

## Rituximab in Branched Retinal Artery Occlusion Subset of Susac's Syndrome

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### Abstract

Susac's Syndrome (SS) is a neurologic condition that presents with encephalopathy, branch retinal artery occlusion and hearing loss. There are two forms of SS. The encephalopathic form is associated with headaches and distinct MRI changes. The branch retinal artery occlusion (BRAO) form is a more prolonged course with minimal MRI changes but with recurrent active retinal vasculopathy. Many patients with SS can effectively be treated with corticosteroids. Little data exists for the treatment of patients with the BRAO subset of SS who are resistant to corticosteroid therapy. We report the use of rituximab in a 31-year-old male who was diagnosed with the BRAO subset of SS. Despite treatment with high dose steroids and immunosuppressive therapy, the patient experienced progressive non-occlusive arteriolitis on fluorescein angiography and worsening hearing loss. The decision was made to treat the patient with rituximab, an anti-CD20 monoclonal antibody. After treatment there was improvement in exam with no new retinal infarcts. To our knowledge, this is the first case report of using rituximab in a patient with the BRAO subset of SS. These findings suggest that rituximab may be a viable option in patients with recurrent disease who are resistant to conventional treatment modalities.

### Keywords

rituximab; susac's syndrome; branched retinal artery occlusion; primary central nervous system vasculitis; encephalopathy

### Abbreviations

SS: Susac Syndrome; BRAO: branch retinal artery occlusion; HL: hearing loss; PCNSV: primary central nervous system vasculitis; CC: corpus callosum; MRI: magnetic resonance imaging; IV: intravenously; FA: fluorescein angiogram

### Introduction

Susac's Syndrome (SS) is an immune mediated endotheliopathy defined by a clinical triad of symptoms consisting of encephalopathy, branch retinal artery occlusion (BRAO), and hearing loss (HL) [1]. It primarily affects the precapillary arterioles of the brain, retina and inner ear. While SS mimics other forms of primary central nervous system vasculitis (PCNSV), it may be differentiated by the presence of hyperintense lesions in the corpus callosum (CC) on T2-weighted magnetic resonance imaging (MRI). Two forms of SS have been defined: the encephalopathic form and the recurrent BRAO subset [1].

The encephalopathy is commonly associated with headaches and distinct changes in T2 sagittal

flare images on MRI scan resulting in a “string of pearls” sign in the corpus callosum from multiple small “snowball” infarcts [1, 2]. Patients with the BRAO subset generally have a less severe, more prolonged course, with minimal MRI changes, recurrent active retinal vasculopathy and concurrent or potential future tinnitus, vertigo and HL [1].

Distinguishing between the two forms is paramount as pharmacological management varies. Treatment of SS is immunosuppressive in nature with initial treatment generally consisting of pulse methylprednisolone 1 gram on 3 consecutive days followed by high dose oral prednisone therapy (60-80 mg/day for 2-4 weeks) [2]. For patients who are unresponsive to steroid therapy, cyclophosphamide has been effective for both induction and maintenance therapy [2]. To our knowledge, limited data exists in regards to using rituximab, an anti-CD20 monoclonal antibody that is found on mature B cells, in the BRAO subset. A 2014 case report described the successful use of rituximab in combination with corticosteroids in a patient with PCNSV [3]. Two 1 gram doses of rituximab administered intravenously (IV) at 2 week intervals resulted in improvement of symptoms and improvement in repeat imaging when assessed at 2 months [3]. Two other cases reported successful use of rituximab doses at 375 mg/m<sup>2</sup>/week for 4 weeks but none of these reports define diagnosis of SS with BRAO [4]. Here, we report successful use of rituximab in a patient with imaging studies suggestive of SS with BRAO in the setting of idiopathic vasculitis.

## Case Presentation

This is a 31 year old Caucasian male with past medical history of factor V Leiden deficiency and migraine headache who was diagnosed with SS in April of 2013 in the setting of headache and loss of visual acuity. Patient was initially treated outpatient with high dose prednisone 100mg PO daily and methotrexate 20mg PO once weekly when BRAO was identified in the right eye. In January 2015, evidence of active vasculitis with occlusion was noted in the left eye and cyclosporine 100mg PO daily was initiated. In March of 2015 patient was switched to mycophenolate 1000mg PO twice daily in addition to cyclosporine 100mg PO daily and prednisone 10mg PO daily in the setting of worsening vision loss. In April of 2015, he had new onset retinal edema and scotoma in right eye with fluorescein angiogram (FA) showing arterial vasculitis. Patient was subsequently admitted to the hospital and started on methylprednisolone 1 gram IV daily for 3 days and then transitioned to prednisone 80mg PO daily thereafter.

MRI showed decreased signal intensity within the Splenium of the corpus callosum on sagittal image with corresponding mild increased signal intensity of FLAIR sequences (Figure 1). Remainder of corpus callosum was unremarkable in appearance and the body of the corpus callosum demonstrated no focal lesion (Figure 2). The lack of focal lesions in the corpus callosum is common with the BRAO subset of SS. Magnetic Resonance Angiography (MRA) and Magnetic Resonance Venography (MRV) of the brain showed punctate infarct in the periventricular white matter adjacent to the anterior horn of the left lateral ventricle and was considered unremarkable.

Blood tests with normal or negative findings included complete blood count with differential, basic metabolic panel, liver function tests, coagulation studies (including prothrombin time, INR, PTT, antithrombin activity, protein C activity, protein S functionality and antiphospholipid antibodies), and immunology studies (including complement C3 and C4, beta-2 glycoprotein antibody IgG, IgA, and IgM,

ANA, extractable nuclear antigen abs group, and lupus anticoagulant). Evaluation studies for infectious disease (sedimentation rate, urinalysis) were negative. Cerebral spinal fluid showed 1 red cell, 1 nucleated cell, 84 lymphocytes, 16 monocytes, glucose of 55 mg/dL and elevated protein, 85 mg/dL (normal <50) and no oligoclonal bands.

In May 2015, patient presented to ophthalmologist for routine office visit. On exam, FA showed evidence of new non-occlusive arterioles, worsening HL in left ear, and new onset HL in right ear despite high dose steroid therapy with prednisone 80mg PO daily. Given worsening clinical picture patient was sent to ED for evaluation. He was subsequently admitted and reinitiated on high dose corticosteroids (methylprednisolone 1 gram IV daily x 3 days). Upon audiology evaluation, moderate sensorineural HL in both ears (left > right) were noted with significant asymmetry noted from 6-8 kHz. Decision was made to treat patient with rituximab 1 gram IV x 1 dose and prednisone 80mg orally daily and to re-dose rituximab 1 gram IV in 14 days. Patient was evaluated by ophthalmology 2 weeks later and was found to have evidence of new non-occlusive arteriolitis on FA in left eye. Patient was sent to ED for pulse methylprednisolone and second rituximab dose. Patient was discharged home on prednisone 80mg PO daily. One month follow-up visit showed improvement of previous non-occlusive arteriolitis in left eye and no new vasculitis or infarct on FA. However, at two month follow-up there was evidence of recurrent arteriolitis and decreased perfusion on FA in left eye but no new retinal infarcts were noted.

## Discussion

The optimal treatment for SS has yet to be determined. To our knowledge, there are few case reports reporting treatment of SS and only two published case reports with successful use of rituximab in this patient population, although none with BRAO involvement [3,4,5].

Majority of patients presenting with SS will demonstrate microinfarcts along the corpus colossal as seen on MRI [1]. These findings are most common in patients with the “encephalopathic form of SS”, which is characterized by the predominance of encephalopathy at the time of diagnosis. The use of rituximab in patients presenting with these symptoms were discussed in previous case reports and was shown to improve MRI abnormalities and clinical status in all patients [3,4]. In the present case, patient's findings were consistent with recurrent BRAO subset of SS generally defined as a more prolonged course with recurrent active retinal vasculopathy, concurrent or potential future HL, tinnitus and vertigo, and minimal MRI abnormalities.

To our knowledge, this is the first case report to discuss the use of rituximab in patients with this subset of the disease. Our patient was initially treated with conventional therapy that consisted of corticosteroids and immune modulating agents. The patient had persistent recurrence of BRAO and worsening HL despite conventional therapy. Upon receiving rituximab, the patient showed clinical improvement with resolved vasculitis and absence of infarct on one month follow up exam. At subsequent two month follow-up visit, evidence of new arteriolitis was seen on FA as well as areas of decreased perfusion but no new retinal infarcts were noted. During this time, prednisone dose was decreased to 50mg PO daily given intolerable side effects. Recurrent arteriolitis seen on FA may have been attributed to decreased steroid dose.

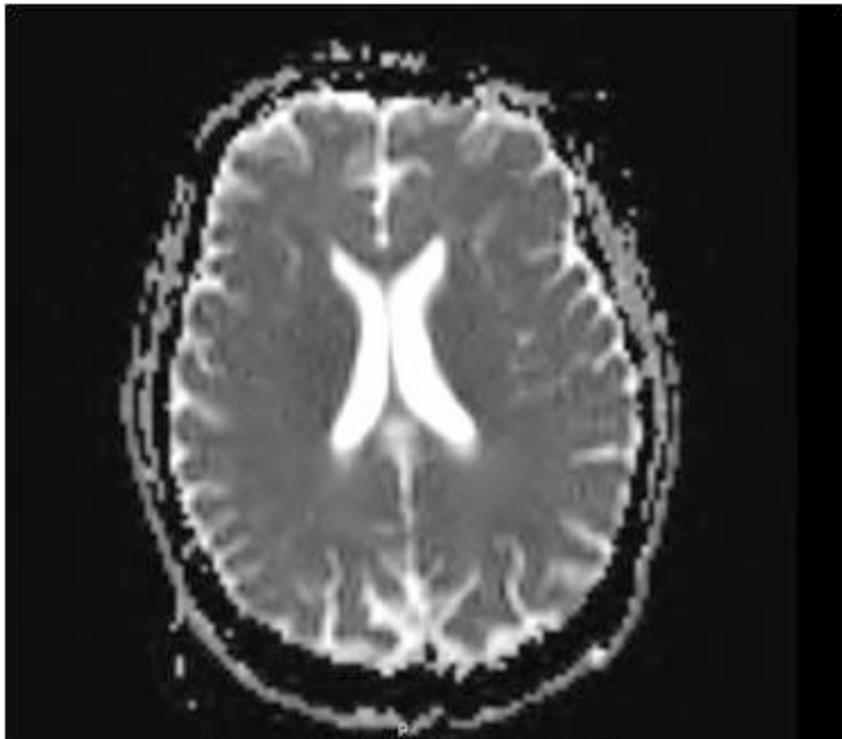
## Conclusion

Our case suggests that the use of rituximab may be a viable option in patients with SS, specifically those with recurrent BRAO subset who are not adequately controlled with conventional treatment modalities.

## Figures



**Figure 1:** Saggital T1 Flair showing no abnormalities



**Figure 2:** Axial DWI showing no lesions in the splenium

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