ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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Management of Fistulas in Patients With Crohn's Disease

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G&H How common are fistulas in patients with Crohn's disease, and which patients are at greatest risk of developing them?

AL Approximately 25% of patients with Crohn's disease will have a perianal fistula and 10% of female patients with Crohn's disease will have a rectovaginal fistula. The main risk factor is proctitis, or inflammation of the rectum; thus, a higher proportion of patients with proctitis will have perianal disease or perianal fistula involvement.

G&H What are the current treatment options for fistulas?

AL There are medical and surgical therapeutic options. The medical side consists of biologics and monoclonal antibodies. There will often be symptom improvement with these agents and potentially resolution of proctitis, but only perhaps one-quarter of fistulas will heal. Although there are a number of medical treatments currently being used for Crohn's disease, none of these agents, including the newer biologics, have been shown to be better than others specifically for treating fistulas. Thus, the majority of patients will need some type of surgical intervention. The surgical treatment that is most often performed is placement of a seton, which acts like a drain and prevents infection or abscess from building up in this area. It does not heal the fistula, and many patients will live with setons for years. If a patient does not have any rectal inflammation and only has 1 fistula tract, then surgical treatments such as a mucosal advancement flap or a ligation of intersphincteric fistula tract procedure can be performed. Unfortunately, however, many patients will have some type of rectal inflammation or they will have multiple tracts or branching tracts. The options to treat such patients surgically are limited. Many times, the only treatment options are setons. Currently, treatment efficacy is better for perianal fistulas compared with rectovaginal fistulas (approximately 30% vs 10%-20%, respectively). Unfortunately, the fistulizing phenotype of Crohn's disease is notoriously difficult to treat effectively.

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G&H What complications may occur when performing surgical treatment for fistulas?

AL The main potential complication is incontinence. Owing to the closeness of the sphincter, the surgeon may

injure the sphincter complex and cause a degree of incontinence when performing any surgical intervention. That is why the surgeon has to be especially careful when performing a fistulotomy, which cuts through the fistula tract. This is only performed when little to no sphincter is involved.

G&H How are patients typically followed after surgical treatment for fistulas?

AL Patients are seen by the surgeon approximately 6 weeks after surgery. They are regularly followed by gastroenterologists, as they are often on medications for intestinal disease that they may have as well. They will typically contact the surgeon if they continue to have fistula symptoms.

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G&H Are there any other treatment approaches that should be considered, such as those involving endoscopy, lasers, or video-assisted technology?

AL Currently, no endoscopic techniques have shown much benefit for the treatment of fistulas. Lasers are being used more often in Europe; they are not used much for fistulas in the United States at this time. Video-assisted technology has been used in this country for fistulas, but I do not have much experience with this approach.

G&H What clinical trial data have been reported on stem cell therapy for fistulas in patients with Crohn's disease?

AL There is an increasing number of clinical trials in this area, and more and more data are showing that this approach is safe. No significant adverse events have been reported with stem cell therapy or the direct injection of stem cells. Additionally, there is no risk of incontinence, and the efficacy of this approach is quite high. Most recently, a phase 3 clinical trial was completed with nearly 300 patients that showed a significant benefit with stem cell therapy compared with placebo. Healing rates were greater than 50% with stem cell therapy compared with approximately 33% in the placebo group. Healing is thought to be related to the anti-inflammatory and immunomodulatory benefits of stem cell therapy.

G&H Have clinical trials looked at different stem cell doses, sources, and modes of delivery?

AL Different doses have not been compared or studied to date in large clinical trials. Sources of stem cells used in trials have been either bone marrow or fat tissue, but trials have not directly compared outcomes from the 2 sources. Modes of stem cell delivery have been limited to direct injection or placement on a plug. Stem cells placed on a plug were studied only in one trial of 20 patients to date. The other trials have all included direct injection of stem cells by the internal opening of the fistula tract and around the external opening parallel to the tract.

G&H How long do the effects of stem cell therapy appear to last?

AL The largest and only phase 3 study that has been conducted to date goes out to 1 year. In this study, patients who had healed at 6 months were still healed at 1 year. Smaller studies have reported that healing is sustained out to 4 years. Thus, it appears that the effects of stem cell therapy are long-lasting and that healing rates are durable.

G&H What is the risk of fistula recurrence, and how can this risk be reduced?

AL The risk of recurrence is very high; fistulas will recur in two-thirds of patients. The best way to reduce recurrence is to maintain good disease control in the rectum and prevent inflammation from developing there. This is most often done by being on maintenance medical therapy, usually with biologics.

G&H Are there any considerations that should be kept in mind in terms of managing Crohn's disease patients who have fistulas?

AL It is important to make sure that physical examinations of patients with Crohn's disease are performed looking for fistulas because patients may not want to talk about their symptoms. Examination is very simple; it can be performed in the office and just requires looking at

the patient's perianal area. In addition, it is important to ask patients specifically about symptoms. The main symptom of fistulas is drainage, so patients with fistulas may describe having to wear a pad because they have ongoing drainage.

G&H What are the next steps in research in terms of fistula management? Are there any promising therapeutic approaches in development?

AL The main promising therapeutic approach currently being investigated is stem cell therapy. Further research is required before it can be used in clinical practice. Thus, the next steps in research involve trying to expand stem cell therapy, particularly in terms of identifying the optimal dosage, as well as determining whether it can be used to treat more severe phenotypes of fistulas.

Disclosures

Dr Lightner has served as a consultant for Takeda, Ossium, and Mesoblast.

Suggested Reading

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