Obinutuzumab in a patient with overlap syndrome of systemic sclerosis and myositis with perimyocarditis and renal crisis

Sirs,

Systemic sclerosis (SSc) is an autoimmune disease with the potential to be life-threatening. Patients with organ involvement or rapidly progressive SSc reveal a high mortality (1) and should be treated with immunosuppression (2, 3). Some patients can develop overlap syndrome with immune-mediated myositis (IIM), particularly if they have diffuse cutaneous SSc and anti-PM/Scl autoantibodies, as was the case with our patient.

Recent studies have demonstrated the efficacy of obinutuzumab in systemic lupus erythematosus and lupus nephritis (4). Data concerning the utilisation of obinutuzumab in patients diagnosed with SSc or IIM are rare (5-7). This report presents a successful case of obinutuzumab in a patient with SSc/IIM overlap and perimyocarditis, renal crisis (SRC) and vasculopathy.

A 36-year-old female patient diagnosed with SSc/IIM overlap, characterised by antinuclear and anti-PM/Scl100 ab, presented with severe renal and cardiac organ manifestations and vasculopathy. Following the initial diagnosis twelve years prior, the patient was treated with methotrexate, leflunomide, cyclosporine, azathioprine, rituximab and mycophenolate mofetil (MMF) and was recently escalated to cyclophosphamide in a peripheral rheumatologic hospital. Rituximab was administered over a period of nine years, with treatment cycles occurring every six months. The treatment was terminated due to a decline in efficacy.

SRC manifested with hypertension, hydropic decompensation and the necessity of haemodialysis. Cardiac involvement presented as a decreased left ventricular function (LVEF) and perimyocarditis in magnetic resonance imaging (MRI). Due to vasculopathy, all fingers and toes were amputated. In light of the life-threatening organ involvement and the persistent disease activity, this patient was sent to our hospital for further therapy.

We decided on a treatment with obinutuzumab, which was given intravenously at a dose of 1000 mg on day one and fifteen. In addition, MMF (2000 mg per day) and bosentan (250 mg per day) were administered.

Obinutuzumab demonstrated a favourable response in absence of adverse effects. After the six-month follow-up period, troponin levels returned to normal, N-terminal pro-brain natriuretic peptide levels decreased to 342 ng/l. A new MRI showed improvement of LVEF from 35% to 47%. The myocardial oedema was only slightly detectable and there was no evidence of pericardial effusion anymore. Creatinine levels decreased to 1.4 mg/dl, with no more need for haemodialysis. Vasculopathy manifested as mild Raynaud's phenomenon (RP). Skin sclerosis was determined using the modified Rodnan skin score (mRSS), which revealed a mRSS of 4 before the administration of obinutuzumab and a mRSS of 0 following the follow-up period.

This case demonstrated the safety and efficacy of obinutuzumab in a patient with SSc/IIM overlap and life-threatening organ manifestations.

Obinutuzumab is a humanised glycoengineered type II anti-CD20 monoclonal antibody. Compared to rituximab, it has been shown to induce more cell death, antibody-dependent cellular toxicity, B-cell depletion and a weaker binding affinity for C1q, which may be associated with reduced drug resistance (8).

Obinutuzumab is approved for the management of active lupus nephritis (4, 9, 10). A small number of case series have been published on the utilisation of obinutuzumab in connective tissue disease and/or IIM (5-7). In addition to these case series, it was possible to demonstrate the efficiency not only in skin, muscle, lung, renal and joint involvement, but also in the case of perimyocarditis. The impact of obinutuzumab on vasculopathy remains to be elucidated. Obinutuzumab can be considered a promising treatment option in particular in cases of severe organ involvement and/or ineffectiveness of rituximab.

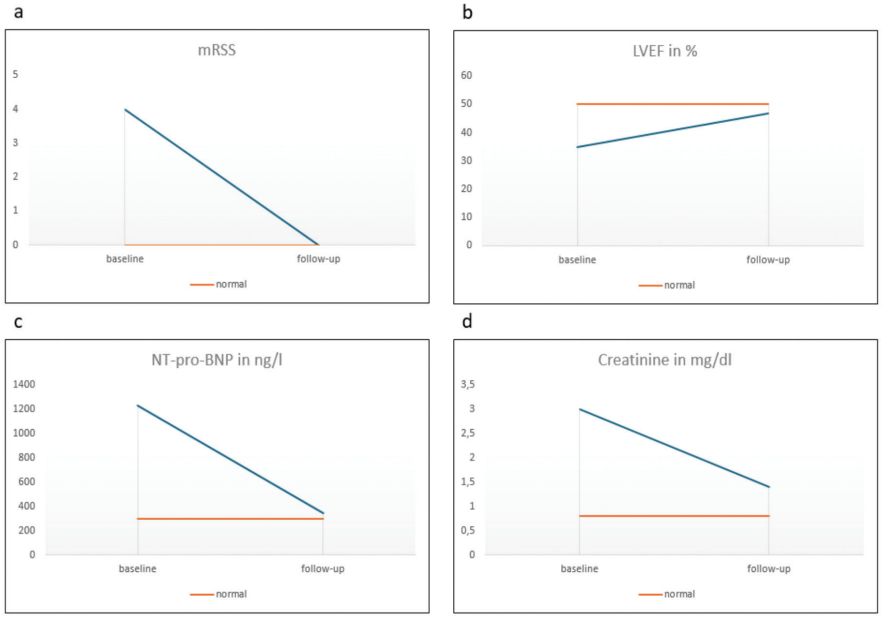

Fig. 1. Treatment effect of obinutuzumab in terms of **a**. modified Rodnan skin score (mRSS); **b**. left ventricular ejection fraction (LVEF); **c**. N-terminal pro-brain natriuretic peptide (NT-pro-BNP); **d**. creatinine, at baseline and follow-up (after two cycles of obinutuzumab, day 1 and 15 each).

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Competing interests: A.C. Pecher has received honoraria from UCB, AstraZeneca, GSK. J. Henes has received honoraria and is member of speaker's bureau of Roche. The other authors have declared no competing interests.

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