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).\textsuperscript{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/m\textsuperscript{2} 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 only 15 m despite ambulatory oxygen. Repeat HRCT demonstrated progression of

---

**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, x200). (C) Improvement in lung function following rituximab. FVC, forced vital capacity; DLco, diffusing capacity for carbon monoxide.
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, DLco 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 cells⁴ 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.

Harpreet K Lota,¹ Gregory J Keir,¹ David M Hansell,² Andrew G Nicholson,³ Toby M Maher,¹ Athol U Wells,¹ Elisabetta A Renzoni¹
¹Interstitial Lung Disease Unit, Royal Brompton Hospital, London, UK
²Department of Radiology, Royal Brompton Hospital, London, UK
³Department of Histopathology, Royal Brompton Hospital, London, UK

Correspondence to Dr Harpreet K Lota, Interstitial Lung Disease Unit, Royal Brompton Hospital, Sydney Street, London SW3 6NP, UK; h.lota@rbht.nhs.uk

Contributors All authors contributed to this case report.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; internally peer reviewed.


Received 15 January 2013

Revised 19 February 2013

Accepted 21 February 2013

Published Online First 20 March 2013

doi:10.1136/thoraxjnl-2013-203265

REFERENCES

Novel use of rituximab in hypersensitivity pneumonitis refractory to conventional treatment

Harpreet K Lota, Gregory J Keir, David M Hansell, Andrew G Nicholson, Toby M Maher, Athol U Wells and Elisabetta A Renzoni

Thorax 2013 68: 780-781 originally published online March 20, 2013
doi: 10.1136/thoraxjn-2013-203265

Updated information and services can be found at:
http://thorax.bmj.com/content/68/8/780

These include:

References
This article cites 5 articles, 3 of which you can access for free at:
http://thorax.bmj.com/content/68/8/780#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Interstitial lung disease (559)
- Pneumonia (infectious disease) (579)
- Pneumonia (respiratory medicine) (562)
- TB and other respiratory infections (1273)
- Inflammation (1020)
- Airway biology (1100)
- Lung function (773)
- Chemotherapy (183)
- Screening (epidemiology) (366)
- Screening (public health) (366)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/