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Managing Extraintestinal Manifestations in IBD

Dr. Buch:

Welcome to GI Insights on ReachMD. I'm your host Dr. Peter Buch, and joining us today to discuss extraintestinal manifestations in inflammatory bowel disease, or IBD, is Dr. Katherine Falloon. Dr. Falloon is a gastroenterologist at the Cleveland Clinic, and her research focuses on extraintestinal manifestations in IBD.

Dr. Falloon, welcome to the program.

Dr. Falloon:

Thank you so much for having me.

Dr. Buch:

To start us off, Dr. Falloon, could you give us an overview about the extraintestinal manifestations of inflammatory bowel disease, or IBD, and does the presence of extraintestinal manifestations indicate a worse prognosis?

Dr. Falloon:

Absolutely. Extraintestinal manifestations of IBD are basically any manifestation of IBD that occur outside the gastrointestinal tract. They're actually quite common, at least 50 percent of patients with IBD will ultimately develop an EIM, and about a quarter of patients will present with an EIM before the diagnosis of IBD is even established.

What is actually considered an EIM depends a little bit on which definition you use. The classical EIMs involve the joints, so peripheral and axial arthritis, the skin, so things like erythema nodosum, pyoderma gangrenosum, sweet syndrome, and cutaneous Crohn's, the liver, and biliary tree, so PSC, autoimmune hepatitis, and the eyes, so episcleritis, uveitis, scleritis.

However, there are a number of other conditions that are more commonly seen in patients with IBD, either as a result of the disease itself or of our treatment choices that also can be considered a fall under the EIM umbrella. These include autoimmune pancreatitis, blood clots, anemia, fatigue, pulmonary manifestations, the list can really go on and on.

The relationship to disease activity depends on the EIM. Some are thought to run alongside disease activity, such as erythema nodosum, and then others run classically independently of the underlying IBD disease course, such as PSE. For your second question surrounding prognosis, as we just discussed, EIMs can be associated with disease activity, and they have also been shown to be associated with increased rates of treatment escalation for IBD and of surgery.

They've been associated with morbidity and at times, unfortunately, even increased mortality. I do think it's important to highlight that EIMs are also associated with decreased quality of life for our patients, which makes intuitive sense. Just think, for example, about a patient with peristomal pyoderma gangrenosum.

They're going to have pain, they're going to have issues with pouching, and that's really going to limit their quality of life.

Dr. Buch:

Thank you very much. Moving on to skin manifestations, how do you treat pyoderma gangrenosum? And how does the treatment of erythema nodosum compare with pyoderma?

Dr. Falloon:

So great question. I'll start, if it's okay, with a quick overview of PG, and then I'll move to treatment because I think the first step of treating PG is actually making sure that you're diagnosing PG. The diagnosis isn't always so easy to make. So it presents initially as this painful skin lesion or pustule that progresses into this ulcerated lesion and will have this violaceous undermined border around it.

It can present anywhere, but classic locations are peristomally, like I talked about, and then also on the legs. The buzzword for PG is pathergy, so it's often going to occur at a site of trauma, such as a stoma site. It really needs to be diagnosed and managed with the help of a dermatologist. So when I'm seeing something that's suspicious for PG for me, I'm referring my patients to dermatology right away, and then treating them with a multidisciplinary team approach.

In terms of selecting an IBD medication for these patients, first line is really anti-TNF therapy. There's good data to suggest that the anti-TNF medicines are effective in treating PG, and though I do also want to include the caveat that PG is notoriously hard to treat. JAK inhibitors are usually my second line therapies.

Data for the other IBD medications, such as anti-interleukin therapies is more mixed. We do sometimes use prednisone, azathioprine, and methotrexate. And then depending on the severity of the PG, sometimes dermatology will do steroid injections in clinic. Our colorectal surgeons sometimes do that as well, and then the dermatologist will sometimes prescribe agents focused on the PG, such as dapsone, MMF and IVIG. Erythema nodosum is much more common, it's actually the most common skin manifestation of IBD, and it's much easier to deal with than PG. So it usually goes along with IBD disease activity, and it's classically seen in patients who have active disease and are having a flare. They have these tender, swollen nodules, classically on the extensor surfaces of the lower limb, so over the anterior tibia. And sometimes patients will tell me, it feels like I have a bug bite, but it's painful instead of itchy.

The mainstay of treatment is really controlling the underlying IBD. If you get the luminal inflammation under control, the skin inflammation usually gets better too. If you're running into trouble, steroids can be quite effective.

Dr. Buch:

So what's your approach to treating the arthritis of IBD?

Dr. Falloon:

Yeah, so I like this question because arthritis is one of my big research interests, and I like to break it down really into two categories. So you have peripheral arthritis and axial arthritis. I'll start with peripheral. I led a modified Delphi consensus panel through the Cohort for Healing Arthritis, Skin and Eye Extraintestinal Manifestations, or Chase EIM, and basically we developed definitions and treatment targets for five key EIMs, including peripheral arthritis.

And what you're looking for to diagnose peripheral arthritis is basically some combination of morning stiffness, joint pain, and a swollen or tender joint on exam with exclusion of other etiologies. Peripheral arthritis may or may not coincide with active IBD, but if there is active luminal IBD, that's always the first place I start, I try to get that luminal IBD into remission and see if that helps with my joint pain.

If the pain is severe, steroids again can be really effective, though obviously not a good long term solution for our patients. Similarly to PGE, joint infections can also sometimes be considered with the steroid. In terms of medications, five Aminosalicylates, and in particular Sulfasalazine, have good data, so I'll often start there.

Anti-TNF agents, again, have good data. JAK inhibitors, again, have good data. Mixed data for Vitolizumab, and then also some mixed or limited data for anti-interleukin agents and S1P. For Axial Arthritis, this is presenting as an inflammatory back pain. They're having back pain, morning stiffness. These are often younger patients.

And while I have a really low threshold for involving rheumatology and peripheral arthritis, for axial arthritis, rheumatology involvement early on is a must because this arthritis can progress and lead to joint damage. So you really want to be referring right away if you're thinking about axial arthritis. I just refer to rheumatology, and then taking a multidisciplinary team approach to care is essential. Medication choices for axial are much more limited than for peripheral arthritis. The agents we're really thinking about are anti-TNF agents and JAK inhibitors as medicines that would target both the IBD and the axial arthritis.

I think a question that often comes up is non-steroidal, anti-inflammatory agents in our IBD patients and classically the teaching is don't give any NSAIDs to IBD patients, but they can actually be highly effective in managing joint pain, and there's some emerging data that they can, in particular selective COX-2 inhibitors, be safe.

So I will sometimes use these short term in patients with severe joint pain depending on the clinical scenario.

Dr. Buch:

And a follow up question again for our primary care colleagues who are listening is I think that they sometimes get a little bit concerned about using NSAIDs in patients with ulcerative colitis. Can you comment a little bit about that and make them feel a little bit more comfortable about this process?

Dr. Falloon:

Yeah, so there has been some recent data that hasn't shown that these are really leading to worse outcomes or flares in our IBD patients. So again, I wouldn't be routinely prescribing them or prescribing them in the long term, but if you have a patient who has severe joint pain, and especially if their IBD is under reasonable control and you're just trying to bridge until you can get them in with either GI or rheumatology or both.

I don't think it's unreasonable to do a short course of a selective COX-2 inhibitor.

Dr. Buch:

Thank you so much. So let's move on to this next topic, Dr. Falloon. What should we know about cholelithiasis and nephrolithiasis in IBD?

Dr. Falloon:

So to keep it simple, the IBD patients are at increased risk for both of those. And there was a systematic review that was just published a couple years ago that found an increased risk of gallstones in patients with both UC and Crohn's. To your question earlier in the talk, the risk was higher in Crohn's disease.

It looked like the Swiss IBD cohort study has given us a lot of data about patients with extraintestinal manifestations and they found risk factors for gallstones to include Crohn's disease activity and duration, NSAID use actually, and intestinal surgery, and then other EIMs. For nephrolithiasis, again, it's actually Crohn's disease patients who have been shown to be at increased risk, especially, UC too.

And they can get either uric acid or calcium oxalate stones. And again, from that Swiss IBD cohort, risk factors here were male gender, disease activity, intestinal surgery, NSAID use. And then interestingly, reduced physical activity as well was another risk factor. And then for both, patients being hospitalized increased risk, and then having one increase the risk of the other.

And I think that highlights an important point for EIMs in general. Once you have a patient with one EIM, you want to be looking out for others because they're at increased risk of developing concurrent EIMs.

Dr. Buch:

For those just tuning in, you're listening to GI Insights on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Katherine Falloon about extraintestinal manifestations of IBD. Let's move on to thromboembolism prophylaxis for hospitalized patients with inflammatory bowel disease. What are the guidelines?

Dr. Falloon:

Yeah, so this is an important topic because thrombotic events are more than two times as common in our patients with IBD as those in the general population. And luckily, there are numerous guidelines from various societies that tell us what to do. As the European Crohn's and Colitis Organization, the American College of Gastroenterology, basically all agree we should be using DVT prophylaxis in our patients who are hospitalized and have IBD.

The ECHO guidelines were the most recent, and they recommend the use of either low weight heparin or fondaparinux in this patient population. And I think this really is a key take home point from this session because when we give prophylaxis to our IBD patients, they have over a 50 percent decrease in the risk of clot without an increased risk of major bleeding episodes.

So we really should be giving thromboembolic prophylaxis to our hospitalized patients with IBD.

Dr. Buch:

Yeah, so again, primarily for our primary care providers, very important concept that they need to understand.

Dr. Fallon, that led me to another thought, and are you aware of the compliance out there in the United States with regard to the prophylaxis? How well are we doing?

Dr. Falloon:

Still not great. So there's lots of room for improvement in this area, and again, I think it's just because providers are worried because these patients are already bleeding. But this is a place in our care of IBD patients where we really could improve a lot and help improve their outcomes.

Dr. Buch:

Thank you for that. Let's talk a little about a controversial area. Should outpatients with exacerbations of IBD receive anticoagulation as well?

Dr. Falloon:

Yeah, so this is a trickier question to answer as you pointed to because this hasn't been as well studied. So the absolute risk of clot in these patients remains low. Studies haven't shown as of yet that anticoagulation is cost effective. And so for both of those reasons, the guidelines, I just referenced suggests that for those with severe flare in the ambulatory setting, you can consider thromboprophylaxis, but it's not recommended for all patients.

So basically, in general, my answer is no, but we do want to be making the decision on a case by case basis based on risk. And when you're thinking about risk, the guidelines actually go through very nicely and give you major risk factors, and then mild to moderate risk factors. I'll highlight a few of them.

So major risk factors include surgery, especially if they're having prolonged surgery. So greater than 30 minutes of anesthesia within the past three months. And then other things that make sense if they're immobile, if they have active malignancy, if they're at high risk for clot due to underlying conditions, such as antiphospholipid syndrome or antithrombin risk factors.

Those are major risk factors. And then more mild to moderate risk factors are patients who are over 65, patients who have a central venous catheter in place. Those who are using estrogens for any reason. Other lower risk factor five line and protein C, protein S.

Obese patients, those with recent infections, those on flights, again, a lot of it makes intuitive sense as you're thinking through. I wanted to highlight one risk factor is pregnancy in the postpartum period, especially if you have a pregnant patient with IBD who underwent a C-section, and then I think about history of clot during a prior flare too.

So if you have somebody who tells me the last time I was in the hospital, I got a clot and now they're in a flare again, that's going to trigger me to more seriously consider the anticoagulation.

Dr. Buch:

This has been a spectacular review of the extraintestinal manifestations in IBD, and I'd like to thank my guest, Dr. Kathleen Falloon, for sharing her research and insights today. Dr. Falloon, it's been a pleasure speaking with you.

Dr. Falloon:

Thank you, you as well. I really appreciate you having me here.

Dr. Buch:

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit GI Insights on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.