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How to Identify and Treat Gout After Failure with Oral Urate-Lowering Therapy

Announcer:

You're listening to *Living Rheum* on ReachMD, and this episode is sponsored by Amgen. Here's your host, Dr. Charles Turck.

Dr. Turck:

Welcome to *Living Rheum* on ReachMD. I'm Dr. Charles Turck, and joining me to discuss how we can identify and treat uncontrolled gout after failure with oral urate-lowering therapy, or ULT for short, is Dr. Robin Dore. Not only is she a board-certified rheumatologist in private practice in Tustin, California, but she's also a Clinical Professor of Medicine at the David Geffen School of Medicine at the University of California, Los Angeles. Dr. Dore, thanks for being here today.

Dr. Dore:

Thank you very much for having me.

Dr. Turck:

So if we start with some background, Dr. Dore, would you briefly tell us about the prevalence and impact of gout?

Dr. Dore:

There's about 9.2 million Americans who have gout, and gout is the most common inflammatory type of arthritis in men. And people think that it's, "Oh, it's just related to what I eat in the diet," but in fact, it really has to do more with clearance of uric acid through the kidneys. And this can be very disabling. People can miss work. If the attacks are not prevented with urate-lowering therapy, we can end up with permanent joint damage and disability. Because the urate is processed by the kidneys, people can also end up with kidney stones and with interstitial nephritis, which can interfere with their kidney function. So this is not just a painful toe; it's a systemic inflammatory condition.

Dr. Turck:

Now as I understand it, oral ULTs are often used to treat patients with gout, but what are some common challenges associated with them?

Dr. Dore:

In my experience, the most common challenge has been that the primary care doctors really don't understand how to treat gout. And so what happens is patients go to urgent cares and are started on indomethacin. We're not supposed to use that in patients who are above the age of 55 due to central nervous system side effects. Other options are prednisone and colchicine, but oftentimes, the patient's acute attack is treated, but then they don't go see their primary care doctor for follow-up to get started on urate-lowering therapy. Or they might get started on urate-lowering therapy during the acute attack, and some studies suggest that that prolongs the extent of the attack. So what's recommended to do, and again, it's hard for patient follow-up, is after the acute attack, you go back, usually 4 or 5 days later still on the colchicine, the steroids, or the indomethacin, and then get started on urate-lowering therapy. This is a really time-intensive disease because you're supposed to start the patients on 100 mg of allopurinol, come back 2 weeks later, and check the uric acid again. And every 2 weeks, increase the dose of allopurinol until the uric acid is below 6. But what we see happen is oftentimes the patients are just started on 300 mg and never have another uric acid level check, or the patients are started on 100 mg and they don't have the dose

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of allopurinol or other urate-lowering therapy titrated to keep that uric acid less than 6. And then, if the patients aren't adequately educated, they end up stopping the allopurinol or other urate-lowering therapy and then have more gout attacks, and then they think the medicine isn't working. So there's a big need for better public knowledge of all the aspects of gout and that it is a chronic condition, not just these acute episodes of arthritis.

Dr. Turck:

So with all that in mind, what are the key signs of uncontrolled gout that we need to be on the lookout for?

Dr. Dore:

What I didn't mention is that if the patients have continued gout attacks, tophi form, which are accumulations of uric acid crystals, and those can damage the joints. So when we're looking at uncontrolled gout, where we're looking at a patient who has the uric acid level that's persistently greater than 6 or a patient who has tophi, our goal of therapy includes preventing further gout attacks, trying to prevent any effect that the elevated uric acid level might have on the kidney, and dissolving tophi if any are there. And often these patients are not even examined to see if they have tophi. But tophi are evidence of uncontrolled gout, and then we need to be much more aggressive with our therapy.

Dr. Turck:

For those just tuning in, you're listening to *Living Rheum* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Robin Dore about how we can evaluate patients for signs of uncontrolled gout.

So, Dr. Dore, once we notice that a patient isn't achieving the target urate levels with an oral ULT, how else can we treat them?

Dr. Dore:

Well, at that point, the patient should really be referred to a gout specialist or someone who has experience in treating uncontrolled gout. At the present time, these patients are usually started on an intravenous medicine called pegloticase, and this is an infusion that's given every 2 weeks. But it's really important that the prescribing provider understands how to prescribe this medicine because when it first came on the market, there were a lot of unknowns. It was great at treating uncontrolled gout, but many patients ended up having infusion reactions. And what we've learned is, one, when the patient is started on the infusions, they need to stop their urate-lowering therapy; and two, they need to be started on an immunosuppressive medicine. The pegloticase is a porcine derivative; it's derived from pig so that the patients can make antibodies directed against the pegloticase. So it's important that the patient be on an immunosuppressive therapy to prevent them from developing antibodies that make it so that the pegloticase infusions are not effective.

In clinical trials that were performed by Jeff Peterson, one of my friends up in Seattle, and others, they looked at using methotrexate. But again, methotrexate can be used, leflunomide can be used, and azathioprine can be used, but the patient needs to continue on that the entire time they're on the pegloticase; otherwise, the medicine might be ineffective.

The other thing that needs to be done is the patients need to have a serum uric acid level measured before each infusion. And typically, if the infusion is helping, the serum uric acid level will be less than 1. But if you start seeing those serum uric acid levels start creeping up to 5.5, 6, 6.5, or 7, that means the treatment is ineffective, the patient is, even with immunosuppressive therapy, making these antibodies, and the therapy needs to be stopped.

So that's why this treatment needs to be prescribed by someone who is familiar with how to not only manage the infusion, but the medications associated with it to make it so the medicine continues to be effective and does not have the infusion reactions.

Dr. Turck:

And are there any other considerations we need to keep in mind when employing pegloticase or the immunosuppressants you mentioned?

Dr. Dore:

Well, of course, the immunosuppressants can increase the risk of infection and can lower the patient's white blood cell count, red blood cell count, and platelet count. So certainly, monitoring for side effects of the immunosuppressive is very important.

The other thing is to monitor the patient. So I have a patient now who has been on pegloticase for 2 years; he had tophi over most of his joints. And so the patients have to be examined, and once their tophi have all resolved, then they can go back on their urate-lowering therapy and stop the pegloticase. So constant monitoring of the patients. Typically, my patients have been on the pegloticase only for 2 to 3 months. They've had maybe one tophus, or maybe their serum uric acid is staying above 6 and I haven't been able to get it under

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control. Or the other thing is perhaps the patient is needing many doses of steroids to get their acute attacks under control, so I put them on the pegloticase, but then I need to monitor them for not only the side effects of the medications, but when it's time to stop the infusion.

Dr. Turck:

And before we close, Dr. Dore, would you share some key takeaways on how we can actively evaluate and treat patients with uncontrolled gout?

Dr. Dore:

There are several important things. One is patient education so they understand the importance of treating this chronic inflammatory condition rather than just treating the acute attacks of arthritis and that they understand that the diet plays very little role; typically, it's a lack of excretion of the uric acid through the kidneys, as well as overproduction in the body, so stress to them how important it is to take their urate-lowering therapy.

And then for the providers, to make certain that they're monitoring that serum uric acid level. With an upper-limit dose of allopurinol, which is 800 mg a day, if that uric acid level doesn't stay below 6, if the patient is below 6 but continues to have frequent attacks of gout, or if the patient has tophi, they need to be referred for pegloticase therapy in order to try to get their disease under control because it's very possible; it's just a matter of the patients understanding their condition and the providers understanding how to prescribe the pegloticase.

Dr. Turck:

With those final reflections in mind, I want to thank my guest, Dr. Robin Dore, for joining me to discuss identification and treatment strategies for uncontrolled gout after failure with oral urate-lowering therapy. Dr. Dore, it was great having you on the program.

Dr. Dore:

Thank you very much for having me. Gout is one of my favorite topics, so thank you.

Announcer:

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