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Case Report

Dupilumab is a Predominant Treatment for Recalcitrant Bullous Pemphigoid

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Abstract

Bullous pemphigoid is occasionally recalcitrant to established medications. Our 72-year-old male patient was treated with established medications such as systemic corticosteroid (prednisone 1.3_0.7mg/kg), methylprednisolone pulse therapy, 7 doses of monthly intravenous immunoglobulin, cyclosporine. During tapering of prednisone, the disease activity easily flared up, and many complications such as aspiratory pneumonia, chronic urinary infection, hypoalbuminemia were observed. Given the patient's severe disease status and treatment limitations, we introduced dupilumab expecting Th2-suppressive effect, according to the dosing regimen approved for atopic dermatitis. After 2 months of dupilumab therapy, BPDAI (Bullous Pemphigoid Disease Area Index) score halved, and after 3 months, he accomplished the clearance of the lesions. A placebo-controlled phase 3 clinical trial of dupilumab for severe BP is now under way, and it is expected that the effectiveness of dupilumab for BP will be proved in the near future.

Keywords: Keywords: Bullous Pemphigoid, Dupilumab, Recalcitrant Treatment

Introduction

Bullous pemphigoid is occasionally recalcitrant to established medications. Many BP patients are elderly and have other systemic complications, so easily to get a severe infection and occasionally lead to critical condition. Our case is also one of those patients, and we finally tried applying dupilumab to the case. After 3 months since the initiation of dupilumab, the patient had resolved

almost all blisters and erosion.

Case Reports

A 72-year-old man was transferred to our hospital with a 5-month history of extensive bullae and erosion dispersed all over the body, despite ongoing treatment with prednisone 1.3_0.7mg/kg day, and 3-times monthly IVIGs. The clinical presentation is shown in Figure 1, and the clinical course and treatments are in Figure 2. Tapering prednisone to 30mg/day (0.7mg/kg day), bullae easily flared up, so cyclosporine150mg was added and monthly IVIG was continued. Despite these therapies, we could not taper PSL less than 0.7mg/kg. The patient got some complications like aspiration pneumonia, repeated urinary tract infection, and extreme hypoalbuminemia. We did not apply plasma exchange due to the risk of sepsis. Anti-BP180 antibody and peripheral eosinophils continued to be extremely high. To suppress Th2 reaction without immunosuppression, we started dupilumab instead of cyclosporine, with an initial dose of 600mg administered subcutaneously followed by 300mg every other week, according to the dose for atopic dermatitis. Within 1 month of dupilumab initiation, BP-DAI (Bullous Pemphigoid Disease Area Index) score was decreasing and we started tapering PSL. He achieved disease clearance 3

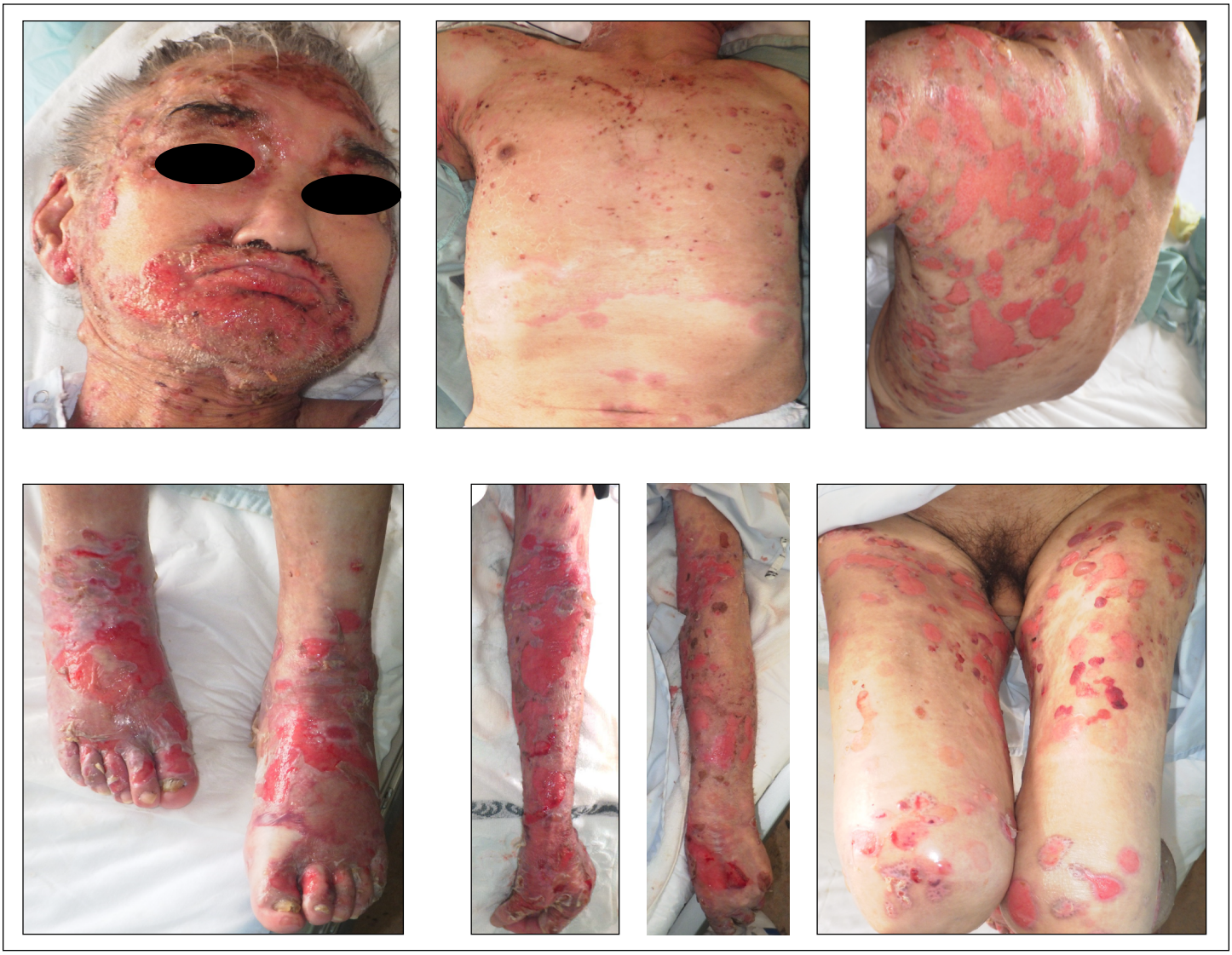

Figure 1: Clinical pictures of the patient when BPDAI score was the worst, 105(/120). Extensive bullae and erosion were dispersed all over the body.

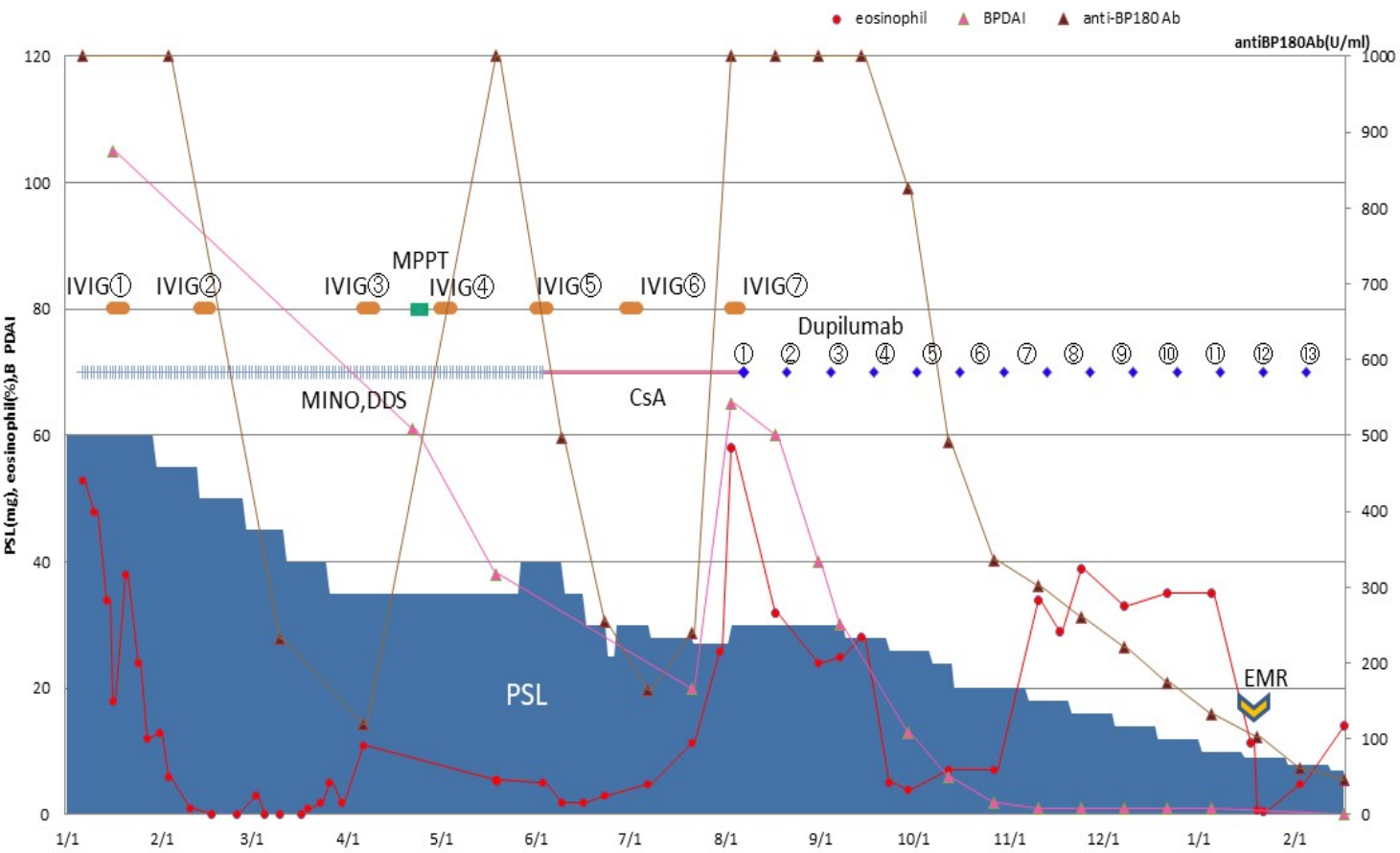

Figure 2: Systemic medications and the clinical course of our BP case are shown. After 4 doses of Dupilumab, BPDAI score halved and anti-BP180 antibody started to decrease. After 3 months, he accomplished the clearance of the lesions. PSL, prednisolone; IVIG, intravenous immunoglobulin; MINO, Minocycline; DDS, Diaphenylsulfone; CsA, cyclosporine; MMPT, Methylprednisolone Pulse Therapy; BPDAI, Bullous Pemphigoid Disease Area Index; EMR, Endoscopic Mucosal Resection for early-stage gastric carcinoma

months after initiating dupilumab and is now tapering of PSL to lower dose without disease rebound. Any specific adverse event, such as injection site reaction, or conjunctivitis, was not observed.

Discussion

Kaye, et al [1], first reported a successful dupilumab treatment for refractory bullous pemphigoid, and Abdat, et al [2], reported 13 cases of refractory bullous pemphigoid treated with dupilumab. It concluded that disease clearance or satisfactory response was achieved in 12 of 13 (92.3%), and total clearance, which means the absence of both bullae and pruritus, was achieved in 53.8% (7 of 13). Furthermore, 3 of 7 that achieved total clearance had no concomitant medications with dupilumab, and one of 7 could taper off concomitant PSL 60mg/day in 3-month period. There was no adverse effect.

Atopic dermatitis and bullous pemphigoid have similar mechanisms in the point that increase in TARC/CCR17 chemokine secreted from keratinocytes leads to the infiltration of Th2 cells to the lesion, which release IL-4, IL-13, which activates eosinophils. Serum TARC levels are related to the disease activity of BP, as well as of atopic dermatitis [3]. It seems logical to consider that dupilumab is also effective to bullous pemphigoid.

Our patient's serum TARC levels before starting dupilumab was 1041pg/dl, and decreased to 212pg/dl 4months later.

Peripheral eosinophils also once decreased, but rebounded in spite of continuing dupilumab. Anti-BP180 antibody has continuously decreased. It was unreasonable dissociation between decreasing

anti-BP180 antibody and continuing hyper-eosinophilia. The patient has had mental illness for many years and had been taking many psychotropic drugs such as chlorpromazine, risperidone, diazepam, carbamazepine, biperiden, and sulfamethoxazole trimethoprim, alfacalcidol , lansoprazole to prevent side effects due to high-dose PSL. Although the administration of these drugs had stopped when he developed aspiration pneumonia, hyper-eosinophilia was continued (Figure 2). In searching for a malignant neoplasm accompanying concomitant BP, the patient was diagnosed with early-stage gastric cancer. Five months after the initiation of dupilumab, we could finally taper PSL to 10mg, and he underwent endoscopic mucosal resection. Around then, hyper-eosinophilia has been moderated (Figure 2).

A placebo-controlled phase 3 clinical trial of dupilumab for severe BP is now under way, and it is expected that the effectiveness of dupilumab for BP will be proved in the near future.

Acknowledgments

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Conflict of Interest Statement

The author has no conflicts of interest to declare.

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