Title

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CLINICAL VIGNETTE

Vedolizumab Treatment of Budesonide-refractory Microscopic Colitis

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Case

A 61-year-old woman with lymphocytic colitis for six years presented with ongoing diarrhea despite use of budesonide 6 mg daily. She had taken Meloxicam when she was diagnosed, but diarrhea persisted. Prior medications included initial treatment with bismuth subsalicylate, cholestyramine, and loperamide which were ineffective. She started an induction course of budesonide the year following diagnosis, with good response. However, due to frequently relapsing diarrhea, she required multiple induction courses of budesonide and eventually required maintenance budesonide. Daily doses alternated between 3 to 6 mg of budesonide, which she continued for nearly four years.

At the time of presentation, she had been taking budesonide 6 mg daily for the preceding ten months. Lowering budesonide below this threshold resulted in increased bowel movements. Despite used of 6 mg budesonide, she reported five to seven watery bowel movements per day. She denied any significant weight loss. Physical examination was unremarkable. Laboratory evaluation for alternate causes of diarrhea were negative, including evaluation for Celiac disease and infectious etiologies.

She was started on Vedolizumab for budesonide-refractory microscopic colitis. After completing induction she had considerable reduction in her bowel movements. Stool output improved to one formed movement daily, with 1-2 watery bowel movement each week. She tapered off budesonide completely within 3 months of starting vedolizumab maintenance infusions. Due to prolonged budesonide use, she developed secondary adrenal insufficiency requiring hydrocortisone. She is following closely by endocrinology, directly tapering hydrocortisone. Baseline bone density testing was normal.

Discussion

Microscopic colitis is found in up to 10% of all patients evaluated for chronic diarrhea.[1] Diagnosis of microscopic colitis requires chronic, watery, non-bloody diarrhea, in combination with a normal (or almost normal) appearing colon on colonoscopy, with distinct histologic findings. Microscopic colitis can histologically as either collagenous colitis or lymphocytic colitis. In collagenous colitis, a sub-epithelial collagen band spanning at least 10 micrometers in thickness is present. Lymphocytic colitis has at least 20 intraepithelial lymphocytes per 100 epithelial cells. Due to the patchiness of the disease, at least 8 biopsies should be taken from different areas of the colon.[2]

Pathophysiology of microscopic colitis involves migration of medications or bacterial antigens into the colonic sub-epithelial space, with dysregulated immune and inflammatory reactions. Proton pump inhibitors and non-steroidal anti-inflammatory drugs are strongly implicated in drug-induced microscopic colitis.[3] There also may be a component of bile acid mal-absorption in this disease.

Treatment for microscopic colitis involves stopping any medication that may be contributing to disease development. Cholestyramine may be useful in mild cases of microscopic colitis.[4] For more moderate or severe cases, budesonide is strongly recommended for induction of remission.[5] However, up to 80% of patients with microscopic colitis will relapse after discontinuing budesonide.[1] Some patients require repeat induction courses of budesonide. Most relapsing patients require long-term budesonide maintenance. Lower doses of long-term budesonide (3 mg daily or every other day), up to 9 years is considered safe with no increased osteopenia, hypertension, cataracts, glaucoma, or diabetes mellitus.[6]

However, patients who do not respond or have a suboptimal response to budesonide need alternate therapy. Currently limited evidence supports the use of biological agents in microscopic colitis, limited to case reports and limited case series. Anti-TNF agents (infliximab and adalimumab) as well as the anti-integrin agent vedolizumab have shown promise in treating budesonide-refractory disease. A paucity of randomized controlled trials makes it difficult to directly compare the efficacy of these agents. Most patients placed on biologic therapy for budesonide-refractory disease respond.[7] Diverting ileostomy is an acceptable alternative for patients failing all medical therapy.

Conclusion

Budesonide is first-line therapy for the induction and maintenance of remission in microscopic colitis. Patients in which a provoking medication cannot be identified and discontinued, have high rates of diarrhea relapse. Biologic therapies like vedolizumab show promise in treating budesonide-refractory disease.

REFERENCES

1. **Boivineau G, Zallot C, Zerbib F, Plastaras L, Amiot A, Boivineau L, Koch S, Peyrin-Biroulet L, Vuitton L**. Biologic Therapy for Budesonide-refractory, -dependent or -intolerant Microscopic Colitis: a Multicentre Cohort Study from the GETAID. *J Crohns Colitis*. 2022 Dec 5;16(12):1816-1824. doi: 10.1093/ecco-jcc/jjac089. PMID: 35793161.
2. **Pardi DS**. Diagnosis and Management of Microscopic Colitis. *Am J Gastroenterol*. 2017 Jan;112(1):78-85. doi: 10.1038/ajg.2016.477. Epub 2016 Nov 29. PMID: 27897155.
3. **Masclee GM, Coloma PM, Kuipers EJ, Sturkenboom MC**. Increased risk of microscopic colitis with use of proton pump inhibitors and non-steroidal anti-inflammatory drugs. *Am J Gastroenterol*. 2015 May;110(5):749-59. doi: 10.1038/ajg.2015.119. Epub 2015 Apr 28. PMID: 25916221.
4. **Miehlke S, Guagnozzi D, Zabana Y, Tontini GE, Kanstrup Fiehn AM, Wildt S, Bohr J, Bonderup O, Bouma G, D'Amato M, Heiberg Engel PJ, Fernandez-Banares F, Macaigne G, Hjortswang H, Hultgren-Hörnquist E, Koulaouzidis A, Kupcinskas J, Landolfi S, Latella G, Lucendo A, Lyutakov I, Madisch A, Magro F, Marlicz W, Mihaly E, Munck LK, Ostvik AE, Patai ÁV, Penchev P, Skonieczna-Żydecka K, Verhaegh B, Münch A**. European guidelines on microscopic colitis: United European Gastroenterology and European Microscopic Colitis Group statements and recommendations. *United European Gastroenterol J*. 2021 Feb 22;9(1):13–37. doi: 10.1177/2050640620951905. Epub ahead of print. PMID: 33619914; PMCID: PMC8259259.
5. **Nguyen GC, Smalley WE, Vege SS, Carrasco-Labra A; Clinical Guidelines Committee**. American Gastroenterological Association Institute Guideline on the Medical Management of Microscopic Colitis. *Gastroenterology*. 2016 Jan;150(1):242-6; quiz e17-8. doi: 10.1053/j.gastro.2015.11.008. Epub 2015 Nov 14. PMID: 26584605.
6. **Tome J, Sehgal K, Kamboj AK, Comstock B, Harmsen WS, Khanna S, Pardi DS**. Budesonide Maintenance in Microscopic Colitis: Clinical Outcomes and Safety Profile From a Population-Based Study. *Am J Gastroenterol*. 2022 Aug 1;117(8):1311-1315. doi: 10.14309/ajg.0000000000001774. Epub 2022 Apr 13. PMID: 35417427; PMCID: PMC9612589.
7. **Taneja V, El-Dallal M, Anand RS, Haq Z, Mishkin B, Feuerstein JD**. Efficacy and safety of biologic therapy in microscopic colitis: systematic review and meta-analysis. *Eur J Gastroenterol Hepatol*. 2022 Oct 1;34(10):1000-1006. doi: 10.1097/MEG.0000000000002409. Epub 2022 Jul 19. PMID: 36052677.