A 51-Year-Old With Musculoskeletal Symptoms

Ronald N. Rubin, MD[1,2] —Series Editor

A 51-year-old woman presents to your office with musculoskeletal symptoms that she had initially thought were exercise-related. The symptoms had started in the summer months but now have persisted for more than 6 months despite the usual attempts of relief using rest and nonsteroidal anti-inflammatory drugs (NSAIDs). The dominant symptoms are in her hands where she notes pain in multiple joints in both wrists, thumb, the metacarpophalangeal joint, and the proximal interphalangeal joint.

The patient reported times when redness and swelling in these areas were visible. She additionally notes a distinct stiffness and heaviness in the hands in the morning, which improves after several hours. These symptoms have markedly interfered with aspects of her life, such as athletic hobbies and work where she has trouble using her computer keyboard.

History

Her health is otherwise good overall. She has had a degree of glucose intolerance; her random blood glucose levels range from 110 to 125 mg/dL with normal hemoglobin A_{1c}. She does not have any major medical diagnoses. She is slightly overweight and does not smoke or misuse alcohol. She currently works as a bank teller.

Physical examination

She is a healthy-appearing woman with a blood pressure of 115/75 mm Hg, a pulse rate of 88 beats/min, and a BMI of 26 kg/m^2. Results of a head, ears, eyes, nose, oral, and throat examination are unremarkable. No enlarged lymph nodes are noted, and a chest/cardiac examination is also unremarkable. No skin rashes are noted. A neurologic examination revealed no abnormalities or lateralizing signs.

A musculoskeletal examination revealed normal overall muscle mass. There is tenderness to palpation and forced motion in both wrists, both metacarpal-phalangeal joints of the thumbs, and the medial 2 metacarpophalangeal joints of the fingers of both hands. The aforementioned thumb joints are red and swollen as well. There is joint swelling and rubor in several proximal interphalangeal joints as well.

Laboratory testing

Results of a complete blood cell count show mild normocytic anemia with a red blood cell count of 11 g/dL and an elevated random blood glucose level of 125 mg/dL. All other results from biochemistry and metabolic panels were within normal limits. Her erythrocyte sedimentation rate was 69 mm/hr. Radiographic evaluation of the hands and feet was pending.

Which of the following is the optimal initial therapy for the presented patient?

A. Initiate an aggressive course of acetaminophen plus NSAIDs for at least 12 weeks before escalating therapy.
B. Consult a hand surgeon for carpal tunnel surgery.
C. Initiate a course of corticosteroids plus methotrexate.
D. Initiate a course of corticosteroids plus chloroquine.
E. Initiate a biologic disease-modifying antirheumatic drug.

Correct Answer: C.

This case involves a middle-aged woman manifesting polyarticular arthritis most pronounced in the small joints of the hands, which should immediately make us think of rheumatoid arthritis (RA). This condition is very common, with a projected incidence rate of 5 cases per 1000 in the United States, a clear over presentation in women, and, although it can occur in any adult, a peak incidence in the 6th decade of life.[1] It is one of the first conditions to be labeled as an "au-

AFFILIATIONS:
[1]Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania
[2]Department of Medicine, Temple University Hospital, Philadelphia, Pennsylvania

CITATION:
Rubin RN. A 51-year-old with musculoskeletal symptoms. *Consultant.* 2022;62(7):e32-e34. doi:10.25270/con.2022.07.000020

DISCLOSURES:
The author reports no relevant financial relationships.

CORRESPONDENCE:
Ronald N. Rubin, MD, Temple University Hospital, 3401 N Broad Street, Philadelphia, PA 19140 (blooddocrnr@yahoo.com)

toimmune disease," wherein antibodies and endogenous inflammatory proteins are noxious and pathological to the host. The cornerstone of pathophysiology in RA is autoimmune-based chronic inflammation targeting the synovial tissues. There is an interaction between the autoimmune process and synovium, which results in the creation of the so-called "pannusm" which is a hypertrophic synovial tissue mass capable of invading and destroying the affected joints' cartilage lining and even the juxta-articular bone nearby.[1] Until recently, this frequently resulted in severe joint morbidity and disability. Recent significant improvements in therapeutics have markedly improved prognosis and quality of life.

The clinical presentation of RA will most often involve middle-aged patients, women more so than men. A feature of RA will be its chronicity—an onset measured in months of pain and stiffness in joints. Joint involvement, though not perfectly symmetrical, will most frequently involve smaller joints with a predilection for the hands and feet. Thus, swelling, pain, and stiffness (especially in the first hours of the morning after awakening) from the wrists down are the classical symptomology of RA. A major differential will be osteoarthritis, but the latter will involve the distal interphalangeal joints more so than the proximal hand and finger joints of RA and will have visible and palpable bony "hard" joint swelling in contradistinction to the spongier "soft" swellings of RA.

Specific diagnosis remains a clinical one. There is no pathologic pneumonic blood test or finding that in itself is diagnostic for RA. Despite the name of an antibody found in RA termed "rheumatoid factor," that finding alone does not confirm the diagnosis. Currently, the diagnosis is made using a scheme modification of the 2010 Rheumatoid Arthritis Classification Criteria.[2] Joint arthritis is "counted" by either physical examination or imaging (ultrasonography or magnetic resonance imaging). Serologies and inflammatory protein studies are performed, and an index score is created and evaluated. Specifically, points are assigned as follows: 1 point for large joint involvement, 2 points if 1 to 3 small joints are involved, 3 points if 4 to 10 small joints are involved, and 5 points if 10 or more joints are involved. In terms of serological abnormalities, the Criteria calculate 2 points for a low but present level of rheumatoid factor, 3 points for a high positive level of rheumatoid factor, and 1 point for an abnormal C-reactive protein level or erythrocyte sedimentation rate. The duration of symptoms for at least 6 months bestows an additional point. The presence of more than 6 such points is consistent with the diagnosis of RA.[2] Our patient already has 7 points, making RA likely. She does not have carpal tunnel, making Answer B incorrect.

Once RA has been diagnosed, early and aggressive therapeutics need to be initiated to prevent the significant morbidity/disability (eg, joint deformity in 80% of patients, inability to work in 40% of patients by 10 years after RA diagnosis) described in the older literature.[3] Tremendous strides in RA therapy pharmacology in recent years have markedly improved these outcomes. A core finding responsible for this is the requirement for medications to not merely address the pain symptoms as with NSAIDs and analgesics but to additionally address the autoimmune/inflammatory pathophysiology as well. Such medications are referred to as disease-modifying antirheumatic drugs (DMARDs). DMARDs will affect disease control and lessen the ongoing destruction with its attendant morbidity and disability, whereas NSAIDs and analgesics will not, making Answer A incorrect.

Without asking us to become involved in the complex, ever-expanding but also even more effective pharmacopeia of RA, a still-excellent initial agent for RA is methotrexate. This is a so-called synthetic small-molecule DMARD in contradistinction to the newer biologics. Methotrexate has been the backbone therapy for RA for decades, and in patients who can tolerate it (eg, no significant renal failure or hepatic disease) remains a first-line therapy, most often accompanied by a short course (no longer than 3 months) of corticosteroids. The therapeutic goals include 50% improvement in joint symptoms and serum markers at 3 months and remission or low disease activity at 6 months.[1] This is Answer C, which is the most appropriate choice here. The antimalarial hydroxychloroquine (Answer D) is another small-molecule synthetic DMARD but has lower efficacy compared with methotrexate and is not the first choice here.[1]

The second category of DMARD is the small molecule–targeted agents that specifically target suspected RA-associated proteins (eg, Janus kinase inhibitors)[4] and the biologic DMARDs, most of which are monoclonal antibodies to tumor necrosis factor.[5] These agents have great television commercial fame and are very effective such that clinicians might consider them early on when ominous prognostics are present. Such prognostics include very high serology and inflammatory markers, early joint damage, or rapid progression. However, most specialists will allow an assessment of a classical methotrexate regimen and consider these newer agents second line for now, making Answer E incorrect, at least for now. A very detailed discussion and tabulation of these complex therapeutics is available in a recent review.[1]

Patient Follow-up

Our patient's hand radiographs revealed joint space narrowing in both thumb metacarpophalangeal joints and small areas of bone erosion in metacarpophalangeal joints of several phalanges. Color doppler ultrasonography confirmed synovial inflammation diffusely in both hands. A chest radiograph did not show interstitial lung disease. Further blood testing revealed a low rheumatoid factor level. Her total RA Classification Criteria score was calculated as 5 points for joint distribution of at least 10, 2 points for low positive RF, 1 point for elevated erythrocyte sedimentation rate, and 1 point for symptom duration of more than 6 months—for a total of 9 points. This was clearly enough to strongly establish the clinical diagnosis

of RA. Therefore, to supply acute symptom relief as well as disease modification to prevent damage progression and disability, a course of glucocorticoids for 4 weeks and initiation of methotrexate, 10 mg with titration toward 25 mg weekly was initiated. Her blood glucose level tolerated the corticosteroid well, and by week 4, her symptoms had greatly (> 50%) improved. Corticosteroids were stopped, and she is doing very well clinically and by the lowering/stabilization of inflammatory markers on methotrexate, 25 mg weekly.

What's the Take Home?

Rheumatoid arthritis is a common autoimmune disorder with the most frequent onset in middle age and with female predominance. It is clinically characterized by chronic (months) onset of polyarticular arthritis affecting the small joints of the hands and feet. It is an autoimmune disease wherein autoantibodies trigger the release of inflammatory mediators that attack the synovial membranes and elicit the formation of an inflammatory, invasive pannus capable of irritating and destroying articular cartilage and juxta-articular bone. When untreated, this process can cause joint destruction and severe disability. A scoring scheme utilizing degree/number of join involvements, presence of inflammatory markers, and abnormal antibody levels (ie, rheumatoid factors) are used to obtain a clinical diagnosis. Early and aggressive therapy aimed at disease modification rather than merely pain relief is required to avoid joint deformity and disability. Available agents include synthetic disease-modifying antirheumatic drugs (DMARDs), of which methotrexate is the prototype and most effective; targeted synthetic DMARDs that target Janus kinases; and biologic DMARDs that are monoclonal antibodies designed to target inflammatory cytokines such as tumor necrosis factor and interleukin-6. Methotrexate is the recommended first-line therapy for now. Appropriate use of these agents has markedly improved the outlook and prognosis of RA patients.

References

1. Aletaha D, Smolen JS. Diagnosis and management of rheumatoid arthritis: a review. JAMA. 2018;320(13):1360-1372. doi:10.1001/jama.2018.13103
2. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2010;69(9):1580-1588. doi:10.1136/ard.2010.138461
3. Wolfe F. The natural history of rheumatoid arthritis. J Rheumatol Suppl. 1996;44:13-22. https://europepmc.org/article/med/8833046
4. Smolen JS, Aletaha D, Koeller M, Weisman MH, Emery P. New therapies for treatment of rheumatoid arthritis. Lancet. 2007;370(9602):1861-1874. doi:10.1016/S0140-6736(07)60784-3
5. Taylor PC, Keystone EC, van der Heijde D, et al. Baricitinib versus placebo or adalimumab in rheumatoid arthritis. N Engl J Med. 2017;376(7):652-662. doi:10.1056/NEJMoa1608345