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Case report

Rituximab as an alternative for patients with severe systemic vasculitis refractory to conventional therapy: report of seven cases and literature review

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ARTICLE INFO

Article history:
Received 14 November 2014
Accepted 1 July 2015
Available online 12 September 2015

Keywords:
Rituximab
Systemic vasculitides
Granulomatosis with polyangiitis
Microscopic polyangiitis
Polyarteritis nodosa

ABSTRACT

The greater understanding of pathophysiology and behavior of systemic vasculitis, together with the development of therapeutic regimens with increasingly better safety and efficacy profiles, dramatically changed the prognosis of patients diagnosed with these clinical entities. Recently, the use of rituximab in the treatment of patients with ANCA-associated vasculitis in randomized clinical trials showed an important alternative in selected cases, especially patients refractory or intolerant to standard therapy with cyclophosphamide and corticosteroids. This article presents the report of seven cases of systemic vasculitis successfully treated with rituximab.

O rituximabe como uma opção para pacientes com vasculite sistêmica grave refratária à terapia convencional: relato de sete casos e revisão de literatura

Palavras-chave:
Rituximabe
Vasculites sistêmicas

RESUMO

O maior entendimento das bases fisiopatológicas e do comportamento das vasculites sistêmicas, aliado ao desenvolvimento de regimes terapêuticos com perfil de segurança e eficácia cada vezes melhores, modificou drasticamente o prognóstico dos pacientes

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http://dx.doi.org/10.1016/j.rbre.2015.07.016

Granulomatose com poliangeíte
Poliangeíte microscópica
Poliarterite nodosa

diagnosticados com essas entidades clínicas. Recentemente, o emprego do rituximabe no tratamento de pacientes com vasculites ANCA associadas em ensaios clínicos randomizados se mostrou uma opção importante em casos selecionados, especialmente pacientes refratários ou intolerantes à terapia-padrão com ciclofosfamida e corticosteroides. O presente artigo traz o relato de sete casos de vasculites sistêmicas com tratamento bem-sucedido com rituximabe.

Introduction

The introduction of glucocorticoids and, later, of cyclophosphamide (CYC) in inducing remission of systemic vasculitis (SV) dramatically changed the prognosis of these patients, resulting in symptomatic improvement, high rates of remission and in increased survival.[1,2] However, a significant portion of patients remains refractory or intolerant to conventional therapies,[3] justifying the growing interest in new safer and more effective therapeutic options. Recent evidence points to a crucial role of B lymphocytes in the development of SV.[4] Rituximab (RTX) is a chimeric anti-CD20+ B cell monoclonal antibody widely used in B cell lymphomas, and more recently has been used for various autoimmune conditions in selected cases.

We report seven cases of patients diagnosed with SV treated successfully with RTX.

Case report

Patient 1

Male, 46, with fever, weight loss, severe pulmonary vasculitis (Fig. 1), pauci-immune glomerulonephritis and neuropathy of lower limbs, with Birmingham Vasculitis Activity Score (BVAS) = 20 and ANCA-negative. Treated under a diagnosis of microscopic polyangiitis (MPA), subjected to pulse therapy with methylprednisolone (MP) followed by cyclophosphamide associated with prednisone 40 mg/day. The patient developed hyperglycemia and liver toxicity; thus, this treatment was suspended, with the introduction of weekly doses of RTX 375 mg/m^2 for 4 weeks. After a year of treatment, the patient achieved complete remission without maintenance therapy.

Patient 2

Female, 31, presenting edema and fixed cyanosis of extremities, polyarthralgia, subcutaneous nodules, limb ischemia and acute respiratory failure (BVAS = 15), with a diagnosis of polyarteritis nodosa (PAN) and HBsAg positive for 6 years. Skin biopsy showed fibrinoid necrosis and medium-caliber vessel infiltration. Subjected to pulse therapy with MP and CYC with poor response. Treatment was started with two fortnightly doses of RTX 1 g, with dramatic improvement. Treated with a maintanance infusion of RTX after 6 months, maintaining complete remission without steroids.

Patient 3

Male, 56, admitted with arthritis, nephritis, retinal vasculitis, pulmonary nodules and peripheral neuropathy (BVAS = 17). With a diagnosis of granulomatosis with polyangiitis (GPA) for 3 years with cANCA 1/40, refractory to 7 pulses of MP and CYC. After rescue therapy with 4 weekly infusions of RTX 375 mg/m^2, the patient showed complete remission of the disease for three years, with maintenance therapy with RTX every 6 months.

Patient 4

Female, 47, with ongoing fever, weight loss, hearing loss, palpable purpura, glomerulonephritis and hemoptysis for the duration of 3 years (BVAS = 38 at admission), with a diagnosis of GPA. A chest CT scan revealed multiple pulmonary cavitations. Ancillary and therapeutic tests negative for tuberculosis, with subsequent weekly RTX infusion for 4 weeks. The patient remains in complete remission after 1 year, without maintenance therapy.

Patient 5

Male, 26, with an early weight loss, arthritis, sinusitis, conjunctivitis and abdominal pain for 5 months (BVAS = 12), pANCA 1/20. After ruling out differential diagnoses, the patient was treated as with GPA, beginning with two biweekly infusions of RTX. A maintenance schedule with half-yearly infusions of RTX was chosen.

Patient 6

Male, 24, with manifestations of nephritis and with a biopsy revealing pauci-immune glomerulonephritis, compatible with a diagnosis of MPA, refractory to multiple pulses of MP and CYC over 5 years. A scheme of 4 weekly infusions of RTX was started, with early BVAS = 12, achieving complete remission; as maintenance, half-yearly infusions were scheduled.

Patient 7

Female, 45, with weight loss, arthritis and mononeuritis multiplex over 5 years, with p-ANCA 1/40. The patient received a diagnosis of MPA, and started a weekly RTX infusion schedule for 4 weeks, resulting in complete remission.