Fulminant Colitis Following Rituximab Therapy

Seth Lipka, MD
Seymour Katz, MD
James M. Crawford, MD, PhD

Rituximab (RTX; Rituxan, Genentech) is the clinical formulation of a murine immunoglobulin G (IgG) 1 monoclonal anti-CD20 antibody and is widely used in the initial treatment of CD20-positive hematologic malignancies and a variety of autoimmune disorders. Rarely, fulminant colitis has been reported with the use of RTX (Table). We report a patient who developed 2 episodes of fulminant colitis after 2 infusions with RTX for the treatment of disseminated B-cell marginal lymphoma. The first episode of colitis required subtotal colectomy, and the second episode required completion proctectomy.

A 62-year-old woman presented in October 2002 with a left lower abdominal wall mass. The patient's peripheral blood smear showed atypical lymphocytes. After an excisional biopsy and histologic and flow cytometry, the patient was diagnosed with marginal zone B-cell lymphoma. The patient was offered a combination treatment of CHOP chemotherapy with RTX or RTX alone. The patient decided to undergo therapy with RTX alone.

After receiving several cycles of RTX therapy from 2002 to 2005 and another 4 doses in September 2005, the patient developed severe abdominal pain and diarrhea. Her stool studies were negative for an infectious etiology. A computed tomography scan showed diffuse wall thickening and distention of the entire colon with areas of pneumatosis. The patient's condition deteriorated and required a subtotal colectomy with ileostomy. Three months later, the ileostomy was closed.

In September 2010, after receiving a second course of 4 cycles of RTX therapy for recurrent lymphoma, the patient developed severe abdominal pain and diarrhea. Her stool studies were again negative for an infectious source. Diffuse severe colitis was noted on a sigmoidoscopy. The biopsies revealed severely inflamed tissue (Figure). The patient's clinical course worsened later, requiring a proctectomy.

Discussion

Recent case reports have cited RTX as a trigger for severe colitis. Rituximab is a murine IgG 1 monoclonal anti-CD20 antibody that has become a successful treatment for several hematologic malignancies. The CD20 antigen is expressed on more than 90% of B-cell lymphomas. B cells regulate a number of immune functions, including production of both cytokines and immunoglobulins as well as antigen presentation.
In conclusion, RTX therapy is extensively used in a variety of hematologic malignancies and autoimmune diseases, but acute severe colitis is an underappreciated complication. B cells have both an inflammatory and anti-inflammatory function in humans, and disruption of this equilibrium in susceptible individuals may result in severe colitis.

The authors have no relevant conflicts of interest to disclose.

### References


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**Table.** Cases of RTX and Colitis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, Sex</th>
<th>Indication(s)</th>
<th>Treatment(s)/Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>67, M</td>
<td>Relapse of follicular lymphoma</td>
<td>Subtotal colectomy; died of recurrent bacterial pneumonia 4 months after surgery</td>
</tr>
<tr>
<td>2</td>
<td>26, F</td>
<td>Non-Hodgkin lymphoma treatment</td>
<td>Colectomy</td>
</tr>
<tr>
<td>3</td>
<td>45, F</td>
<td>Clinical trial for Grave's disease</td>
<td>Mesalazine-induced remission</td>
</tr>
<tr>
<td>4</td>
<td>58, M</td>
<td>Long-standing ulcerative colitis unresponsive to corticosteroids, immunosuppressants, and biologics</td>
<td>5-ASA, corticosteroids, and ciprofloxacin; patient suffered from 10-15 loose stools/day and was considered for proctocolectomy</td>
</tr>
<tr>
<td>5</td>
<td>4, M</td>
<td>Refractory minimal-change disease nephrotic syndrome</td>
<td>Corticosteroid-induced remission. Eventually, the nephrotic syndrome relapsed</td>
</tr>
<tr>
<td>6</td>
<td>34, unknown</td>
<td>Corticosteroid-, cyclophosphamide-, and methotrexate-resistant bullous systemic lupus erythematosus</td>
<td>Episode of acute appendicitis with appendectomy. Later developed ulcerative colitis. When RTX was withdrawn, symptoms resolved</td>
</tr>
<tr>
<td>7</td>
<td>38, F</td>
<td>Refractory seronegative rheumatoid arthritis</td>
<td>Corticosteroid- and 5-ASA–induced remission</td>
</tr>
<tr>
<td>8</td>
<td>62, F</td>
<td>Disseminated marginal zone B-cell lymphoma</td>
<td>Initially patient underwent subtotal colectomy and on subsequent RTX re-exposure patient experienced active proctitis requiring completion proctectomy</td>
</tr>
</tbody>
</table>

5-ASA, 5-aminosalicylic acid; F, female; M, male; RTX, rituximab. The table continues on page 63.


16. Gonnella PA, Waldner HP, Weiner HL. B cell-deficient (mu MT) mice have alterations in the cytokine microenvironment of the gut-associated lymphoid tissue (GALT) and a defect in the low dose mechanism of oral tolerance. *J Immunol.* 2001;166(7):4456-4464.


