Pulmonary artery aneurysm in a marfanoid adult patient with unoperated functional single ventricle and levo-transposition of the great arteries

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Abstract: We report a sudden death case of a 33 years old male with Marfan-like syndrome, having a medical history of unoperated congenital heart disease (double outlet right single ventricle with levo-transposition of the great arteries) complicated by heart failure and rhythm disorders; cardiologists also suspected an aneurysm of the ascending aorta. The autopsy confirmed the Marfan-like habitus and the presence of a single ventricle with double inlet - double-outlet of the right ventricle morphology and levo-transposition of the great arteries; it also revealed the presence of a pulmonary artery aneurysm and an anomalous origin of the left anterior descending coronary artery in the right coronary sinus. Medico-legal judgement of such an unusual case is a complex process, implying not only morphologic assessment of the case, but also reconstruction of the abnormal physiology and clinical stage of the disease.

Key Words: Congenital heart disease, univentricular heart, single ventricle, double inlet - double outlet right ventricle, transposition of great arteries, pulmonary aneurysm, anomalous origin of LAD, Marfan syndrome.

INTRODUCTION

Congenital heart disease (CHD) are the most common anomalies found in new-born, the reported incidence varying between 9 to 12 per 1000 live births [1, 2]. They represent an important cause of morbidity and mortality, with highest rates in infants and among young adults 18 to 34 years of age [3].

CHD are subject to various physiological and anatomical classifications due to their high variability [4]. They include a group called either “functional single ventricle” or “univentricular heart” (SV) designating those CHD, characterised by the lack of two completely developed ventricles; some of these cases may be described as double outlet ventricles, either right (DORV) or left (DOLV) accompanied by hypoplastic left or, respectively, right ventricle [5, 6]. Conotruncal malformations resulting in an abnormal ventriculocardial connection (transposition of the great arteries -TGA-) may also be encountered in SV patients [7, 8]. Despite improvements in cardiac ultrasound techniques, such cases with completely altered cardiac anatomy, are frequently subject to inaccurate diagnosis. This is particularly true for prenatal diagnosis (reports show that DORV cases
are the most likely conotruncal malformation to be misdiagnosed [9–11]), but is encountered in adults, when examination is performed in centres with low expertise in CHD.

CASE PRESENTATION

We present the case of a 33-year-old man who died in hospital after a cardiac arrest at home followed by cardiopulmonary resuscitation. He has been known since childhood with a complex CHD and great vessels transposition; at adult age he had been diagnosed with NYHA class II heart failure, longstanding atrial fibrillation, single ventricle with double outlet and Marfan syndrome; repeated transthoracic echography, performed in the five years preceding patients death, found a large single ventricle 84 x70 mm, with moderately depressed ejection fraction (40-45%) and mild regurgitation of both AV valves; neither pulmonary hypertension, nor subpulmonary stenosis were ever mentioned at those examinations; some ultrasound studies noted the dilation of a great artery (“possibly the ascending aorta”). The patient had been receiving a chronic treatment with Digoxin, Furosemide, Acenocumarol, Carvediol and Spironolactone. Arterial oxygen saturation ranged between 91-93% and the Haemoglobin was 15.0g/dL. The family stated a reduction in effort capacity over past weeks.

Following initial successful cardiopulmonary resuscitation (CPR), the patient was hospitalized for 3 hours. The investigations showed tachycardia (120 beats/min) and “biventricular hypertrophy” on the ECG; transthoracic echography identified a single ventricle from which both great vessels were arising, the aorta being situated anteriorly and to the left of the pulmonary artery, low ejection fraction (20%), atrio-ventricular regurgitation, and a much-dilated pulmonary artery. The measurement of the great vessels diameter by thoracic CT scan were: 28 mm ascending aorta, 18 mm descending aorta, 63 mm pulmonary artery, 44 mm right pulmonary artery, 41 mm left pulmonary artery (Figs 8 to 11).

Being classified as sudden death, a medico-legal autopsy was ordered and performed 4 days later. The external examination revealed a marfanoid habitus with muscular-adipose hypotrophy (height =194 cm, weight=63 kg) and signs of CPR and emergency medical

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**Figure 1.** PA: pulmonary trunk; AA: ascending aorta; RA: right atrium; RCA: right coronary artery; LAD: left anterior descendent coronary artery; LCxA: left circumflex coronary artery; CRV: “common” right ventricle; HLV: hypoplastic left ventricle.

**Figure 2.** Common right ventricle, lateral cut: MV: mitral valve; MO: mitral opening; TV: tricuspid valve; PO: pulmonary opening; AO: aortic opening; RA: right atrium.

**Figure 3.** Aortic valve, anterior cut: RCA: right coronary artery; LAD: left anterior descendent coronary artery; LCxA: left circumflex coronary artery.
manoeuvres: electrical burns on the skin of the trunk, vascular punctures, and thoracic fractures. The internal autopsy showed signs of congestive heart failure: bilateral pleural effusion (right: 450 mL, left: 500 mL), agonal food aspiration in trachea and bronchi, pulmonary haemorrhage, basal right pulmonary emphysema.

The inspection of the heart in situ revealed an enlarged heart (670 g), relatively large atria, hypertrophic and dilated right ventricle (RV), severely hypoplastic left ventricle and levo-transposition of the great arteries (the arterial valves were placed in a side by side position, with the aortic valve placed anteriorly and to the left of the pulmonary valve). There was a frank aneurysm of the pulmonary artery (6.3 cm in diameter) (Fig. 1).

For heart dissection we incised the right lateral margin of the RV and found a large and hypertrophic ventricular chamber with coarse trabeculations, one of them suggesting a moderator band (RV type SV), connected to both atrioventricular valves and to both great arteries. Posteriorly and to the left of the RV there was a severely hypoplastic (slit like) nontrabeculated LV; the LV had no identifiable inlet (Figs 2, 4). An anomalous coronary pattern was associated: left anterior descending coronary artery (LAD) originated from the right coronary sinus, through a separate ostium placed just above the right coronary ostium (Figs 1, 3, 4). In conclusion, the autopsy identified in a Marfan adult patient with situs solitus and D-loop, a functional single right ventricle of the double inlet - double outlet type, with levo-transposed great arteries, pulmonary artery aneurysm and anomalous LAD origin.

The microscopic examination pointed out alveolar haemorrhage and food aspiration due agonal state, bronchopneumonia, mild signs of chronic stasis in liver and kidney, low grade signs of pulmonary hypertension (class I and II Heath-Edwards)(Figs 6 and 7), and myocardium hypertrophy.

**Figure 4.** Transverse cut of the heart: LAD: left anterior descendent coronary artery; RV: right ventricle; HLV: hypoplastic left ventricle; VS: incomplete ventricular septum (inferior part).

**Figure 5.** LA: left atrium; MV: mitral valve; MO: mitral opening.

**Figure 6.** PAB: pulmonary artery branch; SIH: subintimal hypertrophy; AH: alveolar haemorrhage + oedema; (HE stain).

**Figure 7.** PAB: pulmonary artery branch; SIP: subintimal proliferation; AH: alveolar haemorrhage (HE stain).
DISCUSSION

“Functional single ventricle” (or univentricular heart) (SV) is a heterogeneous group of CHD including different morphologic entities [12] such as double inlet ventricle (i.e. connection of both atria through separate atrioventricular valves to the well-developed ventricle); more frequently (~2/3) [5], the dominant ventricle is the left one - double inlet left ventricle (DILV) -; when the RV is dominant, double inlet right ventricle (DIRV) is defined; other subtypes of are: absence of one atrioventricular connection (tricuspid atresia or mitral atresia), unbalanced atrioventricular channel (common atrioventricular valve with one well developed and one hypoplastic ventricle), single ventricle in the heterotaxy syndrome.

Functional single ventricle represents 7.7% of all CHD, with an incidence at birth of 4-8 per 10000 [13]. The literature is scarce in describing the natural history of uncorrected SV, since most cases undergo surgery early in life and most reports focus on post therapeutic results. Even if precise figures for survival without any surgical treatment are lacking, all authors agree that the natural history of the disease is severe. It depends on different factors: the anatomic type, the physiologic profile, associated lesions. The hypoplastic left heart syndrome (HLHS) has a catastrophic natural history: almost all patients die before 3 months of age [6]. Double inlet ventricle has a somehow better natural history than HLHS, but still a grim one. It depends on the degree of pulmonary blood flow (PBF) restriction, the morphology of the dominant ventricle and the associated lesions. Patients with unrestricted PBF (implying early congestive heart failure and if that overcome, late pulmonary vascular obstructive disease and Eisenmenger syndrome) have the worse prognosis. Restriction of the PBF (due pulmonary stenosis) was not shown to be life protective [14]. There is however a group of patients with moderately restrictive blood flow (with well-balanced systemic and pulmonary flows) in which a less steep survival curve was noted. Occasionally long survival (up to 66 years) was reported in such patients with “balanced” SV [15]. Overall, DILV was associated with a better natural history than DIRV [14] (particularly in cases with moderate pulmonary stenosis) [16]. The reason may lie in the decreased capacity of a ventricle with RV architecture to adapt its pump function to volume overload and systemic pressure. In a group of SV cases diagnosed at the mean age of 7 years and unrepaired, the 50% survival was 14 years after diagnosis, in DILV cases, but only 4 years in DIRV patients [14].

At autopsy a double inlet - double outlet RV (DI-DORV) was identified [17]. An associated levo-Transposition of the great arteries (l-TGA) was also present in the case (as it was certificated shown by the CT exam, in which the pulmonary valve assumes the normal central position of the aortic valve (Fig. 9) - , which was displaced anteriorly and to the left (Fig. 10).

No severe pulmonary stenosis was noted at post-mortem examination of the heart. However, below the pulmonary valve there was a short infundibulum, barely permitting the introduction of the index (Fig. 2), which intra vitam might have acted as a moderate subpulmonary stenosis. The attested peripheral O₂ saturations (SpO₂) of over 90% at various examinations in the years preceding the patient’s death are consistent with a case of SV with a PBF surpassing the systemic blood flow. The magnitude of pulmonary hypertension (PHT) is difficult to assess at the post mortem examination. Some degree of PHT
was certified by the lung histology (Heath-Edwards Class I and II changes); however, presence of an Eisenmenger syndrome is highly improbable, based on the SpO₂ values and the lung histology.

An interesting find was the pulmonary artery aneurysm (PAA). PAA were reported in association with various types of CHD [18], but to our knowledge this is the first report of a PAA in an unoperated univentricular heart. On an adult CHD population it was found that atrial and ventricular left-to-right shunts and pulmonary stenosis were the lesions most frequently associated to a PAA; only 42 % of PAA patients with CHD had PHT and, surprisingly, PA diameter was not correlated significantly to PA systolic pressure[19], probably due a mix of disease with a diverse impact on pulmonary artery pressure (left-to-right shunts and pulmonary stenosis). However, in a recent study, prevalence of PAA cases (defined as PA diameter > 40mm) in patients with PHT (defined as mean PA pressure >25 mmHg) was up to 38% [20].

The PA dilation was one of the former Ghent criteria for Marfan syndrome [21]- later withdrawn from their revised edition [22]; it was proved associated with Marfan syndrome MRI [23] and echographic studies – with an 15.3% incidence of aneurysms (if defined as PA diameter >4 cm), but with no case over 6 cm [24]. Probably, as the aortic root dilation is usually more significant than the PA dilation, [23] only five cases of clinically relevant PAA in Marfan patients are to be found through a PubMed search; three of them were associated to PHT[25–27] but two developed without this trigger [28, 29]; there is no mention of any PAA complicating a single ventricle case.

The most frequent causes of death in patients with SV are congestive heart failure, arrhythmias and sudden death [30]. Our case could be coded as sudden death, presumably secondary to an arrhythmic event.

The discussion of the case should assess if the patient could have been treated surgically. In patients with functional single ventricle, the surgical repair to a normal anatomy (i.e. biventricular) is not possible. Surgery is usually aimed to create a Fontan circulation (using the well-developed ventricle as pump in the systemic circulation, while the pulmonary circulation is driven by central venous pressure). This may be accomplished either in a single stage (usually after 2 years) or in a dual stage: bidirectional cavo-pulmonary anastomosis (i.e. Glenn shunt) followed later by completing the Fontan physiology through a connection of the inferior vena cava to the pulmonary arterial tree. This “functional repair” is not recommended very early in life, so that, in critical clinical settings, it may be preceded by a palliative operation aimed to improving survival during that period (pulmonary banding, in cases with unrestricted PBF, or a systemic-pulmonary shunt, in patients with severely diminished PBF). Though sometimes performed even in the adult patient, instauration of a Fontan physiology requires some morpho-functional conditions (“The 10 commandments of Choussat”[31]); at least some of them were probably not met by this case: absence of PHT (a mean PAP<15 mmHg), lack of ventricular dysfunction, competence of the AV valve(s), absence of atrial fibrillation. Even if many question or attenuate the strength of all these conditions [32], the maintenance of the first two of them is still largely supported [33]. So we may conclude that, in this particular case, a functional repair could have been attempted at a much younger age (before development of PHT and ventricular dysfunction), but was no longer advisable in the late stages of the disease.

Also, one particularity of this case is the unusual long, 33 years natural survival. Despite the complex nature of the CHD, the right morphology of the single ventricle that developed a significant hypertrophy and the conotruncal malformation associated with a PAA, the patient had an unexpectedly long life spans and a relatively normal life with only medical treatment. This comes to show that in the case of such complex CHD it is difficult to establish an accurate prognosis. Furthermore, in today’s era of prenatal ultrasound screening the most challenging tasks besides establishing a correct diagnosis in the case of complex CHD, has become counselling the parents regarding the prognosis and outcome of such cases.

CONCLUSION

Unoperated complex congenital heart disease may survive to adult age. In such cases a sudden death event can complicate the forensic process, as conclusions should be drawn only after thorough understanding of the morphologic and physiologic features of the specific disease, and of their clinical implications. A double inlet - double outlet RV case, with a 33 years natural survival is reported. The patient associated a pulmonary artery aneurysm and Marfan-like syndrome. Death occurred after a documented history of congestive heart failure, presumably due to the limited capacity of a SV with RV architecture to adapt to systemic pressures.

Conflict of interest. The authors declare that there is no conflict of interest.

References


