Successful Treatment of Pemphigus Vulgaris with a Modified Regimen of Rituximab Biosimilar(CT-P10) Combined with IVIG

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Dear Editor,

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Pemphigus Vulgaris (PV) has been known as fatal autoimmune bullous diseases affecting the skin and mucous membranes. Here, we report that a patient with PV responded rapidly to a modified regimen of rituximab biosimilar (CT-10, Truxima®) combined with Intravenous Immunoglobulin (IVIG).

A 53-year-old man presented with extensive erosions due to blistering on the whole body following initial mucosal erosions which started at 3 years ago. Laboratory tests revealed an eosinophil count of 16.7% (normal range: 0~5%) with normal liver and renal functions. Antinuclear antibody was a nuclear membrane pattern with a titer of 1:40. Anti-dsDNA, anti-Ro/La, anti-Scl-70, and anti-phospholipid antibodies were negative. Myeloperoxidase and PR3 antineutrophil cytoplasmic autoantibody were both negative. Histological examination showed suprabasala cantholysis, while direct and indirect immunofluorescence assays demonstrated a deposition of immunoglobulin G (IgG) on an intercellular surface at 1:640 dilutions (Figure. 1a, b). Based on the blistering on the whole body and characteristic biopsy result, the patient was diagnosed as PV. Although he was initially treated with topical and high-dose methylprednisolone (1000 mg/day) pulse therapy for 3 consecutive days, there was no significant improvement in skin blistering lesions. We decided to administer CT-P10 combined with IVIG. We treated the patient with CT-P10 (500, 500, and 1000mg once weekly for 3 weeks) combined with IVIG (1g/kg at first and third week). During the treatment of CT-P10 combined with IVIG, a clinical response rapidly appeared, and levels of antibodies were decreased from 1:640 to 1:40 (Figure. 1c). Disease activity was dramatically controlled within 3 weeks. It achieved the end of the consolidation phase for PV within 5 weeks after starting CT-P10 combined with IVIG (Figure. 1d-g). Then, we tapered oral prednisolone and steroid-sparing

agents including mycophenolate mofetil and cyclosporine for maintenance therapy. Until now, there has been no recurrence of PV on 36 months follow up.

Rituximab, a monoclonal anti-CD20 antibody, was approved by the Food and Drug Administration for PV treatment with the dosage of 375 mg/m² (once a week, four times) in 2018. Biosimilars such as CT-P10 are currently being developed for use in oncology, endocrinology, and rheumatology [1,2]. CT-P10 is a rituximab biosimilar developed in 2015 and named Truxima® with non-inferiority and similar safety profiles. According to a recent report, rituximab biosimilar has efficacy and safety for both newly diagnosed and previously treated PV patients[3]. However, there is no consensus on the dose regimen and duration for PV. A previous report suggested various successful rituximab regimens for pemphigus such as rheumatology, oncology, and IVIG combination protocols [4]. Other reports demonstrated that low-dose rituximab (375 mg/m², 2 times, 1-2 weeks apart) had similar effects in autoimmune diseases compared to high-dose rituximab (1000mg, 2 times, 2 weeks apart) in the time to achieve rapid improvement[5-7]. Based on these reports, we hypothesized that mixing with low-dose and high-dose regimen of CT-P10 combined with IVIG would be more effective to achieve endpoints of PV compared to other protocols. This modified regimen of CT-P10 combined with IVIG demonstrated significantly rapid improvement for PV with outside effects. The previous report showed that the mean time to disease control was 7.5 weeks in patients of PV (n=15) who were treated with various regimens of rituximab[4]. Another report showed that the median times of disease control and the end of consolidation phase were 7 and 16 weeks[6]. However, our patient achieved disease control and the end of consolidation phase within 3 and 5 weeks, respectively. Collectively, we suggest that the modified regimen of rituximab biosimilar combined with IVIG may be an effective treatment method for PV patients. These biosimilar contain the active substance of the original products, so they have the same effects as the original products. Moreover, they can reduce the cost of

Figure 1: (a) Skin biopsy showed suprabasallacantholysis (Hematoxylin and eosin stain, x 200). (b, c) Deposition of immunoglobulin G (IgG) on the intercellular surface with 1:640 dilution before starting CT-P10 with IVIG, and 1:40 dilution at 16 days after starting CT-P10 with IVIG in indirect immunofluorescence assays. (d) 3 days before starting CT-P10 with IVIG. (e) 10 days after starting CT-P10 with IVIG and debridement. (f) 28 days after starting CT-P10 with IVIG. (g) 35 days after starting CT-P10 with IVIG.

treatment, which alleviates the economic burden of a promising treatment for both the patient and healthcare professionals. Further investigations about this modified regimen method for PV patients are needed.

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