REFERENCES

- 1 Bland J. Rheumatoid arthritis of the cervical spine. *J Rheumatol* 1974;1:319–42.
- 2 Kauppi M, Sakaguchi M, Kontinen YT, Hamalainen M, Hakala M. Pathogenetic mechanism and prevalence of the stable atlantoaxial subluxation in rheumatoid arthritis. *J Rheumatol* 1996;23:831–4.
- 3 Neva MH, Kotaniemi A, Kaarela K, Lehtinen JT, Belt EA, Kauppi M. Atlantoaxial disorders in rheumatoid arthritis associate with the destruction of peripheral and shoulder joints, and decreased bone mineral density. *Clin Exp Rheumatol* 2003;21:179–84.
- 4 Neva MH, Isomaki P, Hannonen P, Kauppi M, Krishnan E, Sokka T. Early and extensive erosiveness in peripheral joints predicts atlantoaxial subluxations in patients with rheumatoid arthritis. *Arthritis Rheum* 2003;48:1808–13.
- 5 Neva MH, Kauppi MJ, Kautiainen H, Luukkainen R, Hannonen P, Leirisalo-Repo M, et al. Combination drug therapy retards the development of rheumatoid atlantoaxial subluxations. *Arthritis Rheum* 2000;43:2397–401.
- 6 Winfield J, Cooke D, Brook AS, Corbett M. A prospective study of the radiological changes in the cervical spine in early rheumatoid disease. *Ann Rheum Dis* 1981;40:109–14.
- 7 Naranjo A, Carmona L, Gavrilu D, Balsa A, Belmonte MA, Tena X, et al. Prevalence and associated factors of anterior atlantoaxial luxation in a nationwide sample of rheumatoid arthritis patients. *Clin Exp Rheumatol* 2004;22:427–32.
- 8 Neva MH, Kaarela K, Kauppi M. Prevalence of radiological changes in the cervical spine—a cross sectional study after 20 years from presentation of rheumatoid arthritis. *J Rheumatol* 2000;27:90–3.
- 9 Kauppi M, Hakala M. Prevalence of cervical spine subluxations and dislocations in a community-based rheumatoid arthritis population. *Scand J Rheumatol* 1994;23:133–6.
- 10 Paimela L, Laasonen L, Kankaanpää E, Leirisalo-Repo M. Progression of cervical spine changes in patients with early rheumatoid arthritis. *J Rheumatol* 1997;24:1280–4.

Rituximab in the treatment of antisynthetase syndrome

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The presence of autoantibodies directed against aminoacyl tRNA synthetases in the sera of patients with idiopathic inflammatory myopathy defines a specific clinical subset that has been called antisynthetase syndrome.¹ The prognosis of these patients is conditioned by the increased incidence of interstitial lung disease compared with other types of myositis.² We report a case of antisynthetase syndrome treated successfully with rituximab.

A 57 year old white woman had a 2 month history of painful synovitis of both hands, typical lesions of mechanic's hands, and moderate proximal muscle weakness. Her laboratory evaluation showed a raised erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and muscle enzymes. Electromyography findings were consistent with the diagnosis of inflammatory myopathy. Prednisone 30 mg/day was immediately started with a good response and then progressively tapered to 10 mg/day.

After 3 months, she had a relapse with increased muscle enzyme levels and worsening of articular symptoms, leading to the introduction of methotrexate with gradual increase up to 15 mg/week. Despite the combination of methotrexate and prednisone 10 mg/day for 5 months, her condition deteriorated with severe muscle weakness, painful symmetrical arthritis, and skin rash. Her laboratory evaluation showed highly increased serum levels of muscle enzymes

(table 1). Immunology tests were positive for anti-Jo-1 and anti-Ro antibodies, but antinuclear antibodies and rheumatoid factors were negative. Magnetic resonance imaging (MRI) of the thighs showed diffuse muscle oedema consistent with inflammatory myopathy (fig 1A). Pulmonary functions were within normal range, but diffusion capacity was decreased (72% of normal values). Echocardiography was normal; in particular, there was no indirect sign of pulmonary hypertension. A high resolution chest computed tomography (CT) scan showed the presence of mild signs of alveolitis in lower lobes bilaterally (fig 1C).

In view of the severity of the relapse, we decided to use rituximab (2×1 g infusions). She had a urinary tract infection between the two infusions of rituximab, which resolved rapidly with antibiotic treatment. During the following weeks her strength gradually increased while creatine kinase (CK), CRP, and ESR levels normalised. After 6 months, the presence of muscle inflammatory oedema on MRI resolved completely and lung abnormalities on high resolution chest CT scan had disappeared (figs 1B and D). After 8 months, she had a relapse with increased muscle enzymes and mild muscle weakness. A second course of rituximab (2×1 g infusions) led to a rapid decrease of CK levels and improvement of muscle strength. She exhibited acute sinusitis just after rituximab treatment, which required

Table 1 Evolution of biological values and treatment

Values	Before rituximab	After 1 month	After 3 months	After 6 months	After 8 months	Three months after second course of rituximab	Normal values
CK (U/l)	8274	3138	287	128	7116	1396	(33–187)
Aldolase (U/l)	<0.2	ND	6.3	5.5	92.9	ND	(0.6–9.4)
CRP (mg/l)	78	17	10	8	16	18	(0–10)
ESR (mm/1st h)	40	32	18	30	16	31	(0–20)
CD19 (/mm ³)	82	<1	8	8	44	2 *	(90–660)
CD3 (/mm ³)	786	984	900	1125	378	627*	(690–2540)
Anti-Jo1 (U)	214	ND	186	153	179	ND	(<20)
Anti-Ro (U)	134	ND	131	113	113	ND	(<20)
IgG (g/l)	12.3	12.5	10.7	11.2	11.7	ND	(6.70–13.18)
IgA (g/l)	0.74	0.79	0.66	0.92	0.85	ND	(0.67–2.96)
IgM (g/l)	1.59	1.01	0.61	0.71	0.67	ND	(0.40–2.61)
Prednisone (mg/day)	30	20	15	7.5	5	10	
Methotrexate (mg/wk)	15	15	15	15	15	15	

ND, not done; U, ELISA test arbitrary unit.

*One month after the second course of rituximab.

Figure 1 Evolution of muscle and lung involvement after rituximab treatment. MRI (T₁ sequences after gadolinium injection) of the thighs before rituximab shows diffuse inflammatory signal in the muscles (A), which resolved completely 6 months after rituximab treatment (B). A high resolution chest CT scan before the treatment shows interstitial inflammatory infiltrates of the lower lobes (C) that disappeared 6 months after rituximab treatment (D).

antibiotic treatment and sinus drainage; the infectious process resolved completely.

The association of myositis, arthritis, interstitial lung disease, mechanic's hands, Raynaud's phenomenon, and anti-Jo-1 antibodies is consistent with antisynthetase syndrome.¹ Treatment with rituximab according to the protocol used in rheumatoid arthritis³ resulted in a rapid resolution of myositis and other inflammatory features. Thus, as recently described in dermatomyositis,⁴ this case further suggests that rituximab is a highly active treatment of idiopathic inflammatory myopathies. The occurrence of two infectious adverse events is of potential concern for the use of rituximab, although the evolution was rapidly favourable after appropriate treatment. Data from clinical trials in rheumatoid arthritis did not show a significant increase of superimposed infections in patients treated with rituximab. However, it is necessary to obtain more information on B cell depletion in other inflammatory rheumatic diseases.

Autoantibody levels remained high and showed no correlation with disease activity or relapse. In contrast, circulating B cell depletion preceded the clinical response and the disease flare coincided with reappearance of the B cells. This finding is consistent with previously published results in dermatomyositis⁴ and in rheumatoid arthritis.⁵ In our case, the disease relapsed despite the use of methotrexate and prednisone, suggesting that in most cases a single course of rituximab does not protect indefinitely from relapse.

These observations emphasise the need for additional studies to assess the optimal regimen of rituximab treatment in different subsets of idiopathic inflammatory myopathies, including the initial dose, combination of treatments, and

re-treatment schedule. The efficacy of rituximab on the interstitial lung disease which governs the vital prognosis of antisynthetase syndrome⁶ also requires confirmation.

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REFERENCES

- Marguerie C, Bunn CC, Beynon HL, Bernstein RM, Hughes JM, So AK, *et al.* Polymyositis, pulmonary fibrosis and autoantibodies to aminoacyl-tRNA synthetase enzymes. *Q J Med* 1990;**77**:1019–38.
- Schnabel A, Reuter M, Biederer J, Richter C, Gross WL. Interstitial lung disease in polymyositis and dermatomyositis: clinical course and response to treatment. *Semin Arthritis Rheum* 2003;**32**:273–84.
- Edwards JC, Szczepanski L, Szechinski J, Filipowicz-Sosnowska A, Emery P, Close DR, *et al.* Efficacy of B-cell-targeted therapy with rituximab in patients with rheumatoid arthritis. *N Engl J Med* 2004;**350**:2572–81.
- Levine TD. Rituximab in the treatment of dermatomyositis: an open-label pilot study. *Arthritis Rheum* 2005;**52**:601–7.
- Cambridge G, Leandro MJ, Edwards JC, Ehrenstein MR, Salden M, Bodman-Smith M, *et al.* Serologic changes following B lymphocyte depletion therapy for rheumatoid arthritis. *Arthritis Rheum* 2003;**48**:2146–54.
- Marie I, Hatron PY, Hachulla E, Wallaert B, Michon-Pasturel U, Devulder B. Pulmonary involvement in polymyositis and in dermatomyositis. *J Rheumatol* 1998;**25**:1336–43.