Background

Rituximab, a well-known chimeric monoclonal antibody directed against the CD20 antigen on B-cells, depletes CD19-positive and CD20-positive B-cells. It is used for treatment of NHL, CLL, RA, and multiple sclerosis (MS). There are 4 case reports of “rituximab-associated colitis”. We report a patient treated with rituximab, developed fulminating severe colitis when the B-cells were depleted and resolved once the B-cells were restored.

Case Report

We present a 34 year-old Caucasian female receiving rituximab for refractory MS. She would receive one infusion on day zero and day 14 with a dose of 375mg/m2/24h. After her infusion her MS improved and her levels of B-cells were undetectable. She had a repeat infusion eight months after initial infusion. Several days after her second treatment, the patient developed nausea. Her nausea continued and then one month later the patient developed watery diarrhea. Four months later she had a colonoscopy to evaluate her persistent diarrhea. The endoscopic findings appeared normal; however, the biopsy showed lymphocytic colitis (LC) associated with surface injury. Immunohistochemistry revealed that B-cells were depleted with absence of CD20+ B-cells in the mucosa. Of note, there were abundant macrophages in the mucosa. The patient improved and after eight months the patient was at her baseline and received her third infusion of rituximab. Twelve hours after infusion, the diarrhea recurred accompanied by arthralgias. The non-bloody diarrhea persisted and when she presented to neurology clinic she was unable to tolerate a diet. A CT scan showed, circumferential thickening of the left colon. Infectious etiologies were negative. The CRP was 212 and ESR was 32. A repeat colonoscopy was performed to evaluate abdominal pain and diarrhea. Findings were of severe colitis with ulcerations in the entire left side of the colon. The biopsy showed fulminant active colitis with frequent cryptitis, crypt abscess, and ulceration. Immunohistochemistry revealed absence of B-cells by CD20 immunostaining. The number of macrophages was similar to that of the initial biopsy. Though steroids were offered to the patient, she opted to be treated conservatively. She was discharged and monitored closely as outpatient.

Eight months after her previous infusions of rituximab, she finally had a detectable level of CD19 and CD20 cells. A colonscopy with biopsy revealed normal colon without colitis or injury. Immunostaining of CD20 confirmed partial recovery of B-cells in the colon. There was no significant change in the number of macrophages.

Results

- There was a clear relation between colitis and lack of B-cell in colonic tissues
- Severity increased with each infusion of Rituximab
- Resolution of both clinical and histologic findings was obtained after discontinuation of Rituximab.

Conclusion

Review of the literature and this case seems to be showing an association between depletion of B-cells, specifically CD19+ and CD20+ cells and severe colitis with ulcerations. In our case each subsequent infusion of rituximab led to more severe gastrointestinal symptoms. It has been proposed that B-cells both prevent the development of these autoimmune diseases and reduce their severity. It appears that although the depletion of B-cells improve the symptoms of MS, that there is a severe dysfunction of regulation of the cellular immunity that can lead to autoimmune processes. We are hypothesizing that the loss of B-cells causes dysfunction of the cellular immunity and lead to severe colitis with ulceration. Currently our patient is off all therapy for her MS and doing well but further investigations are underway for future options that do not work by affecting the B-cells.

References:
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Severe Colitis Induced by Rituximab
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