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Case Review: Targets Are Met—Can You Stick the Landing?

Announcer:
Welcome to CE on ReachMD. This activity is provided by Prova Education and is part of our MinuteCE curriculum.

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Ms. Geremia:
This is CE on ReachMD, and I'm Jennifer Geremia and have the pleasure of being joined by Dr. David Rubin. And we're discussing next steps when we have met our treatment targets in IBD. How do we maintain the improvement, and what should we do when patients start failing treatment after an initial response?

Let's take a look at a case. This is a 28-year-old male with a 2-year history of Crohn's disease involving specifically the terminal ileum. This has been confirmed by ileal colonoscopy and MR enterography. His initial treatment was with corticosteroids, with transition to vedolizumab, which led to some early symptom relief. At his most recent follow-up, he reports persistent abdominal pain, loose stools, and persistent back pain that's worse in the morning and improves with movement. Workup reveals an elevation in CRP and fecal calprotectin, and repeat imaging shows active small bowel inflammation. Despite months of receiving vedolizumab, there's been no meaningful improvement in either his GI symptoms or his joint involvement.

Dr. Rubin, in a case like this where an anti-integrin isn't controlling symptoms, how do you think about next steps, and when do you consider switching to another class?

Dr. Rubin:
Thanks, Jennifer. This is a really good point and a very important question, because many patients with Crohn's disease and ulcerative colitis do not respond to their first therapy. So the first thing we want to make sure is that we have given the drug enough time to do its job. There was nothing wrong with selecting vedolizumab as an excellent first choice for a patient with newly diagnosed Crohn's disease, but now this patient's been on the therapy long enough that we should have seen resolution of symptoms and improvement in the inflammatory markers.

So when somebody is having persistent symptoms or losing response, the first thing we want to know is, are they still inflamed? And you've shown us that with the measure of the CRP, the calprotectin, and the imaging study. The second question is, are they infected? Is that complicating response to therapy? Remember that patients with IBD have a higher risk of having infections, whether it's a Clostridioides infection, even without an obvious exposure to antibiotics, or whether they have another infection because of some other exposure. So doing a GI panel and ruling out C. diff is very important.

The third part is, where is the drug? Is the drug present? Has the patient been adherent to the dosing regimen? And this patient, we

would presume, has been. But when they're not taking the drug, or when you suspect there might have been increased clearance, sometimes it's appropriate to measure a drug level. I don't measure drug levels with vedolizumab; the data don't support doing that. But if it were an anti-TNF, there are guidelines that recommend we would want to check a drug level and then try to optimize.

So when somebody is not responding and we have objective measures that it's still inflamed and noninfected, it's time to consider another therapy.

Ms. Geremia:
Thank you. How does the presence in this case of axial spondyloarthritis change your treatment approach in this patient with Crohn's disease, especially when this therapy is addressing both the GI symptoms and the EIMs?

Dr. Rubin:
So really important learning point is that up to 30% or even 40% of people with IBD will have extra-intestinal manifestations, the most common of which is joint pain. And the more common joint pains people get are the peripheral joints—the small joints—but there is a coexisting axial spondyloarthropathy in about 8% of people. That means back pain that can manifest from inflammation of their vertebral bodies and the spaces between them or sacroiliitis involving the pelvic joints.

So you mentioned this patient has ankylosing spondylitis. An anti-integrin therapy, vedolizumab, works specifically and selectively in the gut, so it's not going to treat that problem. So when we're selecting our therapies, if we knew that the patient had this, we should be thinking about either a different treatment added to the vedolizumab, or in this case where there's primary nonresponse, we should pick a therapy that's going to address both problems, and hopefully this person will be feeling much, much better.

Ms. Geremia:
Well, that was a great segue. Do you refer these patients to a rheumatologist given the EIM here?

Dr. Rubin:
It depends on your comfort level. If you're not comfortable evaluating and treating these other conditions, then you might be best working as a team with your rheumatology colleagues. I think that's completely reasonable. In my practice as an IBD specialist, I'm very comfortable treating these, and I obviously know about some of our therapies, whether it's anti-TNF or our Janus kinase inhibitors, the JAK inhibitors that are approved by the FDA for treatment of both problems. The axial spondyloarthropathies and the inflammatory bowel diseases.

So for me, the next treatment in this patient with Crohn's disease would be either an anti-TNF or one of our JAK inhibitors. And specifically here, I would be thinking about upadacitinib, because that most recently had a label update that enables us to give it after someone's been on any other systemic therapy if we think TNF inhibition might be not appropriate for that person.

So you have a couple options here that I think are very reasonable, and should address both problems. But getting back to your point, sending to rheumatology for team approach to management is completely appropriate.

Ms. Geremia:
And in this patient with ongoing small bowel symptoms and elevated biomarkers, what would be your treat-to-target monitoring strategy with this therapeutic change?

Dr. Rubin:
Well, fortunately, you already have some symptoms that you can follow, but you do want something objective. Treating to a target is about quality of life, and it's about making sure that you're matching symptom resolution with objective measures. In this case, it can be your CRP or your calpro, perhaps. In my practice, it would also include intestinal ultrasound of the small bowel, which is a point-of-care test that we now have available at some centers. But if you don't have that, relying on these other markers and then considering repeating the MR enterography and at an appropriate interval, usually 6 months or so down the road, repeating a scope is the best way to know that you're achieving your targets.

Ms. Geremia:
With that, our time is up. Thank you for a great discussion, Dr. Rubin, and thanks to our audience for tuning in.

Dr. Rubin:
Thank you.

Announcer:
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