EJCRIM
European Journal
of Case Reports
in Internal Medicine

RHEUMATOID ARTHRITIS AND PERICARDIAL EFFUSION – A UNIQUE MAJOR MANIFESTATION

Isabel Cruz, Bruno Bragança, Rafaela Lopes, Rui Santos, Aurora Andrade

Centro Hospitalar Tâmega e Sousa, Penafiel, Portugal

Corresponding author: Isabel Cruz **e-mail:** isabelmarticruz7@gmail.com

Received: 21/10/2023 **Accepted:** 27/11/2023 **Published:** 09/01/2024

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: The authors declare that written consent for submission and publication of this clinical report including images has been obtained from the patient according with COPE guidance.

How to cite this article: Cruz I, Bragança B, Lopes R, Santos R, Andrade A. Rheumatoid arthritis and pericardial effusion – a unique major manifestation. *EJCRIM* 2024;**11**:doi:10.12890/2024_004159.

ABSTRACT

Introduction: Pericardial effusion is common in the setting of rheumatoid arthritis (RA); however, it is rarely its first manifestation.

Case description: An 82-year-old male presented with abdominal pain, vomiting and fever. Blood analysis revealed elevated systemic inflammatory markers, and an abdominal computed tomography scan revealed non-specific alveolar condensation of the right pulmonary base and pericardial effusion subsequently quantified as medium size by transthoracic echocardiography. A large aetiological panel was requested, with the autoimmunity study revealing high levels of rheumatoid factor (RF) and anti-citrullinated cyclic peptide (anti-CCP) antibodies. Since the patient did not present articular involvement, the initial hypothesis was pericardial effusion due to pneumonia and no specific treatment for RA was started. At follow-up, the pericardial effusion recurred and a pericardiocentesis was performed. The pericardial fluid analysis was sterile, and no malignant cells were identified. A new serological study confirmed high levels of RF and anti-CCP antibodies, and immunomodulatory treatment was initiated. After one year, the pericardial effusion recurred due to non-compliance with immunomodulatory therapy. A surgical pleuro-pericardial window was performed, and the cytological study of the pericardial patch revealed submesothelial thickening and foci of perivascular lymphocytic infiltrate. The patient remained asymptomatic.

Discussion: After exclusion of a large spectrum of infectious and non-infectious causes and the relapse after suspension of immunomodulatory treatment, the most probable aetiology for the pericardial effusion remains RA.

Conclusion: Pericardial syndromes can be the first manifestation of AR even in the absence of articular symptoms and this disease must be considered in the aetiological investigation.

KEYWORDS

Pericardial effusion, rheumatoid arthritis, pleuropericardial window

LEARNING POINTS

- The occurrence of pericardial effusion in the setting of rheumatoid arthritis (RA) is a usual finding but this form of extra-articular manifestation is possibly the first and only presentation of the disease.
- In the case of recurrent pericardial effusion, the diagnosis of RA must be considered in the aetiological investigation even in the absence of more common manifestations of the disease.

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune inflammatory disorder of unknown aetiology, that most typically presents as inflammatory polyarthritis[1]. It can be accompanied by systemic symptoms such as myalgia, fatigue, low-grade fever and weight loss[1]. Some patients may present several non-articular symptoms, which may pre-date the onset of polyarthritis by many months[2]. The cardiac involvement by RA is relatively frequent and can occur in the form of pericarditis, pericardial effusion (mostly without tamponade) and conduction abnormalities[3]. Patients may rarely present extra-articular disease in the absence of clinical arthritis; however, this is rarely the presenting sign of undiagnosed RA[4]. We report a case of 82-year-old male with recurrent pericardial effusion as the sole presentation of RA.

CASE DESCRIPTION

An 82-year-old Caucasian male with a past medical history of arterial hypertension and atrial fibrillation presented to the emergency department due to abdominal pain and vomiting. At physical evaluation he presented blood pressure of 136/95 mmHg, heart rate of 105 beats per minute, peripheral saturation of 96% with inspired oxygen concentration of 21%, tympanic temperature of 37.8°C, pulmonary auscultation with reduced breathing sounds at the pulmonary bases, normal cardiac auscultation and tympanised abdomen with pain at deep palpation of the lower abdominal quadrants. Blood analysis presented haemoglobin of 13.8 g/dl, elevated white blood cells at 21.68 × 10^3/µl (82.8% neutrophils), platelets of 221 × 10^3/µl, C-reactive protein of 118.9 mg/l, creatinine of 1 mg/dl, potassium of 4 mEq/l and normal aspartate aminotransferase and alanine transaminase. An electrocardiogram presented atrial fibrillation, right bundle branch block (previously present) and normal ST-T and PR segments. An abdominal and pelvic computer tomography scan was performed and revealed non-specific alveolar condensation of the right pulmonary base and a large volume circumferential pericardial effusion in the upper cuts, with no further abnormal findings. Due to the finding of pericardial effusion, a transthoracic echocardiogram (TTE) was performed, showing preserved biventricular systolic function with a left ventricular ejection fraction of 56% and a medium-sized circumferential pericardial effusion (with a maximum size of 20 mm in the posterior and lateral region of the left ventricle) with no signs of cardiac tamponade. The patient was admitted to the ward for surveillance of the pericardial effusion and aetiological study, prescribed with anti-inflammatory therapy (ibuprofen 600 mg three times a day and colchicine 0.5 mg daily) and started on ceftriaxone due to presumed community acquired pneumonia. TTE was repeated and the pericardial effusion maintained its previous dimensions. A vast aetiological study was performed presenting sterile blood cultures, negative urinary antigen test for legionella bacterium and streptococcus pneumoniae, negative serologic testing for Borrelia, leptospirosis, hepatitis B, hepatitis C, human immunodeficiency virus 1 & 2, Epstein-Barr virus, Leishmania and syphilis. Thyroid hormone levels were normal; a high erythrocyte sedimentation rate was found, as well as high levels of RF to 177 IU/ml (negative <14 UI/ml) and strongly positive anti-CCP to 381 IU/ml (positive >10 UI/ml). Finally, a thoracic computed tomography scan revealed no relevant findings. Since the patient did not present any articular symptoms or signs suggestive of arthritis and because the pericardial effusion was of presumed infectious aetiology, no specific therapy for RA was started. A strategy of clinical and echocardiographic surveillance was adopted. At follow-up, a new serologic study was performed, showing high levels of RF (57 UI/ml; negative <14 UI/ml) and anti-CCP antibodies (283.0 UI/ml; positive >10 UI/ml). At the one-year follow-up, the patient presented exertional dyspnoea and a new TTE was performed, revealing worsening of the pericardial effusion with 33 mm at the posterior and lateral region of the left ventricle. The patient denied constitutional symptoms or symptoms suggestive of active infection. Blood analysis presented normal inflammatory markers. A pericardiocentesis was performed with the removal of 850 ml of serous pericardial fluid. The pericardial fluid showed no growth of bacterial or fungal cultures, the interferon-gamma release assay was negative, and no malignant cells were identified. Since the patient maintained high levels of RF and anti-CCP antibodies, RA was the only identified cause for the pericardial effusion. Treatment with methotrexate and prednisolone was started with good clinical response. The patient was discharged asymptomatic under corticosteroid therapy. At the 9-month scheduled follow-up TTE, the pericardial effusion had recurred. There was again a large volume effusion with 34 mm at the posterior and lateral regions of the left ventricle. The patient admitted he had abandoned corticosteroid therapy the previous month. Since it was the second relapse and taking into consideration the age and comorbidities of the patient that limited the start of biological therapies for AR, a surgical pleuropericardial window was performed by a left lateral approach. The cytological study of the pericardial patch revealed a serous layer with submesothelial thickening and foci of perivascular lymphocytic infiltrate, findings in correlation with the clinical context of RA; there was a negative adenosine deaminase test result. At follow-up, the patient remained asymptomatic without new relapse of pericardial effusion.

DISCUSSION

RA is a chronic inflammatory arthritis of autoimmune nature that mainly affects people in the third and fourth decades of life[3], presenting an estimated annual incidence of 0.3%–1.0% and prevalence of up to 1%[5]. The major clinical feature of RA is inflammation and erosion of synovial joints in a typically symmetrical form, which, if uncontrolled, can lead to erosion of cartilage and bone, causing joint deformities and irreversible disability[6,7]. The disease may also cause the presence of fever, weight loss and fatigue[4]. Since RA

is a systemic disease, other organs can be affected, such as skin, eyes, lungs and heart[2]. Extra-articular involvement may pre-date the onset of polyarthritis by many months[8], and occurs in about 40% of patients. However, extra-articular manifestations are rarely the presenting signs of undiagnosed RA[2]. Asymptomatic cardiac involvement occurs in up to 50% of patients, with pericarditis, pericardial effusions, myocarditis, coronary vasculitis, diastolic dysfunction and valvular heart disease the most frequent cardiac manifestations in RA[3]. During the course of the disease around 40% of patients present pericardial involvement from the disease with one-third of patients presenting pericardial effusion, mostly asymptomatic[1]. On rare occasions, pericardial effusion may be the first manifestation of the disease. The diagnosis of RA is highly individualised, being based on clinical manifestations. Although no diagnostic criteria exist, classification criteria that include clinical manifestations and serological assays guide clinical diagnosis[5,9]. The systemic inflammation and autoimmune nature of this disease is reflected by the presence of various useful biologic markers such autoantibodies, and evidence of an acute phase response. Autoantibodies are found in about 75% to 80% of patients (seropositive RA)[10] and can be detected up to 10 years before the onset of clinical arthritis[11]. The main clinically useful autoantibodies are RF and anti-CCP; anti-CCP positivity occurs less frequently than for RF but anti-CCP antibodies testing is more specific than RF. On the other hand, both the sensitivity and specificity for diagnosis markedly increases in case of both positive RF and anti-CCP antibodies, and appears to be associated with a more aggressive clinical course[11]. As such, the presence of such autoantibodies has diagnostic, therapeutic and prognostic implications. Positive antibodies can also be found in other diseases including other autoimmune rheumatic diseases, active tuberculosis and chronic obstructive pulmonary disease[10]. In this report we present a rare first manifestation of an RA (pericardial effusion) in a seropositive patient without non-articular manifestation of the disease. After study of a large spectrum of infectious and non-infectious causes, the patient was found to have RA without identification of any other likely causes for the pericardial effusion. This is supported by the recurrence of pericardial effusion after the patient had suspended treatment with prednisolone.

CONCLUSION

This case highlights that pericardial syndromes can be the first manifestation of AR even in the absence of articular involvement and this disease must always be considered in the aetiological investigation.

REFERENCES

1. Imazio M. Pericardial involvement in systemic autoimmune diseases [Internet]. 2022. Available from: https://www.uptodate.com/contents/pericardial-involvement-in-systemic-autoimmune-diseases
2. Davis JM. Overview of the systemic and nonarticular manifestations of rheumatoid arthritis [Internet]. UpToDate. 2018. Available from: https://www.uptodate.com/contents/overview-of-the-systemic-and-nonarticular-manifestations-of-rheumatoid-arthritis
3. Owlia MB, Mostafavi Pour Manshadi SM, Naderi N. Cardiac manifestations of rheumatological conditions: a narrative review. *ISRN Rheumatol* 2012;**2012**:463620.
4. Whitfield N, Krasniak A, Nguyen H. Concomitant large loculated pleural and pericardial effusions in a patient with rheumatoid arthritis on methotrexate. *Perm J* 2020;**24**:1.
5. Taylor PC. Update on the diagnosis and management of early rheumatoid arthritis. *Clin Med (Lond)* 2020;**20**:561–564.
6. Alivernini S, Tolusso B, Petricca L, Ferraccioli G, Gremese E. Rheumatoid arthritis. In: Perricone C, Shoenfeld Y, editors. The mosaic of autoimmunity: the novel factors of autoimmune diseases, Amsterdam: Elsevier; 2019, p. 501–526.
7. Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. *Bone Res* 2018;**6**:15.
8. Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD, Tanasescu R. Extra-articular manifestations in rheumatoid arthritis. *Maedica (Buchar)* 2010;**5**:286–291.
9. Van Hoovels L, Studenic P, Sieghart D, Steiner G, Bossuyt X, Rönnelid J. Impact of autoimmune serology test results on RA classification and diagnosis. *J Transl Autoimmun* 2022;**5**:2022.
10. Taylor PC, Deleuran B. Biologic markers in the diagnosis and assessment of rheumatoid arthritis [Internet]. 2023. Available from: https://www.uptodate.com/contents/biologic-markers-in-the-diagnosis-and-assessment-of-rheumatoid-arthritis
11. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid arthritis. *Nat Rev Dis Primers* 2018;**4**:18001.