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Rheumatoid cachexia: A challenge for the clinician

Caquexia reumatoide: Desafio para o clínico

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ABSTRACT

Rheumatoid cachexia can be described as a complex syndrome, where the patient loses muscle mass, and may or may not maintain weight, through the gain of fat mass. Active inflammatory cytokines in rheumatoid arthritis appear to be the pivot of this process; high levels of TNF-alpha and IL-1 are associated with protein degradation. In this case report, information was collected from the hospitalization period through a search in medical records, where the patient was admitted to the hospital a little more than 1 month after surgery to repair an aortic aneurysm, reporting inappetence and weight loss, which had been occurring for three months, even before surgery. During hospitalization, hypotheses were raised about the cause of weight loss, especially neoplasms. Finally, any diagnoses from other specialties were discarded. The importance of recognizing cachexia as a warning symptom for patients with rheumatoid arthritis without clear manifestations of the disease was highlighted.

Keywords: Rheumatoid Arthritis, Cachexia**,** Consumptive syndrome.

INTRODUCTION

Rheumatoid Arthritis (RA) is a low-incidence disease that mainly affects women between the 4th and 6th decade of life. It has a systemic characteristic, with an autoimmune background, whose mechanism and etiology have not yet been fully elucidated. The disease is marked by a set of symptom signs arising from marked destruction of cartilage and joint bones.

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The whole process is mediated by inflammatory cytokines, which become more pronounced during disease activity1.

Cachexia is a clinical condition where the body begins to lose muscle mass, the result of a set of factors that culminate in malnutrition and/or protein degradation. This clinical condition can translate into an accentuated weight loss by the patient, characterized by a consumptive syndrome2. There may also be weight maintenance, if there is an increase in fat at the same time that skeletal muscle is lost. Therefore, in some cases, weight loss may not manifest itself or may still be limited3.

Weight loss is usually indicative of some underlying disease, such as AIDS, Chron's disease, COPD, cancers, psychiatric diseases, rheumatological disorders, among others, and are therefore an important cause of hospitalizations. A weight loss will be considered significant when the individual has a weight reduction in the range of 5% of usual weight over a period of 6 to 12 months. Losses greater than 10% are an indication of malnutrition related to mediated cellular action4.

The mechanisms of muscle destruction and reduced protein synthesis will vary between each of the diseases that can cause cachexia. In the case of RA, a set of inflammatory cytokines that mark the activity of the disease acts on cellular catabolism, in a way that is not yet fully understood. What is known so far is that these cytokines can accelerate the degradation of protein complexes, reducing muscle mass indices in affected individuals5.

It is believed that the inflammatory cytokines TNF-alpha and IL-1 beta are the main ones involved in the pathophysiological process of RA cachexia. Both are produced by several cells of the human body, such as defense cells (T lymphocytes, macrophages) and cells that make up the musculoskeletal system, such as skeletal muscle cells1,5.

Studies reinforce that the accentuated expression of pro-inflammatory cytokines, present in RA, are capable of interfering in the basal maintenance of protein metabolism, inducing degradation. The balance of the body's protein ecosystem is complex and very sensitive to variations, and the increase in mediated inflammatory activity is capable of interfering with this sensitive system, causing cachexia. Because cytokines are present from the onset of the disease, it is common for weight loss in these patients to be one of the first signs of RA6.

The amount of muscle mass is easily modifiable, responding to atrophy stimuli, such as disuse and severe inflammatory conditions; Hypertrophy occurs in response to growth stimuli and increased protein synthesis in parallel. Cachexia resulting from the marked loss of muscle mass – atrophy due to inflammatory complications of systemic diseases such as RA – can lead

to a significant loss in the quality of life of patients with the disease, with loss of independence to perform simple daily tasks, and also increased mortality rates6.

In the past, cachexia was believed to be a result of rheumatoid arthritis activity; As the patient began to suffer from increasingly intense and long-lasting joint pain, he became less active, and the physical limitations imposed by the disease generated a sedentary lifestyle that was responsible for muscle atrophy. However, observations revealed that complaints of weakness and weight loss sometimes preceded the more classic manifestations of the disease, such as morning stiffness. It was noted that cachexia could be one of the first signs of the disease, and not a secondary sign to the activity of the disease itself6.

This fact is very similar to the clinical picture of the patient, which became the object of study in this case report. He had recently undergone a major surgery, and at the admission in question, he complained of inappetence and significant weight loss; Several hypotheses emerged, which was finally established as a rheumatological condition. In the description of the report, it is possible to observe that the main complaint was in fact weight loss, and there was no report of muscle limitations or joint pain, although clinical changes compatible with rheumatoid arthritis were later observed.

This case report will aim to describe the clinical condition of and the evolution during the hospitalization period of a patient who was affected by a marked weight loss, which did not present clinical evidence suggestive of rheumatologic disease at admission. Thus, the importance of recognizing cachexia as an important sign for the diagnosis of rheumatoid arbitrary will be highlighted, even before the appearance of the expected clinical profile of patients with this disease.

METODOLOGY

This is a case report based on the medical records of a well-documented 62-year-old male patient. The study was approved by the ethics committee of the Presidente Prudente Regional Hospital. This study followed the guidelines of the National Council for Research Ethics (CONEP) during its elaboration. To complement the content, searches were carried out in electronic databases, such as PubMed, Lilacs and Scielo.

CASE REPORT

G.S.S, 62 years old, male, was admitted to the service on 07/29/2021 with a clinical picture of malaise and adynamia for 1 month, with worsening for 3 days. The patient reported

that he was still having difficulties in performing his daily activities due to muscle weakness. The daughter who accompanied him reported weight loss of around 15 kg in 1 year, 6 kg after a surgery performed at the same hospital, on 06/01/2021, to repair a thoracoabdominal aortic aneurysm. There were no complications in this surgery.

A thorough physical examination was performed, which indicated a good general condition, discolored mucous membranes 1+/4+, hydrated, acyanotic, anicteric, afebrile, eupneic, oriented, with no changes in the cardiopulmonary system, with flaccid abdomen and painless palpation, without the presence of visceromegaly. The physical examination of the wrists was normal, symmetrical and the capillary refill time was less than 2 s. Muscle strength was graded to grade 5.

G.S.S. had a personal history of smoking, alcoholism and hypertension, and was continuously using losartan, ASA, metoprolol and risperidone.

Shortly before, on 07/25/2021, the patient had already been admitted for weight loss investigation in the medical clinic ward. Some tests were ordered, but the diagnoses were not conclusive in determining the origin of the patient's consumptive syndrome.

During the first hospitalization, the patient progressed without intercurrences or other complaints. He was discharged on 07/06/2021. As he returned less than 20 days after the last discharge, with a new worsening of symptoms, and now reporting worsening of weakness and adynamia, he was hospitalized again and several consultations were requested by the medical clinic team.

Throughout the 13 days in which he was hospitalized, the patient was called for all consultations with the specialties referred to by the diagnostic hypotheses.

Among the laboratory tests that showed alterations, we had normocytic normochromic anemia, indicating a chronic disease in early stages; C-reactive protein was 28.7 mg/L (RV: 0 to 9.9 mg/L); Westgreen's result for erythrocyte sedimentation was 82 mm/h.

The rheumatology consultation was the one that drew the most attention from the team. The patient presented with morning stiffness, with symptomatic polyarthritis. The rheumatoid factor test came back positive. Based on the clinical history and the condition of consumptive syndrome/cachexia, the diagnosis of rheumatoid arthritis was given on August 8th.

Immediately, treatment with hydroxychloroquine sulfate 400 mg/day, methotrexate 2.5 mg (take 6 tablets, totaling 15 mg every Monday), folic acid 5 mg every Tuesday, was prescribed, and outpatient follow-up was scheduled. After the beginning of rheumatologic treatment, the patient was hemodynamically stable, without intercurrences. She was discharged

on 08/10/2021 with a scheduled outpatient return with rheumatology. At the time of discharge, he was in good general condition, with no further complaints.

RESULTS

In view of the celebrations presented by the patient, the diagnosis for weight loss was rheumatoid cachexia, a clinical condition associated with the early stages of rheumatoid arthritis, and which sometimes goes unnoticed in patients with few classic symptoms of this rheumatologic disease, such as painful arthritis.

The patient in this case had the diagnosis of rheumatoid arthritis confirmed through specific laboratory tests, and his treatment was instituted correctly, and it is expected that his arthritis will evolve in a mild manner, without diminishing his quality of life. This result was obtained thanks to the team's attention and recognition of cachexia as a possible early sign of rheumatoid arthritis.

DIVISION

Although it is a disease of low incidence, rheumatoid arthritis has a great impact on the quality of life of patients, as it results in limitations and loss of full functional capacity of the musculoskeletal system. Because its mechanisms are not fully elucidated and depend on clinical correlation for diagnosis, it is essential that they know how to notice the signs and symptoms of the disease in order to reinforce diagnostic hypotheses1. The consumptive syndrome, although not specific to a disease, is characteristic of generally severe involvements, and, therefore, this sign should be noted and the patient should always check with the patient if there was any trigger for weight loss. In the case of the patient G.S.S., the consumptive syndrome presented was actually rheumatoid cachexia4.

Rheumatoid cachexia in the patient in this case manifested immediately before the diagnosis of rheumatoid arthritis, which is in line with what is described in the current literature; although it is more common to suspect RA through joint complaints and laboratory and imaging tests, sometimes severe weight loss occurs earlier, and if properly investigated, can accelerate the diagnosis of RA6.

The medication method chosen by the rheumatology team is the first-line approach recommended by the Ministry of Health; Methotrexate and hydroxychloroquine are synthetic disease-modifying medications. Methotrexate (MTX) is associated with considerable levels of intolerance, but it has been observed that its administration followed by folic acid

administration approximately 36 hours later considerably reduces the chances of MTX intoxication. Hydroxychloroquine is preferable to chloroquine, as it has a profile that is more compatible with the modulation of the course of the disease that is intended7.

In view of what has been reported, we conclude that, although it is not a common disease, rheumatoid arthritis has important systemic repercussions that justify health professionals to have a good understanding of the signs and symptoms of the disease, in order to accelerate the diagnosis and favor a better treatment for the patient.

G.S.S. presented a very broad complaint, and not at all specific, and for this reason it demanded the attention of so many specialists. The patient's weight loss could be related to many findings that were described in the tests performed, such as myeloma, gastritis or some otorhinolaryngological alteration that was disturbing their nutrition.

When he was seen by rheumatology, the signs and symptoms made a lot of sense for rheumatoid arthritis, and the hypothesis was supported by positive laboratory tests. The treatment started was correct, and the patient has excellent chances of living with RA and maintaining their quality of life if they have good adherence to treatment.

The fact that he was hospitalized twice in such a short period of time, with such extensive complaints, is indeed striking. In view of the many hypotheses that were being analyzed, rheumatoid arthritis may not have been one of the most expected to be found as a diagnosis, due to the lack of more expressive joint complaints.

Finally, we emphasize the need to pay attention to symptoms and signs that are not very specific, but which can be very important signs of disease. We must remember that in the case of rheumatoid arthritis, sometimes cachexia sets in even before the patient complains of joint pain and other classic symptoms, and, therefore, unexplained consumptive syndromes should always draw attention to rheumatologic disorders as well.

PROJECTS OF INTEREST

The authors declare that there is no potential conflict of interest that could interfere with the impartiality of this scientific work.

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