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CLINICAL POSTERS

P-019

Ustekinumab IV 6 mg/kg Loading Dose Re-induction Improves Clinical and Endoscopic Response in Crohn's Disease: A Case Series

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CASE: Ustekinumab, a monoclonal antibody to the p40 subunit shared by interleukins-12,23, is approved for treatment of patients with moderate to severe Crohn's disease(CD) with a weight-based intravenous ustekinumab induction followed by subcutaneous maintenance therapy (Feagan et al, 2016). TNF inhibitors are associated with clinical and endoscopic response. Among anti-TNF experienced patients receiving induction at Week 6, higher serum drug concentrations are associated with clinical response, suggesting that there may be a therapeutic benefit to optimizing ustekinumab drug concentrations to augment clinical response (Sandborn et al, 2012). We present our preliminary experience at a tertiary care center to support this hypothesis.
We report 3 patients with moderate to severe anti-TNF experienced CD initiated on ustekinumab therapy, who had minimal response after non-weight based subcutaneous induction; loading with intravenous weight-based Ustekinumab led to clinical and/or endoscopic improvement (Table 1).
Patient 1 was a 35-year-old woman with ileocolonic CD with prior intestinal resections and colectomy with ileoanal pouch who had failed multiple anti-TNF therapies and vedolizumab. The patient had improvement in clinical and endoscopic measures after intravenous reloading with ustekinumab. Initiation of ustekinumab combination therapy as well as steroids did not improve disease activity; however, pouchoscopy three months after reloading dose showed improvement in endoscopic disease activity, and the patient was able to wean off corticosteroids.
Patient 2 was a 44-year-old man with history of Crohn's ileocolitis with perianal fistulas with prior small bowel resections. The patient was a primary non-responder to Infliximab and did not respond to Vedolizumab combination therapy. He was initiated on ustekinumab combination therapy with improvement in ulceration at the ileocolonic anastomosis; however, he had ongoing abdominal pain, diarrhea, and perianal drainage. After intravenous induction with ustekinumab, his clinical symptoms improved and was able to taper off steroids.
Patient 3 was a 26-year-old man with history of ileocolonic Crohn's disease who had secondary loss of response to Infliximab therapy, primary non-response to adalimumab, and was started on ustekinumab combination therapy. He was subsequently hospitalized with an intra-abdominal abscess requiring drainage and antibiotics. After intravenous reinduction of ustekinumab, he had clinical and endoscopic response and successfully tapered off steroids.
All 3 patients showed improvement in clinical response after intravenous dosing of ustekinumab with successful tapering of corticosteroids. Endoscopic evaluations showed endoscopic as well as histologic improvement. With further development of therapeutic drug monitoring for ustekinumab, drug concentrations may aid in the use of intravenous loading of ustekinumab, identifying appropriate patients where a rescue dose may augment a sub-optimal response. Based on these preliminary findings, re-induction dosing of ustekinumab in patients on maintenance therapy with sub-optimal clinical response or ongoing steroid dependence may improve outcomes. Prospective studies in patients with Crohn's disease receiving ustekinumab therapy are warranted to elucidate the best approach for optimizing drug therapy.

P-020

Therapeutic Effect of Vancomycin in UC Patients Associated With PSC: Case Series

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BACKGROUND: Up to 5% of patients with ulcerative colitis (UC) have primary sclerosing cholangitis (PSC). Small studies have shown a decrease in alkaline phosphatase (ALP) in PSC patients treated with vancomycin, suggesting its potential therapeutic role. In our practice, we observed clinical benefits of vancomycin in controlling UC disease activity in patients with UC with PSC, and in the absence of C. difficile infection.
METHODS: A retrospective chart review of those with active UC refractory to standard treatment with PSC was conducted at Georgetown University Hospital. Prior treatments, endoscopic findings, and blood work results were collected.
RESULTS: Six patients with active UC with PSC were treated with vancomycin 125 mg PO QID for 4-8 weeks to induce remission, followed by maintenance with vancomycin 125 mg PO TID. All were female with age between 17-52 and tested negative for C. difficile prior to initiation of vancomycin. Two patients had a remote history of C. difficile. Five had UC pancolitis; one had indeterminate colitis. Three patients were post-OLT with evidence of recurrent PSC (with two patients on tacrolimus and one on mycophenolate mofetil). UC duration ranged from 6-21 years.
All had documented active disease by colonoscopy (Mayo score 1-2) and/or inflammatory markers and were assessed at 4-6 weeks after vancomycin initiated: all achieved clinical remission and maintained remission at follow-up (0.5-2 years). Colonoscopy results at 1 year after initiation of vancomycin were available for 4 patients: Three patients had Mayo score of 0 and one patient had a Mayo score 1, with an average reduction of UC Mayo score on vancomycin of 1.67. Four patients had a decrease in ALP. All tolerated the drug well without reported side effects.
CONCLUSION(S): In our subset of patients with active UC/PSC, who have failed standard treatments (mesalamine, immunomodulators, biologics), vancomycin was effective and safe at inducing clinical, biochemical and endoscopic remission. Clinical remission with vancomycin occurred rapidly within 4-6 weeks of initiating treatment and was maintained for up to 2 years of follow-up. Liver enzymes improved on vancomycin. Prospective studies with a larger number of UC/PSC patients and a long-term follow-up are needed to better establish the therapeutic role of vancomycin in this subset of patients. Proposed mechanisms of action are the induction of regulatory T cells, increased TGF-B via TNF-alpha pathway, and/or shifting aberrant cytokine profiles through gram-negative bacteria composition.

P-021

Young Investigator

Common Variable Immunodeficiency Masquerading as Ulcerative Colitis

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V.R. is a 24 year old, African American female, with a history of Lupus, recurrent UTI's, sinus infections, ear infections, pneumonia and a family history of Crohn's disease, who was originally referred to gastroenterology clinic for microcytic anemia. Over the two months prior to her initial visit, she was having multiple episodes of bilious emesis daily. Additionally, she was experiencing diffuse abdominal cramping and was having 3-4 loose BM's per day with occasional bright red blood coating her stool. She reported that she had been known to have anemia for many years but without a definitive explanation. She did endorse heavy menses which had not previously been evaluated. Repeat blood work noted iron deficiency anemia and there were no findings consistent with sickle cell. As a result of her anemia, she was scheduled for an EGD and colonoscopy.
Her EGD was notable for monilial esophagitis as well as erythematous gastropathy and gastritis with biopsies reported as atypical lymphoid infiltrates. Her colonoscopy findings were notable for prominent lymphoid nodules in the ileum which were biopsied and found to be atypical lymphoid infiltrates. She had an inflamed appendiceal orifice consistent with a cecal patch which was biopsied and returned as atypical lymphoid infiltrates. Additionally, she had mild to moderate patchy proctosigmoiditis with biopsies again returning as atypical lymphoid infiltrates. The biopsies were reviewed by an expert pathologist who noted a paucity of plasma cells, confirmed with negative CD 138 immunostaining. Furthermore, staining for a malignant process such as lymphoma was found to be unlikely.
Given the constellation of findings, immunoglobulin electrophoresis to check for Common Variable Immunodeficiency (CVID) was done as was flow cytometry to rule out lymphoma. Clonality was not established on flow cytometry and serum immunoglobulin electrophoresis was consistent with CVID with her IgG being low at 72, her IgA low at less than 7 and her IgM low at 29.
She was referred to an immunologist who started her on immunoglobulin infusions. She has done well for nearly one year.
CVID is defined as reduced concentrations of IgG along with low levels of IgA and/or IgM, a poor or absent response to immunizations, and not having another diagnosis of an immunodeficiency state. The majority of patients are diagnosed between ages 20 and 45. In a nearly forty year study looking at nearly 500 patients with CVID, it was found that 15% of them had gastrointestinal inflammatory disease. Diarrhea is the most common symptom in patients who have gastrointestinal disease and the most common presentation is one that resembles IBD, either ulcerative colitis or Crohn's disease. One theory regarding the IBD like inflammation in CVID patients may be related to abnormal cytokine production through a T-cell related pathway, however, given the variability of the presentation, there are likely multiple mechanisms involved.
This case is significant for the practicing gastroenterologist. The patient's endoscopic presentation, clinical symptoms and lab findings were consistent with a diagnosis of ulcerative colitis. One must keep a broad differential in mind as it impacts treatment and surveillance.

P-022

Young Investigator

Novel Therapy for Collagenous Colitis - A Case Report

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Microscopic colitis is a chronic, inflammatory disease of the colon that is characterized by chronic, non-bloody, watery diarrhea, insidious or acute onset. It typically occurs in middle-aged female patients. On endoscopy, the colon is typically normal in appearance, with changes of abnormal collagen layers and intraepithelial lymphocytes identified on biopsies. There are two subtypes of Microscopic colitis, lymphocytic and collagenous colitis. The underlying pathophysiology is poorly understood. There may be a mucosal immune response in genetically predisposed patients. Research has been able to identify triggers amongst some patients who use nonsteroidal anti-inflammatory drugs, various prescription drug therapies, smoking and Clostridium difficile and Yersinia infections. Microscopic colitis can be associated with several other autoimmune conditions. Numerous treatment studies for Microscopic Colitis have included use of Budesonide, Mesalamine, Bismuth salicylate, Prednisolone/Prednisone, Cholestyramine + Mesalamine, Boswellia serrata and probiotics.
Vedolizumab is a humanized monoclonal antibody that specifically binds to the α4β7 integrin and blocks the interaction of α4β7 integrin with mucosal addressin cell adhesion molecule-1 and inhibits the migration of memory T-lymphocytes across the endothelium into inflamed gastrointestinal parenchymal tissue. Vedolizumab is approved for adults with moderate to severe Ulcerative Colitis and Crohn's Disease, who have had an inadequate response with, lost response to, or were intolerant to a tumor necrosis factor (TNF) blocker, immunomodulator or corticosteroids; or became corticosteroid dependent.
This patient is a 70-year-old female with a history of refractory Collagenous Colitis, Arthritis, Dermatitis Herpetiformis, COPD, Osteoporosis and Sleep Apnea. She was originally diagnosed with Collagenous Colitis on Colonoscopy 2/16/2012. Initial steroid therapy led to personality changes. Lialda and Colestid therapies were tried and found to be ineffective as single agents. Very minimal benefit experienced with use of Loperamide therapy. High dose Budesonide again led to personality changes; she has tolerated lower doses. Given her history of steroid therapies for her COPD and high dose Budesonide for her Collagenous Colitis, she was diagnosed with Adrenal Insufficiency. An EGD in 2012 was negative for Celiac Disease. Stools have been negative for Clostridium difficile.
In May of 2016, our patient began use of Vedolizumab. She experienced an initial response with decreased stooling. She was previously experiencing >10 stools daily, which diminished to 2-3 stools daily. A repeat Colonoscopy 2/10/16 again confirmed the presence of Collagenous Colitis on biopsy. On 5/12/16, she met with a Dietician to further explore dietary changes that could enhance her disease control. Some changes were found to be of benefit, however, this did not result in a significant change. Overall, her quality of life has been improved on Vedolizumab and continued use of bile sequestering therapy, Mesalamine, anti-diarrheal therapy and one Budesonide 3mg. Although Vedolizumab it is not currently FDA approved for the use of Collagenous Colitis, it is a novel therapy for the treatment of this condition.