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Pleuro-Pericardial Inflammation and Effusion: A Rare Acute Initial Presentation of Rheumatoid Arthritis

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Abstract

Background: Rheumatoid arthritis is a systemic inflammatory arthritis characterized by joint pain and morning stiffness. The affected joints are typically symmetrically affected, and given the inflammatory nature of this condition, patients often present with warmth and erythema around affected joints as well as fatigue. Extra-articular manifestations, especially pleuro-pericardial inflammation, are rare initial presentations, although may be seen in advanced or undertreated disease. Case Presentation: We describe a case of a rheumatoid arthritis presenting atypically in a middle-aged male who came to the emergency department complaining of diffuse muscle pain and swelling in the distal extremities. Cardiac ultrasound revealed pleuro-pericardial inflammation and effusions. Myositis and infectious causes were ruled out and bilateral hand x-rays did not show erosions or any evidence of arthritic changes. All rheumatological auto-antibodies were negative except for rheumatoid factor and anti-cyclic citrullinated peptide (CCP) and a diagnosis of rheumatoid arthritis was made. The patient was started on prednisone with excellent response. Conclusions: This case highlights that rheumatoid arthritis can uncommonly present initially with extra-articular manifestations that are often manifested in advanced disease. Typically, extra-articular manifestations, especially those as severe as this patient's, occur with untreated, advanced disease and could accompany extensive arthritic joint changes. Thus, it is important to have an understanding of rare, atypical presentations of rheumatoid arthritis so that a high index of suspicion can be maintained to make the diagnosis and initiate treatment in a timely manner.

Keywords

Rheumatoid Arthritis, Atypical Rheumatoid Arthritis, Pleuro-Pericardial

Inflammation, Pleuro-Pericardial Effusion

1. Background

Rheumatoid arthritis (RA) is the most common systemic inflammatory arthritis. RA is an autoimmune condition where immune cells target specific tissue, often in joints, causing patients to present with symmetric pain and stiffness in multiple joints, inflammation, and fatigue. RA most often affects women, smokers, and those with a family history of the disease. The lifetime prevalence of RA is 1% globally. RA typically presents between the ages of 30 and 50 years old with symmetric pain and stiffness in multiple joints and morning stiffness lasting more than one hour. The wrist, metacarpophalangeal, and proximal interphalangeal joints are most commonly affected while distal interphalangeal and lumbar spine joints are not usually affected. Systemic symptoms including fatigue, weight loss, and anemia may also be present [1]. Diagnosis can be made with consistent symptom presentation as well as positive serology for rheumatoid factor and anti-citrullinated protein antibody. Extra-articular symptoms that affect other bodily systems can develop as well, however, typically, patients present initially with articular symptoms before severe systemic manifestations develop.

Without proper treatment, RA can progress to involve other systems, including pulmonary and cardiovascular systems. These are known as extra-articular manifestations (EAM) and they usually occur later in the course of disease as a result of undertreatment or treatment resistance. The most common EAM is rheumatoid nodules, affecting about 30% of patients [2]. One such EAM is Felty Syndrome, characterized by RA, neutropenia, and splenomegaly [3]. Caplan Syndrome, also known as rheumatoid pneumoconiosis, is another EAM, characterized by an inflammatory lung condition in reaction to exposure to coal, asbestos, and/or silica, in patients with diagnosed RA [4]. Rarely, severe pleuro-pericardial inflammation and effusion may occur early in the course of disease as an initial presentation. It is rare for patients to present initially with extra-articular manifestations of rheumatoid arthritis that, in these cases, making the proper diagnosis is difficult and often delayed. These cases are usually published in the literature to highlight the possibility of these atypical presentations. However, to our knowledge, there are no published cases in the literature that are identical to the case presented here. This case presentation describes an atypical initial presentation of rheumatoid arthritis in the form of severe pleuro-pericardial inflammation and effusion with other non-specific symptoms in the absence of arthritic joint changes.

2. Case Presentation

The patient is a 45-year-old male who presented to the emergency department

with approximately two weeks of worsening generalized muscle pain, cramping, and diffuse swelling in the distal extremities. The patient's only past medical history was a three-month hospitalization when he was an 8-year-old child for muscle and joint pain that began after moving to a new state. He was treated for allergies, although the true cause was never determined. He continued to deteriorate at that time, and the patient's family moved again to a different state where the patient's symptoms spontaneously resolved. He never took any medications long term, and was not taking any medications at presentation. Two weeks prior to the patient's initial presentation, he felt extreme cramping and proximal muscle weakness after spending an afternoon mowing his lawn. He then noticed a rash appeared on his medial ankles and shins, as well as the dorsal aspects of his hands bilaterally. He wrapped his extremities in ice packs, took ibuprofen, and the pain resolved by the next day. One week later, the patient took a flight to Toronto for a vacation and endorsed heavy alcohol consumption. His muscle pain and weakness returned during the return flight and progressively worsened over the following four days despite consistent ibuprofen use. During this time, distal extremity swelling appeared, and the patient was no longer able to cope at home and presented to the emergency department.

Musculoskeletal examination revealed profound proximal muscle weakness and pain in the bilateral upper and lower extremities. Diffuse swelling and secondary skin tightening was visible in the dorsal aspects of the bilateral hands and feet not limited to the wrist, metacarpal and phalangeal joints. Skin examination revealed erythematous papules over the metacarpophalangeal joints bilaterally and the proximal interphalangeal joints on the left. At the emergency department, an erythematous rash was seen at the periorbital area along with flushing in the anterior and posterior aspects of the neck. Erythema was also present over the extensor surfaces of the bilateral elbows and knees and a maculopapular, erythematous rash was appreciated at the medial aspects of the bilateral ankles and shins.

Given the proximal distribution of acute-onset muscle pain and weakness coupled with the cutaneous findings potentially consistent with a heliotrope rash and gottron papules, dermatomyositis was high on the list of differential diagnoses, but creatine kinase was normal. Given the recent travel history and significant amount of time spent outdoors in his yard and garden, infectious causes were highly considered. Inflammatory and infectious markers were measured as shown in **Table 1** and **Table 2**. Arthrocentesis was performed on the right knee but gram stain and cultures were negative. A panel of rheumatologic autoantibodies was also sent early in the hospital course due to a high index of suspicion of rheumatological disease in the setting of multiple confounding variables in his presentation.

A focused cardiac ultrasound, shown in **Figure 1**, was then performed since he continued to deteriorate and developed mild, vague chest achiness. It revealed extensive pericardial inflammation and effusion including left-sided pleural

Table 1. Values for inflammatory markers for each day of the hospital stay (NR: normal range).

	Day 1	Day 2	Day 3	Day 4	Day 5
Creatine Kinase (U/L) NR: 39 - 308	68	72	35		
C-Reactive Protein (mg/L) NR: 0 - 8	199.6	177.5	147.4	145.8	61.2
Sedimentation Rate (mm/hr) NR: 0 - 14	83	72	70	99	75
White Blood Cell Count (count $*10^9$/L) NR: 3.5 - 10	13.8	13.0	12.6	13.6	14.3

Inflammatory markers measured and tracked throughout the 5-day hospital stay.

Table 2. Values for rheumatologic autoantibodies and infectious markers sent (NR: normal range).

	Day 1	Day 2	Day 3
Anti-nuclear antibody (NR: <1:40)	<1:40		
Anti-dsDNA (IU/mL) (NR: <4)	1		
Anti-Jo (AI) (NR: 0 - 0.9)	<0.2		
Anti-RNP (AI) (NR: 0 - 0.9)	<0.2		
Anti-Scl70 (AI) (NR: 0 - 0.9)	<0.2		
Anti-Smith (AI) (NR: 0 - 0.9)	<0.2		
Anti-SSA (AI) (NR: 0 - 0.9)	<0.2		
Anti-SSB (AI) (NR: 0 - 0.9)	<0.2		
Rheumatoid Factor (IU/mL) (NR: <13)		46.7	
Lyme Reflex (NR: <0.9)		0.19	
Anti-CCP (U/mL) (NR: 0 - 2.9)			>300.0
Myeloperoxidase antibody (AI) (NR: 0 - 0.9)			<0.2
Proteinase 3 antibody (AI) (NR: 0 - 0.9)			<0.2
Quantiferon TB values (2) (IU/mL)			−0.02
Anti-streptolysin O (IU/mL) (NR: <201)			28
B. Burgdorferi PCR			Negative
B. Garinii/D. Afzelii PCR			Negative
B. Mayonii PCR			Negative

Rheumatologic autoantibodies and infectious markers measured on days 1 - 3 of the hospital stay with abnormal values indicated in red.

effusions. Interestingly, the patient denied shortness of breath, and never required supplemental oxygen. By this time, all infectious and most rheumatological auto-antibodies were negative thus far except for rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP), which were pending. Rheumatology was consulted and the patient was started on prednisone for symptom control, which resulted in significant relief. Colchicine was never required to treat the pericarditis. Finally, RF and anti-CCP came back positive, and a final diagnosis of rheumatoid arthritis was made. Bilateral hand x-rays were obtained, shown in Figure 2, which did not reveal any erosions or evidence of arthritic changes, suggestive of an atypical acute presentation.

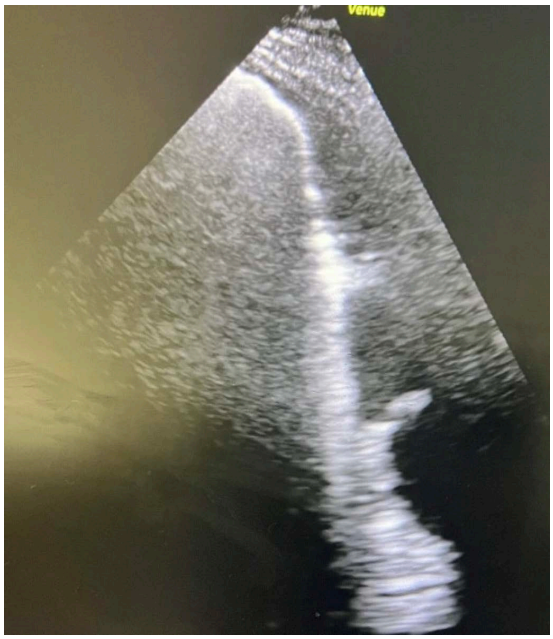
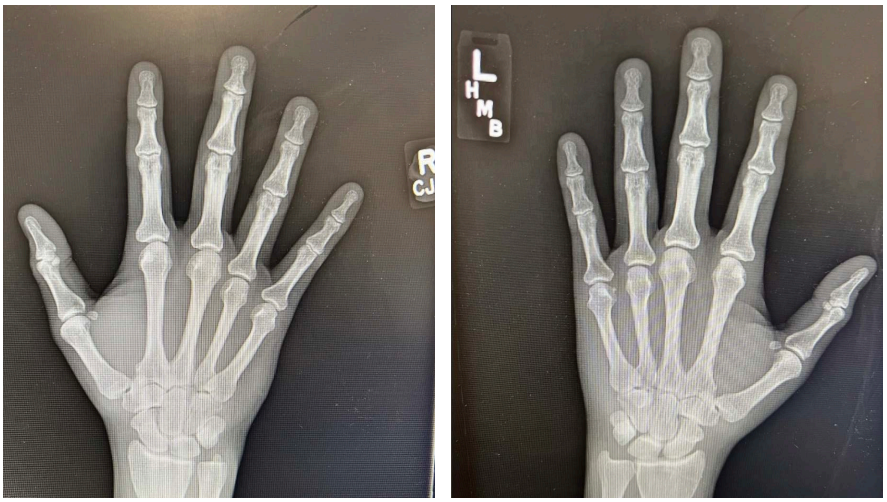


Figure 1. Cardiac ultrasound.



(a) (b)

Figure 2. (a): Right hand X-ray; (b): Left hand X-ray.

The patient was started on 40 mg prednisone as well as oxycodone and morphine for pain management in the hospital, which resulted in significant improvement. He was discharged on 40 mg of prednisone and advised to follow-up with rheumatology as an outpatient and his primary care provider. One week later, he was seen by rheumatology and all of his symptoms had significantly improved. At this time, he was started on methotrexate 15 mg daily and folic acid and advised to avoid alcohol use. The patient was seen again one month later and was doing well without functional limitations.

3. Discussion

Rheumatoid arthritis (RA) is the most commonly diagnosed systemic inflammatory arthritis. Without sufficient treatment, EAM affecting other bodily systems may develop. Given that the disease process is usually quite advanced when extra-articular manifestations develop, it is very unusual that these would be part of an initial RA presentation in the absence of joint changes suggestive of an inflammatory arthritis. EAM are most frequently seen in patients with severe disease and are associated with increased mortality [5]. The major risk factors that are clinical predictors of the development of EAM include male gender, smoking, advanced joint disease, low level of functioning, and very elevated inflammatory marker levels [2]. Clinicians must follow patients with these risk factors extremely closely to ensure their disease remains under control.

Given that the primary characteristic of RA is joint inflammation resulting in joint damage especially in chronic settings, it is unlikely that EAM occurs as part of an initial, severe presentation in the absence of any joint changes [5]. Our question of whether this could be a missed insidious late presentation was answered by the normal bilateral hand x-rays that did not show erosions, suggesting that this case was an acute onset of disease rather than a chronic ongoing process. Although the patient's alcohol use preceded the onset of disease, the literature on the association of alcohol and risk of RA is inconclusive with mixed evidence of increased, decreased and in some studies showing no association [6] [7] [8]. Furthermore, only few cases of RA initially presenting with pleural and/or pericardial effusion have been reported, however, of those that have, all patients complained of chest pain and/or shortness of breath [9] [10] [11] [12]. Our patient denied both these symptoms, making this presentation even more unusual.

According to the American College of Rheumatology, methotrexate continues to be recommended as a first-line agent for treatment of RA. The literature suggests that treatment recommendations do not vary depending on the presence or absence of EAM. During acute flares of the condition, steroids such as prednisone can be added to the treatment regimen. For patients that cannot tolerate methotrexate or have a risk factor for hepatotoxicity, other medications, such as disease-modifying antirheumatic drugs (DMARDS) can be used. These medications include, but are not limited to, leflunomide, hydroxychloroquine, and sul-

fasalazine [1]. The appropriate treatment regimen may vary between patients so it is important to consider medical history, risk factors, and side effect profiles in determining the optimal regimen. When EAM of RA are present, a more aggressive therapeutic approach is taken because EAM are typically associated with a far more advanced and severe disease state, which increases morbidity and mortality in these patients. Additionally, worse long term outcomes associated with EAM leave patients susceptible to functional impairment depending on the complications they experience. However, since this is an initial presentation of RA with EAM, the patient described here responded well on a standard prednisone and methotrexate regimen without the need for an aggressive treatment approach.

4. Conclusion

This case highlights how RA can rarely present initially with predominantly extra-articular manifestations and non-specific musculoskeletal symptoms. Given that many organ systems can be affected by EAM, it is important that RA be considered as a possible diagnosis when an inflammatory process is evident and cannot be explained by another diagnosis. Recognizing these inflammatory signs and symptoms is crucial because EAM of RA is associated with increased mortality, so it is essential that a proper diagnosis be made and treatment initiated in a timely fashion to avoid as much permanent damage as possible. It is also important to be mindful of the possible need to collaborate with other specialists depending on which organ systems are affected so that the appropriate treatment regimen and follow-up plan can be put in place for the patient in order to achieve the best possible outcome. Early diagnosis and treatment with steroids to control acute RA flares are highly effective and other therapies, such as methotrexate, the first-line agent according to the American College of Rheumatology, can be initiated in conjunction or thereafter, typically with very good response, as demonstrated in the case presentation.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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