Rituximab is effective in the treatment of patients with idiopathic inflammatory myopathy

Sirs,

We have read carefully the article in which Ríos Fernández *et al*. reviewed the published experience in treating idiopathic inflammatory myopathies (IIM) with rituximab (RTX) (1). We have significant experience in treating resistant systemic autoimmune diseases, including IIM (2-8). Although we previously assessed the outcome of patients treated with RTX for resistant IIM (7), the number of treated patients and administered treatment cycles has increased to 20 (17 females, mean age 51) and 33, respectively. Disease was considered resistant if the characteristics alterations (muscular, cutaneous or respiratory) did not improve (or reappeared after treatment) with GC and at least one immunosuppressant. The treatment schedule consisted of 4 infusions of RTX (375 mg/m^2 on days 0, 7, 14 and 21), 2 of cyclophosphamide (500 to 750 mg on days 2 and 16, in absence of contraindications) and glucocorticoids (GC) (1 to 3 intravenous methylprednisolone pulses when deemed necessary followed by deflazacort, 60 mg/day for 1 to 2 months with subsequent dose adjustment and withdrawal according to evolution). Remission was considered complete (CR) if alterations returned to the baseline and partial (PR) if significant but incomplete improvement occurred: increase of at least one grade in the scale of muscle strength (MRC) and reduction in plasmatic levels of CK and myoglobin greater than 50% in the event of myopathy, and significant reduction in the extent of skin lesions if present. In cases with respiratory compromise, CR was considered if force vital capacity (FVC) value returned to baseline ± 10%, and PR if FVC value improved more than 10% when CR did not occur. Diagnosis, basal clinical manifestations and immunosuppressants previously used are summarised in Table I. Protocolised evaluation after 1, 6 and 12 months was completed in the 100, 81,8 and 66.6% of cycles, respectively. PR or CR was achieved after 1, 6 and 12 months in the 57.6, 88.9 and 63.6% of courses evaluated, respectively. Mean level of CK (2142 IU/l at baseline, 864 after 1 month, 666 at 6 months and 566 at 12 months) and myoglobin (1077 mg/l at baseline, 419 after 1 month, 210 at 6 months and 346 at 12 months) decreased significantly. Initial dose of glucocorticoids was reduced significantly, and most patients evaluated six months after RTX stopped it after a maximum period of four months (26/27 treatment cycles, 96.3%). Complete depletion of peripheral B lymphocytes was obtained in all the treatment cycles with available data (27). There were 15 relapses in 10 patients (mean time to relapse: 13 months). The rate of response to treatment was not reduced after re-treatment (85.7% after 6 months), number of relapses was not increased and mean time to relapse was not significantly shorter. Six patients (9 cycles) had an impaired lung function, although at present developmental data are only available in 5 cases (7 cycles). One patient, with multifactorial respiratory impairment, did not improve but the other 4 did it (all with interstitial pneumonitis with or without respiratory muscles weakness). Eight patients had positive anti-Jo-1 antibodies. Results in this subgroup of patients did not differ significantly from those achieved in other patients. Serious adverse events were scarce. Patient number 4 (see Table I) received 2 treatment cycles 11 months apart; after second rituximab and first cyclophospamide infusions of the second treatment cycle, she was diagnosed of *Corynebacterium sp* meningitis. Patient number 8 had benign intracranial hypertension 4 months after finishing RTX infusions, with favourable evolution, and 16 months later she died of severe pulmonary hypertension. Finally, patient number 1 died of colon cancer diagnosed 18 months after finishing RTX infusions while her myopathy remained inactive. Adverse events of these last 2 patients were not considered to be related to the study medication.

Table I. Baseline characteristics of patients.

Patient	Sex	Age (yrs)	Type of IIM	Ground for treatment with RTX	Previous treatment
1	F	58	DM	Muscle involvement	GC, CP
2	F	47	DM	1st Muscle and cutaneous involvement 2nd Cutaneous involvement	GC, AM, MT, LF, CS, ET
3	F	51	DM	1st Muscle and cutaneous involvement 2nd Muscle and cutaneous involvement	GC, CP
4	F	77	PM	1st Muscle involvement 2nd Muscle involvement	GC, CP, CS, Ig
5	F	35	DM	1st Cutaneous involvement 2nd Cutaneous involvement	GC, MT, CP, CS, MPA, ET
6	F	63	PM	1st Muscle involvement 2nd Muscle involvement 3rd Muscle involvement	GC, CP, CS
7	F	34	PM	Muscle involvement	GC, MT, AZ, CP, CS, Ig
8	F	24	PM (MCTD)	Muscle involvement	GC, AM, MT, CP
9	F	23	PM-ES + ITP	1st Muscle involvement 2nd Muscle involvement	GC, CP, CS, Ig
10	F	38	DM	Muscle and cutaneous involvement	GC, AM, MT, CS
11	M	54	DM	1st Muscle involvement 2nd Muscle and cutaneous involvement	GC, CP
12	F	73	DM	Muscle and cutaneous involvement	GC, CP
13	F	72	PM	1st Muscle involvement 2nd Muscle involvement 3rd Muscle involvement	GC, AZ, CP, CS, Ig, MPA
14	F	58	PM-ES	Muscle involvement	GC, CP, CS, MPA
15	M	52	DM	1st Muscle involvement 2nd Muscle involvement 3rd Muscle involvement	GC, AM, MT, CP, CS, Ig, ET
16	F	69	PM	Interstitial pneumonia	GC, CP
17	F	45	PM	Muscle involvement	GC, AM, CP, CS
18	F	26	DM	1st Muscle and cutaneous involvement 2nd Muscle and cutaneous involvement	GC, CP
19	M	72	DM	Muscle and cutaneous involvement	GC, CP
20	F	59	DM	Muscle and cutaneous involvement	GC, CP

F: female; M: male; DM: dermatomyositis; PM: polymyositis; PM-ES: polymiositis-scleroderma overlap; MCTD: mixed connective tissue disease; ITP: idiopathic thrombocytopenic purpura; GC: glucocorticoids; CP: cyclophosphamide; AM: antimalarials; MT: methotrexate; LF: leflunomide; CS: cyclosporine; ET: etanercept; Ig: immunoglobulins; MPA: mycophenolic acid; AZ: azathioprine.

This series of patients with IIM treated with RTX is the largest issued. The high response rate achieved in this group of multi-drug resistant patients accounts for its use in the rescue of patients with therapeutic failure. Its high cost should be balanced with the savings of hospital stays and its good safety profile.

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