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Diagnosing & Treating Pyoderma Gangrenosum

Dr. Cheeley:
A rare condition called pyoderma gangrenosum, otherwise referred to as PG, is known to cause large and painful sores on the skin, mainly the legs. According to the Mayo Clinic, it is unknown what causes PG. However, patients who may have inflammatory bowel disease, arthritis, or other disorders of the immune system are at an increased risk for developing this condition. So how do we treat our patients with PG?

Welcome to *DermConsult* on ReachMD. I'm Dr. Mary Katherine Cheeley. And joining me today to discuss the best management practices for patients with this rare condition is Dr. Justin Cheeley. He is the assistant professor in the departments of General Internal Medicine and Dermatology, as well as the director of Inpatient Dermatology at the Emory School of Medicine.

Justin, thanks for meeting me on the couch.

Dr. J. Cheeley:
Thanks for being on our couch together.

Dr. Cheeley:
So to start us off, can you tell us how these pyoderma gangrenosum patients generally present in your world?

Dr. J. Cheeley:
So I mostly encounter these patients on the inpatient setting. One of the more common consult reasons I receive is because of an ulcer, and sometimes those ulcers are due to pyoderma gangrenosum. So the patient will come in after having failed multiple rounds of antibiotics on an outpatient for a purulent, suppurative, painful ulcer that's thought to be infectious. And so the patient is admitted for intravenous antibiotics, for surgical consultation, and possible debridement, and something just doesn't look quite right, and that's where dermatology gets called, and that's where I come in. I'll also see these patients on an outpatient basis; however, a little bit less frequently compared to inpatient. That may be in part due to access issues because it's difficult to get in to see a dermatologist. Our practice is not immune to that fact. So I see them both but mostly inpatient.

Dr. Cheeley:
In these patients that you see, have you seen ones that are more at risk of getting this condition?

Dr. J. Cheeley:
So pyoderma gangrenosum usually is a manifestation of some underlying disease. It's estimated anywhere between, I believe, 30 to 70 percent of patients with pyoderma gangrenosum will have some sort of underlying condition. It's just difficult to diagnose these sometimes and to capture them, but yes, underlying conditions make pyoderma gangrenosum more or less likely. The conditions that underly pyoderma gangrenosum, include inflammatory bowel disease, seropositive rheumatoid arthritis—especially that which has been longstanding—other types of inflammatory arthritides, patients with hidradenitis suppurativa, patients with monoclonal gammopathies—

particularly IgA monoclonal gammopathy—individuals with hematologic malignancies or disorders—particularly acute myeloid leukemia and myelodysplastic syndrome—and then sometimes those with solid organ malignancies as well. All carry with them a higher risk of pyoderma gangrenosum. And when I see an ulcer in those individuals with a known underlying disorder that I just mentioned, my suspicions for pyoderma does increase.

Dr. Cheeley:
For those folks that you see in your outpatient practice, I assume you probably catch them earlier in the disease progression. What's the symptomatology look like? How do you normally capture that?

Dr. J. Cheeley:
So usually, the patients will experience what they describe as a spider bite. They think it's some sudden-onset, painful, red bump, sometimes even looks more like a deep bruise. However, it tends to be very painful, so the pain tends to be a little bit increased compared to what you'd expect just visibly seeing the area on the skin. Like you alluded to in the intro, it usually shows up on the legs. And what I find incredibly helpful is when the patient comes to me with an ulcer, I like to know how it progressed. And so thankfully, most patients have cell phones. Those cell phones have cameras. And if they have some gnarly, out-of-this-world, painful ulcer, hopefully they would have taken a picture of it, and so I find it extraordinarily helpful to see visually how this ulcer has progressed up until the time where the patient has seen me. So I find that to be incredibly helpful to deduce the diagnosis because sometimes ulcers converge on a somewhat shared phenotype that is a somewhat dedifferentiated state, and so seeing the ulcer in front of me can be challenging to know if it's from pyoderma or if it's from venous insufficiency or arterial insufficiency or a thrombotic disorder.

Dr. Cheeley:
What treatment options are available for PG?

Dr. J. Cheeley:
Pyoderma gangrenosum responds well to systemic corticosteroids, so usually, systemic corticosteroids dosed at about one milligram per kilogram are my go-to. I want to give them a sufficient dose of steroids to assess response because I find that responsiveness to corticosteroids is one of my more helpful diagnostic tools, so it's both diagnostic and therapeutic. For those patients who are young and have healthy kidneys, cyclosporin can also be used. The challenge with cyclosporin is that while it used to be on the shelves of most pharmacies with the burgeoning biologic boom with psoriasis, cyclosporin is now an order-only medication. And so I'll prescribe cyclosporin for this patient with this painful ulcer, they'll go to the pharmacy, and then the pharmacy has to order it, and it takes a couple more days for the pharmacy to get it in and the patient to get their medication. But if I know of a pharmacy that carries it, cyclosporin is also a really helpful initial step. And so usually, I'll start with cyclosporin and/or systemic corticosteroids and determine a response, and then the responsiveness, for example decrease in pain, decrease in the amounts of suppurative purulent discharge will help guide my diagnostic certainty, and then I can proceed on to some steroid-sparing agents.

Dr. Cheeley:
How long does it normally take to see that responsiveness?

Dr. J. Cheeley:
So having a giant, gnarly, several-centimeter large ulcer that's down to the tendon, you're not going to expect that to heal within a couple days of steroids, so you don't want to look and see that the ulcer heals entirely with your treatment. What you want to see at first is that the patient has decreased pain and that the amount of discharge and drainage decreases and that the wound bed looks healthier. I find that when pyoderma is active, the wound bed tends to be somewhat pale; it has a lot of fibrinonecrotic slough that's sort of yellow, brownish, black that's adherent to it; and then the borders tend to be a little bit more edematous, erythematous, violaceous; and so those things tend to respond within five days or so to corticosteroids or cyclosporin.

Dr. Cheeley:

For those just tuning in, you're listening to *DermConsult* on ReachMD. I'm Dr. Mary Katherine Cheeley, and I'm speaking with Dr. Justin Cheeley about pyoderma gangrenosum, or PG for short.

So let's move a little bit further into the treatment. What would you say is the hardest part of treating pyoderma gangrenosum?

Dr. J. Cheeley:
I think not every patient responds to the same therapies. It's a little bit of a trial and error so to speak, and the problem is, is that as you encounter error and you encounter patients who just aren't responding, you are losing tissue; the patients continue to ulcerate; patients continue to be in pain and agony, social isolation. So finding a therapeutic option that's effective for the patient, much less affordable and obtainable is difficult. Pyoderma gangrenosum is one of those somewhat orphan conditions for which we don't have any FDA-approved treatments. One of the go-to treatments, once I get them bridged and cooled down with cyclosporin or corticosteroids, I might add on like a dapsone or a colchicine, some non-immune-suppressive but immunomodulatory antineutrophilic agents, is to bridge that into some sort of biologic medication. I usually go for tumor necrosis factor inhibitors, like adalimumab, and I typically dose it at the higher end of the dosing spectrum, so typically, the Crohn's disease dosing or hidradenitis disease dosing is what I shoot for. If patients don't respond effectively or if the patient has commercial insurance and I can't find an underlying diagnosis that has an FDA-approved indication for that tumor necrosis factor inhibitor injection, then I will try and pursue infliximab, which is an infusion. And that one sometimes is easier to obtain because it goes through a different part of the patient's insurance plan rather than their drug coverage plan, and I'm able to get that one approved more readily for those patients.

Dr. Cheeley:
It sounds like these patients have to deal with a lot, whether it's the pain or these ulcerations. Are there other comorbidities that are associated with PG?

Dr. J. Cheeley:
I would say the other complicating factor to treating pyoderma is wound care, just the practicalities of wound care. Wound care supplies are challenging to obtain. They are ungodly expensive if you wanted to purchase them just by yourself, so I try and get some sort of outpatient wound care for them. Sometimes I will send them to a wound care clinic. That's another way to get them the wound dressings and wound care that they need with the caveat that wound care clinics I found often have peculiar and particular ways of dealing with wounds. And those are usual wounds. Those are decubitus ulcers and lower extremity, like venous insufficiency ulcers for which debridements and other practices that you'd apply to the wound that you would not want to use on pyoderma wounds. So sometimes you can send them to a wound care center, and they are doing things that actually are making the pyoderma worse, so that can be challenging.

Dr. Cheeley:
I think there's a nugget in there that we often talk about on our way home from work that I want to make sure our listeners hear. Do you debride pyoderma gangrenosum wounds?

Dr. J. Cheeley:
I do not. So debridement is a no-no. Pyoderma manifests something called pathergy, which is where the disease gets worse with tissue trauma, and so debriding the wound, usually surgical debridement, often times revs up the neutrophilic activation and worsens the pyoderma wound over time. Sometimes, I will autolytically debride the ulcer, meaning by keeping the ulcer occluded and in a somewhat balanced moist environment, that allows the body to do its own gentle debridement. That's necessary for that sort of yellow-brown necrotic fibrinous slough that hangs out in the top of these ulcers, but I typically never take a scalpel to these ulcers.

Dr. Cheeley:
So let's switch gears a little bit and talk through the other things that you look for in these PG patients. Do you recommend screening all of these patients for inflammatory bowel disease or other underlying immune disorders?

Dr. J. Cheeley:
I do. When I make a diagnosis of pyoderma gangrenosum, that's not my mic drop moment. I don't stop there. That prompts me to look further and figure out what condition is underlying this that is driving the pyoderma gangrenosum. If I'm able to diagnose or find an underlying condition, chances are that underlying condition may have an FDA-approved indication for a biologic, such as a tumor necrosis factor inhibitor, an IL-12/23 or IL-23 inhibitor that can be effective for pyoderma gangrenosum, and so that enhances my therapeutic armamentarium and affords me and the patient the ability to get medications more readily. The other benefit is that if I'm able to reasonably diagnose with some confidence an underlying condition, that further increases my confidence that what I'm dealing with is indeed pyoderma gangrenosum. And then the last reason why I screen patients for associated conditions is that there is some evidence that finding a comorbid condition and perhaps treating that comorbid condition improves outcomes in pyoderma gangrenosum.

There's a study that was published in the *Journal of the American Academy of Dermatology* back in the summer of '22 that looked at a panel of patients from The Ohio State University who had pyoderma gangrenosum, and those who had an identifiable underlying condition, comorbid condition, overall had better outcomes.

Dr. Cheeley:
What's on the horizon for patients with pyoderma?

Dr. J. Cheeley:
Newer biologic medications that are approved for other conditions are being used in patients with pyoderma, whether they are used for the sole purpose of treating the pyoderma or whether they're used because the patient has a comorbid condition, and some of these newer biologic medications are being used to treat that comorbid condition, and lo and behold it helps their pyoderma. That's kind of a mixed bag. But beyond tumor necrosis factor inhibitors, there's some evidence of using IL-12 and -23 inhibitors like ustekinumab. There's evidence that IL-23 is important in the pathogenesis of pyoderma gangrenosum, and therefore IL-23 inhibitors have been shown to be beneficial in a small cohort of patients as well. And then the newer exciting kids on the block, the Janus kinase inhibitors, or JAK inhibitors, are also being used in the treatment of pyoderma gangrenosum with reportedly good results. So I think that as the landscape of targeted and biologic therapies expand, dermatologists are going to find more and more ways to reapply those medicines to pyoderma to see if there's therapeutic benefit, and thus far it looks promising.

Dr. Cheeley:
Those are some great and important takeaways when it comes to treating our PG patients. I want to thank my guest and husband, Dr. Justin Cheeley, for joining me from the couch today and sharing his insights. Thanks for joining me.

Dr. J. Cheeley:
Thank you for having me.

Dr. Cheeley:
For ReachMD, I'm Dr. Mary Katherine Cheeley. To access this episode and others from DermConsult, visit ReachMD.com/DermConsult where you can Be Part of the Knowledge. Thanks for listening.