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https://reachmd.com/programs/cme/update-psoriasis-and-psa-best-practices-dermatology/10100/

Released: 04/20/2018
Valid until: 04/20/2019
Time needed to complete: 30 minutes

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Update on Psoriasis and PsA: Best Practices in Dermatology

Dr. Ogdie:
About 30% of patients with psoriasis will develop psoriatic arthritis. Left untreated, psoriatic arthritis can progress to severe symptoms, joint damage, disability, and greatly reduce quality of life, so the earlier we diagnose and treat psoriatic arthritis the better. Dermatologists play a key role in recognizing the signs and symptoms of psoriatic arthritis and referring patients to rheumatology for full evaluation and management. Following referral, close collaboration between dermatologists and rheumatologists can greatly improve the management of both the skin and joint manifestations of psoriatic disease.

I'm Alexis Ogdie from the University of Pennsylvania.

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

Dr. Ogdie:

On today's program we'll be discussing Best Practices in Dermatology for Psoriasis and Psoriatic Arthritis. So, Joe, help us set the foundation for our discussion. How is our understanding of psoriatic disease evolving?

Dr. Merola:
So I think we really have come a long way in the last 10, 20 years for sure, particularly in our understanding of psoriatic skin disease. I think since that time we know that psoriatic disease is really a multisystem inflammatory disease with a complex immunopathogenesis that is really still evolving. We have gotten a little bit closer to understanding some of the environmental triggers, certainly some of the genetic factors, and then even some factors such as the microbiome, which I think have helped us to better understand at least an early, but complex, picture of psoriasis and psoriatic arthritis as well as the systemic nature of disease. We've gleaned a better understanding for sure of the immunopathogenesis with regard to both innate and adaptive immune responses and a whole host of cytokines that seem key to the pathogenesis of disease and have really become the target for the multitude of therapeutics that I think we'll touch on at some point during our discussion today.

One of the things I like to remind dermatologists in particular, is that psoriatic arthritis is really incredibly common and probably the most common and relevant comorbidity of psoriasis along the long list of comorbidities that we know of in this disease, and you mentioned already about a third of patients, which is what I usually remind my dermatology colleagues, which is not insignificant at all and has a tremendous impact on quality of life and potentially quantity of life as well. So, it's not just a bothersome skin and joint condition but can be potentially a progressive, erosive joint disease.

Dr. Ogdie:
Great. And I think you've already started to address this, but what is the dermatologist's role in identifying psoriatic arthritis?

Dr. Merola:
So really the dermatologist is at the forefront of the screening of psoriatic arthritis. I think we know that most of the psoriasis is treated by the dermatologist or by physician extenders and other folks that are embedded in the dermatology office. So really I think it's our responsibility. It's on the dermatologist to be the person who is asking about joint pain, asking about the potential for psoriatic arthritis when seeing patients with psoriasis and referring for appropriate care, or at least considering whether or not they want to take on some of the management role of this particular common comorbidity. I think one of the things that we talk about with dermatologists is there was a study a number of years ago, and I think it's pretty frequently quoted, that I think underscores the nature of the under diagnosis of this

condition. So, they had a dermatology group who saw patients with psoriasis who were subsequently seen by rheumatologists, something like 300 patients. About 41% of those patients had not previously been given a diagnosis of psoriatic arthritis prior to seeing the rheumatologist, and that's, I think, a really important number because it underscores to me how much psoriatic arthritis is potentially floating under the radar, and particularly in the setting of a dermatology office.

So with that in mind, I think there are a number of ways that dermatologists can start to think about psoriatic arthritis screening. And having a very busy practice myself, I know there are a number of challenges to an already packed schedule to be sure without starting to ask patients about joint pain and joint complaints in an office, but I think there are a number of relatively easy ways to get screening done in an appropriate way within the dermatologist's office. So, one of those is just breaking down the barrier of understanding what inflammatory arthritis signs and symptoms look like. I think as a dermatologist—and I get to wear both hats as both a dermatologist and a rheumatologist—I've had some of the benefits of seeing and learning about inflammatory arthritis signs and symptoms, and it can be a challenge for those who have not been trained in musculoskeletal diseases to feel comfortable with screening and diagnosis of psoriatic arthritis.

So, there was a mnemonic that we published several years ago in the *JAD* just as a reminder for dermatologists around some of the signs and symptoms of psoriatic arthritis. So the mnemonic is PSA, which stands for joint pain, so remember to ask your patients about pain in the joints, S for stiffness—and this is probably one of the most important elements, I think, at getting at whether or not the patient has inflammatory arthritis that's sitting in front of us. So, do they have stiffness in their joints that occurs after a period of inactivity or upon wakening that lasts at least 20, 30 minutes or more? And that's really a key sign, I think, that signals to the rheumatologist that this might be inflammatory in nature, so this sort of stiffness that actually improves with activity or pain that improves with activity. If you can remember a second S, the sausage digit for dactylitis is a helpful one, and then A for axial disease, remembering that we can also have back or spine involvement of psoriatic arthritis. So if someone is presenting with back pain, particularly a younger patient with psoriasis, and then has that same qualifying S, the stiffness that lasts for a period greater than 20 or 30 minutes and improves with activity, I think that's a really easy way to remember that there might be inflammatory arthritis going on and then think about the next step.

For us, one of the things we found easiest for the practicing dermatologist is to consider using a screening tool. So there are a number of validated screening tools out there that are freely available, including one called the PEST. There's the PASTE, the ToPAS. There are many others. And these have relatively good sensitivities and specificities for psoriatic arthritis, and it's something that the dermatologist doesn't have to do or administer themselves. It can be administered in a waiting room or

by staff in the office, and this is something I think that really could make the screening and referral, much easier for the busy dermatologist. And these are also freely available, for example, online and through an app. There's the GRAPPA group. G R A P P A has an app where you can download these tools for free and use them on a Smartphone device. So I think those are a few things to think about when we think about screening among the psoriasis population, really something that faces dermatology well.

Dr. Ogdie:
Great, so let's now talk about a case of psoriasis and how you might go about assessing for psoriatic arthritis. So this is a patient with psoriasis, Sandy. She's a 46-year-old woman who works as an office manager. She has plaque psoriasis on her legs and trunk, and she's had this for about 16 years. She follows regular with her dermatologist. Most of the time in the past she's only been on topical therapies, but most recently, in the last year, she's been on phototherapy. This has reduced her body surface area from 4% to 3%, but her skin worsened in the last 6 months, so it's around 4, maybe 5% now, and she's got more active itching and scaling. She is currently only on topical therapy and phototherapy, so how would you go about talking about systemic therapy, and how would you go about assessing for symptoms of joint pain in this particular patient?

Dr. Merola:
Yes, so this is not an uncommon scenario, and certainly, this is a person who's at risk for psoriatic arthritis just by the very nature of having psoriasis. We haven't heard about any other features yet that might suggest psoriatic arthritis in the case, but we'll talk about screening. I think one of the things that's important here is the patient has had, it sounds like, a pretty good trial run of phototherapy. Sometimes we'll have patients who really haven't had enough time in the phototherapy booth, for example, and have claimed failure before it's really been given a good shot. I mean, here it sounds like the patient's been receiving phototherapy for at least the past year and really has had marginal benefit with a BSA from 4 to 3%. If you go by the NPF definition of severity of disease, she would still be in the moderate skin disease severity category. So the NPF uses 3% as a cutoff between mild and moderate disease and 10% as a cutoff between moderate and severe disease, so this patient would still be sitting in the moderate category, and so this is certainly someone who I would want to have a discussion about what are her goals in terms of her therapy? So if this is a person who says, "My itch, my scaling, the areas of involvement for me are highly impactful on my life," then I think this is someone where we may have an aggressive treatment discussion, whereas other people may come and say, "You know, the 4% really just doesn't bother me much, and I'm happy with using topicals as needed," and certainly, we're not going to push too hard beyond what the patient's treatment goals are.

I think that said, we have an ever-increasing understanding of some of the comorbidities of disease,

the fact that skin inflammation probably means systemic inflammation, including even endovascular inflammation, so that's certainly an evolving area and something that we would mention to the patient and may come up as a consideration in our treatment discussion. And so, I think that this is certainly someone where we're going to start now having a discussion about what the benefits and potential treatment options are for oral and/or other systemic or injectable medications as she's already failing topical and UV therapy as I've seen it. To come to your point, this is a patient where a question and screening about psoriatic arthritis really makes all the difference, because we want to know if there is psoriatic arthritis at this point, it's going to dramatically change, or potentially dramatically change, our treatment approach and algorithm to this patient.

This would be a perfect point in care intervention to offer one of those screening questionnaires that I mentioned earlier, and if the patient were to screen positive, to think about co-managing with a rheumatologist at least early on for screening if they were to screen positive.

Dr. Ogdie:
That makes a lot of sense to do the screening as you're thinking about therapy changes because then that informs your therapy selection. So, can you talk a little bit more about therapy selection in psoriasis? So this patient with moderate psoriasis, what might you think about if the patient has just skin disease versus skin and joint disease?

Dr. Merola:
Yes, that's a great question. So if the patient has just skin disease, I think we're often breaking the next sort of decision point, after "is there psoriatic arthritis or not?" is "how severe is the skin disease?" So, if it turns out that Sandy in this particular case really has only skin disease, then our decision is going to be about how severe her disease is. And I think using just body surface area alone is not enough. I think there is some guidance but not enough on this point, so asking the patient about how heavy a burden in terms of quality of life psoriasis is really is crucial, what areas are involved? So, 2 or 3% body surface area when it's on your face or in the genital region or affecting palms and soles is actually quite a heavy burden of disease, whereas some other hidden areas or a low body surface area maybe on elbows or knees in the winter that are otherwise covered may be less of a burden. And everyone's experience varies based on itch and other aspects, so I would try to gauge first how severe is the disease for this individual patient.

In this particular case, if Sandy were tremendously bothered, if she's now failed topicals and UV light therapy, I think there are a number of systemic options based on certainly payers, because it's not always just up to us, but we're at least in the United States subject to—most of us—to step therapy and such. I think this would be a case where we may be talking about an oral agent maybe up front, have a

discussion about methotrexate with this individual, less likely but possibly acitretin, which is an oral vitamin A analog. We may be talking about medications like apremilast, which there have been some more recent data, some shown at the EADV meeting in 2017, for example, looking at apremilast for more mild to moderate disease, which is where she may fit based on her body surface area alone before thinking about whether, say, a systemic biologic might be the right next step after having failed potentially an oral therapy.

And I think there really are rich discussions, because for me, a lot of the discussion will come to not just safety and efficacy but also tolerability of medications. We certainly have some challenges with regard to GI tolerability of apremilast and/or methotrexate, some of the fatigue that patients will experience on methotrexate, for example, so I think there's a lot to discuss. And if you layer all of these different mechanisms on top of the potential decisions around comorbidities, so we may decide—and we haven't gotten this information yet—but is this really a patient who's a candidate for methotrexate? Do they have a fatty liver? Do they drink alcohol? So there's really a lot to be considered.

To come to your second point of what if Sandy has psoriatic arthritis, that's an even more potentially complicating factor, and in that case, I think we're still having a discussion about oral versus systemic agents. We may come much more quickly to the discussion of oral and injectable systemic agents if she does have psoriatic arthritis, certainly again depends on the severity of her psoriatic arthritis. Is it 1 or 2 joints? How much is it impacting her life? And this is something where a discussion with the rheumatologist may be really in order because there are so many different aspects of psoriatic arthritis. And I think one of the points I'd like to emphasize among my dermatology colleagues is not all psoriatic arthritis is the same, so if someone has, for example, back involvement or spine involvement, axial spondyloarthritis as part of their psoriatic arthritis, some agents are known to work better than others. For example, methotrexate really is not a go-to in the setting of back disease, and we may quickly be moving to, say, an anti-TNF or an anti-IL-17 drug in that setting. So there's really a lot to consider and hopefully some that we can unpack during our discussion today.

Dr. Ogdie:
So let's say that Sandy screens positive for psoriatic arthritis on one of the screening tests, and so the dermatologist refers her to a rheumatologist, and the rheumatologist does a full evaluation and finds that she has some low back pain and some stiffness, she has pain in her ankles, elbows and hands, so they initiate a workup, and after the end the workup find basically that she has polyarticular inflammatory arthritis, enthesitis, and sacroiliitis on her SI joints, or at least evidence of sacroiliitis on the x-rays. So, now you started this discussion already, but how do you use her symptoms, or the

active aspects of her disease, to guide therapy selection?

Dr. Merola:
Yes, so that's a great question. I mean, this is a case that is quite complex, I think, from a rheumatologic standpoint, and it quickly turned from a fairly simple mild to moderate skin disease patient to a little bit more complex rheumatologic patient. What's interesting here is—at least in this case, whether it's real or imagined—I think is that fortunately it sounds like Sandy came to the attention, or at least her joint disease came to the attention, of her dermatologist. I have a number of patients where if they are not aware themselves that the psoriatic arthritis is part of psoriasis, they may not think to even tell their dermatologist, so I'm glad that it sounds like some sort of a discourse happened during the course of a visit and this came out. That said, the fact that Sandy now has what sounds like a rheumatologist diagnosis of psoriatic arthritis, including this polyarthritis and enthesitis--and just to clarify for those who maybe don't deal with enthesitis as frequently, enthesitis refers to inflammation at the site of tendon or ligament insertion into bone and is really a hallmark feature of this disease, in some ways thought to be even maybe key to the pathogenesis of the disease, and so this is probably helpful to the rheumatologist to see. But this presence of enthesitis as well as spine disease I think really—and the fact that we're told that this was moderate to severe disease activity—I think really would push us to move in terms of thinking about systemic therapy at this stage.

And there are a variety of guidelines out there for how to now think about this patient. I think one that I will turn to often is—there are a few—but the GRAPPA guidelines which were published in 2016 I believe give us a little bit of an insight by domain of disease into how to think about approaching the treatment for this patient. So the fact that she has peripheral arthritis, that she has skin disease, that she has axial and enthesitis, we can sort of go down their algorithm and think about which therapeutics would make the most sense in this particular case. Given the severity, I would certainly think about a biologic right out of the starting gate in this case. I mentioned earlier that methotrexate is probably not the most appropriate therapy when there's axial spine involvement and/or enthesitis based on a variety of bits of data that exist. That said, we don't have wonderful methotrexate therapy-controlled studies in psoriatic arthritis, but I think it's quite commonly used and is part of step therapy approaches in rheumatology.

That said, for the reasons I mentioned and because of some newer guidelines I think that are coming out, there is some guidance coming from the ACR and National Psoriasis Foundation I believe this year that may, again, push us a little bit closer to using a biologic, a systemic biologic, closer to first-line in the setting such as this. And so, I would absolutely have a discussion with the patient about a TNF inhibitor; I would certainly think about an IL-17 inhibitor as well at this stage given the severity of the axial and peripheral arthritis. And there are a number of agents approved for a patient just like this. We

fortunately, I think, from a dermatology standpoint, could offer her tremendous hope about getting her skin clear with some of these agents, or at least much closer to clear, and we have really good—not perfect but good—numbers in terms of efficacy with these agents in psoriatic arthritis as well, so I would certainly have this discussion I think at this stage with the patient.

Dr. Ogdie:
So let's move into what dermatologists should know about ongoing management for a patient with psoriasis and psoriatic arthritis. Joe, can you take us through what dermatologists should know?

Dr. Merola:
So I think that there are really a lot of considerations in this population. It really is a complex disease. I think we talked a little bit earlier about the nature of the skin disease, that upwards of 30% of patients, or so, have psoriatic arthritis concurrently with their psoriasis. And if we layer on top of that the increasing number of comorbidities that come with this disease state, whether it be cardiovascular disease, some of the metabolic syndrome features (obesity, diabetes, hypertension), the fact that there is co-prevalent increased risk of inflammatory bowel disease, of the anxiety, depression and some other features of mental health disease that come with the condition, and for a rheumatologist, there are some other confusing factors—I mean the fact that patients may have accelerated osteoarthritis, they may have gout—it really makes the diagnosis and treatment a challenge. I think in some ways, from a clinician's standpoint, it's quite an interesting puzzle often to piece all of these bits together with your therapeutic plan, and with the patient's preference and side effects and drug-drug interactions, it really is a rich discussion and often a very busy visit. And that can be a challenge, to be honest—and if we're being practical and feasible about this—for a dermatologist in a busy practice to be thinking about all of these elements of disease. And so I think a lot of this happens in a collaborative fashion and in a multidisciplinary fashion in terms of pairing with primary care, pairing with a rheumatologist, for example.

When I think about patient characteristics again, I think as we're deciding on therapeutics, we certainly want to know what domains of disease are involved. And just to recap, that includes: Does the patient have skin disease? How severe is it? Do they have nail disease? Do they have a peripheral arthritis, an axial or spine involvement? Do they have enthesitis or inflammation at site of tendon insertion into bone and/or dactylitis or the so-called sausage digit as part of their disease?—because not every therapy faces each of those domains in the same way. And as I alluded to earlier, there are some nice reference materials for the practicing physician who wants to take a deeper dive, including the GRAPPA treatment scheme, for example, that gets a little bit at each of these domains and how to approach them.

That said, I think there are also some layering of therapeutics, not just in terms of efficacy and domain of disease but in terms of comorbidities; so something that comes up for us, for example, is: Does the patient have comorbid liver disease, whether it be fatty liver disease or alcohol use that changes our approach with regard to maybe methotrexate? Does the patient have inflammatory bowel disease, which may push us, for example, toward anti-TNF drug, which may better face 2 co-prevalent diseases in that setting? Is the patient on other medications that may cause a drug-drug interaction? It can be a challenging discussion. There is also some guidance, I think, with regard to comorbidities and treatment considerations that's helpful. There was a publication by Laura Coates that came as well from the GRAPPA group that looks at comorbidities and medications and helps a clinician decide which medication might be the best for a given patient in the setting of this complex disease.

So it is complicated, and I think the idea is not to overwhelm anyone. I think from my perspective, I envision that a patient who comes to me with skin psoriasis, we're certainly going to focus on how severe their skin disease is, focus on optimizing their skin therapy, and then if I am not comfortable with the psoriatic arthritis aspect, I'm going to pair with the rheumatologist in thinking about what are the patient characteristics, disease characteristics, and try to infuse patient preference into the discussion and communicate with the rheumatologist all of these features to try to get patient to the right therapeutic.

Dr. Ogdie:
I think that was an excellent discussion of what patients should know about management of psoriasis and psoriatic arthritis for patients with both diseases. Can you talk a little bit more about the role of the rheumatologist and the dermatologist in multidisciplinary care and what that might look like?

Dr. Merola:
We're big fans of multidisciplinary approaches to this disease. If nothing else, I think one of the biggest take-homes from our discussion today is how complex this disease state is, and the complex nature of psoriatic disease I think most often requires a multidisciplinary approach to care. In our center I can talk a little bit about how we've approached this. And then I'm going to briefly mention, if I may, the PPACMAN group, or P-PACMAN group, that's trying to address this gap to some degree.

So in our combined clinic at the Brigham, we have myself, as well as another dermatologist and another rheumatologist, some rheum fellows, derm residents, as well as trainees all seeing these patients together in the same place at the same time, and it really makes for a very rich learning environment for the trainees. I think from an educational standpoint, the rheum fellows are learning to be much more skin savvy. They're learning that skin disease and psoriasis is not just cosmetic but really is highly impactful on quality of life. They learn about the differential diagnosis of presenting skin

disease, and they learn about some of the nuances of psoriasis, such as hidden inverse and intertriginous disease and general disease and such. The derm residents get to learn about musculoskeletal disease, and we actually make sure that they all are comfortable with a joint exam, reporting on tender, swollen joints and on use of screening tools and screening the psoriasis patients. So I hope when they leave our institution, they're at least screening their psoriasis patients for psoriatic arthritis and feel more comfortable with the approach to care. So it's a very rich training environment. The patients, you know, we've done some surveys of this as well, the patients feel that it's a really high-yield visit, it's 1-stop shopping, and they have a combined discussion with the providers. We've shown that there's a quicker transition to approach systemic DMARDs, and the patients are offered a wide array of therapies. So I think the patients are quite happy with the model as well, and it offers us an opportunity academically to do a lot of research.

I think in the community we're as excited about the potential for these models in the community as we are in these formal combined clinic models, and one of the goals, for example, of this PPACMAN group—and PPACMAN is spelled P P A C M A N, stands for the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network is trying to nucleate these combined clinics and centers to really advance a multilevel approach to psoriatic patients. The idea is to also help support the development of local, regional derm/rheum partnerships. We've seen a variety of centers around the country where private practices are getting together to facilitate communication, expedite patient visits. There's a lot of, I think, satisfaction in terms of the approach to this kind of care, and ultimately, it really helps the patients get to the best possible treatment, particularly when they are complicated. And so we're hoping that this model and this group can really advance multidisciplinary care. Part of that multidisciplinary care also involves other specialties—it's not just derm and rheum—but the role of the primary care, I think, in terms of managing the metabolic syndrome, the cardiovascular disease, comorbidities. So I think the summative statement here is a complex disease requires often a complex fix to the problem, and these multidisciplinary clinics and combined clinics I hope start to address that.

Dr. Ogdie:
That's great. Just to offer another way of doing it, I think what you said is exactly right then. It's really about partnerships, and so even if it's just someone that you can call to discuss cases and so on, and even if it's not in the same room—and in fact, that's kind of similar to what we do here, so we see patients in tandem or even on different days sometimes. We have a really close working relationship between dermatology and rheumatology such that we can text or call or talk about patients at any point in time, so even salvaging those close relationships can be really effective for advancing multidisciplinary care much.

Any other tips or insights you want to offer our audience today, Joe?

Dr. Merola:
Yes, I just think in summary, particularly for the dermatologists, I think it really is our responsibility as the frontline providers for our psoriasis patients to be screening for psoriatic arthritis, whether it be, again, with a simple psoriatic arthritis screening tool, which can be done in the waiting room, mailed to a patient before or after their visit, so trying to take some of the burden away from the physician while still accomplishing the goal. Really, collaborative management with a rheumatologist is often a great way to go if we're suspecting psoriatic arthritis. It's a rewarding time, I think, to be treating this psoriatic disease spectrum with all of the new therapies that we have at our fingertips. I can say from a dermatology perspective, it's really wonderful to have therapies that are pushing the envelope in terms of getting patients truly clear and to goals such as the NPF treat-to-target goal, which is quite an aggressive one. And as much as we can, we try to collaborate with specialists to optimize disease control, patient's function, and ultimately patient quality of life.

Dr. Ogdie:
Well, this has been a great discussion. I'm Dr. Alexis Ogdie.

Dr. Merola:
And I'm Dr. Joseph Merola.

Dr. Ogdie:
Thanks so much for joining us today.