Combination therapy of rituximab and corticosteroids for patients with refractory chronic immune thrombocytopenic purpura: report of two cases

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Introduction

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder. Corticosteroids, usually prednisone, are often the first-line treatment for ITP. However, about 70% of adult patients experience a relapse after the discontinuation of corticosteroids. Moreover, approximately 20% to 30% of chronic ITP patients do not respond to corticosteroid therapy [1, 2]. Rituximab has been proven to be an effective treatment for ITP, and the response rate was reported to be about 60% in refractory ITP patients [3]. However, the response time with rituximab is slower than expected, and at least three months might be necessary to observe an effect. Therefore, sometimes, the use of a combination therapy with rituximab according to different patient conditions is necessary.

For this reason, we performed a clinical analysis of the combination therapy of rituximab and corticosteroids in two patients to evaluate the efficacy and safety of this treatment.

Case report

Case 1

An 82-year-old man presented with sustained blood-tinged sputum and bleeding in the skin for more than six months. He has a history of hypertension, and his platelet count was about 1 × 10^9 to 10 × 10^9/l. No splenomegaly was observed. His bone marrow showed an increased number and maturity disturbance of megakaryocytes without morphological evidence of dysplasia, and his platelet-associated immunoglobulin G (PAIgG) level was normal. His antinuclear antibody and rheumatoid factor test results were negative. He was diagnosed with chronic ITP, based on the criteria reported in a previous paper [4]. He was initially treated with prednisone, 40 mg/day, which resulted in a rapid increase in his platelet count to around 100 × 10^9/l. However, he developed steroid-induced diabetes after a short-term prednisone therapy and relapsed on a prednisone taper, with his platelet count decreasing to 18 × 10^9/l. His blood glucose was controlled after insulin therapy. No response to the second course of 40 mg/day prednisone was observed. He refused splenectomy and other immune suppressive drugs, and thus we gave him weekly intravenous infusions of 375 mg/m² of rituximab for four weeks combined with 10 mg of dexamethasone. After his first dose of dexamethasone followed by rituximab, within 24 h, his platelet count had increased to 65 × 10^9/l and his bleeding symptoms were significantly improved. During the succeeding three-week treatment period, his platelet count fluctuated between 30 × 10^9/l and 60 × 10^9/l and then dropped to a minimum of 19 × 10^9/l. Considering the patient’s slow response...
Platelet autoantibody production results from autoreactive T-helper cell activation and autoreactive T-B cell cognate interaction. The activation and expansion of autoreactive T cells are induced by antigen-presentation in the spleen that present apoptotic platelets to T cells [5–7]. The mechanism of action of rituximab (a monoclonal anti-CD20 antibody) in ITP may be due to the selective depletion of CD20+ B cells, which affects autoantibody development and normalizes abnormal autoreactive T-cell responses in patients with ITP [8]. The peripheral B cells of the two patients were almost eliminated even at different doses of rituximab. Although the platelet count of the male patient was significantly improved, it was continuously below the normal level. For the female patient, no favorable response to rituximab was observed. The result suggests that ITP is a heterogeneous disorder. Not only B cells but also cytotoxic T lymphocytes [9] or other unknown factors that do not depend on B cells might play important roles in the pathogenesis of ITP. Considering the varying treatment effect of rituximab in different ITP patients, as well as the slow response time, we believe that the use of combination therapy with rituximab for refractory ITP patients. Moreover, because both patients had steroid-related complications such as steroid-induced diabetes and Cushing’s syndrome, we used a low dose of dexamethasone (10 mg, weekly) combined with rituximab and a smaller dose of prednisone (10 mg, daily) as maintenance therapy. In the first case, the quick increase in platelet count after the first administration of rituximab and dexamethasone therapy suggested that multiple immunological mechanisms are involved in ITP pathogenesis and that the mechanism of action of rituximab in ITP needs to be further investigated.

The authors declare no conflict of interest.
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