

## Commensalism or symbiosis: The potential use of rituximab in steroid-refractory Evans syndrome in a patient with ulcerative colitis

Eyad Ahmed<sup>1</sup> , Kok Hoe Chan<sup>1</sup> , Sindhusa Veeraballi<sup>1</sup> , Theodore Dacosta Jr<sup>2</sup> , Hamid Shaaban<sup>3</sup> 

<sup>1</sup>Department of Internal Medicine, Saint Michael's Medical Center, New York Medical College, Newark, United States

<sup>2</sup>Department of Gastroenterology, Saint Michael's Medical Center, New York Medical College, Newark, United States

<sup>3</sup>Department of Hematology/Oncology, Saint Michael's Medical Center, New York Medical College, Newark, United States

Evans syndrome (ES) is defined as simultaneous or sequential association of direct Coombs-positive autoimmune hemolytic anemia (AIHA) with superimposed immune-mediated thrombocytopenia (ITP) and, in some cases, neutropenia.<sup>1</sup> In this report, we present a case of ES with ulcerative colitis (UC) that was refractory to steroids, but responded to rituximab, which also surprisingly maintain the remission of UC.

A 68-year-old male with a past medical history of recently diagnosed ES on prednisone 60 mg daily, UC on mesalamine, and prostate cancer (in remission for 16 years) was found to have low levels of hemoglobin (8.0 g/dL, normal range: 13.5 to 17.5 g/dL) and platelet count (6,100/ $\mu$ L, normal range: 150,000-400,000/ $\mu$ L) during an office visit. He was diagnosed with ES with co-existence of ITP and AIHA at one of the hospital visits. During hospitalization, he received intravenous immunoglobulin (IVIG) and solumedrol which improved his reticulocyte count, hemoglobin level, and platelet count. He was initially responded to the steroids, but developed refractoriness after six months with counts slowly decreasing every outpatient visit, which at a

point required a high dose of oral prednisone (1 mg/kg). The decision was made to administer rituximab in the setting of steroid-refractory ES. The steroid was discontinued, as the patient failed the steroid therapy. He responded to rituximab with remission of his ES at one month with hemoglobin of 10.5 g/dL and platelet count of 252,000/ $\mu$ L. At the current visit, the hemoglobin level was 14.3 g/dL and platelet count was 173,000/ $\mu$ L. Although there was a concern of the flare in his UC, he remained in remission despite the addition of rituximab. A written informed consent was obtained from the patient.

Evans syndrome has a naturally relapsing and progressive course and is almost always fatal, if left untreated. For a long time, the primary treatment option for ES has been steroids and even IVIG; however, the duration response may vary and more than half of cases relapse.<sup>1</sup> An alternative option currently emerging as a treatment for ES is rituximab, which exerts its effect as a chimeric monoclonal antibody acting against CD20 expressed on the surface of B cells. Rituximab may be considered in patients who are refractory to steroids and may be used

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**Correspondence:** Kok Hoe Chan, MD. Division of Hematology, Department of Internal Medicine, McGovern Medical School, University of Texas Health Science Center at Houston, Texas, United States. Tel: 713.500.6774 e-mail: kokhoedelcos.chan@gmail.com

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in conjugation with corticosteroids showing as high as 76% remission rates.<sup>2,4</sup> The average dose used to achieve a response and remission was 375 mg/dose for three to four doses.<sup>3</sup>

Recently, the discussion of both rituximab and UC has circulated and drawn wide opinions. The pathogenesis of UC, although not well understood, is believed to be related to anti-goblet cell antibodies and perinuclear anti-cytoplasmic neutrophil antibodies (pANCA), which may point toward B cells as contributors to the disease.<sup>5</sup> Several studies have also pointed to the risk of rituximab-induced colitis, even if the patient at times has no past history of inflammatory bowel disease.<sup>6,7</sup> Nonetheless, Leiper et al.<sup>8</sup> reported the potential safety of rituximab in patients with UC, although it has no roles in inducing or maintaining remission. For our patient, we interestingly found that the use of rituximab was beneficial for both treatment of ES and remission of UC. It is possible that the mechanism of UC is more complex than originally thought, and that, through another unknown pathway, there exists a potential mechanism which allows for remission of UC along with treatment of ES.

In conclusion, the present case successfully demonstrated the potential use of rituximab in a UC patient presented with steroid-refractory ES. Although there are case reports documented of its potential risk of fulminant UC flare-up, in our patient, the use of rituximab was not only beneficial for the treatment of ES, but also able to maintain the remission of UC.

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## REFERENCES

1. Norton A, Roberts I. Management of Evans syndrome. *Br J Haematol* 2006;132:125-37.
2. Shaikh H, Mewawalla P. Evans Syndrome. [Updated 2020 Jun 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK519015>
3. Jaime-Pérez JC, Aguilar-Calderón PE, Salazar-Cavazos L, Gómez-Almaguer D. Evans syndrome: Clinical perspectives, biological insights and treatment modalities. *J Blood Med* 2018;9:171-84.
4. Kashif M, Qureshi A, Adil SN, Khurshid M. Successful use of rituximab in Evans syndrome and refractory immune thrombocytopenic purpura. *J Pak Med Assoc* 2010;60:64-5.
5. Bossuyt X. Serologic markers in inflammatory bowel disease. *Clin Chem* 2006;52:171-81.
6. Lipka S, Katz S, Crawford JM. Fulminant colitis following rituximab therapy. *Gastroenterol Hepatol (N Y)* 2016;12:58-60.
7. Ardelean DS, Gonska T, Wires S, Cutz E, Griffiths A, Harvey E, et al. Severe ulcerative colitis after rituximab therapy. *Pediatrics* 2010;126:e243-6.
8. Leiper K, Martin K, Ellis A, Subramanian S, Watson AJ, Christmas SE, et al. Randomised placebo-controlled trial of rituximab (anti-CD20) in active ulcerative colitis. *Gut* 2011;60:1520-6.