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CASE REPORT

ACUTE HEART FAILURE SECONDARY TO SEVERE THREE-VESSEL CORONARY ARTERY DISEASE IN A YOUNG INDIVIDUAL AND ALTERATION OF LIPOPROTEIN A.

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ABSTRACT

Atherosclerotic coronary artery disease is ranked as the leading cause of acute and chronic heart failure in the world. When we thoroughly evaluate the modifiable and non-modifiable risk factors for atherosclerosis, we are faced with global cardiovascular risk scores, which delimit preventive and later therapeutic goals, with the objective of reducing morbidity and mortality from cardiovascular diseases. The present case report shows us a severe coronary disease, with diffuse atherosclerosis, in a patient with a low global risk score and alteration of lipoprotein A (LpA), raising questions about the improvement of measures for global restratification of cardiovascular risk.

KEYWORDS: ATHEROSCLEROSIS; HEART FAILURE; LIPOPROTEIN(A); MYOCARDIAL INFARCTION; PATHOPHYSIOLOGY

INTRODUCTION

Despite significant advances in the diagnosis and therapy of cardiovascular disease (CVD), individuals continue to experience acute myocardial infarction, stroke, peripheral arterial disease, and the need for revascularization. Advances in the identification of modifiable risk factors for CVD, including smoking, hypertension, dyslipidemia, diabetes mellitus and obesity, allowed the development of evidence-based guidelines, with medical and revascularization therapies, which contributed to the reduction of cardiovascular mortality. However, despite advances, 40% of all deaths are attributed to CVD. Furthermore, only 20 to 30% of patients benefit from therapies, and more events occur in patients who are on active therapy than in prevention. These observations suggest the presence of additional modifiable risk factors that contribute to cardiovascular risk[1,2].

Among these risk factors, there is a recent highlight in the atherogenic scenario of dyslipidemias involving lipoprotein A (LpA), similar to LDL in lipid and protein composition. Dyslipidemias can be divided into four clinical categories: elevation of LDL, reduction of HDL, elevation of triglycerides and, finally, elevation of LpA. Currently, it is known that an isolated elevation of apolipoprotein B-100 (apoB), which contains lipoproteins (LDL, VLDL and LpA), can casually be associated with an increase in cardiovascular risk. In contrast, genes that elevate HDL or drugs that increase its concentration do not promote risk reduction. The main difference between LpA and LDL is the presence of apoA glycoprotein linked to apoB-100 [3,4]. Serum levels of LpA vary between populations and are determined by genetic factors. Serum values up to 30 mg/dL are considered normal, except in the black race, which presents much higher levels of this lipoprotein under normal conditions. ApoA is very similar to the plasminogen molecule. In vitro studies have shown that LpA, at high levels, competes with some functions of plasminogen in the coagulation and fibrinolysis cascade and, thus, may have thrombogenic properties. Because it is similar to the LDL particle, LpA also has atherogenic potential. Epidemiological studies have shown that high rates of LpA are associated with an increased incidence of atherosclerotic cardiovascular disease, especially in patients younger than 60 years of age. Furthermore, LpA particles were found in arterial intima, particularly in association with atherosclerotic plaque [5,6].

In view of this atherogenic process, coronary artery disease stands out, as the ischemic substrate is the main cause of acute and chronic heart failure (HF) in the world. Acute HF is one of the main causes of hospitalization in Brazil and in the world and is related to an increase in mortality and the need for short and long-term readmissions. When all this atherosclerotic process and subsequent cardiac dysfunction is triggered in young patients and apparently without risk factors, evaluated by global cardiovascular risk scores as low/intermediate, questions about additional measures and screenings – as well as LpA me-

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asurement – are put in agenda with the objective of risk restratification and change in preventive and therapeutic approaches [7,8].

The present report describes a young patient, with no previous risk factors (hypertension, diabetes, dyslipidemia, family history, obesity and smoking), with acute HF and severe, chronic, three-vessel atherosclerotic coronary artery disease, who would previously fit into low risk scores. for cardiovascular disease, showing a high value of LpA in the investigation.

The Research Ethics Committee of the Hospital de Urgências de Goiânia, linked to Plataforma Brasil, approved the present study (CAAE: 85497418.2.0000.0033).

CASE REPORT

Male patient, 42 years old, white, married, born in Goiânia-GO, commercial representative, BMI 29.62 Kg/m², sought the emergency room on 05/07/2022 reporting dyspnea on minimal exertion for three weeks, with orthopnea and paroxysmal nocturnal dyspnea, in addition to swelling in the lower limbs up to the middle third of the legs. Patient denied chest pain in the period, cough, fever and had no urinary complaints. He had been reporting diarrhea for 30 days, without blood or pus, without associated fever and without abdominal pain, with an average of four to five episodes in the period, not associated with prostration.

He was seen in the emergency room without signs of dehydration, with systemic congestion, with mild dyspnea and a respiratory rate of 19 bpm, saturating 96% to room air, pulmonary rales up to the middle third, bilateral, stable, with a blood pressure of 110 x 83 mmHg, good peripheral perfusion, conscious, and with edema in the lower limbs. An electrocardiogram was performed on admission, which showed sinus rhythm, with a heart rate of 98 bpm, low-amplitude QRS complex in the frontal plane, slow progression of the R wave in the horizontal plane, delay in the end of ventricular activation by the right branch and diffuse changes in ventricular repolarization (Figure 1).

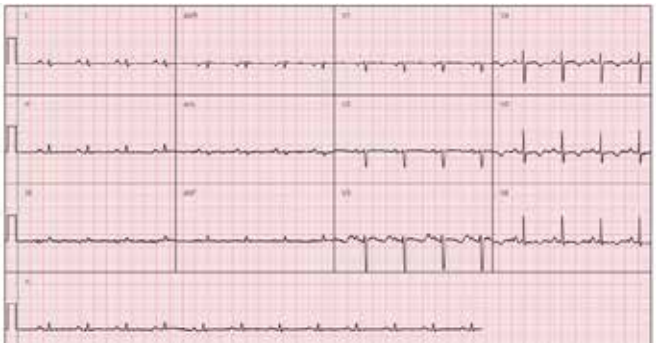

Figure 1 - Electrocardiogram 05/07/2022

Ultrasensitive troponin was measured, with a value of 49.26 ng/L (reference value < 14 ng/L). The patient was hospitalized with diuretic therapy and a transthoracic echocardiogram and cardiac magnetic resonance imaging were requested to assess probable myocarditis.

The patient denied previous comorbidities, referred only to social drinking, on weekends, of mild intensity. He denied diabetes, high blood pressure, dyslipidemia and a previous history of thrombosis. No family history of early coronary artery disease and sudden death, as well as thrombophilia in relatives. He reported a lack of physical activity (sedentary lifestyle), but active due to his profession, and reported sporadic smoking, on weekends, for only one year (2019). The patient was overweight and had an abdominal circumference of 109 cm, without stigmata of chronic liver disease and chronic alcohol consumption. Unhealthy eating habits.

On 05/08/2022, a chest computed tomography was performed, which showed a small pleural effusion on the right, with compressive atelectasis over the adjacent lung parenchyma and enlargement of the left heart chambers. On the same day, he continued with serum tests, with a new troponin of 40.20 ng/L and normal renal function (creatinine 1.4 mg/dL and urea 41 mg/dL). Blood count with leukocytes of 15900 /µL, hemoglobin 15 g/dL, hematocrit 44.3%, platelets 219,000 /µL, C-reactive protein 22.7 mg/L, ESR 10 mm/h, d-dimer 1985 ng/mL, ck- mb 18.8 Ui/L, cpk 92 Ui/L, sodium 133 mmol/L, potassium 4.1 mmol/L, ionic calcium 4.63 g/dL, magnesium 1.88 mg/dL and urine summary without leukocyturia and negative nitrite. Thyroid functions within normal limits by laboratory reference (TSH 2.75 µUi/mL and free T4 8.8 µg/dL). A metabolic profile was performed with HbA1C 5.3%, LDL 90 mg/dL, HDL 28 mg/dL, triglycerides 133 mg/dL, total cholesterol 141 mg/dL.

Transthoracic echocardiogram of 05/09/2022 with 33 mm aorta, 49 mm left atrium with indexed volume of 45 ml/m², left ventricular end-diastolic diameter of 63 mm, left ventricular end-systolic diameter of 52 mm, with fraction Teicholz ejection rate of 33%. Diastolic septum thickness of 10 mm and diastolic thickness of the left ventricular posterior wall of 10 mm. Diffuse hypokinesia of the ventricles, with an estimated PASP of 34 mmHg, mild dilatation of the left ventricle and right atrium, impairment of right ventricular systolic function and marked left ventricular diastolic dysfunction. Simpson ejection fraction of 29%.

With therapy already optimized for heart failure with reduced ejection fraction, the patient underwent cardiac magnetic resonance imaging (05/09/2022) which showed mild dilatation of the right atrium and moderate dilatation of the left heart chambers. Left atrium with a diameter of 49 mm (rv 19 to 43 mm) and a volume of 66 ml/m² (rv 21 to 52 ml/m²). Right ventricle with diffuse hypokinesia of the walls and an ejection fraction of 38%, with a diameter smaller than 52 mm (rv: 22 to 44 mm) and larger than 76 mm (rv: 65 to 95 mm), and an end-diastolic volume of 156 ml (rv: 119 to 219 ml) and end-systolic of 96 ml (rv: 32 to 92 ml). Left ventricle with anterior septum of 7 mm and posterior wall of 7 mm, ejection fraction of 25%, end-diastolic diameter of 66 mm (rv: 37 to 53 mm) and end-systolic

diameter of 57 mm, with end-diastolic volume of 259 ml (rv 119 to 203 mm) and end-systolic of 194 ml (rv 33 to 77 ml) with thinning and akinesia of the basal lower segment and hypokinesia of its other segments, as well as mild pericardial effusion and moderate pleural effusion on the right (Figure 2A) . Absence of edema and lipomatous infiltration in the myocardium. Basal lower segment hypoperfusion during dynamic resting perfusion. Late enhancement (fibrosis/necrosis) of an ischemic, transmural pattern, in the lower basal segment and in part of the lower middle segment (Figures 2B and 2C), in addition to mild late non-ischemic, linear mesocardial enhancement in the basal inferoseptal segment. Mesocardial enhancement at right ventricular insertions at the basal portion of the interventricular (junctional) septum, often associated with cardiac chamber overload/pulmonary hypertension. In conclusion, myocardial fibrosis with a multivariate pattern and absence of alterations compatible with acute inflammatory activity in the myocardium/pericardium, which cannot exclude coronary artery disease and Chagas disease.

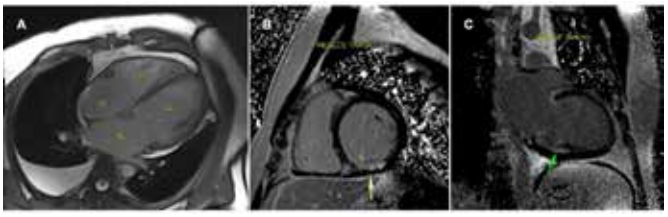

Figure 2 – Cardiac magnetic resonance 05/09/2022: (A) SSFP CINE in 4 chambers – mild dilatation of the right atrium and moderate dilatation of the left chambers, right ventricle with increased dimensions, showing mild pericardial effusion and moderate pleural effusion on the right. (B) delayed short-axis enhancement sequence – delayed transmural enhancement, with an ischemic pattern, in the lower basal segment of the LV. (C) late enhancement sequence, in two left ventricular chambers (2 ECH), ischemic pattern, transmural, of the lower basal segment of the LV.

Serology was performed for Chagas disease, with non-reactive IgM and IgG and negative hemagglutination. Serology for HIV, hepatitis B and C, VDRL, HTLV, all non-reactive. IgM negative for CMV and Epstein Barr virus, and IgG reagent for CMV and Epstein Barr. Non-reactive covid serology (IgG and IgM). Negative PCR for covid on admission.

On 05/12/2022, coronary angiography was performed, showing a severe multivessel obstructive pattern, with mild diffuse atherosclerosis in the right coronary artery, emitting posterior descending artery with 80% obstruction at its origin and right posterior ventricular with 90% obstruction at its origin (Figures 3 A and B). Anterior descending artery with 90% obstruction in the proximal third (Figures 3 C and D) and circumflex artery with 95% obstruction in the proximal third (Figure 3 E). First marginal with 70% obstruction at the origin and proximal third, second marginal with 60% obstruction at the origin and proximal third, and left posterior ventricular artery with 90% obstruction at its origin (Figure 3 F), showing a Syntax I score of 32.

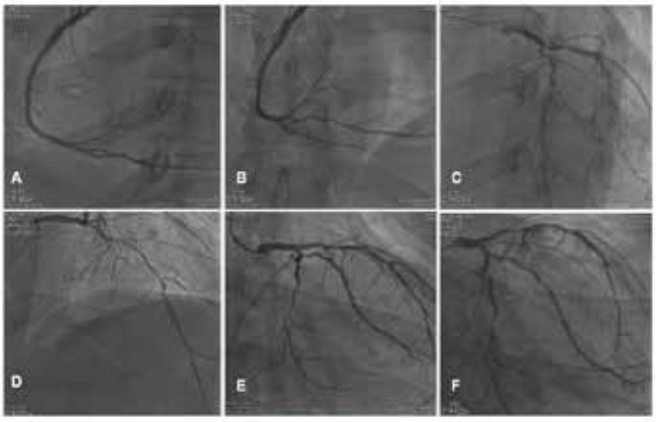

Figure 3 – Coronary angiography evaluation on 05/12/2022: (A) Right coronary artery with mild diffuse atherosclerosis. (B) posterior descending with 80% obstruction at its origin and right posterior ventricular with 90% obstruction at its origin. (C) and (D) anterior descending artery with 90% obstruction in the proximal third. (E) circumflex artery with 95% obstruction in the proximal third. (F) first marginal with 70% obstruction at the origin and proximal third, second marginal with 60% obstruction at the origin and proximal third, and left posterior ventricular artery with 90% obstruction at its origin.

Due to a complaint of pain in the right calf during hospitalization, followed a few days later by sudden and mild chest pain in the dorsal region, the patient was diagnosed with deep vein thrombosis in the right lower limb seen on Doppler US (05/10/2022) , and anticoagulation with full enoxaparin was started, and pulmonary thromboembolism was documented due to failure of filling of the subsegmental arterial branch at the right lung base (Chest angiotomography on 05/17/2022).

With the patient compensated, in profile A of heart failure, apoA 106 mg/dl (rv 79 to 169 mg/dl), apoB 72 mg/dl (rv 46 to 174 mg/dl) collection was performed on 05/18/2022 dl) and LpA 53.8 mg/dl (rv less than 30 mg/dl). He was discharged on 5/20/2022 with optimized therapy: sacubitril/valsartan 100 mg twice daily, carvedilol 50 mg twice daily, ASA 100 mg once daily, atorvastatin 80 mg once daily, spironolactone 25 mg once daily, dapagliflozin 10 mg once daily and warfarin 5 mg one and a half tablets daily. He was then evaluated by the gastroenterologist, being diagnosed with dysbiosis, receiving intestinal flora replacement treatment, with subsequent improvement of gastrointestinal symptoms.

On 06/29/2022, the patient was readmitted for myocardial revascularization surgery, with implantation of the left mammary artery in the anterior descending artery, implantation of the left radial artery in the marginal artery and left posterior ventricular artery, and a saphenous vein bypass in posterior descending artery and right posterior ventricular. The patient was extubated in the operating room, without complications during the surgery, with hospital discharge on 07/06/2022, maintaining previous medications and referred for clinical follow-up.

DISCUSSION

The present case report draws attention to the high morbidity and mortality risk in a young patient with low cardio-

vascular (CV) risk according to Framingham, but with diffuse and three-vessel coronary atherosclerosis, with signs and symptoms of acute heart failure, evidencing an increase in LpA . LpA contributes to CV risk through multiple pathways. Quantitatively, it carries the entire atherogenic risk of LDL particles, including a greater propensity for oxidation after entering vessel walls, creating highly immunogenic and proinflammatory particles[9]. However, its main pathognomonic component is found in apoA, a plasminogen-derived structure that potentiates the atherothrombosis process, including inflammation through oxidized phospholipids, as well as a decrease in its clearance by impairing the anchoring in LDL receptors and potentiating the antifibrinolytic effects by inhibition of plasminogen activation [10].

The CV risk mediated by LpA should be considered by its amount/absolute mass value, given that 70 to 80% of patients at risk have low levels of LpA and elevated LDL. However, as we observe increases above 25 to 30 mg/dl (which represents 30% of the population), a linear increase in CV risk is observed. In addition, oxidized phospholipids carry a high pro-inflammatory power by increasing monocyte-mediated cytokine production and their migration to vessel walls, resulting in atherothrombotic risks [11,12].

Recent data have shown that values above 30 mg/dl of LpA infer a higher risk of AMI13, and this observation is confirmed by a large meta-analysis of 124,634 participants, where an acceleration of risk was observed with values already above 24 mg/dl [14]. In light of these advances in dyslipidemia, in 2016, the Canadian Society of Cardiology scored a value > 30 mg/dl as a risk factor and recommended measuring LpA mainly for intermediate-risk patients, as well as individuals with an early history of coronary heart disease in the family. These findings are of great interest to physicians and patients as they would restratify intermediate risk patients to higher or lower risk, and would lead to changes in therapies and therapeutic targets [15]. The Bruneck study with a prospective follow-up of 15 years showed a reclassification risk in 39.6% of subjects (both high and low risk), and concluded change in risk in 4 out of 10 patients if the measurement was included in the Framingham score [16].

More than 90% of circulating LpA have their concentration genetically determined, with little influence by diet and external factors and with little fluctuation in their dosages 17. It is postulated that its measurement should be evaluated at least once, mainly in the first lipidogram of any individual, and a new collection is unnecessary in case of normality, regardless of changes in treatment. In 2010, the European Atherosclerosis Society recommended LpA measurement for all patients with premature CVD, familial hypercholesterolemia, early family history, CVD recurrence despite statin therapy, and for reclassification of patients at borderline risk [18].

Regarding drug therapy, previous studies suggested intensifying LDL control in view of the increase in LpA. However, new studies (such as AIM-HIGH, JUPITER and LIPID) demonstrated that the elevation of LpA alone reflected residual risks of CVD despite controlled LDL levels [19,20,21]. Another point highlighted by some pre- and post-treatment reports with statins corresponds to the paradoxical increase in LpA with these drugs, as observed by an analysis of 3,896 patients, in which the use of atorvastatin, pravastatin, rosuvastatin, pitavastatin and the addition of ezetimibe, raised LpA levels by up to 11%, and further studies are still needed to better understand this phenomenon [22,23].

CONCLUSION

The reported case reinforces the importance of new and large studies regarding the pathophysiology of the atherosclerotic process, a more accurate risk stratification of the evaluated population, and the application of more in-depth methods in the evaluation of obscure dyslipidemias in clinical practice as well as non-invasive exams (anatomical and/or functional) in individuals at low/moderate risk for changes in LpA. In addition, we must estabçish in high-risk patients, in the presence of optimized therapies and lifestyle changes, but with new atherosclerotic events, what are the non-modifiable risk factors where science and gene therapies could act.

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