Differentiating CTCL from Atopic Dermatitis and Psoriasis in Skin of Color

Ginette Okoye, MD, FAAD, interviewed by Brad Glick, DO, MPH, FAAD

Brad Glick, DO, MPH, FAAD: Welcome to Dialogues in Dermatology. It is June 12th, 2023. I am Dr. Brad Glick and I'm a board certified dermatologist and clinical assistant professor of dermatology at the Florida International University Herbert Wertheim College of Medicine in Miami, Florida. I will be your host.

Our topic today is differentiating cutaneous T-cell lymphoma from atopic dermatitis and psoriasis, particularly in skin of color. And joining me today to discuss this very important topic is Dr. Ginette Okoye, MD. Dr. Okoye is professor and chair of dermatology at Howard University College of Medicine. Her areas of clinical and research expertise are in healthcare disparities in dermatology, and hidradenitis suppurativa.

Dr. Okoye left her native Trinidad and Tobago to attend Barry University in my home state of Florida, where she earned her BS degree. She then earned her medical degree from Columbia University's College of Physicians and Surgeons, and completed her dermatology residency training at Yale University, where she also served as chief resident. She has been recognized by the American Academy of Dermatology with a presidential citation, a volunteerism award, a patient hero award, and the 2023 Mentor of the Year award, and I was honored to witness that, while you received that award. Dr. Okoye, Ginette, welcome and thank you for helping us out today with this very, very important topic. Welcome.

Ginette Okoye, MD, FAAD: Hi Brad. I'm happy to be here. Always a pleasure to chat with you.

Brad Glick, DO, MPH, FAAD: And you as well. Let's go ahead and dive right in. A little bit of an introductory commentary here. And cutaneous T-cell lymphoma, I think of it as an incredible great masquerader, and considering this condition and differentiating it from other inflammatory disorders: psoriasis and atopic dermatitis, is our title, but I think we have challenges. Cutaneous, connective tissue diseases, even inflammatory reactions, drug reactions. It's

sometimes a big challenge, and give us some tips and tricks on how we step away and really properly diagnose cutaneous T-cell lymphoma, and with also the optic through the lenses of how we really properly diagnose it in darker shades of skin.

Ginette Okoye, MD, FAAD: Sure. I am thrilled to be here, because this is one of my favorite diseases to think about and talk about, because it's such a challenge. And I had the privilege of learning about CTCL, not just how to diagnose it, but also how to treat it, from some of the masters at Yale University. And so some of it is just repetition, and I think the more patients you see, and I always tell my residents this, the more patients you see, the more you'll get the patterns.

But I have a few tips and tricks, and so I think it's always good to level set, right? So what is MF? What are the CTCLs there? A heterogeneous group of lymphoproliferative disorders of the skin homing T-cells. And they're interesting and they're tricky because they vary widely in terms of their clinical presentation, their histology, and their immunophenotype, and definitely their prognosis.

Today we'll focus on MF, mycosis fungoides, that's the most common type of CTCL, and MF is extra tricky because it can look like anything, like you said. It can particularly look like atopic dermatitis, which I think has always been tricky, to distinguish it from atopic dermatitis. So when I think about MF, there are two distinguishing features.

The first is its distribution in double covered areas of the body, so parts of the body that are under two layers of clothing. And the second is its morphology. So MF lesions tend to be annular or arcuate. They can have epidermal atrophy, which can actually easily be mistaken for steroid atrophy in people with atopic dermatitis. And in patients with lighter skin, these lesions tend to be erythematous, but in skin of color, this pigmentation is much more prominent than erythema. So patients with skin of color with MF will have hyperpigmentation, hypopigmentation, even depigmentation occurring within their patches and plaques.

And sometimes all three are occurring in the same area. And I think that's one of the tip-offs that I've noticed in MF and skin of color. You'll rarely see in a patient hypo, hyper, and depigmentation in one lesion. If you do, think about MF.

Another subtle clinical sign in MF is an overlap of annular patches or plaques. And this overlap then creates these arcuate borders on the edges of the lesions. And I feel like that's another tip off. That's something you see from the door, right? So if you see a patient you're worried about MF, I would get them totally undressed, and look at them from further away. You're looking at the distribution of the lesion to double covered areas, look for those overlapping lesions, and the dyspigmentation, and then you go in a little bit closer, you zoom in to look for atrophy, for fine scale, and for poikiloderma in some patients.

Brad Glick, DO, MPH, FAAD: You make it sound so easy. And I know from personal experience it really is not, and particularly in darker shades of skin. But it doesn't matter. You describe those whirly lesions with scaly borders, fungoides, atopic dermatitis, connective tissue disease, maybe even psoriasis, some of the challenges in terms of the differential diagnosis, but even in the earlier stages, just seeing that scale. Now, is it more of a trailing scale, an advancing scaly border? Is it more diffuse scaling, or does it vary? I mean, what other clues, and I think you've given some amazing ones, but are there any other separators, before we move on?

Ginette Okoye, MD, FAAD: Sure. The scale I think really varies. I can't say that I could think of a specific type or pattern of scale that I would associate with MF. I actually have a little trick that I would love to share.

Brad Glick, DO, MPH, FAAD: Please.

Ginette Okoye, MD, FAAD: And this I learned from Dr. Peter Heald at Yale. He taught the residents an algorithm, a quick algorithm for diagnosing MF in the clinic. And I still use it today, I

still teach it today. So from his perspective, we have these three categories to consider. We have your lesion morphology, your lesion distribution, and the histopath.

And then, you're evaluating these three characteristics to determine if you think they're classic, consistent, or atypical. So it's like a grid that I have in my head at all times.

So for example, your classic MF morphology, we talked about that: annular and arcuate patches. You have your epidural atrophy scale, dyspigmentation, your overlap, and then you have your classic histology, which isn't easy to find, but epidermotropism, atypical lymphocytes, fibrosis of your papillary dermis, et cetera. If two of these characteristics are classic, so let's say you have a classic morphology in a classic location, then the chances of the patient having MF are really high. So for example, if I see a patient with a nice annular patch with poikiloderma on the buttock, even if I do a biopsy and the biopsy says eczema, I think the patient has MF. We have two classic findings.

Brad Glick, DO, MPH, FAAD: You know, you really-

Ginette Okoye, MD, FAAD: With me so far, Brad?

Brad Glick, DO, MPH, FAAD: Yeah, no, definitely. And you highlight the challenge of, it's not always about a biopsy. It's not always about, "Well, I'm not sure, but I see these patterns." And I think for me as a clinician, what's helped me so far just in listening to you, is that clinical presentation, the location. Even more so than the morphology, which I think that we all learn about. But I really appreciate that, if you will, tripod, of that algorithm. Very, very helpful.

Let me ask you this, and you can continue to expand this very challenging topic. Does CTCL occur more commonly in darker shades of skin? Does it occur more commonly in African Americans, or Hispanic individuals, or people of Indian descent?

Ginette Okoye, MD, FAAD: Yes. So from the data that we have so far, the prevalence is higher, particularly in patients of African descent, so African American, Afro Caribbean, and African ancestry in the US. And though the prevalence in the Black patients is higher than that in our Latino patients, in our Native American patients, and in our Caucasian patients, and we don't really understand why that might be.

And it's not just the prevalence, but the outcomes are different in our Black patients as well. And there may be some biology at play. I mean we use phototherapy to treat MF, and we know that ultraviolet light chases away the skin homing T cells and the dendritic cells that feed them, so to speak. So it's possible that having more pigment in your skin filters out light that would otherwise help you clear those cells. So that might be a biologic basis for the differences in the outcomes.

But we know that the differences in outcomes of diseases, they usually are due to the social determinants of health more so than biology. And of course in dermatology we have those too. Many patients just don't have access to us. They can't come in early enough to be diagnosed early, and early diagnosis in MF is the key to good outcomes.

Brad Glick, DO, MPH, FAAD: Can you expand on that? Can you describe and discuss the healthcare care disparities that we see, particularly with the diagnosis and management of CTCL in individuals of color? Because I have seen that my most challenging cases in my now 29 years of practice, and really specifically, Ginette, in my African American patients, they've been some of the more challenging cases, even when we've hit on it very early. And even if there's been a delay in diagnosis, we've jumped on treatment, and the outcomes have not been good. And yet sometimes as well, I also believe that there may very well be some access issues. Can you tell us about the foundation of these healthcare disparities?

Ginette Okoye, MD, FAAD: Sure. We know, as I mentioned, that our black patients are more likely to have MF, but they're more likely to present with advanced disease, and they're more likely to present at a younger age. And then something else that's very interesting, is there seems to be a male predominance in white patients with MF, but a female predominance in black patients with MF. And that too has not been worked out. And there's even data suggesting that there's a subset of black women who present early, meaning before the age of 40, who have an even poorer prognosis. And I can name five patients, that they were young women, 35, 38, 41 with MF, and within five years they're all gone. We don't understand. We need more research in this area.

Brad Glick, DO, MPH, FAAD: I have to tell you, I have to share this, because what you just described for me is, you said you can think of five patients and I can't think of five, thank God. But in this last year and a half, and maybe a little bit longer during the height of the pandemic, we lost a 35-year-old African American woman to cutaneous T-cell lymphoma. And we worked aggressively, we worked hard, we pulled out all the stops, and then even got her even into a tertiary care center, even beyond the scope of our university practice. And it does need to be further elucidated.

And I wanted to ask you, as we look at the impact and the diagnosis and ultimately treatment, and we'll talk about treatment plans and what have you, how do we meet these challenges?

How do we meet these challenges? How do we get there? A little earlier, and you've already answered some of it, Ginette, by really making sure that all of us take a step back, and we use that algorithm approach that we always have a high index of suspicion, that we consider, if we're thinking MF, that maybe more likely we see the Caucasian male, more severe cases in an African American woman.

But what else can we do to effectively meet these challenges and maybe do even better for our patients?

Ginette Okoye, MD, FAAD: This is the stuff I think about all day long, Brad, and this stuff, I lose sleep over. How can we do this better? And I feel like I am uniquely positioned to think about this because of where I work.

My patient population is 90% African American, and so I do have some thoughts. The first is, often I see Black patients with MF years after they've been diagnosed with MF. And I think part of it is when you make that initial diagnosis of MF in a patient with skin of color, it's really important to sit with them and do some education about MF. Our patients with skin of color may not be aware that they're at risk for skin cancer of any sort, and certainly may not have heard of MF or CTCL. So it's a very scary diagnosis, and it doesn't look like cancer. It doesn't feel like cancer.

So sometimes they don't necessarily believe that we got it right the first time. Some of them are invariably concerned about the word lymphoma, and that conjures up fears of imminent demise, and they lose hope, because maybe we didn't take the time to talk about the fact that in many patients this is a lymphoma, but it's indolent, but we need to treat.

And so if we treat, if we jump on this quickly, your life expectancy is probably the same as someone without MF, if you're in stage 1A. But if you get scared and you run away, and you come back two years later and you have tumors, and that's a very different conversation.

And so I think really taking the time, and none of us have a lot of time in clinic, but bring them back for a second visit, for the biopsy results. Perhaps consider not doing that over the phone, and have a discussion balancing this indolent nature of most cases of MF, yet the need for expedient treatment. I think that's a really important thing that I've learned.

Another important aspect to consider here, I think is actually getting patients the treatment they need. So treatment for CTCL may be as simple as phototherapy, yet depending on where the patient lives and the amount of flexibility they may or may not have with their occupation, coming into your office to do phototherapy two to three times a week may not be possible.

And so I find that sometimes I will prescribe phototherapy for a patient with stage 1A MF, I see them back in three months or four months, and they're no better. I'm like, "Oh my goodness, maybe the phototherapy isn't working." But when I really sit and chat with the patient, I realize that they were really only able to go once a week, because they couldn't leave work more than that. So then that's easy.

I can do FMLA paperwork for them, I can try to help them access a home device to help with compliance, but you wouldn't know that unless you really sit and have a conversation with patients and develop that relationship.

And other challenges that I've seen in my patient population, the therapies for advanced diseases, bexarotene, interferon, topical nitrogen mustard, they're expensive, and may not be covered by my patient's insurance. So I have to be prepared to do prior authorizations, appeal letters, phone calls, to make sure that they have access to those therapies that they need.

Brad Glick, DO, MPH, FAAD: And patient assistance too. We really strive very hard to make sure that those are underrepresented minorities, people that don't have health insurance in general, that we go the extra mile so they can get these drugs, because delays in diagnosis with this condition can be devastating, as you've really beautifully described.

You mentioned some of the therapies. Let's combine thoughts about treatments, and maybe even just a quick review for the audience.

Obviously there's different stages of cutaneous T-cell lymphoma, but when you're looking at your patient population that you described, and you're starting from the basics, and you see someone with patch stage CTCL, you're confident in your diagnosis, you've done a biopsy, it's highly suggestive of CTCL, what other diagnostic tests do you order? Do you order any labs? Are there blood measures that you assess? And then take us from there and then go through, if

you will, your treatment algorithm, starting from more mild severities, like you said, a 1A, and then maybe into some of the more challenging cases that you see.

Ginette Okoye, MD, FAAD: For patients with early disease, 1A, 1B. I still check flow cytometry, to make sure that there isn't any blood involvement, because I've been surprised before. It's uncommon, but at least we get a baseline.

I will check an LDH. I don't think I've ever seen an elevated LDH in a patient with early disease, but again, it's a good baseline to have.

And I'll also do CBC CMP lipid panel, knowing that I may need to use systemic therapies like bexarotene in the future, and so again, having that baseline on board.

If my patient is from the Caribbean basin, I will check an HTLV-1, and actually HTLV-1 is vertically transmitted. So even if they were born in the US, if their mother was born in the Caribbean basin, I will check an HTLV-1, because the smoldering form of HTLV-1 associated lymphoma looks very much like MF, but the outcomes are much, much poorer, and the treatment is totally different. So I really want to rule that out in my patients.

Brad Glick, DO, MPH, FAAD: What would be your treatment in that scenario? What is your treatment?

Ginette Okoye, MD, FAAD: I would send them to an oncologist, because they usually get treated with chemotherapy.

Brad Glick, DO, MPH, FAAD: Gotcha. You and some of the more advanced cases. This is a disease state where at least, through my lenses, over many years we've had topical steroids and phototherapy, and we've tried eczema laser for localized disease. People that start to get more advanced plaque stage disease, maybe we get into the retinoids. I've used several in my career.

What happens when we start to get a little bit more advanced? Now I know you said that you will refer out to oncology. Are there new drugs on the horizon? Is there research being done in this disease? So much is made about our common diseases, Ginette. We have got so many therapies for atopic dermatitis and so many for psoriasis now. We have treatments, thank goodness, for vitiligo and alopecia areata. What about our patients with cutaneous T-cell lymphoma? What does the future hold for them in general, and particularly for our patients of color?

Ginette Okoye, MD, FAAD: No, I think Dr. Christiane Querfeld out in California, she gave us an excellent lecture a few months ago, on some of the drugs that are on the horizon for CTCL. So I think that there are things coming down the pipe, but I think we underestimate the power of skin-directed therapy in this disease.

So of course we have patients who are going to progress pretty quickly. They have blood involvement and they're sort of in a different camp. But the vast majority of patients with MF, we as dermatologists need to keep them as long as possible. We don't want to send them to oncology before we have to, because we are the keepers of skin-directed therapy that can be effective and less toxic to these patients. So I love phototherapy. If your narrowband phototherapy is not working, go look at your dosing, because I think some of our patients with skin of color are underdosed with phototherapy, so try pushing your phototherapy dose.

If narrowband UVB is not working, or the patient has thicker lesions, consider PUVA, oral PUVA, which will penetrate deeper, and it seems to work better in patients with skin of color. Not a lot of data to support that, just anecdotally from my colleagues around the country.

So maximize your phototherapy if it's not working. Again, find out, is the patient going for phototherapy? Are they able to do it?

The other thing that I really like, and we had a lot of experience with this in residency, and the problem is it's not available everywhere, is total skin electron beam radiation. This is still skin-directed therapy. It's a little bit of a hurdle mentally for patients, because they hear "radiation," and they think of all the bad things they've heard about radiation, but really try to impress upon them that it's just in the skin.

That works beautifully in many patients. And then you can do phototherapy as the maintenance treatment, after they've flared with total skin electron beam. Then, if the patient has blood involvement, I like to add ECP or extra corporeal photopheresis, in addition to their phototherapy. At that point, I'll probably add on bexarotene and or interferon as well.

Now, once we start getting there, because I'm no longer at an institution that has ECP or electron beam, I will partner with a CTCL center closest to me, and most of us will hopefully have someone within three or four hours.

By the way, that's how few experts we have in the country. But I think that's the point at which you really need that person's opinion, whether they alternate seeing them with the patient, hopefully they have transportation to get there. I have patients who don't have transportation to get from me in Washington DC to Baltimore to Johns Hopkins, even though it's just an hour away, they simply can't get there.

So I try to co-manage those patients with my colleagues there. So they tell me what to do. They do these severe patients more often than I do. And then after that, then you're in the purview of the oncologist. The patient has blood involvement, it's not responding to ECP, or they don't have access to ECP. Then I have a couple of oncology colleagues that I will send the patient to, and manage from a little further away. But, I think more so than talking about the new treatments on the horizon, because most of them are in the purview of oncologists, I think we need to really maximize, and get really confident in our skin-directed therapy as dermatologists.

Brad Glick, DO, MPH, FAAD: Yeah, I love that. Sorry to interrupt you. I just wanted to say that I really appreciate, moving on to our patients, and holding their hands, to skin-directed therapy, and this is also important. And I find as a clinician that I take care of a fair amount of CTCL. Obviously not to the extent of an expert like yourself, but we really want to exhaust our treatments, and I really appreciate your perspective on that. And I think the one thing, that once we do reach that breaking point, at least compared to a while ago, there are at least a few things that are out there, some monoclonal antibodies that may help our patients.

I recall a patient I had recently, Ginette, just horrendous out of control. We poured in the kitchen sink, tremendous pruritus associated with her CTCL, that sometimes the inflammatory burden and the pruritus is just debilitating, to the point where this particular patient couldn't sleep, and unfortunately progressed to nodules beyond her plaques and needed chemotherapy.

But it is such a good example of we should try to keep it, all the particular, as you say, skin-directed therapies in our toolbox available for the patients along the way. Let me ask you, you've given us some incredible tips and many pearls. I really appreciate the information about the algorithm. I love the reminder to the audience about skin-directed therapies, and exhaust all of them in the toolbox. And I think that we have some more than we did before, and I think maybe we even use them a little bit differently than we did before. But what final comments do you have, from a summary's perspective, for this very difficult to treat condition, and particularly in our patients of color?

Ginette Okoye, MD, FAAD: I think with many difficult to treat diseases, and in derm, we have a fair share of those. I think just continuing to have that empathy for patients, and it might be the fourth CTCL you've seen that week, but it's the first time they've ever heard that they had a lymphoma. And to really sit with patients in that, and get them to a place of acceptance, so that they can trust you and be adherent to your treatment, is the most important message I'd like to share.

And I hope that in the future, our basic science, translational and clinical research will continue to include more patients with skin of color, so that the data we generate can really truly be generalizable to the US population.

And I think that access to us as board certified dermatologists is important. Hopefully one day all communities will have access to dermatologists, especially one who wants to do medical derm, who accepts lots of insurance types. There's still many counties in the US, especially counties with a majority minority population, where there are no dermatologists at all. So just working to increase the reach of our workforce, I think could be a great way to get our patients more access to us and our expertise, because that's the only way we'll catch MF, is if we bring our expertise to the fore.

Brad Glick, DO, MPH, FAAD: Well, Ginette, thank you so much. This has been enlightening for me. I feel like a student of yours today and I've learned so much, and I appreciate your expertise, and I would close by saying that your patients are incredibly fortunate to have you as their doctor. I thank everyone for listening in. Dr. Okoye, thank you so much for your expertise here. We've really enjoyed this Dialogues in Dermatology.

Ginette Okoye, MD, FAAD: Thank you, Brad, for having me.

Brad Glick, DO, MPH, FAAD: Thank you.