Improving the Understanding, Diagnosis, and Management of

Generalized Pustular Psoriasis (GPP)

Podcast Series: Episode 1

Adrian: Hello and welcome to "Improving the Understanding, Diagnosis, and Management of Generalized Pustular Psoriasis," a podcast series brought to you by the American Academy of Physician Associates and the France Foundation. This activity is supported by an independent educational grant from Boehringer Ingelheim.

This is episode one of a five-part series focused on generalized pustular psoriasis or GPP. In this episode, we will discuss the pathophysiology of GPP, with a specific focus on the definition and underlying mechanisms of the disease. We're going to talk about the risk factors that contribute to the development of GPP, as well as disease progression that may be a consequence of delayed diagnosis.

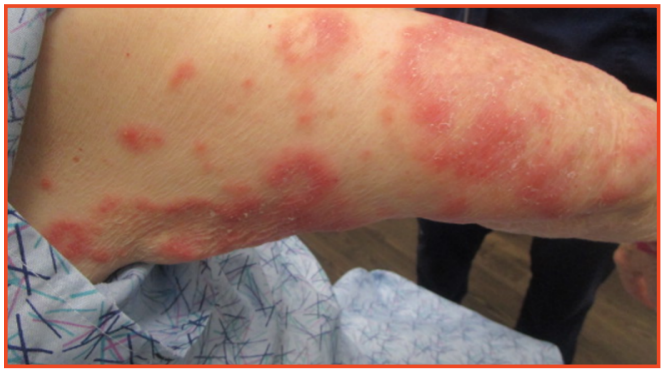
We'll also describe the pathophysiology of GPP related to other skin conditions such as plaque psoriasis. My name is Adrian Banning. I'm a PA and an associate professor in the PA program at Delaware Valley University in Doylestown, Pennsylvania. I'm joined today by my esteemed colleagues, dermatology PA Terri Nagy, and dermatology NP Leigh Ann Pansch, as we discuss generalized pustular psoriasis. Leigh Ann, Terri, thank you so much for being here. Will you each tell us a little bit more about yourselves?

Leigh Ann: Absolutely. I am Leigh Ann Pansch. As you mentioned, I'm a nurse practitioner practicing in dermatology in a private practice setting in the Cincinnati, Ohio area. I've been in practice for about just shy of 15 years. I absolutely love treating inflammatory skin disease.

Terri: My name is Terri Nagy, and as you said, I'm a physician assistant. I've been a PA for actually 25 years, believe it or not, 20 of those years in dermatology. Currently, I'm located in Colorado, but I spent most of my time practicing in Ohio. And like Leigh Ann, I just love taking care of patients who have inflammatory skin diseases, as well as the multitude of other things we get to address every single day.

Adrian: Two absolute all-stars. Definitely the right people to have on today. It is a pleasure to be with both of you today. I can't wait to learn more from you. So let's jump right in. Terri, I wonder if you can talk to us about what GPP is and why it happens.

Terri: GPP stands for generalized pustular psoriasis. You already mentioned this, Adrian. It is actually a really rare diagnosis, which we see in individuals who have a previous history of psoriasis and even in those who do not. Patients usually present with these abrupt, widespread development of very painful erythematous patches and plaques, which soon become covered with these tiny little pinhead pustules. Some of these patients can also have systemic symptoms. They can be very sick with fever, joint pain, and malaise.



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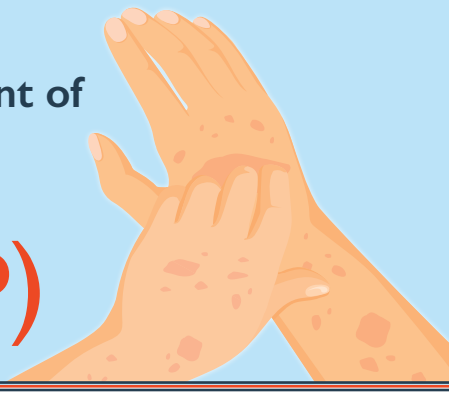

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Terri: The truth about the mechanism of action, unfortunately, it's not clearly understood, but we are learning more every single day. The jury is still out on whether GPP is a variant of plaque psoriasis or if it is completely different disease state. What we do know, GPP differs from plaque psoriasis in regard to what we see histologically, meaning under the microscope, and what is happening genetically.

In some patients, GPP is actually linked to mutations in the IL36RN gene, the IL36RN gene codes for the IL36 receptor antagonist. This regulates inflammation. Because of mutations to the IL36RN gene.

The IL36 receptor antagonist actually doesn't bind effectively to its receptor sites, leading to a dysregulation of the IL36 signaling pathway. This dysregulation, or over-activation of the IO 36 signaling pathway, results in a neutrophilic inflammatory response, leading to proliferation of keratinocytes, and the formation of those sterile pustules that we talked about earlier.

Some patients with GPP actually don't have these genetic mutations in the IL36RN gene. So, what we understand about them is their pathway is believed to be an overreaction or an over-activation of the IL36 signaling caused by mutations and yet other genes.

Adrian: Terri, thank you so much for summarizing that. So, it sounds like GPP is still keeping some of its secrets from us, but we seem to know a lot and it sounds like it's pretty serious. Leigh Ann, now that we know how the process works, sometimes genetics, sometimes not. Will you talk to us about personal risk factors that patients might have that predispose them to GPP development?

Leigh Ann: Absolutely. So, some key findings that might give us little clues that we're actually looking at a generalized pustular psoriasis patient. Our recent corticosteroid use, usually systemic, prior history of psoriasis, and interestingly enough, this is usually mild psoriasis. For instance, they may just have rash on their scalp with little bit of rash, skin infections, hypocalcemia, and we know for pustular psoriasis as a whole, cigarette smoking is a risk factor.

Adrian: I see, so if you see someone and it occurs to you, this might be GPP, you'll ask about those things in their history. Have they ever noticed any psoriasis, even if it's small? Have they had recent steroid use? Things like that.

Leigh Ann: Absolutely.

Adrian: That was so helpful. Okay, so let's say someone with or without those risk factors, that Leigh Ann just outlined for us, finds themselves with the diagnosis of GPP. What can the patient and their healthcare provider expect in terms of disease progression? Terri, can you talk to us about that?

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Terri: That's a really great question, Adrian. What we are hoping for is, with this podcast today, is to develop an increased awareness regarding GPP, its presentation, its triggers, how to diagnose it, and some of the new treatments that are actually available nowadays. The more efficiently and effectively we diagnose and treat these patients, the better the outcome.

Most patients with GPP are more than likely going to need a biologic to control their signs and symptoms. If not, GPP can get scary and it can get scary fast. Generalized pustular psoriasis can actually be life-threatening, as the systemic inflammation associated with the disease states can lead to things such as sepsis, hepatic respiratory, and even renal failure. Sometimes, these patients need to be treated in burn units, as they experience something referred to as erythroderma. This involves at least 90% of the body surface area, and it is an fully exfoliative dermatitis, as these patients are sloughing off all the involved skin. And if you can imagine, if that is over 90% of their body surface area, that's pretty severe.

Adrian: That is something I hadn't considered before, just how serious it is and how much skin loss can occur here. But it makes so much sense when you explain that it can really involve 90%, and then, you're treating these patients kind of like they're burn victims. Thanks for bringing the relevance to this, Terri. That was a really good explanation. So now that we've talked about the mechanisms and the risk factors and progression, Leigh Ann, what are the key takeaways on this material for our listeners in your mind?

Leigh Ann: Personally, I would love to see an increased awareness of the subtleties of generalized pustular psoriasis. I think as providers in this field of dermatology and beyond, it's important that we can recognize that not every time we see a pustule is there actually infection as a cause.

It's also important to recognize that systemic corticosteroids in patients with any history of psoriasis can lead to a significant worsening of their overall disease control. And as providers, we need to focus on encouraging our patients with inflammatory skin disease to avoid smoking, stop smoking, be physically active, and aim to be their healthiest form of who they are.

Adrian: Leigh Ann, thanks for highlighting that systemic steroids are such a problem. I can imagine, for some type of inflammatory conditions, someone who isn't really sure what to do might reach for a systemic corticosteroid at first, so something really important to ask about.

Terri and Leigh Ann, thank you so much for those overviews. They were fantastic about what causes generalized pustular psoriasis and what we can expect as the disease progresses. And listeners, we also want to thank you for tuning into this episode of "Improving the Understanding, Diagnosis, and Management of Generalized Pustular Psoriasis."

Please tune into the other podcast episodes in the series where we talk through the diagnostic challenges, steps to treatment, current and emerging treatments, and implications for patients' quality of life related to GPP. You can find the full list of podcast episodes in AAPA's Learning central catalog at cme.aapa.org.

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