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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Case Challenges in the Management of IBD

Announcer:
Welcome to CME on ReachMD. This activity, entitled “Case Challenges in the Management of IBD” is provided by Prova Education.

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Dr. Nandi:
Through this series, we have reviewed the desirable endpoints to achieve both clinical and mucosal remission for our IBD patients, but this also requires that we also desire to improve patient-reported outcomes. Our path forward requires a proactive treat-to-target strategy and that we educate our patients on the risks and benefits of their individualized therapies. Shared decision-making is critical. Now, let's put what we have reviewed to the test with a patient case scenario. Let's see if you can help make the best decisions possible to achieve long-term remission in this IBD clinical case.

I'm Dr. Neil Nandi, and I know someone who certainly can, and that is Dr. Sunanda Kane, professor of medicine in the Division of Gastroenterology and Hepatology at the Mayo Clinic. Susie, welcome to our discussion of Case Challenges in the Management of IBD. Are you ready?

Dr. Kane:
You bet, Neil. I was born ready.

Dr. Nandi:
I love the energy. All right, so, Susie, let me introduce you to Katherine. Katherine is a 22-year-old, Caucasian female looking forward to graduating from college. A few days ago, she noticed she was having bloody bowel movements with cramps and urgency. She visited her primary care physician who has referred her to you. Now, since that initial episode, she's experienced around 7 bloody bowel movements per day on average, and several of which have been nocturnal. She complains of urgency and tenesmus. Upon exam, you notice some mild tenderness upon the palpation of her left lower quadrant. Laboratory values show mildly decreased hemoglobin and an elevated CRP at 11 micrograms, a fecal calprotectin at 400. She undergoes a colonoscopy a few days later, which reveals pancolitis with erythema. Her colon shows friability, ulceration, loss of vascularity, and spontaneous bleeding. Biopsies do confirm chronic active colitis. Susie, how would you initiate treatment?

Dr. Kane:
Well, thanks, Neil. I want to just point out first in her exam and in her presentation that you have to make sure that you have ruled out infection like CMV [cytomegalovirus] from the biopsies, but also *C. diff*. As you know, it has become rampant and that easily 1 out of every 3 of our patients who is “flaring,” is doing so because of *C. diff*. So you want to make sure that that fecal calprotectin is being driven completely by ulcerative colitis and not *C. diff*. So having said that, let's assume that she is not infected. This description of her endoscopy would be at least a Mayo 2, if not a 3, because there’s spontaneous bleeding. So she's kind of in trouble. So you have to do something sooner rather than later. And I assume that we're thinking that she has moderate to maybe bordering on severe. She is ambulatory, but she's got nocturnal bowel movements. So you want to do something for her. And remember that women can have

mildly decreased hemoglobins because of iron deficiency if they're menstruating. And that is probably the case in our 22-year-old. And so if you look at the guidelines that were published from the ACG, that she meets criteria for moderate to severe disease and that we recommend and the data suggest that you should start with either MMX budesonide or prednisone as a short bridge to something else just to help get her over some of these acute active symptoms while you are discussing with her what the bridge will be to something else.

Dr. Nandi:
So a couple of great points there, right? We have to rule out infection and other causes like NSAIDs, alcohol, all these other things that may contribute to the flare. Why is she presenting this way, right? And then you have to also be thoughtful about your first bridge agent is what you kind of talked about there with prednisone and budesonide.

Are there any other types of factors that you might consider on what type of biologic you might consider at this point in time?

Dr. Kane:
Right. So I do think that she is an appropriate candidate for a biologic, that she should be transitioned fairly quickly from whatever steroid you choose. It is not appropriate to necessarily give her monotherapy of just an immunomodulator. So don't just start her on a thiopurine for this, but yes, you go straight to the biologic. And so the data would suggest an anti-TNF agent or perhaps vedolizumab as your first agent. And you know what a splash the results from the VARSITY study were when they got announced. And for those of you who aren't necessarily familiar, the VARSITY trial was a double-blind, randomized, controlled trial, head-to-head of vedolizumab to adalimumab in adults with moderate to severe active ulcerative colitis in the outpatient setting. And it turns out that clinical remission was observed in 31% of the vedolizumab group, compared to 22.5% in the adalimumab group, and that was statistically significant.

Dr. Nandi:
Let's say that after some good shared decision-making, the insurance approves an anti-TNF, for instance, and that she is induced and maintained on the anti-TNF. How should we look and what do we need to look for in monitoring her response? How should we define that?

Dr. Kane:
Okay, so that's a really good question. And as you know, there is what the literature says you should do, there's what the books and the guidelines say you should do, and then there's real life, right? So in a perfect world, you would have the patient come back to clinic, you would discuss what her symptoms are. And in a clinical index, if she's having now 1 to 2 formed stools per day without urgency, without bleeding, you can feel pretty confident that she's had a very good clinical response. But in order to say that she's actually met true clinical remission, that you'd probably want to get a look and to see what the mucosa looks like and prove healing. And how quickly do you need to do that? Well, I wouldn't jump the gun and do it at 4 or 6 weeks. I would probably wait 8 at least, or if not 12. Now, having said that, if you have a patient in clinic and she says, “My God, I feel so much better. I feel like what I felt like 6 months ago before I got this diagnosis,” do you really need a flex sig or a colonoscopy? I would argue no because the patient isn't going to necessarily want one. But if you really want to feel comfortable that you can now let the patient go for another 6 months before follow-up, then at least some sort of objective testing should be done, whether that's calprotectin and/or a flex sig. Now, Bill Sandborn would tell you that you should do the flex sig, and I have no problem with that. But patients don't like flex sigs. So if I have to pick and choose, I'm going to for sure do a fecal calprotectin and make sure it's under 200 and also see whether I can talk her into that flex sig. And if not, then feel comfortable that I've documented her clinical response and that calprotectin is below 200 so that there's a good response in that objective marker.

Dr. Nandi:
Absolutely. So if I'm listening to you correctly, you know, you don't just set it and forget it; you start a therapy and then you reassess. Right? And you define with the patient shared decision-making as well – we're going to start you on this medicine. And a couple of months down the line, we're going to agree to some type of clinical assessment, some type of endoscopic assessment, some type of noninvasive marker like a calprotectin.

For those just joining us, this is CME on ReachMD. I'm Dr. Neil Nandi, and I'm here today with Dr. Susie Kane. We're discussing case challenges in IBD.

So I'll tell you, Katherine here had a terrific response to anti-TNF therapy. But unfortunately, after 4 years of good adherence, Katherine notices that she had increasing signs of flare, blood in her stool, diarrhea, tenesmus with, again, nocturnal component of awakening returning. Her calprotectin, again, markedly elevated, and her colonoscopy shows moderate to severe disease. *C. diff*, the usual suspect, is checked off the list. It's not the culprit here. Now, her anti-TNF agents, or actually her anti-TNF level is very low and her antibodies to TNF are very high. Since she had an anti-TNF response, a second anti-TNF in class agent is tried, but two years later, the same scenario has occurred.

So she was very lucky, right? She's had 2 agents, extended the shelf life of that class, but ultimately continued to have active disease. Now, at this time, her biopsychosocial world is completely topsy turvy. She just got married. She graduated law school. She defends doctors, okay? She hopes to have a family after graduation and is currently on oral contraceptives but wants to start a family in the future. This flare is really giving her quite a bit of stress. How do we stratify or position the other therapies in our armamentarium for this young lady who has developed secondary nonresponse status to anti-TNF class of agents?

Dr. Kane:
Okay, well, so as you know, this would be an entire hour-long lecture, not just a few minutes of us talking in the hallway here. So the first thing we have to do is, again, address from an objective standpoint where the level of her disease is. And we want to have her not stop her oral contraceptive because we don't want her getting pregnant while she's having active disease. So at this point, we're going to do a colonoscopy. We are going to check her iron levels, her vitamin D and her B12, just to make sure that her tank is full. And now in terms of therapy, that we've done two anti-TNFs, and so what do we have on the menu? We can give her vedolizumab, we could consider ustekinumab, or we could consider even tofacitinib in this scenario because all 3 of them are FDA-approved for ulcerative colitis and all would be considered a second-line agent after anti-TNFs. So here's where the decision-making is shared. You know, shared discussion about which one we should choose next is appropriate.

Dr. Nandi:
Okay, and I think that's appropriate. You know, we're lucky that we have so many other agents that we can offer patients. We certainly shouldn't burn through them. I think you would agree, maximize one class before you move on to the next.

In regards to the JAK inhibitors, and her desire to get pregnant in the future, can you briefly review what we know about fertility and conception and tofa, and any concern about her being on an oral contraceptive pill, her having active IBD, and any questionable DVT [deep venous thrombosis] risk with tofacitinib?

Dr. Kane:
So that's a whole bunch of info there. I will try not to overwhelm people, but let's just, remember that tofacitinib does have a black box warning for increased risk for shingles and thromboembolic events. The real-world data for tofacitinib use in IBD and thromboembolic events is still in the low double digits. So like 20, 25 patients in total. And those patients all had another risk factor for why they developed a thromboembolic event. She's got active disease and she is on oral contraceptives. So she is at higher risk. And so this is where I would leave tofacitinib as my last choice for her.

Your next question, Neil, is: Well, what if somebody's on tofa and they are well and they want to get pregnant or do get pregnant? Then we don't stop it because they are well, but this is somebody who you're going to have a very short leash on and you're going to have them see high-risk OB and that you are going to be monitoring and following them very carefully and closely in that first and early second trimester until we know that there is a very mature placenta and that the fetus is growing appropriately.

Dr. Nandi:
That's right. And if you are a clinician listening to this podcast and you do have a pregnant mother who is on tofa or any of the biologic medicines, we would encourage you to enroll them into the PIANO registry so we can try to learn more about tofa and the other medicines.

Dr. Kane:
Exactly. Thank you for that plug because I often forget to say that, but yes. And if you are not a site that registers patients, that myself and particularly Dr. Mahadevan are happy to just hear about the patient, and we can take care of enrolling them from a distance.

Dr. Nandi:
So far we've really covered a lot of information. We saw this young 22-year-old college grad get diagnosed with moderate to severe ulcerative colitis, have a good response to 2 TNF agents, but ultimately lost response, graduated to a second class of therapy. And I'm going to give you the conclusion. She did well and she got pregnant and it's a happy story. But sometimes it's not always a happy story.

The good news is we do have data from the PIANO registry and we do have great leaders in the field like yourself, Dr. Kane, Dr. Uma Mahadevan, and others who are helping to further the knowledge that we know about the safety of these medicines and pregnancy.

I guess the other thing that I really like from our conversation is that we highlighted the proactive approach, maximizing your drug, monitoring, rechecking and making sure that you have close ties with the patient.

Well, that's our time today, folks. I really want to thank our entire audience for listening to the entire series. And I want to convey a special thanks to the always humble and always wonderful Dr. Susie Kane.

Dr. Kane:
Thanks, Neil, it's been great to talk to you.

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