Case Report

Efficacy of Rituximab in Refractory Polymyositis

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ABSTRACT. We describe the effectiveness of rituximab, an anti-B lymphocyte monoclonal antibody, in a case of refractory polymyositis with interstitial pulmonary disease and anti-Jo-1 autoantibody (antisynthetase syndrome). Rituximab was well tolerated, and its efficacy in inflammatory myositis should be evaluated. (J Rheumatol 2005;32:1369–70)

Key Indexing Terms:
POLYMYOSITIS ANTISYNTHETASE IMMUNOTHERAPY RITUXIMAB

Polymyositis (PM) and dermatomyositis (DM) are disabling and potentially life-threatening autoimmune diseases. Systemic steroids are the gold standard first-line therapy. For patients refractory or intolerant to steroids, intravenous immunoglobulins (IVIG) and other immunosuppressive drugs such as methotrexate (MTX) and azathioprine may be proposed, but there is little evidence supporting their effectiveness and patients often remain disabled[1].

The chimeric anti-CD20 monoclonal antibody rituximab was first introduced to treat B lymphocyte neoplasia. Recently, encouraging results have been reported in its use for the treatment of several autoimmune disorders including rheumatoid arthritis[2], systemic lupus erythematosus[3], and immune thrombocytopenia[4]. Preliminary unpublished data suggest rituximab efficacy in DM[5]. We describe its effectiveness in a case of refractory PM.

CASE REPORT

In 1998, a 47-year-old female nurse with an unremarkable medical history was admitted for diffuse muscle weakness and polyarthralgia. Clinical examination showed hyperkeratotic fingers ("mechanic's hands"). Creatinine phosphokinase (CPK) and aldolase were 342 IU (normal < 150) and 22 IU (< 10), respectively. Chest radiograph and computed tomography scan showed bilateral irregular linear opacities. The ratio of diffusing capacity for carbon monoxide/alveolar volume (DLCO/AV) was decreased (74%). Anti-Jo-1 antibody was positive. Muscle biopsy confirmed the diagnosis of PM, showing T lymphocytes infiltrating necrotic and regenerating fibers.

Prednisone was started at 1 mg/kg/day, with significant muscle and lung function improvement (DLCO/AV 93%), but she remained steroid dependent above 20 mg/day of prednisone. She was unable to work.

In 2000, steroid-sparing agents were tried, but MTX 15 mg/week was ineffective (relapse 4 months after MTX onset) and azathioprine 200 mg/day was stopped because of agranulocytosis after one month. From 2001 through 2002, she received IVIG at the dose of 1 g/kg/mo, with amelioration of symptoms and reduction of prednisone to 15 mg/day. By the end of 2002, she became refractory to IVIG and the prednisone dose was raised to 30 mg/day. She presented significant weight gain and osteoporosis. In September 2003, her muscle disability scale (MDS)[6] was 9, and she was unable to walk outside her house. CPK was increased (1360 IU/l). She was given 4 biweekly infusions of rituximab at a dose of 375 mg/m^2, while maintaining prednisone at 25 mg/day. Four months later, she had significantly improved, with MDS at 2, and normal CPK. DLCO/AV was stable at 93%. The dose of prednisone was gradually tapered to 8 mg/day one year after rituximab, and she was able to resume her job in April 2004. However, anti-Jo-1 antibody was still positive.

DISCUSSION

To our knowledge, this is the first report of the efficacy of rituximab in PM. The patient had PM associated with interstitial lung disease, polyarthralgia, hyperkeratotic fingers, and anti-Jo-1 antibody. This combination defines antisynthetase syndrome, which has a poor outcome despite immunosuppressive drugs[7]. New treatments are required and rituximab, as an effective B lymphocyte-depleting agent[8,9], is of benefit in autoimmune diseases mediated by B lymphocytes. However, PM is a T cell mediated autoimmune disorder as its pathogenesis is mostly marked by muscle infiltration by CD8+ cytotoxic T lymphocytes[1]. The efficacy of rituximab with this patient is therefore intriguing. The role of antisynthetase autoantibodies in the pathogenesis of PM and DM remains unclear[1]. The persistence of anti-Jo-1 antibodies may indicate that B cells contribute to pathogenesis by mechanisms aside from the production of pathogenic autoantibodies, such as serving as antigen-presenting cells, producing cytokines, or by other means of costimulation. Anti-Jo-1 antibody levels are not affected by rituximab, probably because the plasma cells producing autoantibodies are CD20-negative and remain unaffected by rituximab.

Rituximab was well tolerated, and its efficacy in DM and antisynthetase-positive PM, as suggested in our patient, should be evaluated in larger studies.

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