



Severe bronchospasm associated with rituximab for refractory Churg Strauss syndrome

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Severe bronchospasm associated with rituximab for refractory Churg–Strauss syndrome

Rituximab is now used to control antineutrophil cytoplasm antibody (ANCA)-associated vasculitides, eg, Wegener's granulomatosis.^{1,2} In Churg–Strauss syndrome (CSS), a small-vessel systemic vasculitis with asthma and eosinophilia, 39% of patients have ANCA.^{3,4} Rituximab could be effective in ANCA-associated vasculitides, even if ANCA are not present at the time of prescription, because B lymphocytes also play a role as antigen-presenting cells and can modulate the immune response in another way than targeting antibody production. Therapy-refractory CSS⁵ was successfully treated with rituximab in three patients.^{6–8} We would like to draw attention to the potential risk of rituximab-associated bronchospasm, by reporting our experience with two CSS patients.

A 44-year-old woman had been treated for CSS for 2 years. Her initial symptoms included: paranasal sinusitis; persistent cough; weight loss; asthma; hypereosinophilia and bilateral pulmonary infiltrates. ANCA were negative. Despite high-dose corticosteroids, she was hospitalised in extremis three times for severe asthma. Azathioprine then methotrexate were prescribed, but were poorly tolerated (allergy and hepatitis, respectively) and were rapidly discontinued. Intravenous cyclophosphamide pulses were started, but she developed mononeuritis multiplex, a hypereosinophilia flare and severe respiratory manifestations after the fourth infusion. Because of the unusual severity of her disease and the failure of cyclophosphamide, it was then decided to administer rituximab (375 mg/m² per week for 4 weeks). As recommended, after intravenous dexchlorpheniramine (5 mg) and paracetamol (1 g) premedication, rituximab was infused at 50 mg/h. Less than 15 minutes later she developed a sudden and severe bronchospasm. Infusion was stopped and her breathing returned to baseline after two salbutamol inhalations. Rituximab was definitively withdrawn.

The second patient was a 33-year-old woman, whose CSS had been diagnosed 9 years earlier based on the association of polyarthritis, pulmonary infiltrates, recent-onset asthma and hypereosinophilia, without ANCA. She was on long-term corticosteroids and many immunosuppressants (cyclophosphamide, mycophenolate mofetil and azathioprin) had previously been prescribed without success. Moreover, complications of glucocorticoid therapy arose: severe steroid-induced myopathy and bilateral cataracts. During a new exacerbation of the disease with arthralgias and asthenia, to obtain a corticosteroid-sparing effect, an intravenous rituximab infusion was prescribed as above. Again, rituximab was administered as recommended, and again a sudden bronchospasm occurred during the first 15 minutes of infusion. The patient's breathing returned to baseline after salbutamol inhalation; 1 h later, a slower infusion

was resumed, without any incident (nor any further improvement), but the subsequent infusions were not given as initially planned.

Although anti-CD20 therapy may contribute to controlling CSS, our two observations remind us to be cautious, especially in this indication. Rituximab, a genetically engineered chimeric human–mouse anti-CD20 monoclonal antibody, might trigger hypersensitivity reactions, especially in CSS patients, who frequently have allergic manifestations. Another possible mechanism could be the immediate release of proinflammatory cytokines that might trigger the spasm, as it has been shown (mostly for haematological disease indications) that rituximab administration could be followed by a rise in plasma cytokines.⁹

In the specific setting of CSS, more experience is certainly needed, along with mandatory close respiratory monitoring, especially during the first minutes of infusion. An American phase II and III trial was begun in December 2007.¹⁰

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