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Complete atrio-ventricular canal in natural history. A case in adulthood and a mini-review

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SOUHRN

Přirozený vývoj kompletního defektu atrioventrikulárního septa (atrioventricular septal defect, AVSD) bez operačního řešení již byl popsán, přičemž řada autorů uvádí, že pouze 4 % pacientů se dožijí více než pěti let. Bez operace je příčinou většiny úmrtí v raném dětství městnavé srdeční selhání v důsledku velkého levopravého zkratu a nedostatečnosti atrioventrikulární chlopně. Příčinou úmrtí ve věku nad pět let je pravděpodobně postižení plicní vaskulatury vedoucí k nezvratné plicní hypertenzi zatížené nepříznivou dlouhodobou prognózou. Popisujeme případ kompletního AVSD s dožitím páté dekády věku, přičemž u pacienta byl defekt spojen s dextrokardií a společnou síní.

ABSTRACT

The natural history of complete atrio-ventricular septal defect (AVSD) without surgery has been well documented and many authors have reported that only 4% of patients survives beyond 5 years old. Without surgery, most of the deaths in infancy are from severe congestive heart failure caused by the large left-to-right shunt and atrio-ventricular valve incompetence. Deaths after 5 years of age are probably from pulmonary vascular disease that leads to an irreversible pulmonary hypertension burdened by a poor long-term prognosis. We present a case of complete AVSD with a survival till fifth decade of life in whom the defect was associated with a dextrocardia and a common atrium.

Introduction

The term "atrio-ventricular septal defect" (AVSD) covers a spectrum of congenital heart malformations characterized by a common atrio-ventricular junction coexisting with deficient atrioventricular septation. In ostium primum atrial septal defect (ASD) there are separate atrioventricular valvar orifices despite a common junction, while in complete AVSD the valve itself is also shared.

Complete AVSD is also called complete atrio-ventricular canal (CAVC).[1,2]

The estimated incidence of the condition in the era of two-dimensional echocardiography varies from 0.24/1000 live births to 0.31/1000 live births.[1]

CAVC is considered an uncommon congenital heart disease, accounting for about 3% of cardiac malformations. According to Calabrò et Limongelli,[1] atrioventricular canal occurs in two out of every 10,000 live births.

About the aetiology we know that formation of atrioventricular canal results from complex interactions of components of the extracellular matrix. Septation of the atrioventricular junction is brought about by down growth of the primary atrial septum, fusion of the endocardial cushions, and forward expansion of the vestibular spine between atrial septum and cushions.[3] Thus, atrioventricular canal can result from arrest or interruption of the normal endocardial cushion development.

The clinical presentation and prognosis of these pathologies vary according to the morphology and type of defect and they are based on the presence of further associated defects.

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In children with complete AVSD and a non-restrictive interventricular septal defect, the development of heart failure represents an early event, which occurs around the first months of life when the pulmonary arterial resistance decreases.[4]

Signs of heart failure can occur even earlier, during the first weeks of life if there is severe insufficiency of the common atrioventricular valve and if aortic coarctation or left ventricular dysfunction coexist.

Surgical intervention is fundamental for survival and, in the absence of this, many patients die in childhood, or if they survive, develop high pulmonary vascular resistance that lead them to Eisenmenger's syndrome.[5]

Surgery is usually performed between the 3rd and 6th month of life.[1]

There are some patients with complete ASVD and large interventricular septal defect, often with Down's syndrome, in whom heart failure does not occur, due to the persistence of high pulmonary vascular resistance from birth.

Patients with complete ASVD and restrictive ventricular septal defect (VSD) in whom regurgitation of the atrioventricular valve is minimal, may remain asymptomatic or develop only mild symptoms in childhood. In any case, in the absence of surgical treatment, there is a significant increase in mortality and morbidity and only 25% of these patients survive beyond 40 years of age.[4]

The case

A 52-year-old Hispanic man came to the Emergency Room (ER) for worsening dyspnoea in the past two months. NYHA class was IIIb.

In his clinical history there was a congenital heart disease in natural history, described by the patient as 'dextrocardia associated with a single atrium'. Patient told that his mother refused surgical intervention at newborn-hood.

ECG was performed by placing the precordial leads in a mirror-image position on the right side of the chest and reversing the left and right arm leads. The exam (Fig. 1A) documented atrial fibrillation (AF) with average heart rate (HR) of 90 bpm, associated with left axis deviation, inversion of all complexes in lead I, positive QRS complexes in aVR and absent R-wave progression in chest leads (dominant S waves throughout). AF was defined as 'permanent' by the patient who was being treated with furosemide, aspirin and ambrisentan.

On physical examination, cyanosis, digital clubbing, 4/6 systolic murmur along the right anterior axillary line, hepatic margin two-fingered from the costal arch, sloping oedemas were found. Blood pressure (BP) was 80/50 mmHg with body temperature of 38.5 °C.

Chest x-ray showed dextrocardia together with a significant increase in cardiac image and marked lung congestion (Fig. 2B).

Arterial blood gas test revealed a severe hypoxemia with partial pressure of oxygen of 50 mmHg and arterial oxygen saturation of 85%. PaO_2/FiO_2 ratio was 102.

Bloods demonstrated a normal renal function and electrolytes, elevated C-reactive protein, leucocytosis, mild anaemia and low haemoglobin level but negative blood cultures.

Due to dextrocardia, transthoracic echocardiography (TTE) was performed in right lateral decubitus and with acoustic windows to the right of the sternum. The exam confirmed the presence of a "common atrium" but showed also the following findings: 1) the presence of a common five-flaps atrio-ventricular valve (Fig. 2A, video 1) with a double and torrential regurgitation jets from both ventricular chambers to the common atrium (Fig.2B, video 2); 2) membranous VSD and bidirectional shunt; 3) ventriculo-arterial concordance (Fig. 2C, video 3); 4)

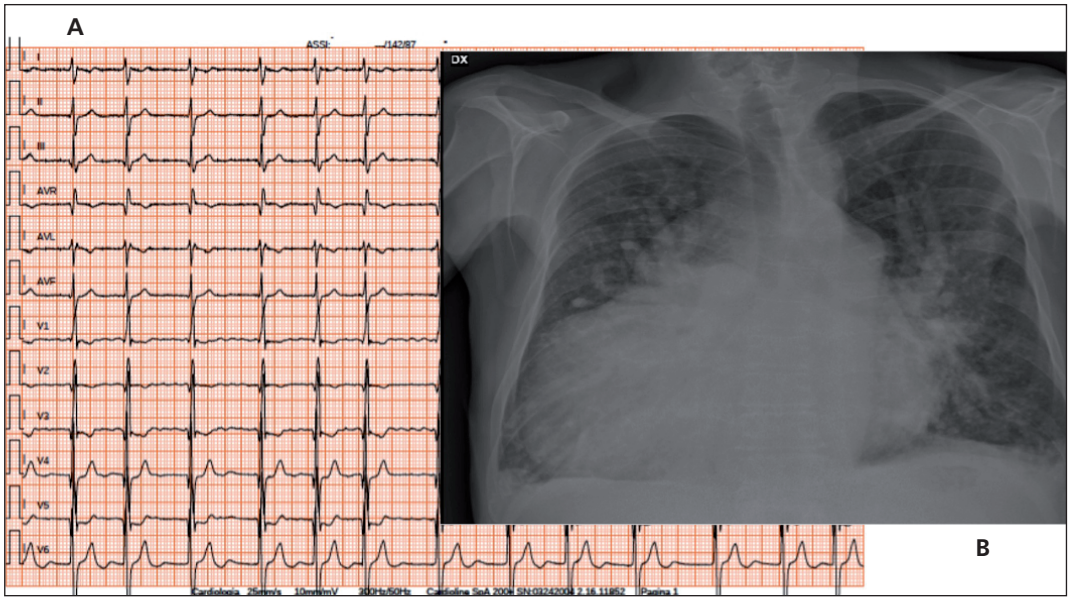

Fig. 1 – (A) 12-lead electrocardiogram obtained by placing the precordial leads in a mirror-image position on the right side of the chest and reversing the left and right arm leads. (B) Chest X-ray demonstrating dextrocardia and cardiomegaly.

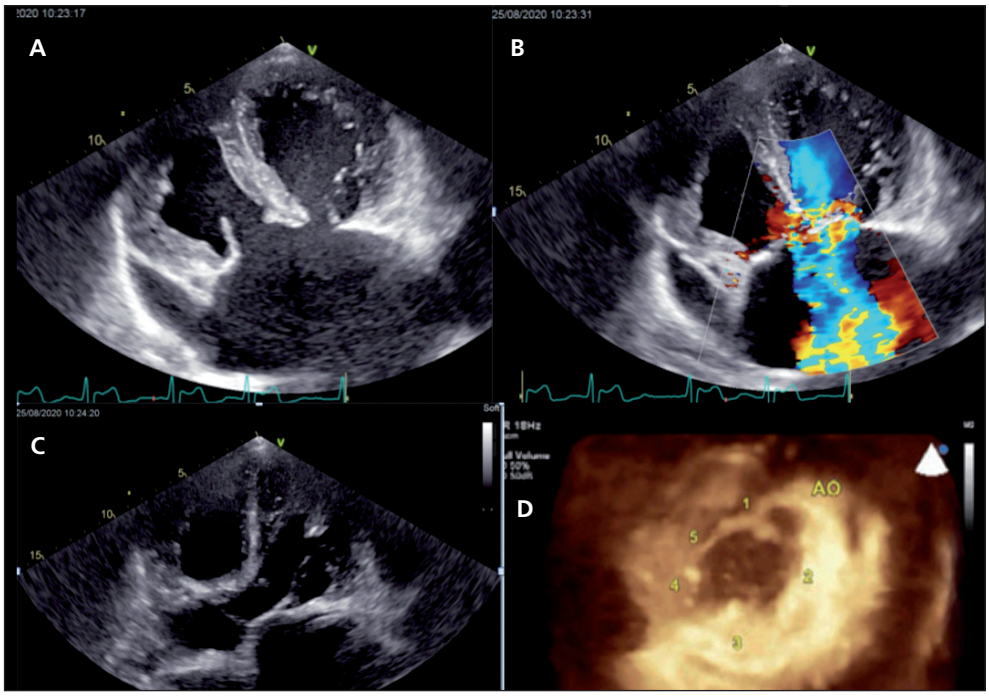

Fig. 2 – (A) 2D-TT echocardiography, apical view demonstrating a CAVC picture. (B) 2D-TT echocardiography, apical view, colour Doppler mode demonstrating massive regurgitation jets through common AV valve. (C) 2D-TT echocardiography, apical view, demonstrating left ventriculo-arterial concordance. (D) RT-3D-TT echocardiography: en face view of the common AV valve showing all five leaflets.

normal biventricular ejection fraction (RVEF: 47%; LVEF: 56%); 5) right ventricle/left ventricle basal diameter ratio of 1,2; 6) peak velocity regurgitation jet coming from right ventricle of 4,8 m/s with an estimated systolic pulmonary artery pressure (sPAP) of 92 mmHg, confirming a picture of Eisenmenger's syndrome; 7) common atrium end-systolic area of 28 cm^2; 8) pulmonary artery diameter of 35 mm; 9) inferior vena cava diameter of 28 mm with decreased inspiratory collapse (20%); 10) no infective vegetations were found.

Real time (RT)-3D-TTE en face view allowed the complete visualization of the common AV valve showing all five leaflets (Fig. 2D).

During Intensive Care Unit (ICU) permanence, patient underwent inotropic support with intravenous dobutamine, non-invasive positive pressure ventilation (NPPV) with FiO_2 of 80% and high dose diuretic intravenous therapy which resulted in a progressive reduction of hypotension, hypoxemia and signs of systemic and pulmonary venous congestion. He was also treated with antibiotics (piperacillin/tazobactam 4.5 g for three times daily), warfarin, digoxin, bisoprolol, ambrisentan plus sildenafil. At discharge clinical conditions and respiratory parameters appeared significantly improved and he was referred to specialized grown-up congenital heart diseases (GUCH) center where he underwent further titration of therapy for pulmonary hypertension and was evaluated for the possible eligibility to cardiopulmonary transplantation. Right heart catheterization confirmed the severe pulmonary hypertension (pulmonary artery pressure [PAP]: 80[max]-51[med]-29[min] mmHg); Qp:Qs shunt fraction resulted of 2,2; arterial pulmonary resistance: 4,2 UW; pulmonary vascular response to inhaled **nitric oxide** (NO) demonstrated no reduction in PAP. The 6-minute walking test demonstrated a distance of 180 meters.

He's actually in waiting list for a combined (heart-lung) transplantation.

Discussion and mini-review

Diagnostic tools

As we know, diagnosis of CAVC might be clinically suspected in patients presenting in the first few months of life with congestive heart failure, cardiomegaly on chest X-ray and left axis deviation, bi-atrial enlargement and bi-ventricular pressure/volume overload on electrocardiogram (ECG). Echocardiography is the key tool for the diagnosis and anatomic classification of this malformation. Over the years, several methods of classification and nomenclature for atrioventricular (AV) septal defects have been proposed. CAVC is characterized by a large septal defect with an atrial component, ventricular component, as well as a common AV valve, and a common AV ring. The common AV valve consists of a single annulus and five leaflets (superior bridging, inferior bridging, mural lateral, antero-superior, and mural inferior). Based on considerations for potential surgical corrections, Rastelli et al.[6] classified the pathology into types A, B, and C. In most advanced form of development (Rastelli type A), the superior bridging leaflet is attached to the crest of the ventricular septum. In type B, the superior bridging leaflet extends over the vent-

Table 1 – Anatomic classification of CAVC[6]
Type A
The superior bridging leaflet is almost completely adherent to the left ventricle and is firmly attached on the ventricular septum by multiple chordal insertions.
Type B
The superior bridging leaflet is attached over the ventricular septum by an anomalous papillary muscle of the right ventricle.
Type C
The superior bridging leaflet is not attached to the ventricular septum (free-floating leaflet).

ricular septum and attaches to an anomalous papillary muscle of the right ventricle. The most primitive form (Rastelli type C) is also the most complex-one: the superior bridging leaflet is free-floating, not attached to the ventricular septum with the lateral margins attached to an anterior papillary muscle in each ventricle.[6,7]

It is important to identify the attachment of superior bridging leaflet to further classify complete AV septal defects using the Rastelli classification system (Table 1).

Additionally, the space between the left ventricular components of the superior and inferior bridging leaflets is traditionally called "cleft". Some morphological studies suggested that this gap functions as a commissure, even though it is not supported by a papillary muscle.[8]

CAVC is frequently associated with other congenital anomalies. Type A CAVC is most frequently associated with left-sided obstructions. Type B is the least common form of atrioventricular canal. Type C is often associated with other complex cardiac malformations such as tetralogy of Fallot. Additional cardiac malformations are the left ventricular inflow and outflow obstructions, mainly due to anomaly of the left component of the common atrioventricular valve, and to ventricular imbalance, with right ventricular dominance.[9–11] Our patient had a Rastelli type A form associated with dextrocardia and common atrium. The association with these two additional malformations was never reported in medical literature.

2D trans-thoracic echocardiography (TTE) is the key technique to accurately assess all these anomalies and is also crucial in assessing the dysfunction of common atrioventricular valve and in detecting pulmonary artery hypertension (PAH).

Singh et al.[12] demonstrated the incremental value of live/real time three-dimensional transthoracic echocardiography (3D-TTE) over 2D-TTE in adult patients with a complete AV septal defect. Authors demonstrated that, using sequential cropping of the 3D data sets, it is possible to accurately assess all five leaflets of the common AV valve by visualizing them en face. Likewise, unlike 2D-TTE, the atrial and ventricular components of the defects can be well visualized en face and their extent comprehensively delineated by 3D-TTE.[12]

In addition, 3DTTE allows direct visualization en face of the vena contracta (VC) of the regurgitation jets, facilitating accurate measurement of its area by planimetry together with calculation of regurgitant volumes.[13,14]

Natural history and the pathology in adulthood

The natural history of children with CAVC is a progressive and irreversible pulmonary vascular disease.[4] However, trans-thoracic echocardiography allows to really detect the pathology in neonates presenting with symptoms of cyanosis[5] and this allows also for a quick and prompt surgical correction of the defect, before the development of congestive heart failure and irreversible pulmonary hypertension.

To date, we know that half of children with untreated CAVC die in the first year of life.[15–17] The main cause of death in infancy is either heart failure or pneumonia while, in surviving patients with unrepaired CAVC, irreversible pulmonary vascular disease becomes increasingly common, and affects virtually all patients older than 2 years of age.[5] Long-term prognosis of the patients with irreversible pulmonary hypertension is poor.

The natural history of complete AVSD without surgery has been well documented by Berger et al.[5] They stated that only 4% survival beyond 5 years old, concluding that, without surgery, most of the deaths in infancy are from severe congestive heart failure caused by the large left-to-right shunt and whatever A-V valve incompetence may be present. At contrary, deaths after 5 years of age are probably from pulmonary vascular disease.

In consideration of the severity of symptoms and the high sensitivity and specificity of current imaging techniques, diagnosis in adulthood is a rare event.[18] There are very few cases described in the medical literature of CAVC in natural history who reach adulthood. One of the first published cases dates back to 1984 and involves a 73-year-old male patient who underwent cardiological consultation before undergoing prostatectomy.[18] The patient knew he had a heart disease, diagnosed as rheumatic heart disease. He had no symptoms and was leading a normal life, but he had experienced one attack of paroxysmal atrial tachycardia several years before. Physical examination revealed normal pulse rate and there was no evidence of congestive heart failure. At chest X-ray there was evidence of right ventricular enlargement. Two-dimensional echocardiography showed a defect in the lower part of the interatrial septum overlying a defect in the upper part of the interventricular septum. Separate mitral and tricuspid components of the anterior common leaflet were present, with probable chordae appearing to cross over just above the interventricular septum.[18] Another case[19] is regarding a 20-year-old patient with Down's syndrome who immigrated to the United States from Mexico. He presented with dyspnoea due to mild exertion, in the absence of other symptoms. He had a history of long standing sleep apnoea, secondary to the macroglossia that's typical of Trisomy 21. At the time of surgical repair, a large ostium primum atrial septum defect was identified, in addition to a large ventricular septal defect with a common atrioventricular valve.[19] Authors reported the hypothesis that one of the factors that allowed this patient to progress relatively symptom-free into adulthood may have been the protective vasoconstrictive effect of hypoxia, secondary to sleep apnoea. Hypoxic vasoconstriction is a defining characteristic of the pulmonary circulation, and a study published by Schneider et al.[20] has found vasoconstriction in the pulmonary

vasculature during obstructive sleep apnoea. This "auto-pulmonary artery banding" phenomenon from enduring hypoxia may have protected this patient's pulmonary bed from the development of an irreversible disease. An emblematic case was described by Atik et al.[21] in Brazil in 2019 and it is regarding a 33-year-old patient with Down's syndrome, who did not develop symptoms from birth. At the time of evaluation, the patient was able to walk for about 30 minutes without developing dyspnoea. At the 2D-TT echocardiogram the patient presented ostium primum-type atrial septal defect measuring 10 mm in diameter and inflow tract ventricular septal defect measuring 15 mm, with an effective 7 mm orifice by interposition of valve tissue, with interventricular pressure gradient of 78 mmHg. There was a single atrioventricular valve with two orifices, of which the right-one measured 23 mm in maximum diameter and the left one 30 mm. There was left valve regurgitation caused by cleft, resulting in a moderate left atrial increase.[21]

All these reported cases add further evidence that occasional prolonged survival is possible in patients with atrioventricular canal, even the complete form.

Ours represents one of the rare cases of patients with CAVD in natural history who reached adulthood despite a severe and irreversible pulmonary hypertension. The uniqueness of the case is further highlighted by the presence of a common atrium and dextrocardia. These anomalies were never described in association with CAVC detected in adulthood.

Conclusions

It is well known that the complete atrioventricular canal (CAVC) defect has an unfavourable evolution, with signs of heart failure that occur in the first days of life, and which are associated with signs of pulmonary hypertension secondary to pressure overload and pulmonary vascular remodelling.

For this reason a timely diagnosis, during the first weeks of life, allows surgical treatment before the development of an irreversible pulmonary hypertension.[22]

Our case is regarding a patient who survived till fifth decade without surgery.

The rarity of our case is also highlighted by the presence of dextrocardia and enlarged common atrium.

In these types of patients there is no agreement about the treatment and, in presence of Eisenmenger evolution, it may include heart-lung transplantation.

In any case, a rigorous and thorough follow-up is of fundamental importance, in order to make the best therapeutic decisions.

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