Polymyositis with pulmonary and renal involvement refractory to combined immunosuppressive therapy treated with rituximab

Sirs,

Polymyositis (PM) is a chronic autoimmune disease characterised by symmetrical and bilateral inflammation of proximal muscles. Course of the disease is diverse with symptoms varying from painless muscle weakness to myalgias and constitutional symptoms, but also affection of pharyngeal and respiratory muscles in severe cases (1). Interstitial lung disease (ILD) is found in 60–70% of patients at the time of diagnosis. Pulmonary complications are a major factor causing mortality and a marker of poor prognosis (2).

About 20% of patients develop renal disease – acute kidney injury (AKI) and chronic kidney disease (CKD). The main reason for AKI seems to be tubular necrosis caused by rhabdomyolysis and myoglobinuria or by therapeutic nephrotoxic regimes. Most of the patients with AKI develop CKD, with various histopathologic types described (3, 4).

Despite the lack of controlled studies, glucocorticoids (GC) remain the cornerstone therapy, as well as for the associated interstitial lung disease. In order to control severe cases and to reduce side-effects, glucocorticoid-sparing agents are often introduced (methotrexate - MTX, mycophenolate mofetil - MMF, azathioprine, cyclosporine-A, cyclophophamide) (5). Biologics are indicated in refractory forms, rituximab (RTX) showing the most promising results (6).

We present a 58-year-old male with unremarkable medical history with dispnoea and dry cough as initial symptoms. Detailed pulmonary work-up (CT) revealed interstitial infiltrates and he was diagnosed with bronchiolitis obliterans organising pneumonia after the lung biopsy. The treatment was started with GC with slow tapering. With the reduction of GC, patient's condition deteriorated with elevated parameters of acute inflammation and extremely high creatin-kinase (CK) level and significant proteinuria. Patient underwent muscle-biopsy which proved inflammatory myopathy and renal-biopsy which was consistent with focal segmental glomerulosclerosis. Serologic tests showed positive antinuclear antibodies and Jo-1 positivity.

The patient was treated with GC pulse-therapy and IVIg and later with MTX. During the follow-up period the patient relapsed several times and was treated with high doses of GS, IVIg and MTX was replaced by MMF.

Taken into account the refractory nature of the disease, and a poor response to standard therapy RTX was introduced (2x1 g two weeks apart) with monthly IVIg applications. Five and a half months after the 1st course of RTX, patient relapsed again and received 2nd course of RTX. Laboratory findings normalised and muscle symptoms improved. The levels of $CD20^+$ B cells were measured and confirmed B cell depletion during the remission period. The relapse of PM occurred approximately 5 months after the first RTX course which was proven with rising levels of $CD20^+$ B cells (repopulation). These data determined the therapeutic strategy, so every other RTX course is planned 5 months after the last one to prevent repopulation with $CD20^+$ B cells and relapse of the disease. The patient remains in remission with stable renal and lung function tests, on stable dose of MMF with no need for GC (Fig. 1).

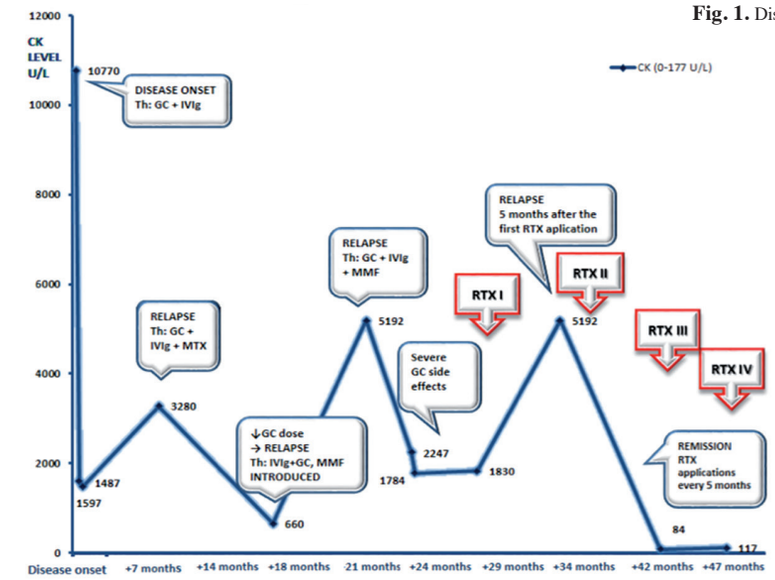

Fig. 1. Disease course.

Although there is a great deal of data regarding idiopathic inflammatory myopathies, the treatment algorithm for the refractory forms remain problematic, since there are no standard therapeutic guidelines (7). The main reason for this is the low incidence and prevalence of the disease, clinical diversity and a small number of randomised, double-blind controlled clinical trials supporting a specific diagnostic and treatment algorithm (8). Regarding RTX, the most promising results come from the blockade of $CD20^+$ B cells, and the reports on successful therapy are increasing (9). Monitoring the levels of CD20+ B cells (depletion) can be a good laboratory marker of the disease activity (as in the case of our patient).

We underline the need for further investigation of aforementioned and novel therapy especially in patients with renal and pulmonary involvement (10).

M. BAREŠIĆ
M. BAKULA
B. ANIĆ

Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, School of Medicine University of Zagreb, University Hospital Center Zagreb, Crotia.

Address correspondence to:
Marko Barešić, MD,
Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, School of Medicine University of Zagreb, University Hospital Center Zagreb, Kišpatićeva 12, 10000 Zagreb, Croatia.
E-mail: markobaresic@gmail.com

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