RESEARCH LETTER

Novel use of rituximab in hypersensitivity pneumonitis refractory to conventional treatment

Hypersensitivity pneumonitis (HP) is treated by removal of the inciting antigen, if identified, and with corticosteroids and immunosuppressive agents in extensive or progressive disease. A minority of patients continue to decline and suffer outcomes comparable to idiopathic pulmonary fibrosis. Rituximab, a B cell depleting anti-CD20 antibody, has shown benefit in interstitial lung diseases (ILDs) associated with connective tissue diseases (CTDs).1–3 We report a novel use of rituximab in a case of HP refractory to conventional treatment.

A 57-year-old female never-smoker, with no previous medical history, presented with a 6-month history of progressive breathlessness and dry cough. Pulmonary function tests (PFTs) were impaired, with 26% of diffusing capacity for carbon monoxide (DLco) and 44% of forced vital capacity (FVC). A high-resolution CT (HRCT) showed changes suggestive of HP (figure 1A). A surgical lung biopsy disclosed chronic bronchocentric inflammation, poorly formed non-necrotising granulomas and mild fibrosis (figure 1B). Immunohistochemistry showed scattered CD20 follicular aggregates on a background of CD3 T cells. A causative exposure was not identified on clinical history, precipitin screening tests were negative and features of a CTD were absent. HP was diagnosed with high confidence by multidisciplinary consensus. Oral prednisolone was commenced, tapering from 40 mg daily to maintenance 20 mg daily over 2 weeks. Following continued deterioration over the next 4 months, three 500 mg doses of intravenous methylprednisolone were administered weekly, followed by six 3-weekly doses of intravenous cyclophosphamide (600 mg/m² of body surface area).

Twelve months after presentation, and despite vigorous immunosuppressant treatment, PFTs had further worsened DLco and FVC, reaching a nadir of 17% and 37%, respectively. Exercise tolerance was

Figure 1  (A) Section through lower lobes showing generally increased attenuation of lung parenchyma with a few pulmonary lobules of decreased attenuation (reflecting small airway component). Appearances typical of hypersensitivity pneumonitis (HP). Both lower lobes are of reduced volume; in the right lower lobe, there is subtle traction bronchiectasis reflecting fine interstitial fibrosis. (B) A bronchiole shows moderate chronic inflammation and a small poorly formed non-necrotising granuloma in its wall, typical of HP (H&E, ×200). (C) Improvement in lung function following rituximab. FVC, forced vital capacity; DLco, diffusing capacity for carbon monoxide.
only 15 m despite ambulatory oxygen. Repeat HRCT demonstrated progression of fibrosis. Further intravenous methylprednisolone (500, 750, 750 mg on consecutive days) was administered together with rituximab (1000 mg repeated after 2 weeks). Oral prednisolone followed, tapering from 30 mg daily to a 10 mg daily maintenance. Two months post rituximab, symptomatic improvement was reported with a corresponding improvement in PFTs (figure 1C). At 4 months, ambulatory oxygen was no longer required. Compared with the pre-rituximab results, D\textsubscript{L}co had risen by 76.5\% to 30\% and FVC by 40.5\% to 52\%.

At 8 months, azathioprine 50 mg daily was added as maintenance therapy. PFT improvement was sustained at 10 months. Our patient’s striking improvement was temporally related to rituximab. Although administered concurrently, earlier treatment with methylprednisolone had been ineffective.

The unequivocal response to B cell depletion therapy suggests an immunopathogenetic role for B cells in HP. Although the inflammatory infiltrate in HP is traditionally considered to be T cell predominant, autoreactive B cells may originate from the T cell zone, accounting for the poorly organised lymphoid structure in HP lungs. Furthermore, marked expansion of plasma cells has been observed in bronchoalveolar lavage, bronchus-associated lymphoid tissue and B cells\(^4\) and high titres of rheumatoid factor have been associated with pigeon fancier’s lung suggesting B cell activation.\(^5\)

This first report of the success of B cell depletion therapy in HP, if confirmed by future studies, widens the range of ILDs that might benefit from rituximab and suggests that immunological overactivity may drive ILD progression outside the context of autoimmune disease.

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