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Successful treatment of severe anti-p200 pemphigoid in a heart transplant recipient with a single cycle of rituximab



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Key words: anti-p200 pemphigoid; heart transplant recipient; rituximab.

INTRODUCTION

Anti-p200 pemphigoid is a rare autoimmune subepidermal blistering disease, first described in 1996.¹ This disorder was initially considered as a more benign condition compared with bullous pemphigoid and epidermolysis bullosa acquisita, but in a recent series of patients, heterogeneous clinical presentations have been described, including cases with a more severe course than previously reported.² We describe a case with a highly active disease in a heart transplant patient who experienced a dramatic and complete remission after 1 cycle of rituximab.

CASE REPORT

A 65-year-old man who underwent a heart transplant for ischemic heart disease in 1995 presented to our department in February 2011 for a severe relapse of a bullous eruption. His antirejection treatment included mycophenolate mofetil at 1.5 g/d, everolimus at 0.75 mg/d, and prednisolone at 15 mg/d. He had a history of a difficult-to-control bullous disease lasting 3 years, which was diagnosed as bullous pemphigoid. This diagnosis was based on histologic examination of a blister, which found a subepidermal blister with mixed dermal infiltrate, and direct immunofluorescence microscopy of perilesional skin, which showed linear depositions of IgG and C3 along the dermoepidermal junction. He had no mucosal involvement. He had a dependency on highly potent topical corticosteroids, the standard regimen in France,³ despite increasing doses of

immunosuppressants (mycophenolate mofetil) reaching 3 g/d. At a diagnostic reassessment, indirect immunofluorescence microscopy on 1 mol L⁻¹ NaCl split normal human skin with positive IgG autoantibodies binding to the dermal side of the skin and immunoblotting found positive IgG4 autoantibodies against 200-kDa dermal protein. The diagnosis of anti-p200 pemphigoid was finally made. There was no clinical, histologic, or ultrasound scan signs for heart graft rejection. The patient had a severely altered quality of life because of his intractable skin disease and advanced steroid-related skin damage. Therefore, a non-steroid-based treatment was sought. After dapsone at 100 mg/d for 3 months and high-dose intravenous immunoglobulin (3 monthly courses at 2 g/d per course) failed to control the disease, and after informed consent, he received 4 weekly infusions of rituximab (375 mg/m²) in June 2012 (Fig 1). His antirejection treatment had not been changed. He experienced a complete remission 6 weeks after the end of the last rituximab infusion (Fig 2). The treatment was well tolerated. Topical corticosteroids were discontinued, and prednisolone was maintained at a dose around 10 mg/d as an antirejection drug. Immunoblot analysis did not identify anti-p200 antibodies in May 2014. The patient remains free of disease after a follow-up of 52 months.

DISCUSSION

Our case illustrates the severity of anti-p200 pemphigoid in a heart transplant patient and that

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Fig 1. Anti-p200 pemphigoid with edematous erythema and tense blisters on the trunk, before first infusion of rituximab.

rituximab (MabThera, Roche, Welwyn Garden City, UK) could be an alternative treatment for refractory and severe anti-p200 pemphigoid. Few cases of immunobullous disease have been described in organ transplant recipients,⁴ most of them occurring in the context of acute or chronic graft rejection.⁵ In contrast, our patient had no signs for graft rejection.

Our patient's disease was highly active despite the antirejection medications and the various systemic treatments attempted. Standard treatment strategy for anti-p200 pemphigoid is not well established, but it is classically based on bullous pemphigoid treatment and topical class intravenous corticosteroids being applied first. In case of highly active disease, systemic medications can be used, including corticosteroids, dapsone, azathioprine, cyclosporine, high-dose intravenous immunoglobulin, and ustekinumab.⁶

Our patient had a dramatic, complete remission with more than 4 years of follow-up after a single cycle of rituximab (4 weekly infusions of 375 mg/m²). Rituximab, a monoclonal antibody against the CD20 antigen, has been administered in various blistering autoimmune diseases, with major efficacy in pemphigus.⁷ It is currently being assessed in mucous membrane pemphigoid and bullous pemphigoid. The long-lasting efficacy of rituximab in pemphigus is thought to stem from a blockage of B-cell maturation, prolonged repopulation with



Fig 2. Anti-p200 pemphigoid, 6 weeks after 4 weekly infusions of rituximab.

naïve B cells, and delayed reappearance of memory B cells, explaining the disappearance of circulating desmoglein-specific IgG-positive B cells in patients with lasting complete remission after a single cycle of rituximab.⁸ Although we did not investigate lymphocyte subpopulations, it is noteworthy that our patient experienced a lasting clinical remission and that anti-p200 antibodies were no longer detectable. Two administration protocols for rituximab are currently used in autoimmune diseases (2 infusions of 1,000 mg each 15 days apart or 4 weekly infusions of 375 mg/m²), without evidence of different efficacy in a retrospective assessment of published data.⁹

This case is the first report of a long-lasting, complete remission of anti-p200 pemphigoid with rituximab. Because publication bias is a serious concern, additional cases of anti-p200 treated with rituximab or other anti-CD20 monoclonal antibodies, including failures, are warranted to ascertain whether rituximab is an encouraging therapeutic approach for highly active anti-p200 pemphigoid.

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