

## Introduction

- Ocrelizumab is an anti-CD20 monoclonal antibody used to treat multiple sclerosis (MS).
- Common side effects include infusion reactions and infections. Rare adverse events have been reported in case reports.
- Serum sickness (SS) is a type III hypersensitivity reaction that can occur with monoclonal antibody therapy.
- Only one case of SS has been previously reported with ocrelizumab.<sup>1</sup>

## Objective

To describe two patients with MS who developed SS post ocrelizumab infusions.

**Table:** Summary of radiologic and laboratory findings of both patients

	Case 1	Case 2
<b>MRI findings</b>	No new/enlarging enhancing lesions	No enhancing lesions
<b>Inflammatory markers</b>	ESR: 102 mm/h ; CRP: 20 mg/dL	ESR: 62mm/h
<b>Liver enzymes</b>	AST: 48 U/L ; ALT: 39 U/L	AST: 169 U/L ; ALT: 198 U/L
<b>WBC counts</b>	28.37 K/cu mm	12.15 K/uL
<b>Complement levels</b>	C3: 209.5mg/dL ; C4: 43.9 mg/dL	CH50: >60U/ml
<b>Infectious workup (Negative results for all)</b>	<p><u>CSF:</u> Cytomegalovirus; Varicella zoster virus; Epstein-Barr virus; JC virus PCR; cultures</p> <p><u>Blood:</u> Hepatitis panel; Parvovirus antibodies; Enteroviral NAT; SARS-CoV-2 NAT; Mayo encephalopathy panel; Human immunodeficiency virus antigen and antibodies; Lyme antibodies titers; Beta-D-Glucan and galactomannan assays; cultures</p> <p><u>Urine:</u> Urinalysis; Neisseria Gonorrhoea NAT; Chlamydia Trachomatis NAT</p>	<p><u>CSF:</u> JC virus PCR</p> <p><u>Blood:</u> Lyme antibodies titers; cultures</p>

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; WBC: White blood cell; CH50: Total complement activity; PCR: polymerase chain reaction; NAT: nucleic acid testing

## Case Presentations

A 45-year-old man with primary progressive MS (PPMS) was admitted for sensory changes and lower extremity weakness 2 weeks after his 5<sup>th</sup> cycle of ocrelizumab infusion.

- Given 1 dose of 1000mg methylprednisolone for a suspected MS flare
- Workup included imaging and blood and CSF laboratory tests (Table)
- Discharged after negative workup

- Re-presented 4 days later with progressive generalized weakness, arthralgias, myalgias, and fever
- Infectious workup was negative (Table)

- Started on prednisone for suspected SS (60mg daily for 2 weeks, followed by a 10mg daily taper)
- Symptoms significantly improved after 2 days

A 59-year-old woman with PPMS presented for stiff, painful joints with abdominal pain 48 hours after her 2<sup>nd</sup> cycle of ocrelizumab infusion.

- Basic blood workup was unremarkable
- Given morphine for pain and sent home

- Re-presented 1 day later with severe abdominal pain, worsening arthralgias, generalized weakness, and myalgias
- Workup included imaging and blood and CSF laboratory tests (Table)

- Ketorolac injection dramatically improved her symptoms
- Started on prednisone for suspected SS (60mg daily for 1 week, followed by a 10mg weekly taper)
- Back to baseline within a few days

## Discussion

- Unlike rituximab (chimeric anti-CD20 monoclonal antibody), ocrelizumab is a fully-humanized antibody and has a reduced risk of inducing antibodies and causing SS.
- SS has been reported with other humanized monoclonal antibodies used in MS (alemtuzumab and natalizumab).<sup>2</sup>
- The presence of all triad components of SS (fever, arthralgias, rash) is not necessary for diagnosis. A systematic review of rituximab-induced SS reported only 48.5% of cases presented with the full triad.<sup>3</sup>
- Infectious causes should always be considered in the differential diagnosis. Viral exanthems and Lyme disease may have overlapping symptoms with SS.
- Treatment depends on symptom severity; nonsteroidal anti-inflammatory medications, antihistamines, or corticosteroids can be used.

## Conclusion

- SS should be suspected in a patient with new-onset arthralgia, fever, or rash following ocrelizumab infusion, with an otherwise negative infectious workup and rapid response to steroids.
- Longer experience with ocrelizumab is necessary to characterize the possible rare side effects.
- It is important to be aware of the possible occurrence of SS in order to properly address it when it occurs.

## References

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