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Restrictive cardiomyopathy. Presentation of seven cases

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ABSTRACT

Restrictive cardiomyopathy is a disease characterized by diastolic ventricular failure with increase in telediastolic pressure and systolic function preserved.

Materials and methods: a retrospective study of patients with diagnosis of restrictive cardiomyopathy. We conducted an analysis of demographic data, clinical manifestation, and studies of patients diagnosed in the last 15 years at Instituto Nacional de Pediatría.

Results: all the patients included had clinical signs of heart failure manifested mainly by medium dyspnea on effort in school-age patients and dyspnea on eating in infants, as well as polypnea and diaphoresis. The most prominent signs were hepatomegaly, ascites, and gallop rhythm. Cardiomegaly due to right auricular dilation was the most common radiological finding. The most common electrocardiographic findings were dilation of both auricles, ST segment depression and negative T waves. The echocardiogram showed biauricular dilation and restrictive pattern in all cases.

Conclusions: our patients had findings similar to those described in the specialized literature. Echocardiogram remains the best study for diagnosis, and the use of functional measurements like Doppler tissue imaging may help detect early diastolic failure. In Mexico, heart transplant remains unfeasible, with 100% mortality.

Key words: restrictive cardiomyopathy, heart failure, cardiomyopathies.

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Restrictive cardiomyopathy (RC) is a disease characterized by diastolic ventricular failure with increase in telediastolic pressure and systolic function preserved.[1,2] The cause may be idiopathic or secondary to systemic diseases such as hemochromatosis, Fabry disease, etc. It is the most uncommon form of cardiomyopathy, accounting for around 5% of cases, and its prognosis is poor. We present the cases diagnosed at our hospital and the characteristics of their evolution.

MATERIALS AND METHODS

A retrospective study of patients with diagnosis of restrictive cardiomyopathy. We analyzed demographic data; clinical manifestation; and radiographic, electrocardiographic, echocardiographic, and hemodynamic studies from patients diagnosed in the last 15 years.

RESULTS

Between 1997 and 2012 our hospital attended to seven patients with diagnosis of restrictive cardiomyopathy. The patients' demographic and clinical characteristics are shown in Tables 1 and 2. All had clinical signs of heart failure manifested primarily by dyspnea on medium effort in school-age patients and dyspnea on eating in infants, as well as polypnea and diaphoresis. The most relevant signs observed on physical exploration were: hepatomegaly, ascites, and gallop rhythm. Cardiomegaly due to right auricular dilation was the most common radiological finding; none of the patients had signs of pulmonary venous-capillary congestion in early stages. The most common electrocardiographic findings were dilation of both auricles, ST-segment depression, and negative T waves; one case had Wolff Parkinson White syndrome (Table 3). In all cases the echocardiogram showed biauricular dilation and restrictive pattern (Table 4). Doppler tissue imaging, which evaluates the movement of the ventricular wall, was performed only in patient number seven, showing diminished S`, which was interpreted as altered systolic function. Three patients underwent cardiac catheterization, finding high telediastolic pressure (Table 5). Evolution was torpid; the patients had to be hospitalized and frequently receive diuretics in large doses. Two patients were referred for heart transplant and died waiting, two died from pneumonia, and the others died at home. In all cases the cause of death was decompensated heart failure. One patient stopped reporting for follow-up.

DISCUSSION

The cardiomyopathies are a heterogeneous group of myocardial diseases not imputable to structural defects. According to the World Health Organization, they are classified in: 1) dilated; 2) restrictive; 3) hypertrophic; 4) cardiomyopathy-arrhythmogenic right ventricular cardiomyopathy-dysplasia.[2,3] Depending on their causes they are divided in: a) primary (genetic, acquired, and mixed)[4] and b) secondary.[4,5] In recent years family groups with the disease have been found, in view of which a molecular classification has been suggested.[6]

RC is rare, accounting for 3 to 5% of all cardiomyopathies.[7] it is characterized by restrictive filling of both ventricles with diastolic dysfunction and systolic function preserved. The idiopathic form is the most common in pediatric patients, followed by that secondary to Pompe disease. In adults, causes secondary to systemic diseases such as amyloidosis, sarcoidosis, Andersen disease, Fabry disease, Loffler disease, etc., are more common. In cases of idiopathica and hereditary restrictive cardiomyopathy mutations in the genes TNNI2, TNNI3, and ACTC have been described, associated with sarcomere protein diseases.[5,8] Also, there are mutations unique to each disease in secondary cardiomyopathies.

Table 1. Demographic characteristics of patients

Patient	Gender	Age at diagnosis (years)	Survival (months)	Age at death (years)	Outcome
1	M	8	UNK	UNK	Awaiting transplant
2	M	3	11	4	At home
3	M	8	UNK	UNK	Loss of follow-up
4	M	1	11	2	Associated pneumonia
5	F	5	UNK	UNK	Awaiting transplant
6*	M	1	15	3	Associated pneumonia
7**	F	2	11	3	At home

UNK: Date of death unknown. The deaths occurred at another hospital.
* Prior diagnosis of Bruton agammaglobulinemia, in addition to Wolff Parkinson White syndrome.
** Thrombus in right auricle.

Table 2. Clinical characteristics and cardiothoracic index

Patient	Clinical	Hepatomegaly	Ascites	Auscultation	CTI
1	Dyspnea	Yes	No	Gallop	0.66
2	Dyspnea	Yes	Yes	Gallop	0.57
3	Dyspnea	Yes	Yes	Gallop	0.46
4	Dyspnea	Yes	Yes	Normal	0.62
5	Dyspnea	Yes	No	Gallop	0.62
6	Dyspnea	Yes	No	Gallop	0.6
7	Dyspnea	Yes	Yes	Second sound reinforced	0.61

CTI: Cardiothoracic index. Clinical data observed in patients at time of diagnosis.

Table 3. Electrocardiographic data from patients in milliseconds

Patient	Age	QRS* ms (70-110)	QTm** ms (290-370)	QTc** ms	Auricular dilation	ST depression+	Negative T wave++
1	8	120	400	500	Right	V2-V6, aVL, aVR, DII	V1-V3
2	3	80	230	320	Biauricular	DI, DII, V2-V6	No
3	8	90	340	420	Biauricular	No	V1-V4
4	1	80	240	300	Right	No	V1-V6, AVF
5	5	90	390	550	Right	V4-V6	V1
6	1	120	320	480	Right	V1-V6, aVL, aVR, DII	No
7	2	120	320	480	Biauricular	V1-V3	V2-V6

* The QRS duration represents the ventricular depolarization time. A prolonged QRS is associated with higher mortality in patients with heart failure.
** The QT interval represents the ventricular repolarization time. The mean QT (QTm) value varies with age.
Because heart rate affects the duration of QT, the corrected QT (QTc) is used. A prolonged QT predisposes to ventricular arrhythmias.
+ An ST segment depression of more than 0.1 mV in pediatric patients is abnormal and is grounds to suspect pericarditis, ischemia, or hypertrophy.
++ The T wave represents part of ventricular repolarization, and is normally positive in all derivations, except in aVR and V1 in children under 10 years. A negative T wave in V4, V5, and V6 indicates alteration in repolarization; its presence suggests ischemia, pericarditis, or severe hypertrophy.
Values indicative of normality for children between 1 and 9 years taken from Hung Chi-Lue: ECG in the Child and Adolescent.[19]

Table 4. Echocardiographic findings

Patient	Age (years)	Auricular dilation	LVDD	FEVI (%)	Relación E/A Mitral
1	8	Biauricular	35	31	Restrictive
2	3	Biauricular	29	80	Restrictive
3	8	Biauricular	38	71	Restrictive
4	1	Biauricular	22	62	Restrictive
5	5	Biauricular	33	55	Restrictive
6	1	Biauricular	35	64	Restrictive
7	2	Biauricular	26	74	Restrictive

LVDD: Left ventricular diastolic dimension. The greatest length between the walls of the left ventricle at the end of diastole. The normal value depends on the patient's height and weight; it was normal in all cases, which indicates that there is no dilation of the left ventricle.
LVEF: Left ventricular ejection fraction. A quantitative measurement of ventricular systolic function, which represents the percentage of blood expelled by the left ventricle and is normal between 55 and 70%. Only one patient had altered systolic function.

Table 5. Results of catheterization and biopsy

Patient	Telediastolic pressure of RV (mmHg)	Histopathological diagnosis of biopsy
1	15	Mild interstitial fibrosis
5	29	Mild lymphocyte infiltration
6	33	Endomyocardial fibrosis

RV: right ventricle. Telediastolic pressure is the pressure generated in a cavity throughout diastole. For the RV a value above 11 mmHg is interpreted as a ventricle with restrictive filling and increases the risk of death in patients with restrictive cardiomyopathy.

In RC there is biventricular diastolic alteration with systolic function preserved. Ventricular filling is altered, causing a disproportionate increase in ventricular telediastolic pressure in response to small volumes of blood, which in turn causes dilation of both auricles.

Macroscopically, dilated auricles and normal-size ventricles are observed. The ventricular wall is abnormal, with a rubbery texture and thickening of the endocardium. Microscopically changes are seen depending on the infiltrating material in secondary causes.[5]

Clinical manifestations are variable, with signs of systemic venous congestion predominating,[9,10] with varying degrees of pulmonary artery hypertension caused by pulmonary venous-capillary hypertension due to difficulty in left auricular emptying. Symptoms such as dyspnea, polypnea, and tachycardia are often confused with respiratory issues.[11] Physical exploration reports signs of heart failure; hepatomegaly is the most constant sign, as well as auscultation of the third and fourth sounds.[11]

In initial stages x-rays often show the heart with normal characteristics, and as the disease advances cardiomegaly due to auricular dilation, which is the most common finding, appears.[8,10] There may be pleural effusion (Figure 1).

The electrocardiogram shows biauricular dilation manifested by high and bimodal P waves; the QRS is narrow and without alterations. Some patients show ST segment depression without signs of ischemia.[10] The T wave may be negative.[10] Due to auricular dilation supraventricular arrhythmias, such as auricular extrasystoles or auricular fibrillation, may appear.

The echocardiogram should rule out any structural abnormality and differentiate RC from other cardiomyopathies. Typical findings are auricular dilation, diastolic dysfunction, systolic function preserved or very similar to normal, and lack of

ventricular dilation.[1,11,12] Some authors refer to such findings as "inverted cavities" (Figure 2).

Varying degrees of pulmonary artery hypertension have been documented.[8] Doppler ultrasound measures the rate of flow entering the ventricles. Rate E represents rapid ventricular filling, while rate A represents filling secondary to atrial contraction. In RC diastolic failure of the ventricles reduces rate E and raises rate A. This is known as restrictive pattern.

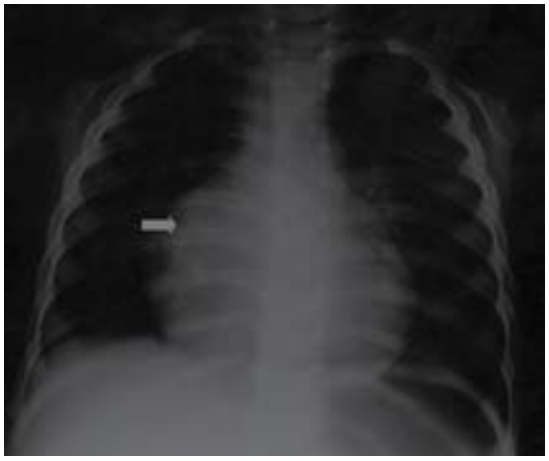

Figure 1. Chest x-ray of patient 1: dilation of right auricle (arrow).

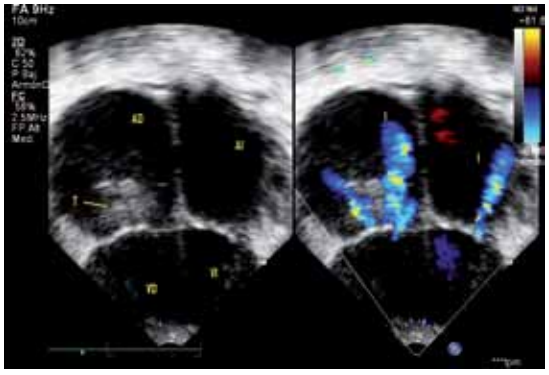

Figure 2. Two-dimensional, comparative four-chamber image of patient 7. Dilation of right auricle (RA) and left auricle (LA) so significant that it makes the right ventricle (RV) and left ventricle (LV) appear small, although they are of normal size. We can also observe a thrombus (T) in the right auricle and substantial insufficiency of the atrioventricular valves (I).

Doppler tissue imaging is very useful as it can identify cases with early diastolic dysfunction, anticipating macroscopic morphological changes. The earliest changes are S` alterations.[12,13]

Cardiac catheterization records high telediastolic pressure in both ventricles with different values for each one. The atrial pressure curve presents early diastolic collapse with rapid elevation and plateau (square root sign). Angiography shows obliteration of the ventricular apex, and areas of hypomotility.[1] The main indication for cardiac catheterization is biopsy in case of systemic disorders, a practice which is tending to disappear with the advance of other molecular and radiological diagnostic techniques such as magnetic resonance.

Magnetic resonance is important in the study of secondary cardiomyopathies where specific findings have been described due to amyloidosis, sarcoidosis, Loffler endocarditis, and endomyocardial fibrosis.[14] It helps differentiate from other cardiomyopathies and in differential diagnosis with constrictive pericarditis.[11,14]

Differential diagnosis should be made with constrictive pericarditis, which may manifest with clinical signs of heart failure and echocardiographic findings of restriction with diastolic failure.[15] Doppler tissue imaging and magnetic resonance are used to establish differential diagnosis.

Treatment should focus on alleviating congestive symptoms with diuretics and hydric restriction. Use of digital is reserved for cases with compro-

mised systolic function and auricular fibrillation (AF). Use of anticoagulants should be considered due to the high rate of thrombus associated with auricular dilation and AF. Cases secondary to metabolic diseases should receive specific treatment. In idiopathic cases (the most common in children) transplantation may be the only option. Survival rates have been reported of 86% at one year and 50% at two years.[16-18] The criteria are not well defined.

The prognosis of the disease is very poor, survival at two years from diagnosis is not above 50% and mortality increases when there is syncope.[12] Other markers of poor prognosis are radiographic evidence of pulmonary congestion, right ventricular telediastolic pressure above 11 mmHg, left ventricular telediastolic pressure above 22 mmHg, and ratio of diameters of left atrium and aortic root greater than 2.[19] Some studies report 100% mortality or need for transplant in the first 5 years after diagnosis.[8] Post mortem studies reveal myocardial infarction with normal coronary arteries, based on which some authors take the view that those patients are at greater risk of ischemia.[8] Sudden death occurs in up to 28% of cases with annual mortality of 7%.[12]

CONCLUSIONS

Our patients had findings similar to those described in the universal literature. Symptoms of heart failure such as dyspnea, hepatomegaly, and ascites, are typical of the disease. Clinical studies such as x-ray and electrocardiogram can provide important data for diagnosis. Echocardiogram remains the best study for diagnosis, and use of functional measurements like Doppler tissue imaging may help evidence early diastolic failure. As the disease advances the most evident findings are auricular dilation and restrictive pattern. In Mexico heart transplant remains unfeasible, with 100% mortality.

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