Updates and Evolving Insight into the Treatment of Hidradenitis Suppurativa

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interviewed by Olayemi Sokumbi, MD, FAAD

JULES LIPOFF, MD, FAAD: From the American Academy of Dermatology, welcome to *Dialogues in Dermatology*. I'm Dr. Jules Lipoff, your Editor-in-Chief. Thanks for tuning in.

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OLAYEMI SOKUMBI, MD, FAAD: Hello, I'm Yemi Sokumbi, Professor of Dermatology and Laboratory Medicine and Pathology at Mayo Clinic in Jacksonville, Florida, excited to be in conversation with colleagues talking about updates and our evolving understanding of the treatment of hidradenitis suppurativa. Dr. Dan Eisen, Director of Dermatologic Surgery at University of California, Davis; and Dr. Martina Porter, Vice Chair of Research at Beth Israel, where she also directs hidradenitis suppurativa clinic. Thank you both for joining me in conversation today.

DANIEL EISEN, MD, FAAD: Thank you so much for the invitation.

MARTINA J. PORTER, MD, FAAD: Thanks for having us.

OLAYEMI SOKUMBI, MD, FAAD: I thought to get us started, it would be important to sort of think through the journey of treatment of hidradenitis suppurativa. We take care of these patients and those of us who care for them are really deeply invested in finding treatments. Dan, do you mind just walking us through the overall treatment paradigm of hidradenitis and how it has evolved in recent years?

DANIEL EISEN, MD, FAAD: If you've been in practice as long as I have, you've seen things change dramatically from where they were back in the late '90s, when I first started. Things

used to be thought of as primarily as an apocrine disease type of issue. You have boils in the pits or the inguinal fold or inframammary area. That changed to follicular occlusion and now people are thinking it's more like of an inflammatory process, like arthritis or inflammatory bowel disease, or rheumatoid arthritis.—

--It's probably a multifactorial disease. I think we're still working out what the primary disease drivers are. I think it's probably different for every patient that's involved. But we now have different treatment options than we had before. Before we just had surgery and we had some antibiotics and we had retinoids. Now things have changed dramatically. I think I'll leave to Martina to talk about what's new on the horizon for that.

OLAYEMI SOKUMBI, MD, FAAD: Well, you set that up very nicely for me, Dan. Martina, what are your thoughts as we think about the options with biologics? I think we've seen our specialty explode just in general in terms of therapeutic options for a number of our inflammatory skin disorders. But when you think about targeted therapies and biologics and how that's changed expectations for hidradenitis, where do we stand today?

MARTINA J. PORTER, MD, FAAD: We've obviously made huge strides. For reference today, and I finished training around the time that adalimumab got approved for hidradenitis. But even then when it first came out, we couldn't get medication to patients. It would take months for our prior authorization to get approved and so the utilization was quite low. Although adalimumab is a groundbreaking drug, it still left a lot to be desired I think in terms of being able to improve patient outcomes, because only about half of the patients would get about 50 percent or more better, which is a relatively low bar when we think of other inflammatory disorders.—

--But in the last two years, we saw the approvals of both secukinumab and bimekizumab for hidradenitis. Three more phase 3 trials have also been completed for two more IL-17 inhibitors and a systemic JAK inhibitor. So the options that we have I think are going to be a lot wider,

even in the next two to three years. But still we're really looking at drugs that only work for about half of the patients and so it becomes difficult.—

--I think it's not like psoriasis, where we can give a drug and expect almost everybody to clear and so it takes a little bit of trial and error and clinical expertise of looking at the lesions and how bad patients are to kind of figure out where you should start with some of these therapies, because we still don't have guidelines telling us to do X, Y, and Z, in this order.

OLAYEMI SOKUMBI, MD, FAAD: I think that you alluded to this, not only do we not have the guidelines, also are there different phenotypes that we need to be thinking of in terms of figuring out who will be a great responder to a particular type of biologic, so we're truly targeted in our decision making? Is that something that has been coming up as you've been thinking through a pipeline?

MARTINA J. PORTER, MD, FAAD: Oh yeah, definitely. I think there's definitely two big categories of patients in the moderate to severe HS category. Those that we think are more follicular or nodular or cystic, where they make these individual abscesses and nodules but they don't tend to make these large coalescing lesion but they can still have dozens of these lesions all over their bodies. And those are differentiated from the patients who are the more classic HS, where they're Hurley stage 2 or 3 and their whole armpits are involved and their buttocks and their groin.—

--I think we have sort of teased out over time that there are certain therapies that work better for these different groups. But even within each group, there's a lot of variability. But they don't unfortunately include any of these phenotypes in any of the trial data and so we have to rely on real world evidence and these sort of post hoc analyses to try to understand who they're working for. But my dream is in five years that we have a pretty set idea of we should try this therapy first for these types of patients, followed up by these other therapies, and this is when

we should implement surgeries or procedures. So I think that will come but we're not quite there yet.

OLAYEMI SOKUMBI, MD, FAAD: I think we all look forward to that. Dan, I tell my patients that HS is both a medical disease and a surgical disease, because we need surgeons. Tell me how you think about your surgical approach to taking care of HS patients, from the early one who might need a little deroofing that a medical dermatologist might feel comfortable with, to some of the bigger surgeries I know you might be involved in, in taking care of patients.

DANIEL EISEN, MD, FAAD: I think you stated very nicely my philosophy on this, just as a multimodal type of disease. You can't just rely on medical treatment. These people need medical and/or surgery many times. I like to group people in my head as kind of mild disease, moderate disease, severe disease. Obviously there's lots of overlaps between those groups. In someone who just gets like the occasional inflammatory nodule, they probably don't need surgery.—

--They might be better managed with medical treatment. But after they start to get scarring, sinus tracts, or even if they have a lesion that recurs in the same place every single time, that's a good indication for surgery, even if it's just a small spot. If that spot comes back like every month, that's a real problem for the patient's quality of life. And that could be easily managed with just a deroofing. Any dermatologist is capable of doing these procedures, they don't have to go to plastic surgery.—

--In fact, it might be more desirable for a dermatologist to treat them than plastic surgery. My personal feeling is that recurrence rate is much higher when you put a graft or a flap over the top of the diseased areas than if you just let it heal by second intent. So you don't need to know any fancy reconstructive methods to deal with these people. Most of us know how to do tumescent anesthesia and if you don't, it's just as easy as mixing together lidocaine and normal

saline with some epinephrine and bicarb and then injecting it into the area you're working in, it's not that hard to do.—

--If you're afraid of cutting an entire axillary vault out, you can just do deroofing procedures like on a large scale. Just doing that can make a huge impact on peoples' quality of life. If first you're not comfortable doing it, if you start limited and you're comfortable, grow with time and so will your expertise and you'll be able to do progressively bigger procedures.

OLAYEMI SOKUMBI, MD, FAAD: Dan, I love that last comment. Because for the audience, I mentioned I'm a dermatopathologist and I had someone say exactly that to me. These are some of my favorite procedures to do and I started small. And truly anyone can do these procedures, you heard it from me. I support what you said, Dan. We talk about treating our patients early. How, when you're thinking about medical treatment, Martina, walk us through because I've gone from using TNFs, used IL-17s.—

--I've had some patients I've had to try IL-12/23, I've tried IL-23, now we have the JAKs. How are you thinking about all of these drugs? How are you doing first? What's your algorithm when you're seeing a patient?

MARTINA J. PORTER, MD, FAAD: Similar to Dan, I do classify patients in categories of mild, moderate, and severe. But there's actually no defined definitions of those. But what I tend to say is patients who have four or more fixed lesions at all times, whether they're a tunnel or abscess or a nodule that keeps recurring all the time, those patients I'll qualify for biologic therapy or systemic immunosuppressive therapy and also would probably do well with small surgeries.—

--So when patients I think are presenting before that, that's when it gets a little bit more difficult because all of our treatment options are really for the severe. But actually what they've found, even looking at the clinical trial data from the secukinumab, for example, and bimekizumab data

is that patients who are moderate and earlier in the disease course, like less than 2-1/2 years of disease actually have much better response to biologic therapy than patients who have longstanding disease and more severe disease.—

--So really I think we should be treating more aggressively earlier on to prevent some of these worse outcomes. I honestly think any biologic would help those patients, of the FDA approved ones now. But we do also use some other therapies I think for the patients who are milder and maybe not quite biologic-eligible, like spironolactone use even in lower doses than we use for acne. Retinoids we'll use, too, sometimes a course of isotretinoin can help more mild patients, although they'll usually have recurrence later.—

--Males can take acitretin, for example, long term, especially if they make a lot of comedones over their body, not just on their face. And then they're also doing trials now for topicals, too. So things like topical ruxolitinib, they tested it in milder patients, so those that were Hurley 1 or 2 and less than 10 lesions and no draining tunnels and they showed benefit for them, as well. And then one other thing I would say, too, is patients who might look normal in between visits but have three or more flares a year where they're developing multiple, large, golf ball-sized lesions, they'd also be candidates for biologic therapy even if you're not seeing those lesions all the time, because those can be just as debilitating I think as having disease constantly.

DANIEL EISEN, MD, FAAD: I think earlier intervention is key. You'd like to suppress the disease before it gets much more severe. If you have a small sinus tract, it's better to intervene with both biologics and surgery then before it gets to be some huge thing where you've got to cut the person's entire armpit or perianal area out. Because once it's developed, you can't get rid of it. The dream would be to help these people earlier so that their quality of life can be better sooner.—

--Not everybody who – I think waiting for biologics until they have stage 3 Hurley disease is a mistake. You want to base the treatment based upon disease severity. Like how much pain are they having? Maybe they don't have sinus tracts yet but they can't sleep at night. Their quality of life is already impacted by that point. Then you might want to consider more aggressive treatment earlier.

OLAYEMI SOKUMBI, MD, FAAD: Both of you make an excellent point advocating for early aggressive treatments to prevent some of the severe ones that we see later. I think the elephant in the room, and I'm not even going to dive into it, is some of the challenges with getting medications approved and the issues with prior auth. It's truly the elephant that can take us off a different path, but I know that presents a challenge to folks as we think through treatment options. Are there lifestyle changes you're recommending? Nutraceuticals? Patients love natural things. Any natural thing on the horizon, Martina?

MARTINA J. PORTER, MD, FAAD: I think that's the patients' number one thing that they ask about. Honestly, I think for HS patients, the treatment discussions about lifestyle changes can be very difficult because a lot of them have been told in their lifetime that the reason they have this disease is because they're overweight, and they don't clean themselves well, and they're smokers. I think that it becomes very stigmatizing because there's many patients I have who lost 50 to 100 pounds and it doesn't make a difference because their disease was so severe to begin with.—

--Taking extra baths or showers is not going to help. It might prevent some secondary infection but it's not stopping the disease. I do think lifestyle modifications like decreasing smoking can make a huge difference because they have shown that patients who are current smokers are much more treatment refractory and have more severe disease than those who do not smoke.

But beyond that, we do try to tell them to make good clothing choices so that they're not really causing any extra friction from the clothing that they're wearing.—

--We try to get things to prevent them from sweating, too, because that can sort of trigger the disease. We do recommend diet and lifestyle changes, I think especially if they have diabetes or prediabetes, because if their blood sugar is not well controlled, that can be really difficult to get their HS under control. Obesity itself, as we mentioned before, is difficult to manage. Then we've employed GLP-1s for this because the patients have difficult exercising.—

--Just in general, I think the same thoughts about following these low inflammatory diets can be helpful but I always tell patients that it's pretty mild in terms of the effect on their overall disease severity compared to taking a systemic immunosuppressant therapy.

OLAYEMI SOKUMBI, MD, FAAD: Dan, anything from your perspective that you're hearing or recommending your patients consider?

DANIEL EISEN, MD, FAAD: I think Martina very nicely advocated for some simple things. Looser fitting clothing, putting yourself in situations where you sweat less, maybe keeping exercise to air conditioned areas, minimizing friction in body surface areas. I just recently heard a talk by Greg (s/l Ojenick) and he recommends giving patients an emergency kit, which is kind of a concept that I hadn't heard before, like sending them home with some syringes and some Kenalog to inject boils in case they have problems on their own.—

--We had some patients there and one of their primary concerns is the fear of developing a boil or an abscess in the middle of an important time. They have no control over when it's going to affect them and that gives them more control. I thought that was kind of an interesting idea, one I haven't tried yet. I don't know, Martina, if you've done anything like that?

MARTINA J. PORTER, MD, FAAD: I have had patients ask if they can take Kenalog home. And I've even had patients secretly put the bottle in the purse and I've had to ask for it back because they thought they could give the injections themselves. We actually published an article about this before but we do a pill in pocket method essentially, where we give patients a couple days of prednisone at about 30 or 40 mg to keep and also about a week or two of antibiotics. We often use amoxicillin clavulanate, the Augmentin, so that if they start to get a flare at home they can take that medication regimen.—

--Only enough for one flare, so they're not continuously taking it. And then they would call us afterwards. It also did help us track how many flares they were having and how severe they were that they would need multiple regimens. So in addition to the exams that we did and the history at the time of the visits, we could go back in the chart and see they took two or three flare regimens since their last visit, so they may not be very well controlled. Or they used to come in and call for 10 ILKs and multiple flares and they haven't called for that at all now, so they must be doing much better.

OLAYEMI SOKUMBI, MD, FAAD: That's an important point, the flares between the visits and how it occupies the triage system and the nurses. So you help the patients by providing a plan, that is an excellent, excellent suggestion. You both are taking extraordinary care of patients. As you consider our audience, who are taking notes or trying to figure out how to care for these patients, what is an insider or something critical that you think they should take away, a high note from you as you think about treatments that have served you, served your patients well in managing patients with HS?

MARTINA J. PORTER, MD, FAAD: I think the most important thing is really setting expectations, both for the patient and for yourself. Because this is a difficult to treat disease and actually my nurse practitioner one time told me, "How can you let this patient leave the office?

They're not any better." I was like, "Well, I actually think they do have signs that they're improving a lot. They might not have fewer lesions yet from their medication but some of that just really takes time, like a good six months."—

--I think when we see them in follow up, we're looking for signs of improvement, knowing they're on the right track. And if they have them, we'll continue on. I'll tell patients usually at the beginning, especially if they're very severe, that it will take us two years to get their disease under control, and I really do mean that, with a lot of different combinations of therapies. And then when we're in follow up, we're looking for signs that they're not responding to treatment at all, so we can change therapies.—

--As you mentioned with the prior authorizations, things have definitely gotten much more difficult in the last five years. The percentage of medications that require a prior authorization has skyrocketed and the time to getting an appeal approved, if you even do those, extended by probably three or fourfold, which I think makes it really difficult. Now we really focus on whatever we can do to get them any medication, rather than trying to find them the best biologic, for example, at first.—

--Because most of these patients will have some response to the therapies and I think getting them on something is the best you can do in a timely manner. And then trying to change from there, rather than setting your sights on one that you might not be able to get for many months can really make a difference for patients. Also, utilizing a lot of the assistance programs for patients can help, too, to try to expedite some of these things.

OLAYEMI SOKUMBI, MD, FAAD: Thank you for your insights. Dan, how about you? What are some lessons we can take about how to do better at the bedside with our patients with HS?

DANIEL EISEN, MD, FAAD: I'm so glad you asked that. I think empathy, probably we all have empathy for our patients. I think you have to express your empathy very like in an extrovert kind of way. People come in, they're frustrated, no one has been able to help them. Having sympathy for their situation I think is very important. Mr. or Mrs. So-and-So, I can see this disease is really affecting you. This is a really hard disease. Like Martina was saying, you have to le them know that what you're going to do is probably not going to be curative but should, with time, improve their quality of life greatly.—

--And that you're going to be there for them and you're going to work with them and get the best care that you can for them. I always like to tell people that it is not a disease of uncleanliness. That is a commonly misconstrued thing. They often get told that by even doctors. One of the plastic surgeons I sent a patient to told her to take a bath and that she needed to be more clean. Come on, did they have no understanding of the disease?—

--So just hearing from a doctor that they understand that it's not something that they've done, this is just a disease that they're susceptible to, to their genetic makeup or situation, and that you care about their outcome. So I think that can make a huge difference. It's a tough to treat disease but this can be one of the most rewarding ones to treat, as well. When you start to see the improvements that people get from the biologics, the surgery, or both, that's as good a feeling as you can get as a physician.

OLAYEMI SOKUMBI, MD, FAAD: That's a wonderful note to end it, empathy. Our patients with HS need empathy. Thank you so much, Dan. Thank you, Martina, for being in discussion as we think through the evolution of treatments of patients with HS. They need our empathy. They need us to hear them. It is truly rewarding to care for these patients. Thank you.

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