A Narrow Window of Opportunity: Diagnosis and Management of Rheumatoid Arthritis in Underserved Populations

Podcast 2: Case Study Continued | Run Time: 22:35

L Friedman: [00:00:00]
Hello, my name is Luis Friedman. I'm a general internist practicing outpatient Internal Medicine in Woodbridge, New Jersey, and I'm here with Dr. Prabhakaran, a rheumatologist, I will let her introduce herself as well.

S Prabhakaran: [00:00:13]
Hi, this is Sajina Prabhakaran, I'm a rheumatologist in Hopewell New Jersey and we're going to talk a little bit more about rheumatoid arthritis during the session.

L Friedman: [00:00:27]
So, we last left off with our case presentation, without going through the whole thing our 20 year-old African-American female presenting to the Rheumatology clinic, and we'll go ahead with her, her lab values. Her hemoglobin, 10.1…MCV, 92… white blood cell count, 3200… differential normal…AST, 36… ALT, 33…alkaline phosphatase, 96…Creatinine, 0.86…rheumatoid factor, 75… CCP greater than 250… ANA 1 to 320, homogeneous pattern… ESR, 55… CRP, 15…Hepatitis B surface antigen, hepatitis A antibody, and hepatitis C antibody all negative. TSH, normal…TB quantiferon gold, negative… and x-ray of hands were completed. So, Dr. P at this point, I know, as certainly as a primary care physician, we have in our software, we have a whole slew of serologies many that were done here. And when we're thinking about rheumatoid arthritis, or other, systemic arthritis, I'm trying to figure out which ones I should order, which ones like shouldn't order…. Can you kind of help clear the path here for us?

S Prabhakaran: [00:01:51]
Absolutely. So, we talked about… a little bit about inflammatory joint pain and that's what I would still concentrate upon. So, when you… when you come to this stage, unless you have a very, very high suspicion of Rheumatoid Arthritis, you're still categorizing your patient as having inflammatory arthritis, possibly, RA. So…I just want to talk a little bit about the differential diagnosis because that's going to determine what tests we are going to order in our patients. So, when we talk about inflammatory joint pain, especially in a young woman such as this, we're looking at rheumatoid arthritis but other conditions that can cause a similar presentation with inflammatory joint pain, more than six weeks, you're looking at lupus, which is a frequent differential diagnosis or could be an overlap with RA, there is psoriatic arthritis that is Sjogren's syndrome. There are other connective tissue diseases such as mixed connective tissue disease and scleroderma and so forth. So, all of these…oh…post-viral arthritis, which is less likely for somebody who's had symptoms for more than six weeks, but something to think about. So, all of these are conditions that could potentially mimic somebody with rheumatoid arthritis. So, one of the most important tests… besides a complete blood count and a metabolic panel to make sure that the patient does not have any other organ disease, which can… or other conditions that can influence our treatment plan as well… including kidney… renal function, and their hepatic function, it would be very important to check markers of inflammation, and I would encourage the primary care physicians to check both the sedimentation rate, as well as a C-reactive protein… as you're aware, both of them are nonspecific, but sed rate is.. more nonspecific than C-reactive protein, so anemia can cause a set rate to go up. Infection can have both go up. Sometimes, SED rate can be elevated because somebody is obese even or has been in stasis changes. So, ordering both markers of inflammation is certainly…a helpful…it's helpful for us to differentiate to a certain extent that you have inflammatory versus non-inflammatory

joint pain. In addition to that, you're looking at serologies. So ordering, both the rheumatoid factor and CCP antibody are both very helpful. So, 25% of patients with rheumatoid arthritis are seronegative, which means their antibodies are negative. However, the majority of patients with rheumatoid arthritis are seropositive…so they have a positive rheumatoid factor… and a rheumatoid factor has got a high specificity for almost 85%, but an anti-CCP antibody has got greater specificity for rheumatoid arthritis…close to 95%. So, there are…there are a minority of patients where CCP antibodies can be false positive…….. Well, those are the two tests that I would encourage our internist to…our Primary Care Providers to order because that does help in our diagnosis of rheumatoid arthritis. In addition, looking at other connective tissue disease…so an anti-nuclear antibody could be helpful. So, in this patient, her review of systems was really negative for anything besides inflammatory joint pain. She did not have symptoms suggestive of dry mouth or dry eyes. You did not have any photosensitivity. She didn't have Raynaud's… so these are all things that we would consider if you were looking at other disease processes besides rheumatoid. So, getting an anti-nuclear antibody by immunofluorescence would be helpful as well as you are moving forward with a diagnosis and treatment of this patient…of a patient with inflammatory joint pain. And I would also mention that when we look at the labs…we have an ANA direct and we have an ANA by IFA or immunofluorescence, please do order the one by immunofluorescence. It is more sensitive and it's more specific… less likely to give you a false positive. And you looking at titers… one in 80 and above…with the right clinical picture to help you make a diagnosis. So at least these are the few tests that I would order from a diagnosis standpoint in a patient with inflammatory joint pain.

L Friedman: [00:06:26]
So, I know that I will often order, the ESR and the CRP, and I'm often told that the CRP is more… more… sensitive...or maybe more specific, maybe more sensitive. Is it definitely worth getting both… because I feel like, sometimes the CRP is positive when the ESR is not…But you will get both all the time. Is that right?

S Prabhakaran: [00:06:49]
Yeah. It's a very good question, actually. I would do both. So…this is the rheumatoid of another patient… ESR by far is interferon driven, CRP is IL-6 driven. So… there are patients where you will find normal CRP and they have a high sed rate or vice versa, but like I mentioned earlier and like you just said, the CRP tends to be more specific, less likely to give you a false elevation as opposed to a solo sedimentation rate. So, if you have a high ESR and normal CRP, you're like hmm, is it true? I mean and then of course you look at a patient again and say well, does it make sense or not? But if you have a normal ESR and a high CRP in the right clinical scenario certainly is very helpful.

L Friedman: [00:07:30]
Okay. And my other question, I have been thinking about this one before…when I first started practicing, someone came to me who I wasn't sure…maybe she had RA… I ordered a Rheumatoid factor on her, and it was, I think 14 or 15 and it was like just above the norm for the lab, and I…kind of wrote it off… or it might have been just under it, but her symptoms were probably somewhat typical. So…I well, I guess you'd say that most of the time when they're seropositive, do those rheumatoid factors numbers tend to be fairly high or could be anywhere on the board….

S Prabhakaran: [00:08:08]
Yes…. I mean as we know, every lab has a margin of error. So, when you have a rheumatoid with a cut-off being 13, which is what most labs do for rheumatoid factor, and you have a rheumatoid factor result, and it's 14 or 15… You're thinking this is within that margin of error, so there's a good chance it's not a true positive. So, I would have done the same thing that you did. If the patient did not have significant

symptoms, suggestive of inflammatory joint pain or if I didn't have a very high suspicion, then I probably would not take that 14 seriously, but it might be worthwhile to repeat that, you know, in six months to see if things change, because sometimes it does and things have to start from somewhere and end somewhere. So, things could change over time… especially if the patient's symptoms are persistent. If they are not you don't have to repeat it again… but if the patient's symptoms are persistent with the continued complaint of inflammatory joint pain with a rheumatoid factor of 14, it may be worthwhile to repeat that. But I agree with the rheumatoid factor of 14, a low tide rheumatoid factor is less likely to be a true positive as opposed to be… supposed to be to a high titer RA factor.…we talked about the markers of inflammation and the antibodies… the other things that I request which would be useful to us would be checking the hepatitis panel because, as we know, we don't see this as much anymore…fortunately…but chronic Hep C can masquerade as a lot of conditions, especially rheumatoid arthritis with…with positive rheumatoid factors. So, checking a Hep C is extremely valuable and indicated… in the population. If you have somebody with RA, a thyroid function test is clearly very important because as we know hypothyroidism can also present a variety… a variety of symptoms and signs including non-specific joint pain… and fatigue… and swelling… and stiffness. So…and QuantiFERON Gold …we always do that, or a TB test of some sort…either a TB skin test or a QuantiFERON Gold. I tend to order the QuantiFERON Gold…It's a lot more convenient for the patient since we are already getting blood tests because it's going to also influence our treatment and in terms of how safely we can continue…on a patient with rheumatoid arthritis.

L Friedman: [00:10:40]
So, one other question…so the ANA should definitely be drawn in…is there a situation where you would be like absolutely do not draw that ANA primary care physician or would you if… if there's some suspicion, you would get it with this whole panel?

S Prabhakaran: [00:10:57]
I would, I would. I've seen a patient once… the patient has told me that the patient's inflammatory joint pain. But…given the demographic, I would check an ANA because like I said, these patients can go on and develop other symptoms such as photosensitivity and other symptoms or other conditions where the ANA is going to be very relevant, but I would treat the patient…the patient or the symptoms in subsequent visits…I would treat them as just being seropositive for rheumatoid arthritis.

L Friedman: [00:11:25]
And I guess the next…my last question…but probably leads into the x-rays…So patients that have zero negative rheumatoid arthritis…I mean, I know I've had situations where their tests were negative…I sent them off and they ended up being treated for psoriatic arthritis and I didn't…. it wasn't even on my list…I didn't even know. It's definitely in the X-rays at that point? Or where… like how do you… that's the next step to differentiate some of these seronegative…you know these seronegative arthritis from other forms?

S Prabhakaran: [00:12:02]
Yeah, one of the important ones with zero negative rheumatoid arthritis's differential diagnosis is psoriatic arthritis. X-rays can be helpful because they both have certain erosions... types of erosion that we see, so there are some X-ray findings in both. That's again, with more long-lasting…long-standing disease as opposed to early on in the disease process. But the distribution of joint…involvement… remember how we talked about it being bilateral symmetrical? Psoriatic arthritis can also be bilateral symmetrical but sometimes it could be all articular and sometimes it's more enthesitis……. So things like that…so there's most soft tissue involvement there, which we don't see as often it with rheumatoid

arthritis…more axial involvement. Typically, rheumatoid arthritis is not associated with sacroiliitis or spinal disease, whereas psoriatic arthritis is. So it's not uncommon that somebody is diagnosed as being seronegative rheumatoid and then after a few years, their disease pattern changes to being more PSA-like with, for example, axial involvement… or they now have psoriasis or there's a family history of psoriasis and then that, you know, leads us more to think that this is probably psoriatic arthritis. So, it does happen that there are seronegative RA patients who finally get diagnosed as psoriatic arthritis or enteropathic arthritis...something other than rheumatoid arthritis down the line. The X-rays can be helpful, but that, like I said, is more later on in the disease process at which time erosions have developed in the joints.

L Friedman: [00:13:57]
And with the x-rays… in this patient, you would…the money sounds like it's in the hand x-rays. Although she had foot symptoms as well, I believe… You would do hand and foot X-rays. You would…or just pretty just start with the hands and know that's probably where you're going to find the answers.

S Prabhakaran: [00:14:14]
Yeah. Yeah, I mean in clinical practice, we could do both. I think when I saw her in the clinic, I didn't do the feet. Honestly, don't know why. I just did the hands, but it might be because she was very young, and I didn't think I needed to give her all that X-ray radiation exposure. I think that was the hands…the story was so classic I just limited my imaging to the hands but you…you can always start with the hands because most often you find something there… You can do all the joints depending on how much what you're looking for. But I typically try to limit to the hands or at least a few body parts which I think I'm most likely to give me what I'm looking for. You know, in terms of the answers.

L Friedman: [00:15:01]
And I know you wanted to touch on some of the comorbidities of RA. So, I'll let you expand on that as well. Sure.

S Prabhakaran: [00:15:11]
So, with rheumatoid arthritis, one of the things is that we always think of rheumatoid arthritis, as the name suggests, a disease of the joints… which it's primarily it is, it is a disease of the joints and it's a chronic illness. It is a debilitating disease. Fortunately, now not as much as it used to be with the advent of newer therapies available to us… the immunotherapy, they've really changed the landscape of rheumatoid arthritis treatment and has changed the prognosis, as well as improved lifespan in patients with rheumatoid arthritis. So, besides the chronic pain and stiffness and disability associated with rheumatoid arthritis, these patients do have a higher risk for higher morbidity risk compared to the general population, as a result of their chronic inflammation, as a result of other organ involvement from rheumatoid arthritis. As we know with chronic inflammation, we do know this association of that with accelerated atherosclerosis. So, patients with any inflammatory disease with chronic uncontrolled inflammation, we do see that they have a…we do know that they are… they have a higher risk for heart disease and strokes as a result of atherosclerosis. Frequently, these patients are treated with steroids, and these…or anti-inflammatories… that they would be taking anti-inflammatories for symptom control... the side effects associated with these medications also contribute to their morbidity and mortality as well. In addition to the, to the disease itself, as involving the joints and the burden that this causes both to the patient as well as the family, both from a medical standpoint and from a financial standpoint, there is the other organ… involvement of rheumatoid arthritis, and the most dreaded one is the lungs. So, RA lung is a true disease. It is… patients with rheumatoid arthritis with lung involvement… they have nine times higher risk of death, compared to patients…to the general population. Because of

just because of how aggressive it can be, and it's characterized by interstitial lung disease where there is inflammation and subsequent scarring, that these patients can develop. And patients who are seropositive with high titer rheumatoid factor, CCP antibodies… patients with long-standing disease, or who have high markers of inflammation. In other words, more aggressive disease process. These are the patients who are more likely to develop rheumatoid arthritis lungs. So, when we see a patient with RA, and we are seeing them in the clinic, in addition to talking to them about their joints and the pain and stiffness and so forth…and going through the side effects of medications…the other important thing you want to ask them also is about their breathing, because it's amazing how quickly people adjust their lifestyle to shortness of breath, that they don't realize that they're actually dyspnic compared to their baseline. So, teasing out that becomes very important, and then ordering appropriate workups and providing appropriate referrals becomes very important to prevent further rapid progression. In addition, rheumatoid arthritis can involve the eyes with inflammatory eye disease, the most dreaded one being keratitis. Scleritis can be seen in these patients…again, much better treated now with our TNF blockers and IL-6 blockers. Rheumatoid arthritis can involve the skin. We see patients with rheumatoid nodules, which are extremely…they're common in patients with seropositive RA presenting as painless lumps over areas of trauma…for example, the elbows and over the knuckles and so forth. So, we do see them often. Vasculitis, like Pyoderma Gangrenosum, can be seen in these patients. Muscle involvement is not that common. You can have in your… myositis…can occur in patients with rheumatoid arthritis. Similarly, involvement of the heart… so pericarditis can occur… similarly, pleuritis as well in patients with RA. Valvular disease is less common than in patients with lupus, but that can be seen in RA patients as well. And one important body organ is the bones. So osteoporosis is seen in higher instances in patients with RA… These patients have a history of smoking. Patients have been treated with steroids, patients are less mobile, all of these contribute to bone loss. So being aggressive about doing a bone density scan in these patients and diagnosing and treating vitamin D deficiency is critical in these patients. And a lot of patients with rheumatoid arthritis, as we know, go on to develop enough joint damage that they require joint replacement. So that's why…we have seen an increased incidence of knee replacements, especially in the African-American population. Elbow surgery…elbow replacement incidence has reduced with current treatment modalities in RA but the financial morbidity and the inability to work in these patients because of that disease and the subsequent surgeries and so forth also can heavily burden the patient as well as their families.

L Friedman: [00:21:05]
And you said, I'd sort of, maybe I didn't get that, right? But not to get into the treatment too much, but the newer drugs because of the newer drugs that are available now that the incidents of some of these comorbidities is less in all of them or the lungs? How does that….

S Prabhakaran: [00:21:22]
Yeah, so the incidence of the comorbidities has definitely reduced with the drugs…and some of the drugs themselves can, unfortunately, cause issues too, but by far with the immunotherapy, we certainly are seeing great success rates and treatment of keratitis and scleritis in patients or ILD in patients with RA… it should be noted that patients with ILD…interstitial lung disease and rheumatoid arthritis, they tend to have a worse prognosis unfortunately, but we do have a, you know, tocilizumab and other medications available now to treat these patients. So certainly, we've been able to arrest…reduce the morbidity. The one comment I will make is there's an unfortunate disparity in the population for receiving this treatment and that has…that's where we see that some parts of the population are still not getting the full benefit of treatment either because they aren't aware that treatment is available to them or they are refusing treatment, whatever be the cause, we still see a lot of mortality and morbidity. But by far, with treatment, we certainly see people…patients doing much better than they did before.