

Case Report

Prevailing Right Ventricular Myocardiopathy for Previous Myocarditis or Arrhythmogenic Dysplasia?

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A clinical case of a 10-year-old male patient is reported. His dilated and prevailing right ventricular myocardiopathy shows diagnostic difficulties between previous myocarditis etiology and arrhythmogenic dysplasia. As the elements are not pathognomonic of one or other cause, the increase of cardiac enzymes in subacute stage maybe tends to the supposition of previous myocarditis. Hence, the questioning that many cases labeled as arrhythmogenic dysplasia can truly correspond to the possibility of evolutionary myocarditis. The controversial clinic management is disputable.

In most of myocardiopathies both ventricles are ill-taken, and in dilated way, left ventricle involvement prevails and in arrhythmogenic dysplasia, is the right ventricle¹. However, as there are no pathognomonic elements from one or the other entity, the prevailing right ventricular dilation may correspond to dilated myocardiopathy or to arrhythmogenic dysplasia of right ventricle. Such doubt may persist even after a careful analysis of the elements that characterize them, according to established diagnostic criteria².

Diagnostic difficulty between those two entities was the reason for this report, in which there was an intense and prevailing ill-taking of right ventricle.

Case Report

A 10-year-old, white male infant, with a 5-month history of tiredness when laying down, without temporal aggravation. A recent thoracic radiography had shown cardiomegaly, which motivates hospitalization for 13 days, having confirmed the diagnosis of "right ventricular myocarditis", especially due to the verification of rise of creatine-phosphokinase in blood serum. In that hospitalization, laboratory exams of interest revealed that inflammatory markers were normal, as 11 mm hemosedimentation, reactive protein C of 0.17 mg/dl, leucocytes 5600/mm³, and negative rheumatoid factor. However, the myocardial injury markers showed a rise troponin I of 37.5 ng/ml, on the first day and of 57.4 ng/dl, on the fourth day, and with maximum normal values of creatine phosphokinase of 166 U/l, glutamic-oxalacetic transaminase of 40 U/l

and pyruvic glutamic transaminase of 20 U/l. Family history emphasized fatherly sudden death, at 36 years of age, in a football match, in whose previous routine assessment, carried out a year before, there was no indications of the presence of any cardiopathy. At the physical exam, the patient was in a good general condition, eupneic, rosy-cheeked and with normal pulse. Weight: 56.5 kg, height: 153 cm, blood pressure (BP): 100/60 mmHg, heart rate (HR): 78 bpm. Aorta was not palpated at furcula. In the precordium there were discreet impulsions on the left sternal edge and the *ictus cordis* was not palpated. Sounds were normophonetic, being the second sound extended changeable and with the two components equal in intensity. Discreet and mild systolic murmur was auscultated in the 4th and 5th left intercostal spaces, without irradiations. The liver was not palpated.

The electrocardiogram showed sinus rhythm and final disorder of conduction through the right ramus of Hiss bundle. There was a widened Q wave at D1 and at aVL, indicating inactive zone of high lateral wall. T wave was negative from V1 to V4. There were no signs of overload of cardiac cavities (fig. 1).

The radiographic image of the thorax showed a discreet enlargement of the cardiac area at the expense of right inferior arch and the ventricular arch with high edge, indications of increase of right cavities. The pulmonary vascular bed was diminished (fig. 2). That image was compatible with the diagnosis of tricuspid insufficiency.

The echocardiogram showed a change in right ventricular function, dilatation of right cavities and moderate tricuspid insufficiency. On the contrary, the left ventricular function was completely preserved (fraction of shortening of myocardial fiber: 40%, FS: 70%) and the left cavities were normal in size. The right ventricle measured 34 mm, the left ventricle 48 mm, the aorta 25 mm, the left atrium 29 mm and the septum and posterior wall 7 mm. Dynamic electrocardiogram showed 150 ventricular extra systoles in 24 hours. Myocardial scintigraphy with gallium-67 was negative and the high-resolution electrocardiogram did not show tardive potentials in QRS complex. Radioisotopic ventriculography showed ventricular function of 31% for the right ventricle and 51% for the left. Magnetic resonance imaging (fig. 3) showed, besides dilatation of right cavities and tricuspid insufficiency, a stressed right ventricular dysfunction with fraction of ejection calculated at 10%, in relation to the function of 52% found for the left ventricle. The intravenous injection of gadolinium showed a filling up of the whole right ventricular anterolateral wall, but also, discreetly, of isolated parts of left ventricle, as in the lateral,

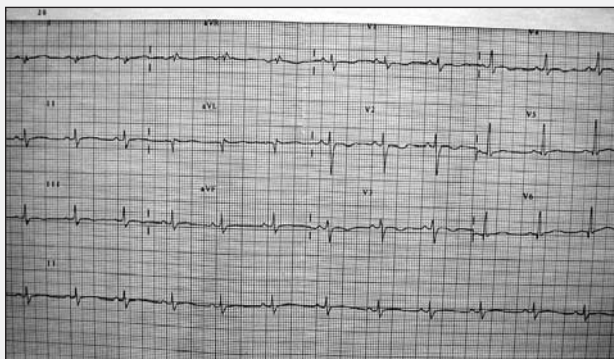


Fig. 1 – Electrocardiogram shows “q” wave thickened in I and aVL, which is an electric characteristic of inactive zone of left ventricular lateral wall and negative T wave from V1 to V4, due to probable right ventricular dilatation.

inferior and septal portions. Furthermore, right ventricular wall slendering was observed, which was regarded as being of stressed level. A hemodynamic study showed normal pressures in right cavities (RA: 10, RV: 30/10, PT: 30/15-17, PC: 10 mmHg) and the angiography (fig. 4) showed a stressed right ventricular hypokinesia with moderate tricuspid insufficiency. A myocardial biopsy was planned for diagnostic confirmation and showed, in seven tissue specimens removed from the right ventricular septum and free wall, myocardium atrophy, with replacement of myocardiocytes for fibroadipose tissue, myocardial hypertrophy and moderate level fibrosis, allied to fat deposition and with discreet histiocytary and lymphocyte reaction (fig. 5).

Regarding the diagnostic thought of the case, clinical elements initially guided to the possibility of a discreet level tricuspid insufficiency. For its turn, the electrocardiographic change of the high lateral wall with final disorder of conduction led to the hypothesis of dilated mycardiopathy, probably of viral origin. The previous finding, on left ventricular preponderant compromising through many complementary exams, led to the diagnosis of right ventricular arrhythmogenic dysplasia, as a premise, given the greater involvement of the ventricle, and the endomyocardial biopsy showed histological changes compatible with that entity. But the endomyocardial biopsy itself place some questions on the other possibility, that such patient could also has had a previous myocarditis with preferential ill-taking of right ventricle, in view of those biopsy elements can be found either in right ventricle arrhythmogenic dysplasia or in previous myocarditis. The increase of myocardial enzymes, verified in the initial stage of the investigation, was added to that finding, in favor of myocarditis. Concerning the established management, in view of the disease being at a stable stage and without tardive potentials present in the high-resolution electrocardiogram, the placement of cardiac defibrillator was discharged and the patient remained under clinical observation.

Discussion

Right ventricular dysplasia is defined as an entity in which the histology, the morphologic features, consists of a severe atrophy of the myocardium, with evidence of death of myocytes and reposi-tion through adipose tissue, as a repairing process that starts in the epicardium and extends towards the endocardium. A percentage of fibroadipose tissue exceeding 43% of the area of biopsy sample³

has been calculated as a diagnosis. The fibroadipose variant shows, in two thirds of the cases, an inflammatory cellular infiltrate, sometimes with focal myocyte necrosis, findings that would be in accordance with the characteristics of a truly myocarditis. Whenever present, the infiltrate consists of positive T CD 43 lymphocytes, also considering the features as a chronic myocarditis. Myocarditis can lead to apoptosis through the release of pro-apoptotic proteins and pro-inflammatory cytokines³.

Other parameters, obtained through histomorphometry⁴, are indicated as suggestive for the diagnosis of that pathology, corresponding to the percentage of adipose tissue greater than 3% and of fibrous tissue greater than 40%, with myocardiocyte atrophy lower than 45%.

That entity clinically makes clear the presence of cardiac arrhythmias that put in jeopardy the life of apparently healthy young people^{1,5}. It constitutes in a myocardial disease of unknown etiology, whose electric instability arises from the right ventricular fibroadipose atrophy. It causes right heart failure, stressed ven-



Fig. 2 – Thoracic radiography emphasizes moderate increase of right heart cavities with diminished pulmonary vascular bed.

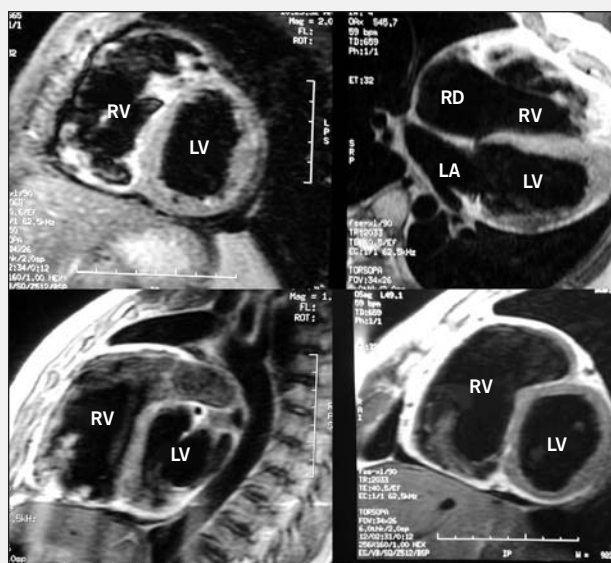


Fig. 3 – Magnetic resonance imaging shows, in many sections, right ventricular dilatation. Slendering of right ventricular anterior wall is clear in left upper quadrant and the its filling up after gadolinium injection, in the other sections, expression of extensive fibrosis. RD = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle.

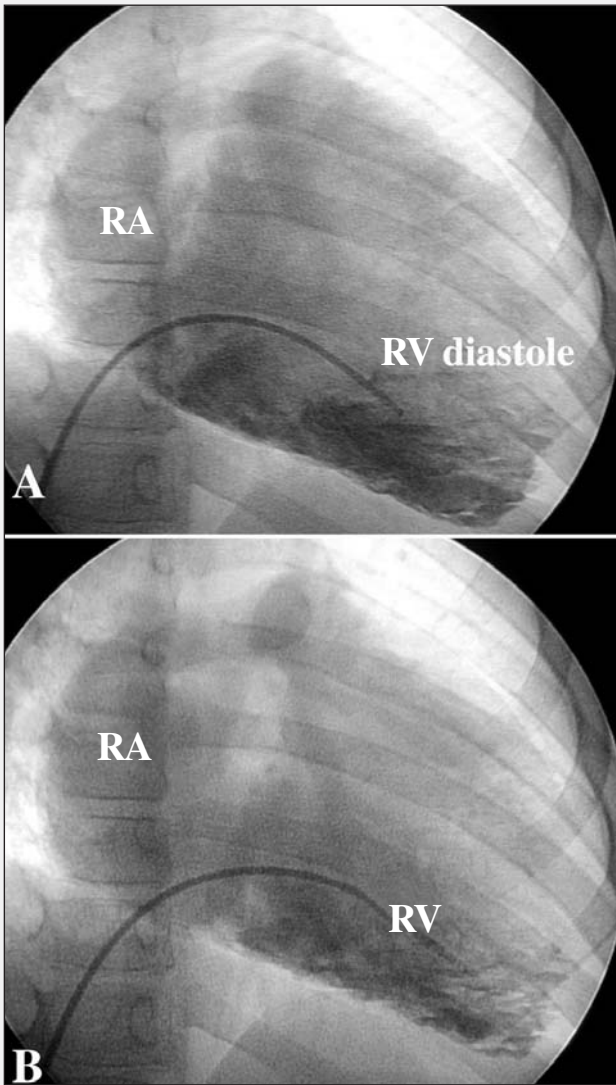


Fig. 4 – Right ventricle (RV) angiography highlights ventricular dysfunction in view of great enlargement of that cavity and discrete variation between systole in B and diastole in A, in addition to right atrial (RA) filling up due to tricuspid insufficiency.

tricular arrhythmias in adults and sudden death in youngsters⁶. Family occurrence has been documented and the responsible gene was found in the chromosome 14q23-q24⁶. The criteria established by the European Society of Cardiology and the Scientific Council on Cardiomyopathies of the World Heart Federation² determine that, to confirm the diagnosis of right ventricular arrhythmogenic dysplasia, it is necessary the presence of two elements considered as major or 4 elements considered as minor or even the presence of a major and two minor elements (tab. I). The analysis of our case under study allowed for the counting of 2 major elements and a minor element, with which the diagnosis of this entity could be possible to establish, by following those same criteria. The major would be the severe dilatation with reduction of right ventricular fraction of ejection, with little ill-taking of the left ventricle and the presence of fibrous and adipose tissues in the myocardium seen at the endomyocardial biopsy and the minor, the inversion of T wave in the right precordial derivations, from V1 to V3, without blocking of right ramus.

However, such elements could be present in previous myocarditis, with cicatricial changes, as demonstrated by the biopsy,

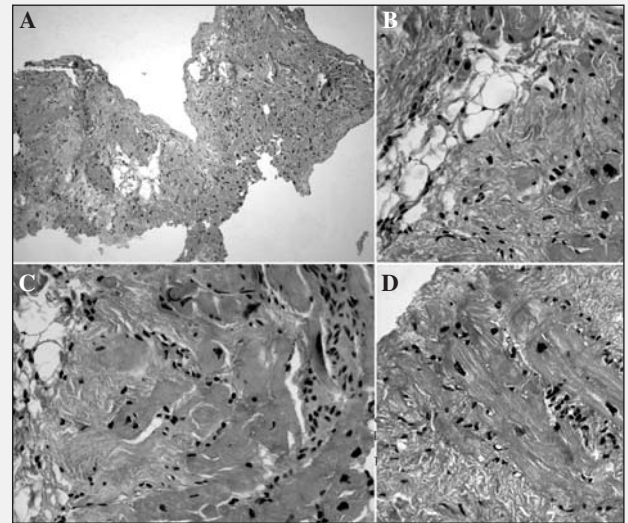


Fig. 5 - Photomicrography demonstrating the histological features of endomyocardial biopsy. In A we observed the myocardium is greatly replaced for fibro-adipose tissue. Hematoxylin-eosin (HE) 100x. In B, C and D, myocardocytes atrophy is observed, with replacement for fibro-adipose tissue, associated to interstitial mononuclear inflammatory infiltrate. Hematoxylin-eosin (HE) 400x

added and strengthened by enzymatic increase at the initial stage of the case investigation. For this reason, separation of those entities became a very complex task.

Such difficulty is shown even clearer when it is noted that, in the literature, there is a prevalence of biventricular involvement^{6,7} in right ventricular arrhythmogenic dysplasia over the isolated ill-taking of right ventricle or even, exclusively, of the left ventricle^{8,9}. So, from 21 cases analyzed in Spain⁷, in 13 of them there was biventricular onset, in 4, isolated right ventricular onset and in the other 4 only left ventricle onset. In another assessment⁶, in Italy, being 27 for necropsy among 30 patients, the onset of the left ventricle along with the right ventricle took place in 20 patients, being 6 in ventricular septum and 14 on the free wall. In the last ones, the differentiation with dilated cardiomyopathy is difficult, in which there is, in most cases, a preponderant left ventricular involvement. So, left ventricular compromising in right ventricular arrhythmogenic dysplasia is well-known and its long-term evolution can be unfavorable to the point of the features be mistaken with was found in dilated cardiomyopathy^{8,9}. Such difficulty grows when reports of myocarditis compromising exclusively the right ventricle are verified in the literature, which makes even impossible to separate such entities^{10,11}, especially that in right ventricular arrhythmogenic dysplasia the lymphocytic infiltrate may come from reaction to cellular death⁶.

So, what is left to us is give a greater importance to the most suitable management, which is not different in either one or another situation.

Since there is no arrhythmia-predisposing elements, such as multifocus ventricular extra-systoles, tardive potentials in the high-resolution electrocardiogram, history of faints and/or syncope and reinforced by absence of right cardiac insufficiency signs, the expectant management could prevail.

Sudden death in those patients is related to a physical strain and the related arrhythmias depend on the catecholamina action, which is released through exercise and, for that reason, they are known as exercise-dependent¹.

Table 1 - Criteria for the diagnosis of right ventricular arrhythmogenic dysplasia (RVAD) according to the European Society of Cardiology and of the Scientific Council on Cardiomyopathies and the World Heart Federation

Family History	
Major	- family disease confirmed through necropsy or surgery
Minor	- family history or sudden death prior to 35 years of age, with suspicion of RVAD
ECG with altered depolarization or conduction/repolarization changes	
Major	- epsilon waves or increase of duration of QRS > 110 ms in right precordial derivations (V1-V3)
Minor	- tardive potentials in high-resolution ECG - inversion of T wave in right precordials in people under 12 years without right ramus blocking.
Arrhythmias	
Minor	- sustained or non-sustained ventricular tachycardia, with CBLR pattern - frequent ventricular extra-systole. Greater than 1000/24 h at the Holter
Global or regional dysfunction and structural change	
Major	- stressed dilatation and reduction of RV fraction of ejection, with little or no LV onset - RV aneurysm (akinetic or dyskinetic areas). Severe RV dilatation
Minor	- moderate global RV dilatation or diminishing of RV fraction of ejection with LV normal ejection. - moderate RV segmental dilatation - regional RV hypokinesia
Tissue characteristics of the wall	
Major	- presence of fibrous/adipose tissue in the myocardium, seen at endomyocardial biopsy
CBLR = complete blocking of left ramus; RV = right ventricle; LV = left ventricle.	

By following that thinking, sudden death in youngsters with right ventricular arrhythmogenic dysplasia, related to physical activity, occurred in 53% of them, and in other 8 (38%) symptoms

dependent on it took place⁷. In another study⁶, sudden death occurred in 24 from 27 patients. In the other 3, it was due to congestive heart failure. The ages varied from 15 to 65 years old, with an average age of 28 years old.

In a Brazilian study¹², the sudden death of 5 patients, among 26 studied, was correlated with right ventricular arrhythmogenic dysplasia, to the extension of QT interval, which constituted in an important predictive factor in that group of patients. QT interval corresponded to 62 ± 17.8 in the risk group and to 51.9 ± 12.8 in the other group.

Once the patient is aware of the necessary physical limitation, allied to an accurate psycho-emotional guidance, by comprising in this context the family action as a constant support, the expectant management can be adopted in the absence of arrhythmias and right heart failure. On the other hand, indications for the placement of defibrillators¹, heart transplantation^{8,9} or cavopulmonary-type operation¹³ are inherent to many clinical situations shown. So, the presence of previous ventricular tachycardia or numerous and multifocus ventricular extra-systoles makes necessary the indication for defibrillators able to be implanted, as the stressed right heart failure requires cavopulmonary operation, and as the congestive heart failure needs heart transplantation.

In those managements, the unusual procedure of total exclusion of right ventricle for the treatment of isolated and refractory right heart failure is distinguished, which can be called upon in the absence of compromising of left ventricle. For such, the tricuspid orifice is closed, the right ventricular free wall is totally dissected and covered with a patch and, then, the total cavopulmonary anastomosis reconstitutes the flow afterwards. The evolution of that procedure can be favorable since the criteria already known for the correct indications are complied with¹³.

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