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Clarifying Best Practices for Treating Fistulizing Crohn's Disease

Dr. Buch:

The best practices for treating fistulizing Crohn's disease requires a coordinated effort involving many disciplines. Welcome to *GI Insights* on ReachMD, I'm Dr. Peter Buch. And joining us today to clarify those approaches is Dr. Miguel Regueiro, who's the Chair of the Digestive Disease and Surgery Institute at Cleveland Clinic.

We're really pleased to have you join us on today's program, Dr. Regueiro.

Dr. Regueiro:

Thank you for having me.

Dr. Buch:

So let's start at the basics. Before we start medications, let's just have a little discussion about seton placement and your experience with regard to that.

Dr. Regueiro:

A seton placement is an important part of the treatment of fistulizing Crohn's disease, and specifically perianal fistula. It is normally placed by a colorectal surgeon or a surgeon. And simply put, it's a small thread, or looks like a rubber band, that is passed through the fistula that allows for any infection or abscess to drain.

Dr. Buch:

Thank you. And when treating fistulizing Crohn's disease, infliximab has been shown to be the most efficacious biologic. Would you comment about the newer biologics, please?

Dr. Regueiro:

It is true that infliximab has the best treatment data and has the best treatment efficacy for fistulizing Crohn's disease and perianal fistula. There are newer biologics and classes of biologic therapies, such as vedolizumab, ustekinumab, risankizumab, to name a few. And out of the newer biologics, there are post-hoc data showing that there may be benefits with these newer treatments in fistula. And while this was not a priority the way it was with infliximab, some of the data look quite compelling and quite good for fistula, as well.

Dr. Buch:

Can you share with us a little bit more about that data that's available?

Dr. Regueiro:

The post-hoc data with ustekinumab and vedolizumab specifically show that there is a higher percentage of patients who are able to heal their perianal fistula compared to Crohn's disease. And while again this was post-hoc, looking back at the data from the pivotal studies this was still enough of a signal that has been beneficial. And then there are open-label studies that have been done with both vedolizumab and ustekinumab that have shown decrease in fistula drainage and improvements in fistula closure.

Dr. Buch:

That's extremely helpful. And with that in mind, when should we be using combination therapy, including anti-TNFs plus antibiotics and/or immunomodulators?

Dr. Regueiro:

Most of us feel that an anti-TNF, such as adalimumab or infliximab, in combination with an immunomodulator, such as a thiopurine, has the best benefit to use that combination approach at healing fistula. One of the questions is the role of antibiotics, and antibiotics have historically been used to treat fistula and the infection related to fistula, but there is some thought that certain antibiotics, such as metronidazole and/or ciprofloxacin in combination with a biologic may lend better healing. But simply put, the best combination that we have for perianal fistula is an anti-TNF, like adalimumab or infliximab in combination with a thiopurine.

Dr. Buch:

And moving on to cutting-edge material, what should we know about fibrin glue, bioprosthetic plugs—and something that you're doing at Cleveland Clinic—mesenchymal stem cell therapy?

Dr. Regueiro:

There have been a number of newer approaches to fistula, and I think it's important to note that perianal fistula has been one of the most vexing diseases to treat and understandably one of the most frustrating for patients, meaning the perianal fistula often—even with the best medication approach or best setons—patients will still have drainage of stool or liquid around their perianal area. And obviously, that can be disconcerting and have a high impact on quality of life. So one of the areas that's been looked at is, can we actually plug or close the fistula in some more direct fashion? So fibrin glue and bioprosthetic plugs have been looked at, and transparently, these have been less than fulfilling in terms of efficacy. Oftentimes, they might plug for a little bit but then drop off, or it might actually lead to just continued drainage of the fistula.

An area that's been most exciting has been more recently at Cleveland Clinic and other sites. The idea of mesenchymal stem cell therapy is where you inject stem cells directly into the fistula tract, and it essentially grows normal tissue or allows for healing of the track. And our hope in the future is this will allow for complete resolution and healing of the perianal fistula.

Dr. Buch:

Thank you very much for that.

For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Miguel Regueiro about fistulizing Crohn's disease.

Let's now move on to other Crohn's fistulas. Dr. Regueiro, what's your approach to treating enterovesicular or rectovaginal fistulas?

Dr. Regueiro:

Enterovesicular fistulas are usually a fistula that emanates from a small intestine or colon and goes to the bladder, rectovaginal fistulas between the rectum and the vagina. These are more internal fistula. So unlike the perianal fistula, which are outside to the skin around the anal area, these are internal. These are some of the more difficult fistula to treat because these aren't ones that a seton can be placed. These are, again, deep inside. And in my opinion, oftentimes, these are fistula that requires some type of surgery to remove that part of the intestine where the fistula is and essentially reconnect and completely heal. So our approach has been medical therapy, like perianal fistula with an anti-TNF and immunomodulator, but sometimes surgery is needed for these.

Dr. Buch:

And when we're thinking about anti-TNF therapy, for instance on these patients, how much time would you give them before you move on to surgery?

Dr. Regueiro:

We usually give the enterovesicular and rectovaginal fistula on an anti-TNF about six months, assuming the patient is doing okay on the anti-TNF therapy, to see if that will heal the enterovesicular or rectovaginal fistula. If at the end of the six-month period of time on an anti-TNF there's still an open fistula to either the bladder or to the vagina and we're not making progress with our medical therapy, this is then a time when more of a surgical approach is needed.

Dr. Buch:

And again, another segue to that question we talked previously about the newer biologics for fistulizing Crohn's disease. In this particular situation, would you head directly to the newer biologics for enterovesicular or rectovaginal fistulas?

Dr. Regueiro:

Not necessarily. Head to the newer biologics if they've been on nothing. So what I mean by that, if somebody comes in bio-naive and has an enterovesicular or rectovaginal fistula, we still might use infliximab for example, being probably the oldest and best studied as the first-line therapy. However, if a patient has been on an anti-TNF—infliximab and/or adalimumab, already—then yes, we would consider one of the newer biologics, such as ustekinumab, risankizumab, or vedolizumab as three of the monoclonal, newer biologic therapies.

Dr. Buch:

Very helpful. Thank you. How do you approach enterocutaneous fistulas?

Dr. Regueiro:

We really have to ask ourselves, "Why is the patient developing an enterocutaneous fistula?" So this is a fistula that usually comes from the small intestine, to the abdominal wall. And in my opinion, these come usually out of two reasons. One is that a patient has developed an abscess around the intestine, and this is percutaneously drained. So for example, the radiologist under CAT scan or ultrasound passes a needle to drain the abscessed cavity, and then leaves a draining catheter in that area to allow all of the infection and abscess to drain out. When the drain is removed, there's essentially a track that is formed from the skin to the intestine because that's where the drain was, and sometimes that does not allow for healing, so the fistula or this fistula is created; this track is created. The other time that we see this is in people who have a stricture in the intestine, and above that their bowel is dilated; they have an obstruction. And if there's an obstruction, high pressure—if you imagine kinking a garden hose, that's the stricture. And above that, you get high pressure. And then you get a little pinhole in that area, like Crohn's disease causes a hole in the intestine, and if that's close to the abdominal wall, that sometimes would track out in the path of least resistance and form a fistula to the skin to allow for drainage.

Dr. Buch:

Before we conclude, are there any other thoughts you would like to share with our audience?

Dr. Regueiro:

I think this is a time for great hope in Crohn's and fistula. For Crohn's in general, we're coming up with newer therapies. We discussed some today. There are some on the horizon that will come out in the next year or two, so there's great hope for treatment, and then with other therapies like stem cells and other treatments. I think this is a time that we are finally seeing remission of Crohn's and fistula in a way we had never seen before.

Dr. Buch:

This was a very practical discussion on the management of fistulizing Crohn's disease. And I want to thank my guest, Dr. Miguel Regueiro, for sharing his insights.

Dr. Regueiro, thanks so much for joining us today.

Dr. Regueiro:

Thank you very much. It was my pleasure.

Dr. Buch:

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can Be Part of the Knowledge. Thanks for listening and see you next time.