

Abatacept as a Therapeutic Option for Rheumatoid Vasculitis

Layth Al Attar¹, Timothy Shaver²

1. Internal Medicine, University of Kansas School of Medicine - Wichita, Wichita, USA 2. Rheumatology, University of Kansas School of Medicine - Wichita, Wichita, USA

✉ **Corresponding author:** Layth Al Attar, lalattar@kumc.edu

Disclosures can be found in Additional Information at the end of the article

Abstract

Abatacept is a fusion protein composed of the fragment crystallizable region (Fc region) of the immunoglobulin IgG1 fused to the extracellular domain of cytotoxic T-lymphocyte-associated protein 4. Our patient presented with lower extremity purpura in the setting of rheumatoid arthritis and common variable immunodeficiency disease. A biopsy of cutaneous lesions confirmed the etiology of rheumatoid vasculitis. Although rituximab is the recommended treatment, it has the potential to exacerbate immunodeficiency. The cutaneous lesions responded well to abatacept after failure to respond to other treatment modalities. This case is the first, to our knowledge, to be reported in North America. Our case may encourage extensive clinical trials on abatacept as a treatment option.

Categories: Allergy/Immunology, Rheumatology

Keywords: rheumatoid arthritis, vasculitis, immunotherapy

Introduction

Rheumatoid arthritis (RA) is a systemic inflammatory disorder of unknown etiology primarily affecting the synovium. Extra-articular manifestations occur in about 40 percent of patients with RA [1]. Cutaneous vasculitis, a clinical manifestation of rheumatoid vasculitis (RV), develops in 5.4 percent of patients with RA [2]. Rituximab has been shown to be effective in inducing remission of RV [3]. It is also documented to be effective in treatment of cutaneous manifestations [4]. On the contrary, abatacept use has been associated with RV. It has been reported that RV may present as a new onset while on abatacept, resolving after being treated with Rituximab [5]. The case we are presenting is of RV managed with abatacept that led to resolution of symptoms.

Case Presentation

We present a case of a 68-year-old Caucasian female known to have multiple comorbidities: seropositive rheumatoid arthritis, common variable immunodeficiency, hypertension, hypothyroidism, and osteoporosis. The patient was diagnosed with rheumatoid arthritis in 2013. She developed cutaneous vasculitis, confirmed by biopsy performed by her primary care physician in May, 2015. She was initially treated with mycophenolate, hydroxychloroquine, and prednisone with initial improvement. The prednisone was tapered off, but she then developed worsening of joint symptoms and synovitis. For this reason, she was switched to methotrexate. Six months later, leflunomide was substituted due to hair loss and inadequate disease control on methotrexate. It was several months later that her cutaneous lesions worsened again. The decision was made to start the patient on abatacept. Arrangements were made with required laboratory testing and screening prior to starting abatacept. On the

Received 03/26/2018

Review began 04/02/2018

Review ended 04/09/2018

Published 04/19/2018

© Copyright 2018

Al Attar et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 3.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

How to cite this article

Al attar L, Shaver T (April 19, 2018) Abatacept as a Therapeutic Option for Rheumatoid Vasculitis. Cureus 10(4): e2506. DOI 10.7759/cureus.2506

following visit, the patient was given abatacept 10 mg/kg intravenous infusion with concurrent therapy of leflunomide, hydroxychloroquine, and prednisone. The patient was reevaluated after two weeks of infusion, with clearing of lesions several days after the first dose of abatacept. On her four-month follow-up visit, the patient continued to demonstrate a satisfactory response to this therapy. Prednisone was discontinued, and the patient was kept on abatacept, hydroxychloroquine, and leflunomide. The patient returned to office a month later without any recurrence of her cutaneous lesions.

Discussion

This was a case of cutaneous vasculitis diagnosed based on biopsy findings. Cutaneous vasculitis is an extra-articular manifestation associated with significant complications. These complications may range from palpable purpura, ulcers, to ischemic lesions [6-7]. The severity of complications depends on the size of vessels involved. The complexity of our case stems from refractoriness to standard therapy, prompting investigation into other treatment options. This prompt search of other treatment option. In our literature review, we found one case of RV responding to abatacept [8]. Consideration of presented comorbidities added limitations to treatment options. Abatacept achieves its effect by binding to the costimulatory molecules CD80 and CD86 on antigen-presenting cells (APC), thereby blocking interaction with CD28 on T-cells [9]. Utilizing abatacept's therapeutic mechanism was shown to be beneficial in treatment of our patient's cutaneous vasculitis.

Cutaneous vasculitis presents as lower extremity purpura. It is managed with glucocorticoids and/or immunosuppressive agents such as cyclophosphamide depending on presentation severity. The recent development of biologic response modifiers showed potential to improve outcomes. Rituximab is considered the current biologic agent of choice for rheumatoid vasculitis treatment [3]. Rituximab binds CD20 on B-lymphocytes and induces B-cell death via natural killer cells, often resulting in hypogammaglobulinemia. This would increase the potential to worsen common variable immunodeficiency. Levy R et al. [10] recommends monitoring serum immunoglobulin levels after initiation of rituximab. Abatacept inhibits T-cell activation by binding to CD80 and CD86 on antigen-presenting cells to interfere with signaling via CD28 [9]. This alternative mechanism of action would preserve B-cell function in our patient.

Conclusions

In conclusion, complex pathophysiology underlies many rheumatologic disorders, providing us an opportunity to explore new treatment options. Newly developed biologic response modifier therapies open up a wider array of possibilities in this regard. While it is premature to recommend the routine use of abatacept in this clinical setting, our case could serve as an impetus for more extensive clinical trials of this agent in the treatment of rheumatoid vasculitis.

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Turesson C, O'Fallon WM, Crowson CS, Gabriel SE, Matteson EL: Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. *Ann Rheum Dis*. 2003, 62:722-7. [10.1136/ard.62.8.722](https://doi.org/10.1136/ard.62.8.722)
2. Kaye O, Beckers CC, Paquet P, Arrese JE, Piérard GE, Malaise MG: The frequency of cutaneous vasculitis is not increased in patients with rheumatoid arthritis treated with methotrexate. *J Rheumatol*. 1996, 23:253-7.
3. Puéchal X, Gottenberg JE, Berthelot JM, et al: Investigators of the AutoImmunity Rituximab Registry. Rituximab therapy for systemic vasculitis associated with rheumatoid arthritis: Results from the AutoImmunity and Rituximab Registry. *Arthritis Care Res (Hoboken)*. 2012, 64:331-9. [10.1002/acr.20689](https://doi.org/10.1002/acr.20689)
4. Assmann G, Pfreundschuh M, Voswinkel J: Rituximab in patients with rheumatoid arthritis and vasculitis-associated cutaneous ulcers. *Clin Exp Rheumatol*. 2010, 28:81-3.
5. Carvajal Alegria G, Uguen A, Genestet S, Marcorelles P, Saraux A, Cornec D: New onset of rheumatoid vasculitis during abatacept therapy and subsequent improvement after rituximab. *Joint, Bone, Spine*. 2016, 83:605-6. [10.1016/j.jbspin.2015.08.016](https://doi.org/10.1016/j.jbspin.2015.08.016)
6. Chen KR, Toyohara A, Suzuki A, Miyakawa S: Clinical and histopathological spectrum of cutaneous vasculitis in rheumatoid arthritis. *Br J Dermatol*. 2002, 147:905-13. [10.1046/j.1365-2133.2002.04933.x](https://doi.org/10.1046/j.1365-2133.2002.04933.x)
7. Scott DG, Bacon PA, Tribe CR: Systemic rheumatoid vasculitis: a clinical and laboratory study of 50 cases. *Medicine (Baltimore)*. 1981, 60:288-97.
8. Fujii W, Kohno M, Ishino H, et al: The rapid efficacy of abatacept in a patient with rheumatoid vasculitis. *Mod Rheumatol*. 2012, 22(4):630-4. [10.1007/s10165-011-0559-8](https://doi.org/10.1007/s10165-011-0559-8)
9. Bonelli M, Scheinecker C: How does abatacept really work in rheumatoid arthritis?. *Curr Opin Rheumatol*. 2018, 30:295-300. [10.1097/BOR.0000000000000491](https://doi.org/10.1097/BOR.0000000000000491)
10. Levy R, Mahévas M, Galicier L, et al: Profound symptomatic hypogammaglobulinemia: a rare late complication after rituximab treatment for immune thrombocytopenia. Report of 3 cases and systematic review of the literature. *Autoimmun Rev*. 2014, 13:1055-63. [10.1016/j.autrev.2014.08.036](https://doi.org/10.1016/j.autrev.2014.08.036)