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Investigating Hidradenitis Suppurativa: A Multifactorial Disease

Dr. Chovatiya:
According to the Mayo Clinic, hidradenitis suppurativa, or HS for short, is a chronic inflammatory skin condition that can cause painful lumps in the skin. Although the exact cause of the condition is still being investigated, it is known to be a multifactorial disease with genetics, environmental, and immunologic factors involved. So what therapies are currently available to treat this painful condition?

Welcome to DermConsult on ReachMD. I'm Dr. Raj Chovatiya. And joining me today to discuss the current treatment landscape for patients with HS is all-around HS superstar herself, Dr. Martina Porter, who is a dermatologist at Beth Israel Deaconess Medical Center and Assistant Professor of Dermatology at Harvard Medical School.

Dr. Porter, welcome to the program.

Dr. Porter:
Thanks so much for having me, and thanks for that introduction.

Dr. Chovatiya:
Well, let's jump right in. It's all truth here. To help us better understand the condition, could you maybe give us a general overview of HS and its pathophysiology? I know that's a little easier said than done, but give it your best shot.

Dr. Porter:
Yeah. I mean, we have learned a lot about this disease over the past 20 to 30 years, and I think one of the first things to just note is that the nomenclature hidradenitis is actually incorrect when we think of the pathophysiology. So this is actually a disease of hair follicles and not of the glands themselves. There is obviously still the inflammation, and that's really the driving factor here. And what we really know so far is that there is some sort of follicular occlusion and then dilation that occurs, and then the follicle tends to rupture, and we have an inflammatory response, and this really leads to this chronic state where the sinus tracts start to connect under the skin, where you really see these hair follicles converging to make those tunnels under the skin. And we've done a lot of different studies, but we still haven't really found a single driver of this disease. And when we ask like, "Oh, which cytokines are involved? Are they the same as psoriasis?" We're still not really sure. We have studies pointing at IL-17, IL-17a, TNF-alpha, interferon gamma, IL-6, and IL-1, and I think it's good in some sense because we have a lot of drugs that target these specific inflammatory mediators, but there doesn't seem to be one specific thing that's driving all of this disease.

Dr. Chovatiya:

And to go down that clinical avenue, how do we think about disease severity in our patients with HS? I know that this has been an evolution over the past decade or so.

Dr. Porter:
Yeah. And as you pointed out before, somehow this ended up being a good part of my career was how do you score these lesions, but essentially, the background is I think most people are familiar with Hurley staging where we had one, two, and three, and it really referred to the extent of the disease and the extent of the scarring or the tunneling that we saw in patients. And they, historically, have thought that about 75 percent of patients are probably Hurley stage 1 where they just have these separated isolated lesions, and then about 25 percent are stage 2 where the lesions start to connect, and, fortunately, only about five percent are stage 3 where they have extensive involvement of a whole anatomic region. But when they started doing clinical trials and as dermatologists started to treat these conditions, the Hurley staging was a surgical staging system. And we do do unroofing now, but most of the medical therapy is not aimed at reversing the scarring. It's reversing the inflammation. And so what we've really been left with is counting individual lesions, but we do say mild, moderate, and severe, and the trials are really for patients who are moderate to severe, which is on average probably having four persistent lesions or more, but I think some patients might have two humongous lesions, and they could be considered moderate to severe as well, so there's not a perfect definition. And we do know that the quality-of-life impact can be really significant even for people who would be rated by their physician as having more mild disease.

Dr. Chovatiya:
It's amazing how that kind of ends up being a recurring trend with a lot of our inflammatory diseases, and I really feel like with HS it's one of those that the symptomatic burden can just be so out of control for our patients and just the overall burden it creates that often times what you may see as probably doesn't look so bad is, in fact, a huge burden in our patients' lives and something they think of as being quite severe.

Dr. Porter:
Yeah, I totally agree. And I think for some patients they might be mild or not affected for nine months out of the year, but for three months they have very severe symptoms, and it could be spread out like a few weeks here and there, and just that constant fear of "When am I going to have a flare, and how can I predict it, and how much of my life do I have to put on hold while I have the flare?"—I think really you should be taken into account when we think about how severe the patients are too because it's just so difficult to live with this disease.

Dr. Chovatiya:
Well, thinking about this reliance on objective measures, which oftentimes is what you need for a phase 3 trial—we've got to make the FDA happy when you get an approved treatment—could you talk me through the general treatment approach at a high level for HS? And then maybe we can delve into at least what we have as improved therapies for the time being.

Dr. Porter:
Yeah. So I think we have some okay treatment algorithms so far. Because we still haven't been able to classify that well different types of HS, and even the severity of the disease to some extent, it's sometimes hard to pick which treatment to use, but the ones that are most commonly utilized for people who have more mild symptoms, I would say are topical washes and, for example, lifestyle changes, like avoiding dairy and some other dietary things. There's even some data for zinc gluconate as well at 90 milligrams a day. But the types of prescriptions that we're really using are things like topical antibiotics, occasionally topical steroids, maybe topical resorcinol, and then we move into more oral or systemic treatment options where we're looking at hormonal therapies, things like birth control pills, spironolactone, and then obviously antibiotics, tetracycline antibiotics, and then even some more broad-spectrum combination of antibiotics to really try to get the disease under control. And then in the last, I would say, about seven or eight years, adalimumab and

infliximab really became the mainstay of treatment for patients who had a lot of inflammation often in combination with surgery. And then now, if you look at clinicaltrials.gov for example, there are a million different therapies it seems, like biologics, that we're really trying for this condition now.

Dr. Chovatiya:
For those of you that are just tuning in, you're listening to DermConsult on ReachMD. I'm Dr. Raj Chovatiya, and I'm speaking to the awesome Dr. Martina Porter about the pathophysiology, disease severity, and treatment options for patients with hidradenitis suppurativa, or HS.

So now that we've talked a little bit about some treatment options, let's zero in on the first FDA-approved therapy we had. You mentioned adalimumab. Dr. Porter, can you tell us a little bit more about this therapy?

Dr. Porter:
Yeah. So as most people know, adalimumab is a TNF-alpha inhibitor. And maybe what people who aren't as deep into the HS world don't know is back in 2012, they actually published the data on adalimumab, and they looked at different dosing regimens, and one of them was, essentially, the psoriasis dosing regimen where they're taking 40 milligrams every other week for maintenance therapy, and then they also looked at the 40 milligrams weekly dosing for patients as well, and what they essentially found in that study was that the every-other-week dosing was ineffective. And this disease was so inflammatory that we needed the 40 milligrams-every-week dosing to really get the disease under somewhat good control.

And so when they did the phase 3 studies, which were the PIONEER studies— those were published probably around 2015—they actually had two arms of the trial; one for patients who were on 40 milligrams weekly and they actually started with a loading dose of 160 milligrams followed by 80 milligrams two weeks later, so it was an even higher dose than we see for patients who have inflammatory bowel disease, for example. And then the other arm was the same adalimumab dose, but they allowed patients to stay on the tetracycline antibiotics as well. And there wasn't really a big difference in the end. Both groups achieved just over 50 percent of the patients meeting the endpoint, which was high score, which is essentially a 50 percent improvement in their overall abscess and nodule count out to week 12 in this study.

And so that's where we started. And I think there's a lot of data now on adalimumab in patients developing, essentially, loss of response or even being primary nonresponders. In clinical practice, that's made it a little bit difficult for this to be the end-all, be-all treatment we have for HS, so there's still a lot of room I think for more therapeutic options.

Dr. Chovatiya:
Very good point. And it does beg the question, do we have any progress in really trying to figure out how we might match the HS patient with the right therapy for them? I know our choices are maybe a little more when it comes to targeted treatment, but do we know? Is there any predictive factors for HS patients that respond better to certain therapies?

Dr. Porter:
I think there's multiple parts to this question. The first thing I'll say is that I think we're doing more work in what I would call, HS phenotype or endotyping, and there's been different categorizations of different types of HS that have been published in different groups across the world essentially. One of the things that I think is really starting to emerge is that there is a type of HS that I would call follicular nodular, but it's also been published in the literature as follicular, and they really define these patients as only having inflammatory nodules, so firm one centimeter lesions, and then small abscesses, like things that didn't really get bigger than one or two centimeters in size ever, and then very rarely they could have one small fistula. In those patients, they have, actually, now published a couple different treatment options for them. And we published a paper on spironolactone saying patients could do better with that type of HS even just taking 50 milligrams of spironolactone daily, and other groups have published dapsone as an option for that type of HS as well. And we always joke now in the HS world that if we see patients like that, they've probably been misdiagnosed as folliculitis many times in their life, but the good news is we have some good therapies that can really help them.

Dr. Chovatiya:

And that leads me to my last question as we close out our discussion, Dr. Porter. Is there additional research needed to understand the pathogenesis of HS? I have a feeling you might say yes, but I'm going to ask you one more question. What might be those things you think that really need to be done for us to have better mechanistic understanding to design better therapies for our patients?

Dr. Porter:
Yeah. Well, you did predict my answer. It was yes. I think, again, there's a couple different things that we're looking at. One is that we really do need to understand the pathogenesis of this disease better, and whether that's understanding it for the entire population or, essentially, teasing out different groups and understanding the pathogenesis for each type I think is to be determined because one of the things we still haven't really done a lot of work in is GWA studies, like finding genetic alterations that may be leading to this disease state. And then I think some of the other things that we haven't fully explored is a therapeutic drug monitoring program for patients who are on TNF-alpha inhibitors. And they do this commonly in gastroenterology for patients who have IBD, and it's actually been really fascinating to me because, essentially, I've tested dozens of patients now who have been on adalimumab and infliximab, some of them for years, and anybody who has antibodies has no disease response. And patients who would be in what we call a therapeutic range for IBD seem to only have partial control with their HS, and so what I'm really finding is that patients need much higher levels of drug in their system, particularly these TNF-alpha inhibitors, to predict response. And so I think we might need to borrow some from other specialties too, like GI, to help us figure out some of these more effective therapies for HS, and then obviously, continued research into more novel therapies that are really designed for HS and not repurposed might also be great in the future.

Dr. Chovatiya:
I couldn't have put it better myself. That was an amazing review of hidradenitis suppurativa. And I really want to thank my guest, Dr. Martina Porter, for sharing her insights. Dr. Porter, thank you so much for joining us today.

Dr. Porter:
Yeah, thanks for having me.

Dr. Chovatiya:
For ReachMD, I'm Dr. Raj Chovatiya. To access this episode and others from Derm Consult, visit ReachMD.com/DermConsult where you can Be Part of the Knowledge. Thanks again for listening.