart malformations found in infants and children (Behrman and Vaughan, 1992; Schmitz and Martin, 2008), responsible for 30-40% of all congenital heart malformations at birth (Lofland and Sabiston, 1994). Incidence of VSD approximately 1.5 to 3.5 per 1000 infants mature and premature infants from 4.5 to 7 per 1000. Based on echocardiography study, the incidence of VSD in newborns around 5-50 per 100 births. Ventricular septal defect (VSD) is more predominant in women (56%) than in men (44%) (McAndiel and Gutgesell, 2008). A study conducted by the Cardiac Substudy of the Collaborative Study of Cerebral Palsy, Mental Retardation, and other Neurological and Sensory Disorders of Infancy and Childhood, published in 1971, found 475 cases of congenital heart malformations. Ventricular septal defect (VSD) is the most widely diagnosed disorder which reached 133 cases out of a total of 457 cases or 30%. Based on research conducted by the New England Regional Infant Cardiac Program from 1968 to 1974, found 2251 cases of congenital heart malformations and 1/6 of the total cases were VSD, while a study conducted in 1981 to 1989 by the Baltimore-Washington Infant Study, found 4390 infants with congenital heart malformations, which is 32.1% or 1411 cases are VSD (McCrindle, 2010).

Discussion

Embriology of the heart

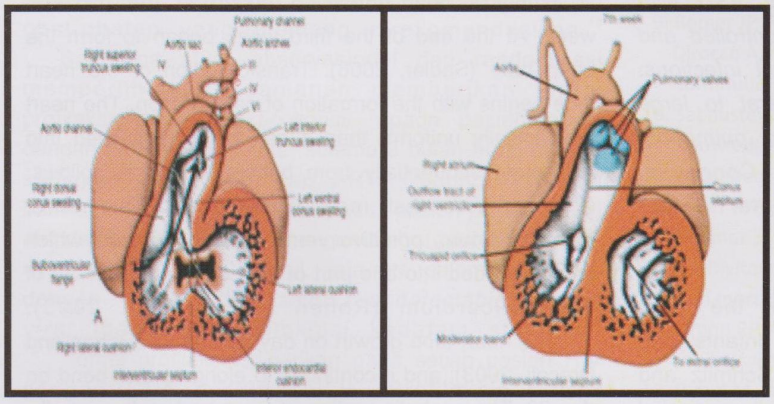
Embryo's heart formation began in the mid-third week. At the end of the third week began to form the heart tube (Sadler, 2006). Transformation of the heart tube begins with the formation of cardiac loop. The heart tube initially uniform, than it can be distinguished into four parts sequentially from bottom to top as follows: sinus venosus that receives blood from the veins, primitive atrium, primitive ventricle, bulbus cordis which can be divided into one part of the cone and trunk out of the pericardium (Rohen and Drecoll, 2003).

The heart tube growth on day 21 and 22 (Rohen and Drecoll, 2003), and it continues to elongate and bend on day 23. The cephalic portion of the tube bends ventrally, caudally, and to the right, and the atrial (caudal) portion shifts dorsocranially and to the left. This bending, which may be due to cell shape changes, creates the cardiac loop. It is complete by day 28, so that the embyos's heart can already see the parts of primitive atrium, primitive ventricle, truncus arteriosus, bulbus cordis and interventricular sulcus (Sadler, 2006).



Embryo's heart : A. 23 days. B. 24 days. C. 28 days (Sadler, 2006)

Interventricular septum formation started at the end of the fourth week, where both primitive ventricles begin to dilate. Medial wall of both ventricles are expanding the line of sight and gradually converge to form the interventrikular septum pars muscularis. Septum formation is not perfect, thus forming a rather deep apical cleft between the two ventricles, namely interventricular foramen. In addition, a thickening of the cone on the right and the left that eventually became conical septum. In the seventh week, the conical septum adjacent to interventricular foramen coalesce and form a interventricular septum pars membranous, so that interventricular septum close properly (Sadler, 2006).



Frontal section through the heart of a 5 week and 7 week embryo (Sadler, 2006)

Failure on the interventricular septum formation can lead to VSD. The defect is often associated with abnormalities in the separation of conotruncal region. Size of the defect that occurs varies and determines the flow of blood to the pulmonary arteries, which can reach 1.2 to 1.7 times more than the blood flow to the aorta (Sadler, 2006).

Etiology

Ventricular septal defects (VSD) is the most common lesion in many chromosomal syndromes, including group of trisomy 13, trisomy 18 and trisomy 21, but in 95% of patients with VSD, the defect is not related to chromosomal syndromes. Malformations is caused by multiple factors, including the interaction between predisposing factors such as hereditary and environmental factors (McAndiel and Gutgesell, 2008), leading to growth factors deficiency and failure of the unification of the components forming the ventricular septum (Ammash and Warnes, 2001).

Some genetic mutations identified as causes of congenital heart malformations, one of which is a mutation in the gene TBX5 (Bruneau et al., 2010). TBX5 gene is a transcription factor containing a DNA-binding motif known as the T-box that plays an important role in the cardiac septum formation (Sadler, 2006). Mutations in this gene can cause a defect in the fossa ovale, muscular VSD and abnormalities in the heart conduction system. Mutations in this gene can also cause extensive abnormalities, a case of hypoplastic left ventricle syndrome, total anomalous pulmonary venous connection and the atrioventricular junction (Bruneau et al., 2010).

Mutations in the NKX2-5 gene can cause defects similar to TBX5 gene mutations, among other deficiencies atrial and ventricular septal, heart conduction abnormalities, left ventricular hypoplasia and other anomalies such as tetralogy of Fallot or Ebstein malformation. Mutations in the gene NKX2-5 gene causes a loss of activity that affects the production of proteins. This can lead to gene transcription and genes can also interact with partner proteins such as TBX5 and GATA-4 (Bruneau et al., 2010). NKX2-5 gene expression as a master gene for heart formation is influenced by a combination of gene activity of BMP and WNT proteins released by the neural tube. BMP gene expression also increased the

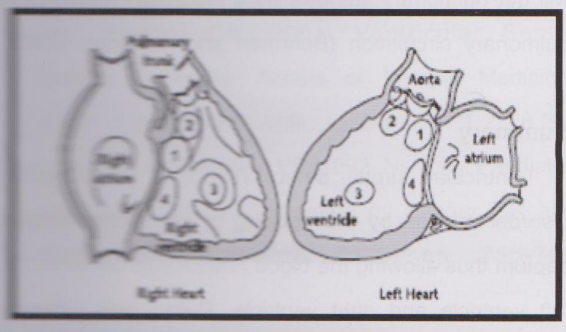
expression of genes that are important for FGF8 expression of cardiac specific proteins (Sadler, 2006). Mutations in the gene GATA-4 also contribute to the occurrence of VSD. Mutations in this gene are thought to cause loss of function of genes and can disrupt the interaction with TBX5 gene, so both of these genes do not have function as a transcription factor for the formation of an atrial and ventricular septal (Bruneau et al., 2010).

Increased use of illegal drugs has been identified as a risk factor most likely to VSD. The incidence of VSD simple perimembranous (isolated) associated with maternal cocaine use and marijuana in men. While VSD multiple perimembranous (multiplex) associated with cocaine, metronidazole and diabetes mellitus (Wilson et al., 1998).

Classification

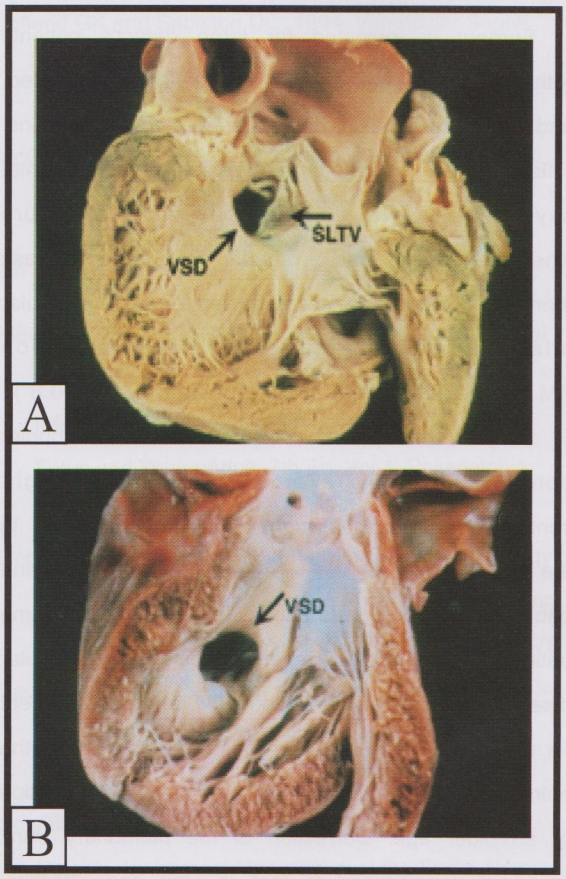
Ventricular septum is a three-dimensional structure consisting of five components, namely membranous septum, trabecular septum or muscular, or subartery infundibular septum, and atrioventricular septal or inlet (Ammash and Warnes, 2001), so based on anatomy, VSD can occur at any site in ventricular septum, among others: VSD subartery, perimembranous, canalis atrioventricularis and muscular (Lofland and Sabiston, 1994).

Ventricular septal defects (VSD) perimembranous is the most frequent of VSD (75% -80%), typically located just below the aortic valve and in the septal crest supraventricular membranosa. Ventricular septal defects (VSD) subartery (supracrista / outlet / infundibular / conoseptal) is a rare defect (5% -7%), except in Asia, the incidence reached 30%. The defect is located under the central part of the right coronary cuspis. From the right ventricle, the defect is located in the part of the outlet or infundibulum of the right ventricle just below the pulmonary valve. Ventricular septal defects (VSD) canalis atrioventricularis (canal / inlet) is the most rare defect occurs (8%), located below the valve leaflets atrioventricularis. Defects of this type are usually large and often found in people with Down syndrome (Ammash and Warnes, 2001; Lofland and Sabiston, 1994).



Types of VSD: 1. Membranous; 2. Subartery; 3. Muscular; 4. Inlet (Ammash and Warnes, 2001)

Ventricular septal defects (VSD), muscular or trabecular occurred around 5% -20%, is located in any place under interventricularis septum surrounded by muscle (Ammash and Warnes, 2001; Lofland and Sabiston, 1994), divided into several types based on location, ie central, apical and marginal. The central type if the defect is located in the moderate of the muscle and marginal type when the defect is located along the right ventrivcle septal junction (McAndiel and Gutgesell, 2008). Ventricular septal defects (VSD) that lies between the muscular crista upraventrikularis and papillary muscles associated with pulmonary stenosis and manifestations more of tetralogy of Fallot, while the defect is located on the crest supraventrikularis less common, but can be found below the pulmonary valve so the aortic sinuses, which can lead to aortic insufficiency (Behrman and Vaughan, 1992).



Membranous and muscular VSD: A. Membranous VSD with partial obliteration of septal leaflet of the tricuspid valve/SLTV); B. Muscular VSD (Ammash and Warnes, 2001)

Management

Patients with small defects are usually asymptomatic and have a good prognosis, so it is not necessary for medication therapy or surgery. Medication therapy is indicated for patients with large defects and exhibit symptoms of congestive heart failure. Drugs used among others furosemide dose 1-3 mg / kg body weight / day divided into two or three doses. Digoxin is given to large defect's patients with congestive heart failure and increased pulmonary blood flow. Many studies report a refinement and improvement in left ventricular contractility due to digoxin use (McAndiel and Gutgesell, 2008).

Surgery is indicated for large defect's patients with severe congestive heart failure and uncontrolled, and presence of recurrent respiratory tract infections. This therapy is recommended for older patients, asymptomatic with normal pulmonary pressure when pulmonary and systemic flow ratio of less than 2:1. Defects are accompanied by left ventricular dilatation often require surgical correction (McAndiel and Gutgesell, 2008).

Surgical therapy is required when the doppler echocardiography examination showed right ventricular pressure is higher than the pressure in the left ventricle at the age of 5 to 6 months and babies have growth retardation. This is because some patients are at risk of irreversible pulmonary vascular disease. There are two options for surgical treatment for newborns. The first option for the correction of the pulmonary trunk and proceed with surgical correction at an older age. Correction of the pulmonary trunk is a palliative procedure that is safe and effective. The second option is to close the defect (primary closure) (Benson et al., 2010).

A large defect's patients with pulmonary hypertension has a high risk of pulmonary vascular obstructive disease, so it can be corrected with surgery as soon as the pulmonary vascular disease is still reversible and not severe. Surgical therapy is not recommended in patients with normal pulmonary artery pressure with a small defect. Surgical correction is indicated in moderate to large defect with left to right shunt without pulmonary vascular resistance (Child and Friedman, 2005).

Prognosis

In patients with a small defect, normal pulmonary artery pressure without left ventricular hypertrophy, usually have a good prognosis (Benson et al., 2010), with little risk for endocarditis, aortic valve insufficiency and arrhythmia (McAndiel and Gutgesell, 2008; Schmitz and Martin, 2008). Based on research conducted by the First and Second Joint Studies on the Natural History of Congenital Heart Defect probabilities obtained 87% VSD's patients can survive up to age 20 years. Prognosis depends on the size of the defect and the presence or absence of pulmonary hypertension (Benson et al., 2010).

About 75% -89% defects may close spontaneously, most often at the age of 2 years (McAndiel and Gutgesell, 2008). Spontaneous closure is rare in moderate or large size defects. Some patients with large defects can get respiratory tract infections, recurrent congestive heart failure and pulmonary hypertension due to increased pulmonary blood flow. A small percentage of patients will get high pulmonary vascular resistance when the defect is not corrected, while others will get pulmonary stenosis as a protection against the pulmonary circulation (Behrman and Vaughan, 1992).

Summary

Ventricular septal defect (VSD) is a congenital disorder caused by the opening of the interventricular septum thus allowing the blood relationship between the left ventricle and right ventricle. Defect lists different types of heart malformations are most commonly found

in infants and children. VSD countless events in approximately 30-40% of all congenital heart disease at birth, the incidence is higher in preterm infants compared with infants mature and more predominant in women than in men.

Ventricular septal defect (VSD) caused by multifactors: the interaction between predisposing factors such as hereditary and environmental factors. Some genetic mutation identified as the cause of this disorder, which is a mutation in the gene TBX5, NKX2-5 and GATA-4 that acts as a master gene and transcription factor for septum formation of the heart. Diabetes mellitus, the use of drugs such as cocaine, marijuana and metronidazole is also associated with the incidence of VSD.

About 75% -89% defects may close spontaneously, most often at the age of 2 years. Medical treatment was given for patients with large defects and accompanied by congestive heart failure, while surgical therapy is indicated for a large defect's patients with severe and uncontrolled congestive heart failure, recurrent respiratory infections and growth retardation. Surgical therapy performed on VSD before the onset of pulmonary hypertension. The severity of pulmonary hypertension that occurs determines prognosis of VSD. Patients with VSD have a high risk for endocarditis, so need prophylactic antibiotics for selective procedures.

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