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Recognizing Atypical Presentations of Inflammatory Dermatoses

Announcer:
You're listening to *DermConsult* on ReachMD. This episode is sponsored by LEO Pharma. And now, here's your host, Dr. Alexandria May.

Dr. May:
This is *DermConsult* on ReachMD. I'm Dr. Alexandria May, and joining me to discuss how we can better recognize atypical presentations of inflammatory dermatoses is Dr. Naiem Issa, a board-certified dermatologist and dermatologic surgeon at Forefront Dermatology in Vienna, Virginia.

Dr. Issa, welcome to the program.

Dr. Issa:
Thank you very much for having me, Dr. May. Looking forward to this.

Dr. May:
So to start us off, Dr. Issa, inflammatory dermatoses can become challenging to recognize when they present outside of their classic clinical patterns. In your experience, what signals that a case warrants a more thorough assessment?

Dr. Issa:
That's a wonderful question because not all dermatoses fit into the textbook pictures, right? And patients are unique, especially when you consider skin of color patients as well.

Let's take a classic example: atopic dermatitis. We think about these erythematous patches and plaques that happen on the extensor surfaces or antecubital fossa as well as popliteal fossa or on the neck and so on, which is great. But then you can have variants of that where you could have a papular version or a bumpy version where sometimes they can resemble hives. And guess what? Skin of color tends to have more papular than the classic patch and plaques, right? And at times you have to even consider, when you do have an odd atopic dermatitis presentation that presents with bumps and with these papules, are there other things that look like that, right? And sometimes that could be arthropod assaults, or it could be some weird lymphomatoid presentation. In older patients, that can be mycosis fungoides, right? So idea here is that don't anchor your diagnosis right away.

Dr. Issa:
The idea is we have to keep our mind broad as we're looking at inflamed skin so that we don't miss the diagnosis.

Dr. May:
Now, patients may not always volunteer symptoms in sensitive or less visible areas such as genital, intertriginous, or acral sites. So how do you approach a patient history and examination to make sure those areas are not missed when evaluating a suspected inflammatory dermatosis?

Dr. Issa:
The idea is first you have to establish the patient rapport, whether you're meeting the patient for the first time or you're seeing them for a follow-up, what have you. You have to ask the tough questions. So you build that rapport and say, "Hey, look, I know I'm seeing you for X condition, but in order to really get an idea of how bad this may be for you, I have to ask some probing questions. So if you're comfortable with me, go ahead and give me the green light." Usually, they say, "Yes, no problem.

Let's go ahead and begin." And I ask them, "Well, let's talk about the private areas. Is there anything that you've noticed there that you

should bring to my attention?" That invites them to answer in an open-ended way. And if they do answer that, then I go ahead and probe further. So I say, "Well, look, if it makes you comfortable, I have an assistant in the room. I can take a look if you'd like me to, or if you'd like to describe what you've felt or what you've seen, that could also help me to paint a picture," right?

So the whole idea is to, to build that rapport, provide comfort in the room, and allow open-ended questions so that the patients are comfortable to go ahead and give you that information.

Dr. May:
Diagnostic uncertainty can also arise when uncommon inflammatory dermatoses resemble more familiar conditions. For example, neutrophilic dermatoses like generalized pustular psoriasis may initially raise concern for infection, a drug eruption, or a severe psoriasis flare. That being said, what clinical features prompt you to broaden the differential diagnosis in these cases?

Dr. Issa:
So first and foremost, the clinician has to be a great diagnostician. And in order to do so, we have to approach the patient, I would say, the same way every single time so that we are not leaving any stone unturned. So while you are thinking that maybe the patient looks like they may have disease A or disease B, like a classic textbook case,

it's always important to have a broad differential diagnosis going into the matter. So you want to put in the pros and cons or what works for or against a diagnosis based on what you see and based on your history taking. In addition, you should always think about wanting to biopsy because a lot of times, the diagnosis, as you just said, is not so clear cut.

But in addition to that—we're talking about that first approach to the patient—but what if you already came up with a diagnosis for a patient and you're putting them down a route of a therapeutic strategy, giving them a certain treatment, and you tell them to come back in X period of time, and they come back and say, “Hey, I've been trying this medication pretty consistently,” topical or systemic or what have you, “and I'm just not getting better.” So that's where you have to pause for a second and say to yourself, “Am I doing the right thing right now? Did I get the right diagnosis?” And I find for myself, a lot of times, if I haven't biopsied yet by this juncture, that I do reach for the biopsy instead of putting my patient through yet another round of medications that may have risk factors and still may not work for them, right? I'm still delaying the right diagnosis, and that delay in time can lead to potential damage, not just in the skin, but also within.

Dr. May:
For those just joining us, this is *DermConsult* on ReachMD. I'm Dr. Alexandria May, and I'm speaking with Dr. Naiem Issa about practical strategies for recognizing atypical presentations of inflammatory dermatoses.

We've talked about clinical overlap across inflammatory dermatoses, but there can also be overlap at the inflammatory pathway level. Dr. Issa, how do shared cytokine pathways, including IL-17, IL-23, and IL-36 signaling, help explain why these conditions may present with overlapping features or symptoms such as pain?

Dr. Issa:
That's an excellent question. And so the way I look at this is nature has built the inflammatory network to be very precise and to be redundant, right? There's only so many ways, so many cytokines, and so many pathways that a cell can utilize to give you a clinical phenotype or a range of phenotypes. And so that's why we see two different major pathways when it comes to inflammatory dermatoses.

We have innate immune system and adaptive immune system. When it comes to the innate immune system, we have, classically, IL-36 in addition to IL-1 and IL-6, and they have their own signaling component. But on the other side, we have the classic, let's say, psoriasis pathway or psoriasis funnel that relies on tumor necrosis factor leading to IL-12 and 23. And then IL-23 will go on to cause the production of IL-17 and signal through their receptor.

Now, they seem to be on opposite ends of a spectrum, but they do, in fact, overlap at some point. Sometimes, when the disease state is going on for some period of time, then you get that crossover between the two. That's why, for example, you'll see plaque psoriasis patients who may also present with, let's say, generalized pustular psoriasis, or you have these classic GPP patients that may morph into some plaque psoriasis. And so it's a gamut of this redundancy of pathways that nature has relied on to give you those different phenotypes.

Dr. May:
Pain can be an important clue in inflammatory dermatoses, particularly when it seems disproportionate to what is visible on the skin or appears early in the disease course. How do you interpret pain, tenderness, burning, or discomfort when assessing whether inflammation may be more active or systemic than it first appears?

Dr. Issa:
Right. So when I'm particularly looking at the "inflamed dermatosis patient," I look at it on two levels: one, from the outside, and two, from the inside. And the "neuropathic component" to this, looking at pain as well as itch for some patients, is a key in for, “Are we headed into trouble?” Because sometimes, if you are early in the process, inflammation takes time to really cause those long-term changes in the skin before the patient presents in a textbook way. So you may miss the diagnosis early if you're not cluing into what's happening from the nerve perspective, because a lot of these conditions, particularly for GPP and psoriasis, they may have changes in those nerve endings, those dendrites, that they are receiving those cytokines that will go and cause those neuropathic changes and elicit pain as well as itch for a subpopulation. And that may precede the changes in the skin, right? So they may have "sensitive skin" before the rash comes in or the pustules. But in addition, as the skin is also changing over time, the severity of that nerve sensitization will also increase over time if we're not intervening early. So both of these are happening in parallel, skin and from within, especially the nerves, and let the nerves help clue you into badness approaching.

Dr. May:
As we bring all of this together, Dr. Issa, what practical strategies can help clinicians improve diagnostic accuracy when an inflammatory dermatosis does not fit a classic pattern, particularly when it comes to targeted symptom inquiry, comprehensive skin examination, and timely biopsy confirmation?

Dr. Issa:
I like to say time is skin and within, right? So the longer that we wait to get a confirmatory diagnosis, the more damage has been done to the patient that may be irreversible.

And especially with some of these conditions such as GPP where you can have systemic involvement, including some end organ damage such as the liver and so on, this could be really debilitating for the patient. So my advice would be first, when in doubt, cut it. And when we talk about skin cancer, we say, “Cut it out,” but in this case here, cut into the skin and get that specimen. Tissue is the issue.

So never be afraid to go ahead and biopsy. That will always lead you down the right path. A lot of times what we find is that we're looking for a classic presentation. But sometimes it doesn't fit in the bucket, right? Some people are going to be splitters, and some are going to be lumpers. And whatever way that you choose to do it, you have to still understand that there are going to be these overlapping phenotypes across inflammatory dermatoses.

So the way I do it is I'm consistent with the way I approach the patient every single time. I have my list of differential diagnoses, starting from the classic presentation. Let's say it's psoriasis or a pustular psoriasis kind of patient. I brought in that differential, and then I put into each differential diagnosis pros and cons, or rather what works for it or what works against it. And sometimes you may find that the patient works for all of them, and you may have that overlap patient as well. But the key is to be systematic in the way you approach your diagnostic acumen. Do it the same way every single time. Don't be afraid to get the tissue, and you'll get your answer.

Dr. May:
With those strategies in mind, I want to thank my guest, Dr. Naiem Issa, for joining me to share his perspective on recognizing inflammatory skin diseases in practice.

Dr. Issa, it was great having you on the program.

Dr. Issa:
Thank you very much for having me.

Announcer:
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