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Successful use of rituximab in a patient with Churg–Strauss syndrome and refractory central nervous system involvement

The major clinical manifestations of Churg–Strauss syndrome (CSS) include asthma, hypereosinophilia and the extrapulmonary manifestation of systemic vasculitis.¹ The involvement of the central nervous system (CNS) is less common (<10%), with significant morbidity and mortality in affected patients.² Glucocorticoids combined with cyclophosphamide represent the treatment of choice in patients with severe involvement of the heart, nervous system or kidney.³ In the case of intolerance to cyclophosphamide, plasma exchange, interferon and mycophenolate mofetil (MMF) have been suggested as alternatives.⁴ A few case reports on the use of rituximab in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis and CSS are available^{5–7}; however, none reported on patients with CNS involvement.

We report on a patient with CSS and refractory CNS involvement who was successfully treated with rituximab.

A 46-year-old white man was admitted with a history of disseminated palpable purpura and blood eosinophilia ($4.95 \times 10^9/\text{litre}$), while more recently paresthesias and palsy in both legs had developed. Mononeuritis multiplex was diagnosed. Laboratory tests revealed the presence of antibodies to myeloperoxidase (MPO)-ANCA (96 U/ml). The patient reported a history of allergic asthma and sinusitis.

CSS was confirmed by a muscle–nerve biopsy revealing epineural vessel involvement. Despite the prompt initiation of cyclophosphamide pulse therapy of 1000 mg monthly and oral steroids,⁸ the patient developed a hemiparesis of the right side. Brain magnetic resonance imaging (MRI) showed two non-enhancing vasculitic lesions in the thalamus, therefore the dose of cyclophosphamide was increased to 1500 mg combined with increased steroids and low-dose acetylsalicylic acid. During the following months the patient received cyclophosphamide initially at 3-week intervals leading to an improvement of clinical symptoms (BVAS = 3) and allowing tapering of steroids to 5 mg/day. As the patient increasingly experienced nausea and vomiting that persisted despite dose reduction, cyclophosphamide was stopped and the patient was started on MMF at 2000 mg/day. Whereas MMF was well tolerated, the patient complained about dizziness 2 months later. MRI showed new vasculitic lesions in the pons and thalamus (figure 1A).

The patient received two infusions of rituximab 1000 mg (2 weeks apart) that were well tolerated while MMF was maintained. Slowly his symptoms started to improve and an MRI 2 months later revealed regression of the pontine lesion (figure 1B) and residual scarring of the thalamic lesion.

At 8 and 16 weeks following rituximab, successful depletion of peripheral B cells and a decrease in peripheral eosinophilia ($0.79 \times 10^9/\text{litre}$) were noted. MPO-ANCA remained almost unchanged during follow-up.

The successful use of rituximab has been reported in a few patients with CSS, complicated by cardiac, renal, gastrointestinal or pulmonary involvement. Hypereosinophilia is thought to occur secondary to T-lymphocyte-derived cytokines (IL-4, IL-5 and IL-13)^{6,9} that are increased in active CSS. T-cell–B-cell

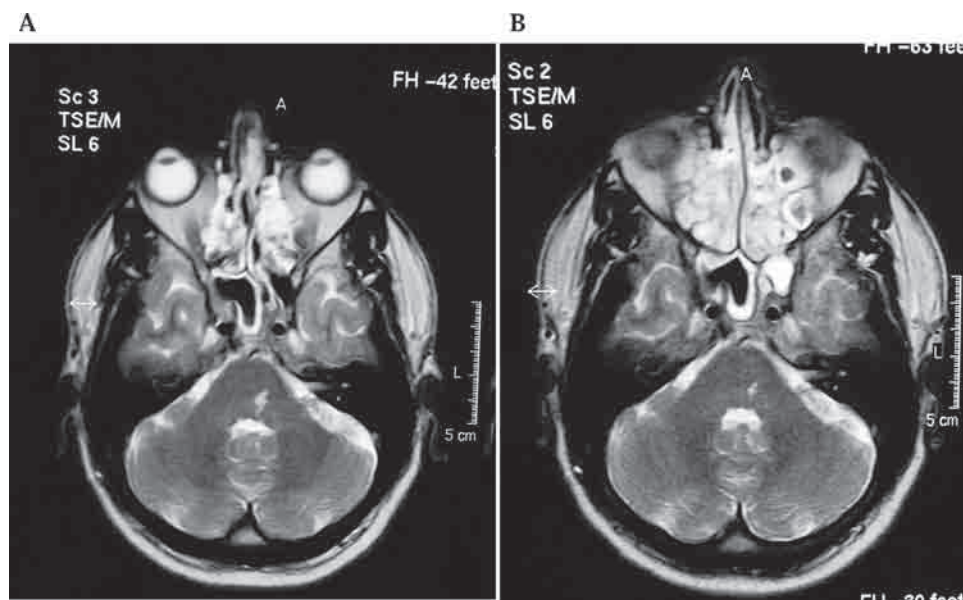


Figure 1 (A) T2-weighted magnetic resonance imaging sequence showing a sharply defined, hyperintense lesion in the left pons, 10 mm size. (B) The lesion in the left pons has decreased to 5 mm and appears less sharply defined.

interaction was shown to be critical for T-cell autoreactivity in some experimental models.¹⁰ The efficacy of rituximab was recently associated with diminished T-cell and IL-5 production, suggesting a link between B cells and eosinophilia through autoreactive T cells.⁶ B-cell depletion may therefore represent an alternative treatment for patients with refractory CSS and CNS involvement.

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