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### Update on Psoriatic Arthritis: Best Practices in Rheumatology

Dr. Merola:

Psoriatic arthritis affects about 30% of patients with psoriasis. Left untreated, psoriatic arthritis can progress to severe symptoms, joint damage, disability, and greatly reduce quality of life; but with timely diagnosis, effective treatment may prevent progression, limit disability, and return patients to normal function and a higher quality of life.

I'm Dr. Joseph Merola from Harvard Medical School and Brigham and Women's Hospital in Boston.

Dr. Ogdie:

And I'm Alexis Ogdie from the University of Pennsylvania.

Dr. Merola:

On today's program we'll be discussing Best Practices in Rheumatology for Psoriatic Arthritis.

So, Alexis, to get us started, how is your understanding and our understanding of psoriatic arthritis evolving?

Dr. Ogdie:

Over the past 10 years, I think we've learned a great deal about psoriatic arthritis. We've learned that this is a multisystem, systemic inflammatory disorder that has a widespread impact on the patients' quality of life and their ability to go about their daily activities. In addition, we learned a lot about the immunopathogenesis of the disease, and from this a number of new therapies have been developed.

Dr. Merola:

Great. So I know there are a number of domains of disease, including peripheral arthritis and enthesitis dactylitis. Can you describe a little bit to us about the relevance of the domains in terms of the diagnosis and treatment of psoriatic arthritis?

Dr. Ogdie:

Psoriatic arthritis is highly heterogeneous, so each patient presents a little bit differently; and as you mentioned, there are multiple different manifestations of the disease, so for a long time we thought about psoriatic arthritis as psoriasis plus inflammatory arthritis but have come to realize that enthesitis can have a major impact on patient's quality of life. So enthesitis is inflammation where a tendon, ligament or joint capsule inserts on to the bone—the Achilles or the plantar fascia is a common area—and those prevent people from walking, obviously. And dactylitis can be a swelling of a whole digit from the base. That's also fairly common. Up to 50% of patients with psoriatic arthritis will have dactylitis. And then axial involvement, in particular the sacroiliac joints, can also cause a lot of problems.

Now, it's important to assess each of these individual domains because this has implications for what therapies you might select, so for example, axial involvement, it's really only responsive to biologics, and so the TNF inhibitors and the IL-17 inhibitors are the ones that will address axial disease. Enthesitis also may respond better in general to the biologics than the typical oral agents. And then the skin disease, depending on the severity of the skin disease, will also drive your therapy selection.

Dr. Merola:

And that's a great segue to focus on some treatments. So, how has the therapeutic landscape evolved in psoriatic arthritis?

Dr. Ogdie:

There's been a rapid evolution in the therapies available for psoriatic arthritis. So back in, let's say, 2006, we still had the TNF inhibitors, but mainly only 3 TNF inhibitors at that time, and that was it for biologics. Now, we have 5 TNF inhibitors, we have 2 IL-17 inhibitors approved for psoriatic arthritis, we have an IL-12/23 inhibitor—ustekinumab—we have tofacitinib recently approved for psoriatic arthritis, abatacept was recently approved for psoriatic arthritis, so a huge range of therapies. And then we also have apremilast, a PDE4 inhibitor. So for the average rheumatologist that's seeing a few cases of psoriatic arthritis here and there, there's a lot to keep up with in terms of the new therapies available and when to choose which therapy and so on.

There are a variety of treatment guidelines now available, so we have the GRAPPA guidelines from 2015 published in 2016, the EULAR guidelines published right around the same time, and then the ACR/NPF guidelines are coming soon. The GRAPPA and EULAR guidelines already are missing a bunch of therapies that were approved since those guidelines came out, but either way, I think in particular the GRAPPA guidelines are really helpful for thinking about how to select a therapy and that they divide therapy recommendations up by the domains. So for patients with bad enthesitis, you might select therapies based on their enthesitis, or for patients with arthritis, severe skin disease and severe nail disease, you might select a therapy based on the most severe part. So I think those are really helpful guidelines and a nice table at the end of the guidelines that shows you each of those different domains and the different classes of therapy.

Dr. Merola:

And can I ask you a little bit about your strategy with regard to target and treat-to-target, because it seems like there are a number of potential treat-to-targets, particularly in the psoriatic arthritis space? Is there something that you follow or that you tend to recommend?

Dr. Ogdie:

Yes, so there are a lot of different targets out there. The TICOPA trial was published in 2017, and that one was the first and only treat-to-target study in psoriatic arthritis. And as you would expect, if you treat to a target—and in that case they used minimal disease activity or MDA—patients do better. They do have more side effects because they get more therapies. And in that particular study in this very early patient population, they didn't necessarily see a difference in radiographic outcomes. But I think regardless, the concept is important, so picking a target and assessing the target objectively at each visit, having a conversation about should we add additional therapy to get to the target or change your therapy to get to the target, I think that hasn't fully penetrated our practice yet across the board. I think I see a lot of patients who have quite a lot of disease activity and are not necessarily switching therapies with other rheumatologists, and I think one of the things that I try to say is, "We should be getting you to a place where you feel good. You might not feel perfect, but we want to get you to a place where you're at least low disease activity, if not aiming for remission."

So in terms of what target, minimal disease activity I think is a really good target, so that's achieving 5 of 7 of different criteria that include things like having 1 or less swollen joints, 1 or less tender joints, 1 or less active entheses, a patient global score that's less than 20 on a scale of 0 to 100, patient pain score that's reaching a similar target, a HAQ, or a Health Assessment Questionnaire, and a similar low range of disease activity. So, basically, it's just asking you to assess a variety of different domains that kind of say where is the patient at. Other targets might be things like RAPID 3 or DAPSA, which is similar to the CDAI in RA, except for it includes a 66/68 joint count. So there's a variety of different measures. I think the key is picking one and following that one objectively at every visit and then discussing with the patient how they're feeling, and if they're not meeting the target, are they ready to make a change.

Dr. Merola:

That's great. And in terms of the outcome measures that have been prescribed by GRAPPA-OMERACT, I know those typically face clinical trials, but is there something that we would glean clinically about measurement in clinic from those outcome measures?

Dr. Ogdie:

So that's exactly right. We developed a core outcome set for GRAPPA-OMERACT and published that back in 2016, and I think the takeaway from that paper is that while that's for clinical trials, what we really found is that patients have a lot of other symptoms that we don't necessarily ask about in a routine clinical visit. So if we think about our usual note, it's about the joint counts, entheses, the dactylitis, the axial disease and so on, but patients are really caring about physical function. Can they do what they need to do? Are they participating socially? How is their emotional well-being? Depression and anxiety are very common. One of the things is addressing all of those concepts.

There is a new outcome measure—it's not so new anymore—called the PsAID, or Psoriatic Arthritis Impact of Disease Questionnaire, and that questionnaire actually addresses almost all of those things that patients reported as important to them—the fatigue, the depression, anxiety and so on. It's a really simple 12-item questionnaire to administer in clinic. It's just a simple addition of the different points. So I think that's something that could be used in clinical practice to address those kind of domains of interest to patients in the

things that really matter to them.

Dr. Merola:

Great, so let's look at a case. This is a patient with psoriasis who is newly diagnosed with psoriatic arthritis. Michael is a 46-year-old marketing consultant. He is obese with a BMI of 32, a history of hypertension and prediabetes, an 11-year history of plaque psoriasis on the scalp and back with a body surface area of about 2%, has been managed by his dermatologist with mostly topical agents to date, and his current medications include a blood pressure medication, lisinopril hydrochlorothiazide, some topical calcipotriene and betamethasone, and at a dermatology visit 6 months ago reported pain in his fingers of both hands and the right knee. An examination identified onycholysis at the fingernail and effusion of the right knee, tenderness of the first to third distal interphalangeal joints on both hands, and the dermatologist decided to refer Michael to a rheumatologist.

So I'm going to pause there for a minute. I'm curious to hear, and before we go on, if this sounds like a pretty common scenario to you, because I tell you sometimes it can be a challenge, I think, to have the dermatologist be comfortable with screening for psoriatic arthritis and even sort of feel comfortable with a musculoskeletal exam to get to this point. What has your experience been with this, either in a combined clinic or from a referral standpoint?

Dr. Ogdie:

Yes, I think that's an excellent point. Sometimes the dermatologists call me and they say, "I think he has a swollen joint," and so I run over and I might see the patient and say, "Yep, that's a swollen joint." And they are like, "I thought it was a swollen joint." So they definitely can do it, but I think the confidence behind it, because they don't see it all the time, is sometimes not there, and so I think for that reason a lot of dermatologists don't do this because this is not something they do on a regular basis and they don't feel comfortable with it. In our centers we have combined clinics or these established relationships between dermatology and rheumatology. It's easier to just say, "I think so. Can you just take a look at it?" So I think that is something that I hope that we can as rheumatologists further establish with other dermatologists these collaborations so that there's an open line of communication to just say, "Can you just take a look at this?"

But aside from all of that, if we just summarize the case a little bit, it's basically mild psoriasis and then had topicals mostly, pain in fingers; they have some comorbidities, so the comorbidities—obesity and hypertension and prediabetes—those are pretty common in patients with psoriasis and psoriatic arthritis. And then the patient has joint pain, onycholysis, so nail disease is also more common in patients with psoriatic arthritis. There's a little bit of debate about that because it's pretty common across psoriasis in general, but it's cited as a risk factor or earlier manifestation of psoriatic arthritis. So we have all those things. This is kind of the right person to have a long duration of history of psoriasis. So this is that population of psoriasis patients that we probably should be having a little closer eye on in terms of maybe being an elevated risk for psoriatic arthritis anyway.

Dr. Merola:

So I'll give a little more history on this particular case, and we can maybe flesh it out a bit more. So the rheumatologist performs an exam and an estimation of disease activity, including, of course, a history, physical exam and some lab studies that include a rheumatoid factor, anti-CCP antibodies, SED rate and the CRP as well as some imaging, and this particular rheumatologist used a validated scale to estimate disease activity as well. And I'll ask you in a moment which you use in your clinic and what you would find helpful over time to measure. The rheumatologist's diagnosis is psoriatic oligoarthritis with moderate disease activity based on his or her assessment and begins to discuss the diagnosis with the patient and discuss his treatment options.

So I guess I would ask you maybe a few questions based on this, because I think it obviously could be quite a rich discussion. There's a lot here. One question I am asked, not infrequently—and I'm curious to hear from you—is about your workup at this stage. So it certainly sounds like an inflammatory arthritis from what you've said and what the rheumatologist has diagnosed. How helpful do you find at this stage the inflammatory markers, baseline imaging, and what would that imaging be? And then which outcome measure or validated scale of disease activity do you consider and document in your patients with psoriatic arthritis?

Dr. Ogdie:

Great question. So, I find the physical exam and history as the most influential in terms of my thinking about the patient's level of disease activity and also the impact of the disease on their lives and whether or not they have psoriatic arthritis. Only about half of patients will have an elevated CRP, and that is highly influenced by their weight, so this person who is obese I would not be surprised if they have an elevated CRP. And then it's not so clear whether it's completely disease related or obesity related. It's a little different than RA in that way. So, I think with RA we routinely follow the serum inflammatory markers, and that may not be as helpful in this disease. So, the CRP, though, if it is elevated... and you can follow it down with disease activity, and you might see it spike up again with disease activity. But again, that's a relatively small portion of patients that are going to have an elevated CRP that you can follow along with disease activity.

The imaging is important for the hands here, probably. I'm not sure that knee imaging would be all that helpful, but to look at the DIPs and see if there are erosions there, erosions would just portend a more aggressive disease, and so that would be helpful. I don't necessarily follow x-rays after this initial imaging, but they might give you some information about the aggressiveness of the patient's disease.

Dr. Ogdie:

I'm not sure that the CCP is so helpful, but I frequently send a rheumatoid factor simply for the CASPAR criteria, and that's partly because we do a lot of studies here, and so a negative rheumatoid factor gets you a point on the CASPAR criteria. And in terms of diagnosis, the CASPAR criteria are really classification criteria to identify a population for studies. However, they can be helpful in terms of diagnosis, so in order to enter the criteria, you have to have either inflammatory arthritis, enthesitis or spondylitis, and then you get 2 points for having active psoriasis, which this person would get, or 1 point for having a personal history of psoriasis or 1 point for a family member having psoriasis. And then you get 1 point for having a negative rheumatoid factor, 1 point for having rheumatologists identify dactylitis, 1 point for the nail disease and 1 point for juxta-articular new bone formation of the feet or hands on x-rays. So, in this case this patient already fits CASPAR criteria because they have inflammatory arthritis, they have active psoriasis, and they have onycholysis, so we wouldn't necessarily need to get the rheumatoid factor or CCP here, but you could just to kind of round that out.

And then you also asked a question about the validated scale to estimate disease activity. It's a little bit tricky because there are a few different scales. So, for example, 1 scale that's commonly used is the DAPSA, and that takes into account the number of tender and swollen joints, the CRP if you have it available, and then a patient global assessment and physician global assessment. So it's pretty easy to do. It's a numerical, like a continuous scale, and there are categories that you can fit people into: mild, moderate, severe disease. The problem with that is that you don't take into account psoriasis, the enthesitis, the dactylitis. It's in some way the dactylitis in that you're counting it in as joints that are swollen, but that is one available option. I actually just look at the individual category, so I just do a 66/68 joint count. I do a **SPARK** enthesitis assessment. That's a kind of full body, mostly peripheral enthesitis assessment. I do a dactylitis count. And then we do a RAPID 3. So, the RAPID 3 is among the most commonly used patient-reported outcomes in rheumatology in the United States, you can use it across different diseases, so it's pretty easy, gives you like a HAQ functional activity, and then a patient global assessment and a patient pain assessment. So I look at the individual pieces rather than using one of the composite measures at this time.

Dr. Merola:

And so for this particular case where we, to sum it up, have a 46-year-old gentleman who has what sounds like a mostly peripheral inflammatory psoriatic arthritis and some more mild psoriasis based on body surface area really using only topicals at present, what would be your initial treatment approach to this particular individual?

Dr. Ogdie:

I think in some ways it depends on how much the patient is affected by their disease, so if it's fairly mild... So this is saying moderate disease activity, or that's what was put into the case, but let's say the patient is feeling not that bothered by their oligoarthritis; the knee is bothering them a little bit; we could inject the knee, perform an arthrocentesis and then inject the knee; and then it's just really the tenderness of the fingers. In that case we might consider just using something like methotrexate. The problem with the methotrexate here is the obesity and the prediabetes, so I would be very careful about the liver. Fatty liver disease is very common in patients with psoriasis and psoriatic arthritis, even above and beyond that which just exists with their obesity alone, so I think you have to be really careful with the methotrexate in this particular scenario. If their disease is causing much more discomfort, it's preventing them from functioning normally in their daily life and their psoriasis is really bothersome, I might think about a TNF inhibitor initially for this patient. Even though it's a first diagnosis of the disease and they are essentially treatment-naïve aside from the topicals, that would be a consideration depending on how much this is bothering the patient and interfering with their life.

Dr. Merola:

Great. And any reason to pick among the biologics if you were going to go there in terms of... You mentioned a TNF, but any reason to not, say, start with an IL-17 inhibitor or some other mechanism?

Dr. Ogdie:

The main reason I don't generally start with something other than a TNF inhibitor is insurance. It's usually easier to get either etanercept or adalimumab first compared to any of the other therapies. They have also been around a lot longer, so you can have a conversation with the patient about the longevity of our data with TNF inhibitors. And as rheumatologists, we're pretty comfortable with the TNF inhibitors.

Now, if the patient had really severe psoriasis, that might be something that you would consider an IL-17 inhibitor first instead. And then thinking about the whole spectrum of other treatments available, this patient may, if they have mild disease activity, may be someone

you would consider apremilast first—mild psoriasis, mild joint disease. Overall, apremilast is pretty mild in terms of efficacy but also somewhat in terms of side effects. You don't have to really watch the labs as much. There's the added benefit of sometimes people getting weight loss. And I should say that's listed as a side effect, not necessarily a benefit, but in this person who's obese, they might benefit from that. But the reason people have the weight loss is the diarrhea and nausea and headaches, and so that can be somewhat, basically, drug limiting sometimes, but not everyone gets that. So I think the discussion with the patient is: How severe is your disease? And then if it's mild or having a mild impact on their life, we might consider methotrexate or apremilast first. If it's having a significant impact, we would consider a biologic, probably a TNF first, IL-17 if they have much more severe psoriasis.

Dr. Merola:

Let's shift over to a discussion about how best to manage the ongoing care of patients with psoriatic arthritis, and we can come back to our case to get us started.

So, the rheumatologists in our case initiated methotrexate 15 mg weekly, titrated up to 22.5 mg per week. After 6 months of treatment, joints were meeting minimal disease activity, onycholysis had improved, but after 6 months Michael reported some worsening of his skin lesions, increased severity of itching and scaling of existing lesions as well as new lesions on the back with a total of about 4% BSA now. You'll remember previously it was about 2%. So at this point, Alexis, in terms of monitoring results of therapy, you had mentioned earlier some concern about this obese individual with prediabetes being started on methotrexate. Maybe we could comment a little bit on what you'd be monitoring and thinking about from that perspective and then how you would approach the patient whose joints are fairly well-controlled but has some breakthrough skin disease in terms of managing on our own versus managing with a dermatologist collaboratively and how you would approach that.

Dr. Ogdie:

Yes, great question. So I had mentioned methotrexate, increased risk for liver disease in patients with obesity or diabetes, and so just following the liver function tests every 8 to 12 weeks; but at this point with the patient's skin really bothering him, one consideration is whether we back down on the methotrexate and add a TNF inhibitor, stay on the same dose of methotrexate and add a TNF inhibitor or a non-TNF biologic, and so I think we'd have a discussion with him and say, "How much is this bothering you?" and then also a discussion with our dermatologists. So this is the perfect example where a collaborative relationship with a dermatologist is really critical, because is there something we could do to maximize his skin therapy without messing with the systemic therapies? So, is he interested in phototherapy or using just topicals to see if we can get things under control, or if not, should we just switch the therapy around? And then which therapy, so should we do a TNF inhibitor like adalimumab or etanercept, or should we switch to ustekinumab or secukinumab? And like I said, the other question is whether we leave the methotrexate on. Usually when a patient is on methotrexate and doing pretty well, I would keep the methotrexate on, but we could lower the dose as we add a TNF inhibitor, but certainly I usually like to keep it on mainly for the prevention of developing antibodies to the biologic drugs.

Dr. Merola:

Great, that's very helpful. And I think it might be worth pointing out that the 4% BSA based on the National Psoriasis Foundation guidance would technically put this individual into the moderate skin disease category where they consider a 3–10% to be in the moderate range. Some use a 5% cutoff for moderate. In any case, it certainly would make sense, it sounds like, to discuss this with the dermatologist or think about treating the skin at this stage.

So, how important is multidisciplinary care for patients with psoriatic arthritis? Maybe we can talk a little bit about the role of rheumatology, dermatology, how we can increase communication between our specialties and perhaps even mention the PPACMAN group a little bit while we're on this topic.

Dr. Ogdie:

Yes, I think we are both very committed to the derm/rheum partnerships, and so to really manage a patient optimally, it's great to have both people at the table thinking about what's the best option for this patient at this time. And I guess I can speak to a variety of different ways of doing that. I know you at your center, you see patients at the same time in the same room. Here we have a derm/rheum partnership where I will run over to the clinic or they'll run over to my clinic, but we don't actually see the patient at the same time, usually in tandem instead, but we also have a lot of conversations. We see each other at least a couple times a week and can mention different patients or talk through things, more than anything just picking up the phone and texting or calling our dermatology colleague to get a better idea of their thought about the patient. But maybe you can talk to what you do.

Dr. Merola:

Exactly, so at our center we're fortunate to have a combined clinic, so we have a dermatologist, a rheumatologist, and myself a dermatologist/rheumatologist, seeing people at the same time in clinic along with some derm residents, rheumatology fellows and medical students, so it's quite a big group that's seeing our patients at any given time. I think, certainly, there are obvious educational



benefits to the rheumatology fellows and dermatologists who are learning about each other's specialties and sort of cross-training. I know for sure our dermatologists are learning how to do joint exams and learn musculoskeletal exams and such. The rheum fellows are getting much more comfortable with topicals and treating to skin therapy targets as well as learning some of the skin differential diagnoses, for example. So I think from that perspective it's really helpful, and I'm sure you have a number of trainees coming through your center as well. I know a number of places around the country—we have about 25 centers or so that we know about as part of our combined clinics group that I'll mention, and so I think that's all very helpful. I think the patients really love the 1-stop shopping and the tailored education and support and such, and there has been some data to suggest that there's a quicker transition to appropriate systemic DMARDs with a wide array of therapies offered to these patients, and they particularly like the combined discussion.

That said, I think we have a number of sites, and we've talked to a number of sites around the country, where it's not quite as formal. There are a number of centers around the country where a dermatologist and a rheumatologist are just facilitating their communication and facilitating patient visits, and so we've been particularly excited about trying to help those form. And so this group I mentioned, PPACMAN, which stands for the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network, is a group that we started to really nucleate psoriasis/psoriatic arthritis combined clinics and centers around the country with lots of support for these models. So we obviously, believe very strongly in these models. I think we'd like to see more local, regional dermatology/rheumatology partnerships and clinics like this spring up and I think, again, our patients certainly appreciate the model, and it's good for patient education.

Dr. Ogdie:

I think it's so professionally rewarding to work with other colleagues that are doing something slightly different from you, and I feel like I learn something every time, so it's really great to hear the dermatologist perspective on what's going on and think, "Oh, yeah, I guess I didn't think about it that way."

Dr. Merola:

And one last point before we wrap up, I think we're familiar with the great burden of comorbidities, I think, that come with psoriasis and psoriatic arthritis. Particularly, I think, what's been highlighted in the recent past few years has been the cardiovascular comorbidities that come with the diagnosis. How are you prescribing the overall management of some of the comorbidity burden that comes with this set of diseases? Certainly, the dermatologists may not be in the position to do all of the cardiovascular screening, and I'm not sure if the rheumatologists necessarily will either. Perhaps they are, but what have you seen as the relative role of the primary care clinician versus the rheumatologist and others in the management of the comorbidity burden?

Dr. Ogdie:

Yes, that's a great point. We've talked a little bit about comorbidities, and in particular, the metabolic comorbidities and cardiovascular outcomes are really important for this patient population. And I think across the rheumatic diseases we've learned so much more about systemic inflammation, its contribution to accelerated atherosclerosis and so on. So I think rheumatologists are becoming more and more aware of this and actually taking on a little bit more of the burden. So here at our center we do a lot of cardiovascular management—risk stratification I should say—in terms of making sure the lipids are checked, making sure the patient knows about it. I think making sure the patient knows about it is really important so that they can also be an advocate for themselves with their primary care physicians.

I think a critical question is how we involve the primary care clinician, so I try to always include in my note, at the bottom of a psoriatic arthritis patient's note, that psoriatic arthritis and severe psoriasis are associated with cardiovascular disease and to pass that on to primary care physicians so that they think about it. I think we need to do a better job connecting with primary care physicians because they get so many letters like that—I can't imagine that they can see and digest all of them. So I think this is something for the future that we need to work on as a field.

Dr. Merola:

Great. So, Alexis, before we wrap up, any last takeaway tips or insights that you'd like to offer our rheumatology audience today?

Dr. Ogdie:

I think one of my always take-home messages is psoriatic arthritis is not rheumatoid arthritis. It's its own distinct disease. It's a multifaceted condition, so you really have to look at all parts of the disease, including the skin, when you're making therapy decisions. And I think the second takeaway that I would put out there and I think you would agree with is that comanagement with dermatology is really important, and getting to know a dermatologist and bringing them into the care of the patient is really important.

Dr. Merola:

Well, this has been a really great discussion. I'm Dr. Joseph Merola from the Brigham and Women's Hospital in Boston.

Dr. Ogdie:

I'm Dr. Alexis Ogdie from the University of Pennsylvania.

Dr. Merola:

Thank you so much for joining us.