

Case series: Monoarticular rheumatoid arthritis

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Abstract

Objective: Monoarticular presentation of rheumatoid arthritis is infrequent and has been previously reported to involve large joints such as the hip and knee joints. Here we report a case series of four patients presenting to the University of Michigan in 2015 with monoarticular rheumatoid arthritis, one with small and three with large joint involvement.

Material and Methods: In total, four patients with monoarticular rheumatoid arthritis were treated in the Division of Rheumatology, University of Michigan. All the patients were retrospectively reviewed with permission from our Institutional Review Board; informed consent was provided by the patients for enrollment in a clinical trial for patients with rheumatoid arthritis. All the patients were assessed using the 2010 ACR/EULAR classification criteria for rheumatoid arthritis.

Results: All the patients presented with monoarthritis; three patients had large joint involvement and one had small joint involvement. Serologies were positive, with each patient having positive Anti-cyclic citrullinated peptide (anti-CCP) antibodies, two patients having a positive rheumatoid factor, three patients having elevated CRP levels, and one patient having positive ESR. All patients met the criteria of the duration of symptoms being at least 6 weeks. The findings of imaging, although not a part of the criteria, were consistent with active rheumatoid arthritis in all the patients.

Conclusion: While the 2010 ACR/EULAR classification criteria are the most sensitive criteria for diagnosing RA to date, the exclusion of these cases of monoarthritis demonstrates that further specificity can still be achieved for diagnosing these types of patients as early as possible using the current guidelines. Further, we suggest the inclusion of an imaging measure added to the inclusion criteria to further increase the yield in establishing diagnosis of rheumatoid arthritis in the current reported patient population.

Keywords: Monoarthritis, rheumatoid arthritis, inflammatory arthritis

Introduction

Rheumatoid arthritis (RA) is a common symmetrical chronic inflammatory arthritis with a prevalence of up to 1% worldwide (1). Untreated RA can result in both short- and long-term complications with an increase in mortality and morbidity. A large U.S. cohort reports that 35% of patients with RA had disability 10 years after diagnosis (2).

The initial 1987 American College of Rheumatology classification criteria for RA have been recently updated to increase the sensitivity to diagnose early RA and enable early intervention (3). The 2010 ACR/EULAR criteria for definite RA consists of a point-based system that includes four domains: confirmed synovitis in at least one joint (higher scores are assigned by a higher number of small joints involved) (0-5), presence of RA antibodies [rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibody (anti-CCP)] (0-3), elevated acute phase reactants [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)] (0-1), and symptom duration of 6 weeks or longer (0-1) (4). Although the presence of symmetrical polyarthritis and morning stiffness has been included in the 1987 criteria, these manifestations have not been found to be significantly important for the purpose of data analysis in the Phase I 2010 ACR/EULAR criteria (3, 5).

Monoarticular RA is a rare entity reported to initially affect large joints such as hips and knees, progressing to a polyarticular presentation within 3-5 years (6, 7). Although the recent 2010 ACR/EULAR criteria are helpful in making an earlier diagnosis of RA, they do not include monoarticular RA because certain patients do not meet the burden of a score of ≥ 6 .

Material and Methods

In this case series, we report four cases of monoarticular, seropositive RA who presented to the rheumatology clinic the University of Michigan in 2015. These patients were analyzed through a retrospective chart review as part of the screening process in an early RA clinical trial, and this retrospective chart review was approved by the Institutional Review Board of the University of Michigan Medical School (HUM00116976). The patients provided informed consent and agreed to have their nonidentifiable information used for research, including publishing purposes.



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Table 1. Summary of patient presentation, 2010 ACR/EULAR ACR criteria, and laboratory results

Patient	Affected joint	ANA	CRP ¹ (mg/dL)	ESR ² mm	anti-CCP ³ (0-19 U/mL)	RF ⁴ (IU/mL)	Duration	2010 ACR/EULAR RA Diagnosis Score
#1								
54-year-old female	Right Ankle	Negative	2.7	18	243	59	2 years	<ul style="list-style-type: none"> • One Large Joint: 0 points • Elevated CRP: 1 point • High titer of anti-CCP: 3 points • 2-Year duration: 1 point Total: 5 points
#2								
56-year-old male	Right Knee	Negative	1.0	14	62	11	2 years	<ul style="list-style-type: none"> • One Large Joint: 0 points • Elevated CRP: 1 point • High titer of anti-CCP: 3 points • 2-Year duration: 1 point Total: 5 points
#3								
48-year-old male	Right Third MCP	Negative	0.4	6	37	11	6 months	<ul style="list-style-type: none"> • One Small Joint: 2 points • Low titer of anti-CCP: 2 points • 6-Month duration: 1 point Total: 5 points
#4								
37-year-old female	Right Knee	Negative	4.7	53	>250	52	3 years	<ul style="list-style-type: none"> • One Large Joint: 0 points • Elevated CRP and ESR: 1 point • High titer of anti-CCP: 3 points • 3-Year duration: 1 point Total: 5 points

¹reference range: 0-0.6 mg/dL²reference range: 0-15 mm for men, 0-20 mm for women³reference range: 0-19 U/mL⁴reference range: 0-15 IU/mL

Figure 1. a-c. Sagittal T1-weighted MR images show extensive swelling and erosive changes over the tibiotalar and subtalar joint with intermediate to low T2 suggestive of chronic inflammatory monoarthritis (a, b); Synovial biopsy of the right ankle shows chronic inflammation with few plasma cells, lymphocytes, and some hemosiderin-filled macrophages diagnostic for rheumatoid arthritis (c)

Results

Case 1

A 54-year-old Caucasian woman with progressive worsening of pain and swelling in her right ankle over a period of 2 years presented after developing stiffness in the ankle that lasted for several hours. There was no history of trauma or other joint involvement. Medical history included type

2 diabetes mellitus and hypertension. Physical examination showed diffuse swelling of the right ankle without skin changes, joint line tenderness, and warmth and loss of anatomical markings. Active and passive plantar and dorsiflexion, inversion, and eversion were markedly limited. Synovitis was not appreciated in other joints. Laboratory data showed an elevated CRP level, normal ESR, high-titer anti-CCP, and elevated RF (Table 1).

Ultrasound of the ankle showed effusion with hyperemia supportive of an underlying synovitis. Magnetic resonance imaging (MRI) of the ankle revealed extensive distention of the tibiotalar joint and posterior subtalar joint with intermediate to low T2 and an intermediate T1 signal process consistent with effusion that likely represented blood products (Figure 1a, b). The differential diagnosis included pig-

mented villonodular synovitis given the MRI findings. A synovial biopsy of the right ankle joint was subsequently performed and indicated hemosiderotic synovitis secondary to RA. The patient was subsequently started on methotrexate with marked improvement in her symptoms.

Case 2

A 56-year-old male with a 2-year history of gout in the right knee presented with worsening of his symptoms. He was initially treated with a tapering dose of prednisone and colchicine. This led to marked improvement of his symptoms of pain and swelling. This regimen was discontinued, and allopurinol was initiated but was not well tolerated. Persistent pain and swelling in the right knee progressively worsened and became associated with stiffness. He underwent several arthrocentesis procedures with aspiration of the fluid and intra-articular corticosteroid injections, which improved his symptoms for 2 months after each procedure. Review of the aspirate indicated an inflammatory arthritis pattern (WBC count of 12,000, comprising 87% neutrophils) and no crystals were identified. Physical examination showed moderate effusion, warmth, and joint line tenderness associated with restriction in flexion up to 90° in the right knee. Synovitis was not appreciated in other joints. Laboratory workup showed normal ESR and RF with positive anti-CCP and elevated CRP level (Table 1). An ultrasound of the right knee showed moderate joint effusion and synovial hyperemia. The patient was started on methotrexate and showed marked improvement in his symptoms.

Case 3

A right-handed 48-year-old man presented to the rheumatology clinic with a complaint of right third finger pain since 6 months. His symptoms progressively worsened to the extent where he could no longer make a fist with the right third digit. Morning stiffness was reported that lasted throughout the day. Physical examination showed swelling and tenderness of the right third MCP, and no synovitis was appreciated in other joints. Laboratory findings revealed positive anti-CCP with normal RF, ESR and CRP level (Table 1). An ultrasound of the right hand demonstrated moderate tendinosis and tenosynovitis of the flexor tendons of the right third digit with underlying joint effusion and synovial hyperemia of the third MCP. Magnetic resonance imaging showed fluid signal surrounding the flexor digitorum profundus and superficialis of the third right digit along their entire extent with joint effusion in the third MCP with no erosive changes. There was associated mild enhancement surrounding

the flexor tendons. Findings were suggestive of inflammatory synovitis. The patient chose to undergo conservative therapy, and occupational therapy as well as naproxen 500 mg BID was initiated.

Case 4

A 37-year-old woman presented with 3-year history of pain and swelling in the right knee. Review of her prior records showed consistently elevated ESR and CRP level as well as a high titer of anti-CCP and elevated rheumatoid factor. She underwent arthroscopic surgery, which revealed significant synovitis of the right knee. She was diagnosed with RA and was started on methotrexate 10 mg as well as low-dose prednisone. Symptoms persisted despite the escalation of therapy with higher doses of methotrexate. Physical examination revealed moderate knee effusion with a limited range of motion and a 10° flexion contracture; synovitis was not present in any other joint. Laboratory findings showed elevated ESR, CRP level, and RF with a high titer of anti-CCP (Table 1). Magnetic resonance imaging of the right knee revealed moderate joint effusion with synovial proliferation and loss of cartilage in the patella and trochlea. She was subsequently placed on adalimumab, which was effective for only 3 months before it was discontinued. She was then started on tocilizumab monotherapy, which provided more effective disease control.

Discussion

In this case series, we present four cases of patients presenting with chronic monoarthritis at the University of Michigan in 2015, which on further workup were diagnosed as having seropositive RA. Untreated RA can result in both short- and long-term complications with an increase in mortality and morbidity. Over the last decade, studies have continually supported the notion of “the therapeutic window of opportunity,” where the current treatment strategy is to initiate early aggressive therapy soon after diagnosis, followed by escalation of therapy guided by disease activity measures aiming to achieve clinical remission and the prevention of radiographic damage and joint deformity. The proportion of missed persistent arthritis patients in early arthritis cohorts is almost 40%, which is likely reflective of the case-load of daily practice (8).

In clinical practice, there is a very low clinical index of suspicion for RA in patients presenting with chronic monoarthritis, and other common etiologies are usually considered. Often, serologies including RF and anti-CCP are not considered. The first question during the evaluation process is to determine the duration of

symptoms and establish whether it is acute or chronic monoarthritis. If symptoms persist for more than 6 weeks, the condition is considered to be chronic. A thorough history and physical examination supported by imaging and laboratory testing can differentiate between inflammatory and non-inflammatory monoarthritis. The possible etiologies of chronic inflammatory monoarthritis include indolent infections such as tuberculosis, fungal and rare parasitic infections, crystal arthropathies, and autoimmune diseases such as arthritis due to seronegative spondyloarthritis (SpA) and, to a lesser extent, RA. The differential diagnosis in the noninflammatory monoarthritis domain includes pigmented villonodular synovitis, single joint osteoarthritis, and neuropathic arthropathy.

Rheumatoid arthritis presenting as monoarthritis has been reported in the literature by Parker et al. (9) with the largest cohort seen in the 1980s. They reported that out of 150 patients evaluated over a 12-month period, 12.6% were diagnosed with RA (9). Interestingly, an additional study examining the clinical and histological presentations of nonspecific monoarthritis defined by synovitis showed that of 34 patients, 15% progressed to a diagnosis of RA within a monitoring period of 5 years; two of these patients had knee monoarthritis (10). Indeed, over the last decade, there have even been case reports documenting monoarthritis as an initial presentation of RA (7).

The aim of the 2010 ACR/EULAR classification criteria for RA is to aid the diagnosis and to identify patients with a relatively short duration of symptoms who may benefit from the early institution of DMARD therapy or entry into clinical trials. Every few years, the criteria are revised to make them more sensitive for diagnosing patients. The ACR/EULAR classification criteria for RA were revised in 2010 from 1987; they were meant to be applied only to eligible patients in whom the presence of obvious clinical synovitis in at least one joint was central. When we applied the 2010 ACR/EULAR criteria to our four cases, they fulfilled 5/10, 5/10, 5/10, and 5/10 criteria (Table 1). The question we faced was whether this subtype of chronic monoarthritis, which did not match the traditional polyarticular natural history of RA and did not meet classification criteria for RA, should be included in the RA continuum. This leads to the question of whether further adjustment to the 2010 ACR criteria is needed, as proposed by Van der Ven et al. (12), to identify more early RA patients in whom early treatment could result in improved patient outcomes. The 2010 ACR criteria do not include a radiological domain

despite the presence of well-established data indicating that imaging can show evidence of disease as well as mounting data suggesting that advances in imaging techniques can help predict and uncover early RA (13-16). Based on our case series, any imaging study such as an x-ray showing marginal erosive changes or advanced imaging such as magnetic resonance imaging or high-power Doppler ultrasound can confirm the diagnosis of RA.

In conclusion, we present four patients with a rare clinical presentation of RA monoarthritis during 2015. Each case highlights the importance of imaging in the early recognition of RA in patients who present with monoarthritis as well as the importance of timely diagnosis and management of this disease to ensure good outcomes.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Institutional Review Board of the University of Michigan Medical School (HUM00116976).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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