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## Abstract

Rheumatoid arthritis (RA) is an inflammatory disease that affects the joints, causing tissue destruction, pain, and deformities. Inflammation accelerates the process of atherosclerosis, progressing to coronary artery disease (CAD). We reported the case of a 64-year-old patient who presented RA for 25 years. The patient evolved with persistently active disease and inflammation markers above the normal value, and was diagnosed with a luminal reduction in the anterior descending artery. He underwent coronary angioplasty. The prevalence of CAD with the risk of premature death increases in these patients due to the chronic inflammatory process. Therefore, annual cardiovascular assessment is essential for patients with RA.

Keywords: Rheumatoid arthritis; Inflammation; Coronary atherosclerosis; Angioplasty.

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### Resumo

Artrite Reumatoide (AR) é uma doença inflamatória que afeta as articulações, levando a destruição tecidual, dor e deformidades. A inflamação acelera o processo de aterosclerose ocasionando o desenvolvimento da doença arterial coronariana (DAC). Relatamos o caso de um paciente de 64 anos, portador de AR há 25 anos, que evoluiu com a doença persistentemente ativa e com marcadores de inflamação acima do valor de normalidade, sendo diagnosticado com redução luminal na artéria descendente anterior e submetido à angioplastia coronária. A prevalência de DAC com risco de morte prematura é aumentada nesses pacientes devido a cronificação do processo inflamatório. Logo, a avaliação cardiovascular anual é imprescindível nos portadores de AR.

Palavras-chaves: Artrite reumatoide; Inflamação; Aterosclerose coronária; Angioplastia.

#### INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects the synovial tissue of the joints, causing tissue destruction, pain, and deformities.<sup>1</sup> This disease is related to an increased risk of coronary artery disease (CAD) because the chronic inflammation accelerates the process of atherosclerosis. As a result, patients with RA have larger coronary plaque than those without RA.<sup>2</sup> Moreover, the clinical manifestations of CAD start earlier and silently in patients with RA, unlike the general population.<sup>3</sup>

The degree of inflammation and the risk of cardiovascular events are directly related.4 Proinflammatory cytokines (e.g., tumor necrosis factor and interleukin-6) impair endothelial function in patients with RA, accelerating atherosclerosis.<sup>3</sup> Other risk factors may be associated, such as age, sex, hypertension, diabetes mellitus, dyslipidemia, obesity, and smoking, influencing the early onset of atherosclerosis.<sup>3</sup>

C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are inflammatory markers that may be associated with cardiovascular risk in RA when elevated.<sup>5</sup> Evidence demonstrates that higher CRP is associated with an increased risk of subclinical atherosclerosis and increased incidence of cardiovascular events.<sup>5</sup> Cardiovascular risk increases by 1% for each 20 mg/L increase of CRP.<sup>5</sup> Therefore, persistent inflammatory markers may identify individuals with RA at increased risk for early CAD.<sup>6</sup>

### **CASE REPORT**

The patient (man, 64 years old) with RA for 25 years, presenting systemic arterial hypertension and dyslipidemia, evolved with persistently active RA, with inflammatory markers (CRP and ESR) four-fold above the upper limit of normal. He presented injuries in the wrist and knees and pain in the hip. He reported the use of non-hormonal anti-inflammatory drugs and glucocorticoids. Blood

pressure was controlled using an angiotensin II receptor blocker, and dyslipidemia was controlled with statin.

In 2013, he reported control of low-density lipoprotein and fasting glucose. The patient underwent myocardial perfusion scintigraphy (MPs) with pharmacological stress that did not reveal electrocardiographic, clinical, or perfusion abnormalities; the left ventricular ejection fraction was normal. On the same occasion, a coronary angiotomography (CT angiography) revealed that the coronary calcium score was zero, and coronary arteries were normal (i.e., no obstructive arterial disease).

After six years (November 2019), he reported atypical chest discomfort unrelated to exertion, attributing it to RA. Due to the persistent inflammatory activity, he underwent a new evaluation with CT angiography and calcium score (figure 1), resulting in a score = 98 (65 percentile) and a severe non-calcified lesion in the proximal third of the anterior descending artery (AD), with significant luminal reduction. A coronary angiography confirmed that the right coronary artery presented a severe lesion (80%) in the proximal third and moderate lesion in the middle third. He underwent coronary angioplasty with drug-eluting stent implantation in the proximal third of the AD.



**Figure 1 –** Angiotomography performed in 2019; 2D reconstruction of the anterior descending coronary artery (AD). According to the white arrow, we note a severe mixed atherosclerotic plaque with severe luminal reduction, predominantly not calcified in the proximal third of the AD. Lilac stripes: a marker for axial cutting of the coronary artery. **Source:** Authors.

## DISCUSSION

The prevalence of CAD with the risk of premature death increases in patients with chronic inflammatory diseases (e.g., RA).6 This risk is mainly due to cardiovascular disease, particularly CAD.<sup>6</sup>

The reported incidence and prevalence of CAD in patients with RA varies according to the specific manifestations of the disease, the population evaluated, and the screening and diagnostic methods.<sup>7</sup> A meta-analysis of 24 observational studies (n = 111,758 patients) concluded that the mortality risk from CAD was 59% higher in patients with RA than in the general population.<sup>8</sup> The risk may increase when symptoms develop and before patients meet the formal classification criteria for the RA diagnosis.<sup>9</sup>

A Swedish cohort study involved 1,135 patients with RA and acute coronary syndrome identified in a national database. They experienced more sudden cardiac death, acute myocardial infarction (AMI) with ST-segment elevation, higher troponin levels, and complications when hospitalized than the general population.<sup>10</sup>

It is unclear why patients with RA and CAD are less likely to report chest pain before or during a cardiovascular event.<sup>11</sup> Possible explanations include that patients with active arthritis or structural joint damage may be less physically active, less likely to increase heart demand enough to trigger angina, and more likely to attribute pain to RA. In addition, nonsteroidal anti-inflammatory drugs, glucocorticoids, or disease-modifying antirheumatic drugs may change the pain perception.<sup>12</sup>

Patients with and without RA share some underlying mechanisms of atherosclerosis pathogenesis.<sup>2</sup> Among the general population, inflammation plays a significant role in the development of CAD, and the innate and adaptive immune systems influence the onset and progression of atherosclerosis.<sup>3</sup>

Inflammation contributes to acute myocardial infarction in patients with RA.<sup>2,6</sup> Chronic inflammation may accelerate the progression of atherosclerosis through cytokines, abnormal functions of T lymphocytes, macrophages, and dendritic cells, immune complexes, coagulation abnormalities, oxidative stress, or a combination of these factors.<sup>3</sup>

The approach to diagnosing CAD is similar in patients with and without RA.<sup>2</sup> Given the higher incidence of CAD, it is suggested to perform an annual cardiovascular assessment focused on history, physical examination, and electrocardiogram in patients older than 50 years.<sup>6</sup> Also, because of the low threshold to proceed to exercise, pharmacologically stressed MPs in those with electrocardiographic symptoms or findings suggestive of CAD may be an option.<sup>10</sup> The evaluation of the coronary calcium score in patients with chronic inflammatory diseases is needed even if they are not in an intermediate risk range.<sup>13</sup> The reassessment of the coronary calcium score, if initially zero, should be shorter; however, previous studies did not indicate the ideal time.<sup>13</sup> A score

greater than 100 increases the probability of myocardial ischemia in the face of a CPM of stress and rest, where the prevalence of myocardial ischemia reaches 40%.<sup>10</sup>

In conclusion, chronic inflammatory diseases, including RA, have an intense and continuous inflammatory activity that accelerates the atherosclerotic process, requiring a systematic approach to detect CAD and myocardial ischemia.

## **CONFLICT OF INTEREST**

No comment.

# **CONTRIBUTIONS OF THE AUTHORS**

**DBL** principal investigator, research elaboration, schedule elaboration, literature survey, data collection and analysis, article writing, article writing correction, final version approval, article submission and procedures; **FAP** co-advisor, research elaboration, schedule elaboration, article writing, article writing correction, and final version approval; **MAF** collaborator investigator, article writing, article writing correction and final version approval; **ARSC** collaborator investigator, article writing, article writing correction and final version approval; **GSSM** collaborator investigator, article writing, article writing correction and final version approval; **LSS** collaborator investigator, article writing, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction and final version approval; and **ELP** advisor, article writing correction approval.

# REFERENCES

- 1. Hochberg MC, Gravallese EM, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, et al. Rheumatology. Vol. 2. Philadelphia: Elsevier, Cop; 2019. ISBN: 9780323680905;
- Løgstrup BB, Olesen KKW, Masic D, Gyldenkerne C, Thrane PG, Ellingsen T, et al. Impact of rheumatoid arthritis on major cardiovascular events in patients with and without coronary artery disease. Annals of the Rheumatic Diseases [Internet]. 2020 Sep 1;79(9):1182–8. https://doi.org/10.1136/ annrheumdis-2020-217154;
- 3. Lee TH, Song GG, Choi SJ, Seok H, Jung JH. Relationship of rheumatoid arthritis and coronary artery disease in the Korean population: a nationwide cross-sectional study. Adv Rheumatol. 2019;59(1):40. Published 2019 Aug 27. doi:10.1186/s42358-019-0084-6;
- Tinggaard AB, de Thurah A, Andersen IT, et al. Rheumatoid Arthritis as a Risk Factor for Coronary Artery Calcification and Obstructive Coronary Artery Disease in Patients with Chest Pain: A Registry Based Cross-Sectional Study. Clin Epidemiol. 2020;12:679-689. Published 2020 Jun 24. doi:10.2147/ CLEP.S251168;
- Erre GL, Cacciapaglia F, Sakellariou G, Manfredi A, Bartoloni E, Viapiana O, et al. C-reactive protein and 10-year cardiovascular risk in rheumatoid arthritis. European Journal of Internal Medicine [Internet]. 2022 Oct (104):49–54. https://doi.org/10.1016/j.ejim.2022.07.001;

- Kang S, Han K, Jung J-H, Eun Y, Kim IY, Hwang J, Koh E-M, Lee S, Cha H-S, Kim H, Lee J. Associations between Cardiovascular Outcomes and Rheumatoid Arthritis: A Nationwide Population-Based Cohort Study. Journal of Clinical Medicine. 2022; 11(22):6812. https://doi. org/10.3390/jcm11226812;
- Daniel CM, Davila L, Makris UE, et al. Ethnic Disparities in Atherosclerotic Cardiovascular Disease Incidence and Prevalence Among Rheumatoid Arthritis Patients in the United States: a Systematic Review. ACR Open Rheumatol. 2020;2(9):525-532. doi:10.1002/acr2.11170;
- Aviña-Zubieta JA, Choi HK, Sadatsafavi M, Etminan M, Esdaile JM, Lacaille D. Risk of cardiovascular mortality in patients with rheumatoid arthritis: a meta-analysis of observational studies. Arthritis Rheum. 2008 Dec 15;59(12):1690-7. doi: 10.1002/art.24092;
- Kokkonen H, Johansson L, Stenlund H, Rantapää-Dahlqvist S. Cardiovascular Risk Factors before Onset of Rheumatoid Arthritis Are Associated with Cardiovascular Events after Disease Onset: A Case-Control Study. J Clin Med. 2022;11(21):6535. Published 2022 Nov 3. doi:10.3390/jcm11216535;
- 10. Mantel Ä, Holmqvist M, Jernberg T, Wållberg-Jonsson S, Askling J. Rheumatoid arthritis is associated with a more severe presentation of acute coronary syndrome and worse short-term outcome. Eur Heart J. 2015 Dec 21;36(48):3413-22. doi: 10.1093/eurheartj/ehv461. Epub 2015 Sep 23. PMID: 26400826;
- Mota LMH da, Cruz BA, Brenol CV, Pereira IA, Rezende-Fronza LS, Bertolo MB, et al.. Diretrizes para o tratamento da artrite reumatoide. Rev Bras Reumatol [Internet]. 2013Mar;53(Rev. Bras. Reumatol., 2013 53(2)):158–83. doi: 10.1590/s0482-50042013000200004;
- Solomon DH, Goodson NJ, Katz JN, Weinblatt ME, Avorn J, Setoguchi S, Canning C, Schneeweiss S. Patterns of cardiovascular risk in rheumatoid arthritis. Ann Rheum Dis. 2006 Dec;65(12):1608-12. doi: 10.1136/ard.2005.050377. Epub 2006 Jun 22. PMID: 16793844; PMCID: PMC1798453;
- 13. Jesson C, Bohbot Y, Soudet S, et al. Is the Calcium Score Useful for Rheumatoid Arthritis Patients at Low or Intermediate Cardiovascular Risk?. J Clin Med. 2022;11(16):4841. Published 2022 Aug 18. doi:10.3390/jcm11164841.