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Case Report

Heart Failure and Dilated Cardiomyopathy in a Young Patient: A Case Report

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Abstract

Introduction: Dilated cardiomyopathy is the most common subtype of a group of diseases in which the primary dysfunction is found in the myocardium. It is characterized by left ventricular dilation, mainly associated with contractile deficit and thinning of its walls. It is responsible for more than 30% of the cases of heart failure in the population; and an early diagnosis and initiation of appropriate treatment influence its morbidity and mortality.

Objectives: Report the case of a patient diagnosed with dilated cardiomyopathy and discuss the diagnostic methods, possible etiologies and the difficulties in defining it.

Methods: Information was collected from the patient's medical record, followed by an interview and analysis of tests performed. About 24 articles were selected using the PubMed, UptoDate and Lilacs platforms, in addition to 3 textbooks and 1 guideline.

Case Story: A 35-year-old male patient who attended the APAE for 6 years began to experience tiredness, dyspnea on exertion and night cough. After outpatient care, radiographic cardiomegaly was evidenced, clinical treatment was initiated and referred to the Heart Failure Clinic. On echocardiogram, he was diagnosed with dilated cardiomyopathy, with multiple symptoms of heart failure with low ejection fraction, with no defined etiology. After stable years, he showed severe worsening, needing to implant a cardiac resynchronizer.

Conclusion: Dilated cardiomyopathy is a multifactorial disease, with variable symptoms, which hinders its rapid diagnosis and definition of the etiology, influencing the patient's prognosis and well-being.

Keywords: *Cardiomyopathy; Dilated; Heart Failure*

Introduction

Cardiomyopathy is defined as all heart disease in which primary dysfunction is located in the myocardium [1], which usually leads to a cardiac dysfunction with pathological remodeling culminating in a Heart Failure [2]. Several types of aggression can lead to these changes such as direct injury to cardiac myocytes, genetic defects and the deposition of substances in the myocardial extracellular matrix

[3]; with consequent alteration of the chamber wall thickness, its size, besides affecting contractility and cardiac electrical conduction, leading to significant morbidity and mortality [1]. There are other alterations that affect the myocardium secondarily such as valvular diseases, coronary ischemia, hypertension and pericardiopathies, but there is no consensus as to its designation as cardiomyopathy or not [1,3]. They are classified according to their morphological characteristics in Hypertrophic, Dilated, Restrictive and Arrhythmogenic right ventricle [4].

Dilated cardiomyopathy (CDM) can be characterized as a disease of multiple etiologies, with ventricular dilation, mainly of the left ventricle, with contractile deficit, that is, the systolic function is the most affected, although in some cases diastolic changes may be present. associated, affecting the prognosis of the disease 5, in addition to reaction myocardial hypertrophy in the unaffected regions6 and thinning of the compromised regions 2. In this, the left ventricular systolic dysfunction is variable and progressive, and as this change may not imply symptoms, the MCD is a factor important risk for the development of heart failure, in addition to the increased risk of developing associated atrial and/or ventricular arrhythmias, due to the impairment of the conduction system 4. Along with the Hypertrophic, the MCD is the most common subtype, affecting 1 each 250 - 500 of the general population, being responsible for 30 - 40% of the cases of Heart Failure 2; more common in men and middle-aged individuals 3. However, the real incidence and prevalence of this pathology is difficult to be evaluated because it presents many variations according to the ethnicity, nationality and diagnostic methods that were used in each research, therefore these values are often underestimated 4. In Brazil, there are no studies conclusive on the prevalence of MCD, making it very difficult to assess the real presence of this pathology in our midst 5.

The etiological definition of DCM has been increasingly studied, due to the great variability of possibilities, such as autoimmune diseases, infections, arterial hypertension, acute myocardial infarction, in addition to toxins such as alcohol [2]. However, more than 50% of the time it is not possible to determine it, receiving the name of idiopathic 3. Of these cases of idiopathic MCD, about 30 - 50% of the cases correspond to the family form, demonstrating the influence of heredity and genetics on its pathogenesis. Mutations in about 57 genes have already been associated with MCD mutations, so we can say that it is a polygenetic disease [2]. Myocarditis is the second leading cause of MCD, corresponding to 12% of the total, followed by coronary disease with 11%, and other causes with 30% may include amyloidosis and Sarcoidosis and Sarcoidosis in this group [5].

Therefore, the study on MCD is essential due to the importance of rapid diagnostic suspicion and initiation of investigation, with the aim of defining an etiology and initiating appropriate interventions that interfere in the prognosis of the patient, whether pharmacological or more invasive as use of pacemakers or cardiac resynchronizers.

Primary objective

Report the case of a 35-year-old patient with Dilated Cardiomyopathy, diagnosed at 6 years of age, and severe intellectual deficit, without previous comorbidities, of unknown etiology and under investigation, which evolved with sudden worsening, requiring the implantation of cardiac resynchronizer.

Secondary objective

To conduct a discussion about the diagnostic methods and possible etiologies for the case presented and the difficulties to define it, with differential diagnosis.

Methods

On October 2, 2018, during a visit to the Heart Failure Clinic of Teresópolis (CLIC), a patient diagnosed with dilated cardiopathy and severe intellectual deficit was consulted. with the patient and his legal guardian, using open questions which were recorded and transcribed

later; and evaluation of the tests performed. The institution's consent and consent terms were acquired, with submission and approval of the project by the institution's Research Ethics Committee with CAAE: 03195918.1.0000.5247. Using the database of platforms such as Pub Med, Upto Date, MEDLINE and LILACS, 10,000 articles were found and from these, 24 articles were selected that fit into papers written since 1998, in English and Portuguese; in addition to 3 textbooks and 1 guideline, using the keywords "Myocardiopathy", "Dilated Cardiomyopathy", "Myocarditis", "Amyloidosis", "Sarcoidosis" and "Smith Magenis Syndrome".

Case Report

EGS, 35 years old, male, white, single, a regular at APAE, born in Rio de Janeiro and living in Teresópolis. All reported information was collected from the patient's mother, her legal guardian. Six years ago, the patient started feeling tired and dyspnea at great efforts besides nocturnal cough. He sought outpatient care at the time without success. After 4 months, in consultation with a clinician, due to ocular hyperemia, he was reported the pre-existing symptoms during anamnesis and after thorough physical examination, he was referred to a cardiologist at the Hospital das Clínicas de Teresópolis, along with a request for Chest X-ray. In the consultation with the cardiologist, she evaluated the radiography performed, detecting cardiomegaly associated with pulmonary congestion, therefore, prescribed Captopril, Spirinolactone and Furosemide, referring the patient to the Heart Failure Clinic of Teresópolis (CLIC).

On 25/07/2012, he made his first consultation at CLIC. In this, he reported tiredness and dyspnea at great efforts, nocturnal cough and edema of the lower limbs, without progression until that time. In the previous pathological history reported tonsillitis and repeated otitis, anemia during childhood, in addition to Rheumatic Fever at 14 years, denied arterial hypertension and diabetes mellitus, denied previous surgeries. In family history, she presents a hypertensive mother and smoker, without other comorbidities; and uncles by the father's family with a history of coronary heart disease; has two healthy siblings. In social history denies alcohol consumption and smoking.

On physical examination, he was in good general condition, cognitive deficit, eupneic, acyanotic, anicteric, hydrated, hearted, afebrile, atugious jugulars. Body Mass Index of 25.89. Cardiovascularpairwith left ventricular Ictus deviated to the left, regular heart rhythm in 3 strokes with accessory sound B3, hypophonetic sounds, with systolic murmur of ++/6+ in mitral focus. Blood pressure: 110x70 mmhg. Heart Rate: 80 bpm. He presented respiratory apparatus with universally audible vesicular murmur, without adventitious noises. Respiratory Rate: 20 irpm. Ectoscopy of the abdomen presented a globous abdomen, with no scars or spots. In auscultation, peristalsis was present. On percussion he had timpanic sound all over his abdomen. No pain was reported to superficial and deep palpation, without palpable masses or visceromegaly. Had lower limbs with bilateral edema of +/4+, free calves and preserved pedial pulses.

In this same consultation, an electrocardiogram was performed in the patient, which showed a sinus rhythm, with a frequency of 82 bpm, PR interval of 0.18, QRS + 60º axis, left ventricle overload (SVE), left atrium overload (SAE) and a complete left branch block (BRE). At the end of the consultation, it was classified as class II on the NYHA functional scale, carvedilol was added to its treatment and an echocardiogram was requested to follow up the diagnostic investigation.

On 17/10/2012, the echocardiogram (ECO) was performed, which demonstrated the following results: left atrium measurement - 41 mm; final diastolic diameter of left ventricle - 69 mm; final systolic diameter of left ventricle (VE) - 54 mm; septum thickness - 9 mm; right ventricle measurement 15 mm; ejection fraction of 43% (according to Teicholz) and 27% (according to Simpson); moderately enlarged left ventricle, restrictive mitral flow, apical akinesia-septal left ventricle, and other segments with moderate hypokinesia at rest. Conclusion of the examination: Dilated cardiomyopathy with increased left cavities. Left ventricle with significantly depressed systolic and diastolic function at rest. Mild Mitral insufficiency on doppler.

On the same day he returned to CLIC to present the echocardiogram result. He reported the maintenance of symptoms. A new electrocardiogram showed a sinus rhythm, with a frequency of 82 bpm, pr interval of 0.24, SVE, SAE, complete BRE and right ventricle overload

(SVD). In this consultation, therefore, the diagnosis of Heart Failure was defined for the patient, based on the Framingham and Boston criteria, stage C, with predominant icfer dysfunction (Heart failure with reduced ejection fraction). But no etiological diagnosis defined. The medications already used by the patient were maintained.

In a new consultation on 08/21/2013, he reported anginal pain to efforts as a recent symptom and brought laboratory tests and a new echocardiogram. Results: total colesterol 221mg/dl; HDL 35mg/dl; LDL 127mg/dl; triglycerides 292 mg/dl; all other parameters evaluated were within normal range; ECHO CARDIOGRAM with ve with important systolic dysfunction and moderate diastolic at rest, mild mitral transvalvar reflux holosystolic at doppler, pseudonominal mitral flow of the reversible restrictive type. 20mg Syvastatin has been added to treat dyslipidemia.

The patient continued to perform multiprofessional follow-up, with periodic consultations in CLIC, usually every 2 - 3 months, with stabilization of the clinical picture, possible symptoms such as headache, dyspnea, edema in the lower limbs, dry cough, always associated with exertion, but of short duration. On an echocardiogram performed on 05/20/2015, he presented an evolutionarily better overall left ventricular systolic function.

On May 10, 2017, he underwent an MRI of his chest as an attempt to investigate one of the possible etiologies for his cardiomyopathy, rheumatic myocarditis. However, no alterations were verified on this examination that meant acute or subacute inflammatory myocardial injury or chronic phase scar lesions. Even with these results, the possibility of myocarditis was not ruled out, with programming for further examinations after a few months.

Until in consultation on 03/07/2017, she reported feeling dyspnea on medium/small efforts such as climbing stairs, a small slope or getting on a bus, associated with pallor, nocturnal cough, orthopnea and during these episodes she rubbed the chest in the sternum region. An electrocardiogram was performed that demonstrated a sinus rhythm, with a heart rate (HR) of 41bpm, with a PR interval of 0.20, with SAE, EVS, SVD, complete BRE and a 2nd degree atrioventricular block (AVB). From this new table, a 24-hour Holter was indicated, showing a minimum HR of 31, an average of 45 and a maximum of 82 with, with BAV of 2nd degree type II during the entire recording, in the wake of driving 2:1 with periods of advanced BAV with 2 blocked P waves and in sleep variable atrioventricular conduction predominated with periods of conduction 1: 1.

Therefore, the patient's beta-blocker reduction was performed as the first approach, followed by suspension to verify whether the blockade was related to the medication, but there was no improvement. For this progressive symptomatic worsening of the patient, cardiac resynchronizer implantation was indicated on 08/26/2017. He had to perform desensitization with loratadine and prednisone to perform the procedure because he is allergic to iodine. After implantation, beta-blockers were restarted, now Bisoprolol, in combination with spirynolactone, chlorthalidona and losartan, in addition to syvastatin.

In a consultation held on March 28, 2018, she presented a significant improvement in her clinical condition, no longer showing dyspnea on exertion. It presented a new laboratory within the normal range, despite the total cholesterol increased by 190 mg / dl. A new ECO was requested at the consultation. This was carried out on April 11, 2018, with ischemic cardiomyopathy, with normal cavity diameters, LV with global systolic function at the lower limits of normality and mild type 1 diastolic dysfunction, preserved RV function, minimal protosystolic mitral valve reflux and visualized resynchronizing cable in DV.

He left the last consultation with a referral to a geneticist in Teresópolis, due to the intellectual deficit he presents and that until now had no diagnosis and it was thought that there was some relationship with his cardiomyopathy. Therefore, on 02/07/2018, he made his first appointment, and in this it was reported that all the patient development milestones were delayed. Sat with support only at the age

of 1, did not kitten, walked only 2 years, spoke the first word at the age of 7 and wrote the first word with more than 18 years, but never any pediatrician suspected anything, with the justification that each child developed differently.

It was reported that he was a child of little interaction, of difficult behavior, dependent on the mother, who did not accept most foods, and even for this it was very weighted. He suffered from a chronic cold, which after diagnostic investigation, he was told it was a psychological problem and was referred to a psychologist at the age of 5. He was enrolled in school for the first time at the age of 5, but never performed well. At the same time he began follow-up with a speech therapist, who carried out several guidelines to stimulate the development of his speech. During this time, it showed no progress in relation to speech, interaction and general development.

At the age of 9, it was reported that the family moved to Teresópolis, and another attempt was made to enter school, without success again. At the age of 10, in consultation with a neurologist, he began using imipramine as an attempt to modulate his behavior, which was suspended a few months later, with the justification that the patient was autistic and no longer needed this medication. He was referred to the APAE, now 12 years old. In this, she performed outpatient care with speech therapist, psychologist and psychomotricity, and began to present pedagogical advances and social interaction. He reported a significant improvement in the institution, mainly in language and intelligence, and began to be more independent performing basic activities alone, such as personal hygiene, and playing sports.

With the onset of adolescence began to present outbreaks of aggressiveness, especially when his routine was interrupted, and difficulties to sleep, with a peak at 17 - 18 years. It was the consultation with a psychiatrist, already 24 years old, who requested an electroencephalogram (EEG) in wakefulness and during sleep for investigation. On 24/11/2007, a wakefulness and spontaneous sleep EEG was performed, which was found to be abnormal, generalized, Grade 1 due to pointed graphoelements, frequent acute waves and tips, of irritative character, of diffuse localization, ativable by the process of numbness.

From this complementary investigation, associated with the patient's mouth movements as if he were "chewing", hyperextension of the upper, lower limbs and head and that were repeated several times during sleep, a diagnosis of nocturnal seizures was made, which, according to reported, the patient had been presenting for years without knowing what it was. Started treatment with Tegretol CR 400 mg twice daily. From there he presented a sudden improvement in behavior, sleep quality and absence of seizures. Makes use of this medication to this day.

After this extensive anamnesis, a series of evaluations were performed in the consultation, and it was concluded that the patient presents severe intellectual deficit with multiple deficits in adaptive life, with intelligence quotient between 20 - 30 and functional age of 3 years, does not present specific dysmorphiasis, absence of dysticchyases, absence of stereotyping, head circumference of 60.5 cm, whichis above the 97th percentile, therefore increased. It was then defined that it presents a phenotype characteristic of a 17p11 microtype called Smith Magenis syndrome, and karyotype was requested to continue the more specific diagnostic investigation protocol and be able to determine the size of this micro-screening and thus be able to correlate or not with cardiomyopathy; in addition, laboratory tests and abdominal ultrasound were requested.

In a subsequent consultation, on 02/10/2018, she had already performed the tests, with the following results: red blood blood diaries 5,12; hemoglobin 17.2; hematocrit 46.8; mean corpuscular volume 91.4; mean corpuscular hemoglobin 33.6; anisocytosis index 12.4; leukometry 6,100; platelet meplatetry 243,000; total cholesterol 171; triglycerides 173; HDL 45; LDL 91; TGO 27; TGP 40; alkaline phosphatase 98; GGT 253; normal bilirubins; protein electrophoresis without alterations; unaltered abdominalultrasound. The karyotype had not yet been performed.

Discussion

The heart's main function is to pump blood into the whole body, regulated by the physiological needs of each person. For this there is a complex system that starts in the sinoatrial node, generating action potentials, propagation by the conduction system, uptake by myocar-

dial cells and large flow of electrolytes such as calcium, allowing interaction between various protein components such as atropomyosin, troponin, actin filaments and myosin, and thus generating muscle contraction, and consequently cardiac output [2].

MCD is a myocardial disease, so this complex interaction suffers a disorganization to the point of ventricular dilation, with the heart acquiring globular shape, endocardic hypertrophy and loss of contractile strength, especially in the left ventricle [6,7]. The integrity of the heart valves are maintained, but the ventricular geometry is modified and thus the papillaral muscles change their positions, altering the functioning of the atrioventricular valves, so the occurrence of mitral insufficiency and/functional tricuspid is a possibility [1,6]. Analyzing microscopically, there are large areas in the interstice and around the blood vessels with fibrosis, with intracellular infiltrate and small necrotic regions [6]. These morphological changes generate important hemodynamic repercussions such as increased volume of cardiac chambers and, consequently, intracavitary pressure, in addition to a decrease in the ejection fraction [8]. The diagnosis of MCD is made based on clinical parameters, identifiable from anamnesis and physical examination, and findings on electrocardiogram (ECG), chest X-ray and echocardiogram, which is the most important [8]. Regarding the clinical picture of the disease, it ranges from asymptomatic to advanced symptoms of mild, moderate or severe heart failure [1,3].

Heart Failure (HF) is a clinical syndrome generated by functional and/or structural abnormalities resulting in low cardiac debit and increased cardiac pressures. Presents very characteristic signs and symptoms such as dyspnea on exertion, orthopnea, nocturnal paroxysmal dyspnea, cough, fatigue, crepitan ralyses to pulmonary auscultation, aquipnea and third bullfight due to increased pulmonary pressures and congestion; jugular turgency, lower limbs edema, weight gain, pleural effusion, ascites, and painful hepatomegaly by increased systemic venous pressure and congestion. In addition to these alterations, the patient may present hypotension, short hand taquicardia, slowed capillary filling time, cyanosis, oliguria and syncope, justified by the reduction of cardiac output, and consequent impaired tissue perfusion [9]. In addition to the increase in intracavitary pressures, an activation of the reinnine-angiotensin-aldosterone system (AAR) as a way to compensate for and maintain cardiac output within normal parameters generates an increase in hydrosaline retention, contributing to pulmonary and systemic congestion [10].

Generally, there is a progression of these symptoms, appearing only during intense physical efforts, until they begin to manifest themselves with less and less effort until rest9. It is a syndrome responsible for 2.6% of hospital admissions in Brazil and 6% of deaths10, mainly among patients over 60 years of age, with an emerging and epidemic incidence and prevalence due to an aging population11. Etiologically speaking, any condition that causes changes in the left ventricle predisposes HF, and myocardial diseases are included in this group9. HF can be classified functionally, by a scale elaborated by the New York Heart Association (NYHA) 9. Although subjective, it is widely used to monitor the progression of the patient's symptoms, evaluate the response to treatment and indicate new therapies (Table 1) [9,10].

Class I: Absences of symptoms during daily activities.
Class II: Symptoms triggered by everyday activities.
Class III: Symptoms triggered by less intense activities than everyday activities or small efforts.
Class IV: Symptoms triggered at minimal effort or at rest.

Table 1: *NYHA Functional Classification for CI [10].*

However, this classification does not take into account that HF is a progressive disease, that even without symptoms, structural damage will continue to evolve, not being reversible in most cases. Taking these factors into account, the American Heart Associancion (AHA) created a new classification, keeping HF in 4 evolutionary categories, associating symptoms and structural changes (Table 2) [10].

Stage A: High risk for developing HF, but without structural changes, signs or symptoms of HF.
Stage B: Cardiac structural disease present, with no current or previous symptoms of HF.
Stage C: Structural disease present, with current or previous signs and/or symptoms of HF.
Stage D: CI refractory to conventional treatment, with indication of specialized interventions.

Table 2: *Ic staging by AHA [10].*

Another way to classify HF is by the measurement of the ejection fraction (EF) of the left ventricle. Those with EF greater than or equal to 50% are classified as having HF with preserved EF (ICFEP); when ef is less than 40% has hf with reduced EF (ICFER) and those with EF between 40 and 49% are defined as carriers of HF with intermediate EF [9].

Using this information to evaluate the described report, it is possible to define that the patient in question did not present apparent risk factors that justified his clinic. She was 29 years old when initiating symptoms, that is, a very young age group compared to the age profile of patients with the same symptomatology and diagnosis, had no comorbidities such as hypertension, diabetes or smoking, no history of coronary heart disease, and also no family history of cardiomyopathies. Their symptoms were not valued to the point of seeking medical help, taking into account the fact that the patient has difficulties in expressing himself; the suspicion arose at random. Chest X-ray requested after this clinical suspicion presented cardiomegaly and pulmonary congestion (Figure 1).

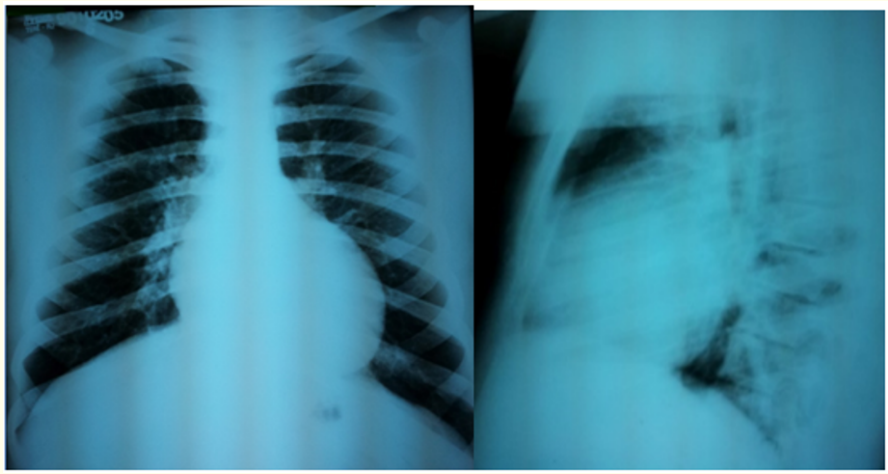

Figure 1: *Thorax Teleradiography.*

From this, he began immediate treatment with an ICIT and two diuretics, one of which was an aldosterone antagonist. As the clinical suspicion should be of an HF, the use of these medications is justified by the fact that large clinical trials have proven that these antihypertensives perform inhibition of neurohormones released by THES, and reduce the symptoms of HF and have an excellent effectiveness interfering in patient survival [12]. In addition, there is evidence that ACIs act in the process of reverse remodeling, that is, in the return to normal ventricular configurations, since HF, regardless of ischemic cause or cardiomyopathies, leads to remodeling with dilation and loss of myocytes [12]. Subsequently, he performed an ECG (Figure 2), an essential tool in THE, with multiple alterations already described. On

physical examination, he presented several signs and symptoms of HF, receiving functional classification II.Mitral murmur reported, evidences the existence of a mitral insufficiency with regurgitation, justified by remodeling and valve deformation. Therefore, a beta-blocker has been added to its treatment, another antihypertensive reported in studies with the same benefits as ACI and Aldosterone antagonists [12].

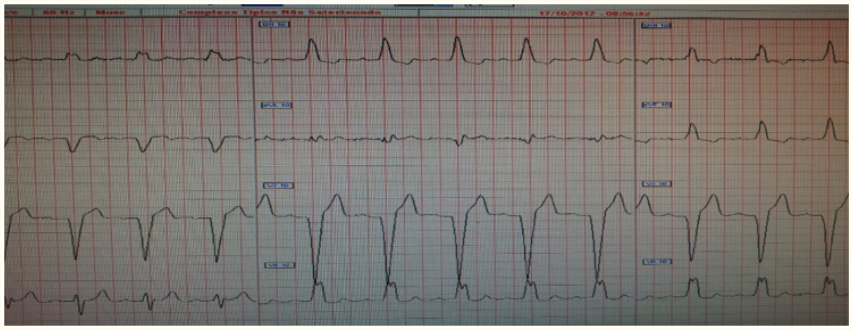

Figure 2

The presence of a BRE demonstrates that the cardiac electrical system is sensitive to any pathology involving myocytes, whether by inflammation, ischemia or fibrosis; being very common in HF and an important predictive factor of sudden death[12]. BRE generates changes in ventricular contraction, diastolic relaxation and mitral and aortic valve functioning, which is why ef reduction, cardiac output decrease, and associated regurgitation May be [12].

The request for a Transthoracic Echocardiogram was the next step and is the main test to be requested for patients with suspected HF, as it promotes a global cardiac assessment, including morphology and chamber diameter, systolic and diastolic function, ejection fraction and heart valves [9]. As shown in the report, the patient presented an increase in the left atrium, the final diastolic diameter of THE, final systolic diameter of THE VE, thickness of the borderline interventricular septum and thickness of the posterior wall also borderline, according to the reference normality indexes; in addition to an ejection fraction by the Simpson criterion of 27%, therefore greatly reduced [13]. All the tests already exposed are sufficient to perform the diagnosis of a CI, but the Framingham and Boston criteria were also used in the case reported, which are scores that indicate high probability of the syndrome, but that have little accuracy to make a definitive diagnosis14, So it will not be afocus on the discussion of this report.

For the diagnosis of MCD, evidence of ventricular dilation and contractile deficit of VE or both ventricles is required, assessed from an EF smaller than 40% or shortening fraction less than 25% [15]. Therefore, all tests performed during the diagnostic confirmation of the patient's HF were also used to confirm THE MCD as the cause of this syndrome. With adequate therapies, patients with MCD can achieve periods of clinical stability, as well as in the report where the patient spent years with the same echocardiographic characteristics, intermittent symptoms and even with improvement in some aspects [3]. Thus, after these quiescent periods, which many patients cannot even reach, some patients present sudden clinical deterioration [3]. Therefore, in the report, the patient begins to present a worsening of his clinic, passing nyha class III, with new alterations to the ECG. There was no improvement with beta-blocker withdrawal, confirming that there was no relationship of these changes with the medication used.

In these cases of patients with symptomatology, in clinical worsening, despite an optimized clinical treatment, the risk of death is very high [10]. There are procedures that can be performed to reduce morbidity and mortality such as cardiac resynchronization (CRT), cardiodefibrillator implantation and heart transplantation. The principle of CRT has the principle of reversing intraventricular dissynchrony, caused by BRE that delays electrical conduction in parts of the ventricle, with consequent late contraction and decreased effectiveness of myocardial contraction, assisting in reverse remodeling and reduction of mitral insufficiency. A pacemaker is implanted with two electrodes in the ventricles, and these resume their synchrony [9,10]. Therefore, the CRT is indicated for those patients with symptomatic HF, functional class III or IV, persistent even after treatment optimization, with EF smaller than 35% and who have a BRE [9,10,12]. Associated with CRT, clinical treatment should continue, as this combined therapy showed a 37% reduction in mortality rates, surpassing any data associated with these isolated therapies [12]. These characteristics were noted in the report, with the patient showing significant clinical and echocardiographic improvement.

As we can observe, the diagnosis of MCD is made based on very limited criteria and parameters, which does not allow us to define the etiology responsible for the process and its prognosis [8]. This justifies the fact that in more than 50% of cases the etiology is not defined, and this is called idiopathic [15]. Myocarditis is, in percentage, the second most mcd-related etiology, and the patient's report of rheumatic fever in childhood corroborates this suspicion.

Rheumatic Fever (RF) is defined as a non-suputive complication that occurs about 2 to 4 weeks after pharyngitis caused *by Streptococcus* group A. It is an autoimmune disease that has several clinical manifestations including polyarthritis or arthralgia, carditis, afirma, margined erythemaand subcutaneous nodules [3,16,17]. It is more common among children aged 5 - 15 years, being the leading cause of cardiovascular death during the first 50 years of age [17]. Its pathophysiology, even if poorly understood, involves B and T lymphocytes and consequent production of IgM and IgG against bacterial proteins; these that have a certain mimicry by host proteins, and therefore there is autoimmune cross-reaction, with formation of immunocomplexes and emergence of rheumatic manifestations [17].

The diagnosis of RF is based on clinical characteristics, aided by nonspecific laboratory tests, and there is no imaging method or laboratory test that confirms the disease. That is why the retrospective diagnosis of RF is difficult, because it is in the acute phase in which the symptoms are exuberant [18]. Rheumatic carditis is the most severe manifestation, with the development of myositis and acute valvulitis. It is considered as pancarditis because it involves pericardium, epicardium, myocardium and endocardium, which is the most commonly affected, with the presence of valve damage in the mitral and aorta [16,18]. It can be totally asymptomatic or oligosymptomatic, making its diagnosis in the acute phase difficult to be made. Moreover, because carditis is a cellular manifestation, it may appear in isolation from other rheumatic manifestations that are mood alums, which also hinders the diagnosis [18].

In the case described, RF is only reported as a previous disease of the patient, but there is no document or evidence of any treatment that proves its existence. However, the patient's history of multiple pharyngotontonsillitis makes us include this diagnosis as existing. The hypothesis constructed was of a RF in adolescence, which because it was treated in the wrong way, since there is no report of the patient having undergone any type of pharmacological treatment or secondary prophylaxis, which evolved late to myocarditis and symptoms of HF, which although not so common, are characteristic of a silent severe carditis [18,19].

Myocarditis is defined as an inflammatory process of the cardiac muscle following any type of aggression, either by exposure to antigens such as viruses and bacteria, or by autoimmune mechanisms [3,20]. It presents a wide variety of clinical presentations, which make its diagnosis and classification difficult. In the adult population, symptoms are more subtle and insidious, most often with IDCD and heart failure due to a more mature immune system, with chronic inflammatory responses, tolerant to the chronic presence of an antigen or autoimmunity [3,20]. For the diagnosis of myocarditis, many of the resources used have low sensitivity and specificity as clinical, laboratory, electrocardiographic and radiography findings. Endomyocardial biopsy is the gold standard, but it is an invasive test and has been little

used for the focal character of the disease [8,19-21]. However, computed magnetic resonance imaging (CMR) has gained prominence, as it is a noninvasive method and allows a general evaluation of the heart, elucidating both etiological aspects of MCD and also of the diagnosis of MCD itself [8,21].

The presence of late enhancement in focal and non-territorial areas is the main characteristic of myocarditis to CMR, and with the evolution of the condition may be a diffuse finding. The lesions are located mainly in the lateral wall in the mesum and epicardium and represent the persistence of gadolinium intracellularly due to necrosis or inflammation of myocytes and cell destruction [8]. Diagnostic accuracy is excellent, with a specificity of 100%, but if the test is negative, myocarditis cannot be excluded in strongly suspected cases[8]. In the report, a CMR was performed, but no changes were demonstrated that suggested the diagnosis of myocarditis, only the characteristic alterations of a DM. The diagnosis was not ruled out, being scheduled for a new CMR, but with the sudden clinical deterioration of the patient and implantation of the cardiac resynchronizer, the performance of a new CMR was contraindicated. This limitation associated with the fact that all other noninvasive tests were performed and inconclusive, there is a possibility that endomyocardial biopsy is indicated, due to the high probability of etiology and because it is the last resource that remains.

Another etiological possibility suggested for the reported case is sarcoidosis or cardiac amyloidosis. Sarcoidosis is a granulomatous disease, characterized by the presence of non-casesine granulomas, reaching multiple organs and systems [22]. It affects mainly young adults, with great clinical variability, which is why, in the vast majority of cases, biopsy is necessary followed by histopathological analysis to confirm its diagnosis [22]. Cardiac involvement occurs at a frequency that is still little known and possibly underestimated, because the symptomatology is little specific or in the case of subclinical disease [22,23]. Myocardium is the most affected region, and is clinically manifested by AVF, arrhythmias, HF and sudden death, and may not present symptoms [15,22,23].

The evolution of a patient with cardiac sarcoidosis (CS) to a cardiomyopathy is less common than the emergence of a tachyarrhythmia, but there have been cases in which CS has been diagnosed after heart transplantation in patients with so-called idiopathic cardiomyopathies. CS can lead to an MCD, with ventricular dilation and low EF, or a restrictive cardiomyopathy, with normal-sized ventricles and preserved EF [22,23]. Therefore, the suspicion of CS in the reported patient is based on the fact that, it is a young adult with changes in the cardiac conduction system at ECG and Holter and with evidence of an unexplained MCD [15,22,23]. The lack of involvement of other systems such as skin, eyes and lung decreases the probability of diagnosis, but a histopathological evaluation is being considered to elucidate this possibility.

Amyloidosis is a disease characterized by extracellular deposition of fibrils composed of low-weight subunits of a wide variety of proteins. This amyloid deposition can occur in multiple organs, including the heart. The frequency at which this occurs is variable, as is the prognosis, depending on the type of amyloidosis. Of the 25 types of amyloidogenic proteins that exist, not all generate cardiac changes, and the most common are light chain (AL), familiar (ATTR) and secondary (AA) [24,25].

Amyloid cardiomyopathy (MA) is manifested by symptoms of HF associated with echocardiographic alterations such as increased pressures and thinning of the VE walls, with normal or moderately increased intracavitary VE size and biatrial enlargement. In addition, they may present alterations in the electrical conduction system such as AV blocks or tachyarrhythmias, especially the AL and ATTR types [24,25]. However, the main presentation of MA is that of restrictive cardiomyopathy, with important diastolic dysfunction, symmetrical thin ventricular walls and granular aspect of the myocardium, associated with a preserved or exaggerated contractile function due to the minimal stress caused by the cardiac walls [26]. Diagnostic confirmation is performed from biopsy and histopathological analysis [24,25]. When we make a relationship between the characteristics of the patient reported with the MA, there are certain symptoms that lead us to suspect this diagnosis, but when comparing echocardiographic findings, the probability of diagnosis decreases, because the patient presents significant systolic/contractile deficit, absence of granular aspect, with important stress of its walls and reduced EF.

As already mentioned, the vast majority of causes of so-called idiopathic MCD have some genetic component. There is a family form of MCD, very common, with variable clinic and various patterns of heredity. However, this is not the case with the report, because for this diagnosis to be defined, it is necessary that 2 or more members of the same family have the diagnosis of MCD [8].

This patient has an ophnotype of Smith-Magenis syndrome. This is a congenital disease caused by a microtype on chromosome 17p11.2, which generates a series of changes such as intellectual deficit, autistic spectrum, aggressive behavior, insomnia, delay in all aspects of neuropsychomotor development, craniofacial abnormalities and metabolic problems [27]. This deleted chromosomal region includes the RAI1 gene, and in 70% of cases the size of the deleteration is the standard, and the rest of the cases have larger or smaller deletes. The RAI1 gene is associated with the regulation of several genes that control a series of physiological processes [28]. Therefore, depending on the amount of genes that have been lost and the size of the deletion, phenotypic manifestations vary, including that they may lead to changes in the cardiovascular system such as mcd [28], even if studies that make this correlation are scarce. The patient even presents alterations of his lipid profile, characteristic of this syndrome [27]. The karyotype test for this type of alteration is normal, but it is mandatory to request for proof of this normality and allow the performance of more specific tests, which can quantify this deletion and define the affected genes. The importance of the diagnosis of this syndrome lies in the fact that therapeutic strategies can be adopted early to stimulate the neuropsychomotor development of affected patients and thus improve their quality of life in a lasting way.

Conclusion

Therefore, we can conclude that Dilated Cardiomyopathy is a multifactorial disease, with great variability of clinical presentations, and that it represents a great danger to the lives of patients. This justifies the importance of an early and rapid diagnosis, to avoid the development of cardiac complications that will not respond to clinical treatment. However, the criteria used may be imprecise, as well as their prognosis. In the case reported, the patient was diagnosed late, because when the symptoms arose, the cardiac alterations were already exuberant and worrying, and even responding well to clinical treatment initially, it evolved severely in need of more invasive measures, with the implantation of the resynchronizer.

Currently, the EGS patient remains without an etiological diagnosis, with all tests already performed showing inconclusive results, which exemplifies the complexity of his investigation. From what has already been exposed, we can conclude that the most likely hypothesis is that of a Rheumatic Myocarditis that evolved silently to a MCD, even if it still requires histopathological confirmation. However, the possibility of cardiac sarcoidosis was not ruled out, and more specific investigation was needed. The investigation of Smith-Magenis Syndrome is active, and has great importance, not only by attempting to justify the patient's myocardial disease, but also for the beginning of specific measures that improve learning and behavior, providing a better quality of life for him and his family.

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