Letters to the Editors

Sustained response to rituximab in a patient with Sjögren's syndrome and severe refractory polyneuropathy

Sirs,

Rituximab has in some studies been reported to have efficacy in primary Sjögren's syndrome (pSS) (1-3). Mekinian and associates have very recently investigated the efficacy of rituximab on the neurological symptoms of pSS (4-5). They found that rituximab was not effective in progressive MS-like manifestations of pSS patients with central nervous system involvement (4). However, they described improvement of peripheral nervous system symptoms evaluated 3 months after rituximab treatment in 65% of 17 pSS patients (5). We have a similar experience of favourable effects of rituximab therapy on peripheral nervous system symptoms in one patient with pSS. Moreover, her good response to the treatment has now been sustained for two and a half years. Her polyneuropathy is associated with systemic pSS, as previously noted in a majority of cases (6).

The patient is a 56-year-old female suffering from pSS since 2000, fulfilling the American-European consensus criteria for pSS (7). In her labial salivary gland biopsy more than two lymphocyte focuses/mm^2 were found. In addition to sicca symptoms, she has presented with fatigue, Raynaud´s symptom, arthralgias, episodic salivary gland swellings and occasional purpuric lesions on the lower extremities.

In 2001 she developed muscle weakness, clumsiness and generalised lymphadenopathy. An IgM kappa monoclonal gammapathy was observed, bone marrow aspiration showed lymphoplasmocytoid cells and lymph node biopsy revealed plasma cell proliferation (IgM kappa), but no signs of malignancy. The clinical neurological examination showed a sock-like sensory loss in the feet and the distal half of the legs, and disturbances in proprioception and vibration in the upper and lower extremities. Sensory or sensorymotor polyneuropathies are among the commonest peripheral neurological manifestations in pSS (8), and the electroneuromyographic findings in our patient were consistent with a symmetric axonal sensorimotor polyneuropathy. In 2001 she received intravenous immunoglobulin treatment, and prednisolone from 60 mg/day was started. For the monoclonal gammapathy, related polyneuropathy symptoms and generalised lymphadenopathy she received chlorambusil treatment from 2001 to 2007.

In autumn 2008 her limb pains increased, and in May 2009 her serum IgM level rose quite suddenly to 25.92 g/L. ESR was 97 mm/h, the RF titer was extremely high, serum beta-2 microglobulin was elevated, and hypocomplementaemia was observed (Table I). Her methylprednisolone dose was increased to 24 mg/day and chlorambusil recommenced without effect on the serum IgM level or the severe polyneuropathy symptoms. In July 2009 she received 15 days apart two 1000 mg i.v. courses of rituximab with methylprednisolone 100 mg i.v., and paracetamol and anti-histamine as pretreatments. By October 2009, serum IgM fell to 4 g/L, the RF titer decreased dramatically, and serum beta-2 microglobulin and C4 levels normalised. In December 2009, the findings in electroneuromyography were comparable to those from 2004 and no more recent findings were observed. The lymphadenopathy disappeared, and up to January 2012 she has felt remarkably better, and her polyneuropathic symptoms have been alleviated. Her methylprednisolone dose has been tapered to 6 mg/day and serum IgM has remained normal up to January 2012. The laboratory and ESSDAI (9) values of our patient before rituximab therapy and at 3 and 30 months follow-up are given in Table I.

Table I. Laboratory findings and ESSDAI levels before and after rituximab infusions in a female patient with primary Sjögren's syndrome.

	Before treatment	After rituximab treatment course	
Variable	Baseline	3 months	30 months
ESR (mm/h)	97	24	2
CRP (mg/L)	2	9.3	<1
Serum IgG (g/L)	15.78	7.19	7.01
Serum IgA (g/L)	3.71	2.71	2.83
Serum IgM (g/L)	25.92	0.98	0.71
Serum beta-2 microglobulin (mg/L)	3.2	2.2	2.0
Serum C3 (mg/L)	1.63	1.54	1.10
Serum C4 (mg/L)	<0.03	0.12	0.13
RF (IU/mL)	3325	23	38
ANA	320	NA	640
anti-SSA antibodies (IU/L)	>240	>240	>240
anti-SSB antibodies (IU/L)	0	0	0
ESSDAI	29	13	5
Methylprednisolone dose (mg/day)	24	12	6
Chlorambusil dose (mg/day)	4	0	0

ESR: erythrocyte sedimentation rate, CRP: C-reactive protein, RF: rheumatoid factor, ANA: anti-nuclear antibodies, NA: not applicable, ESSDAI: EULAR Sjögren's syndrome activity index (9).

Our patient report is in accord with the results reported from the AIR registry (5) in that rituximab was favourable in a pSS patient with a monoclonal gammopathy accompanied by an exceptionally severe polyneuropathy. The systemic activity index ESSDAI has been shown to correlate with serum beta-2 microglobulin in patients with pSS (10), and the good response of our patient was reflected by both of these parameters. Moreover, the good clinical and immunological response of our patient to rituximab treatment has now been maintained for two and a half years.

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