CASE REPORT

Dupilumab monotherapy suppresses recalcitrant pemphigus vulgaris

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INTRODUCTION

Pemphigus Vulgaris (PV) is a subgroup of IgG-mediated autoimmune blistering diseases targeting desmosomal adhesion proteins, desmoglein (Dsg) 1 and Dsg 3.1 Systemic corticosteroids are the current first-line treatment. Other treatments aimed at disease control include immunosuppressive and immunomodulatory agents, such as azathioprine, mycophenolate mofetil, cyclosporine, intravenous immunoglobulin, dapsone, and rituximab.

Dupilumab is a biologic medication targeting interleukin (IL) 4 and IL-13 currently approved by the Food and Drug Administration for the treatment of atopic dermatitis, asthma, chronic rhinosinusitis, and eosinophilic esophagitis. Successful disease control of PV complicated by pulmonary tuberculosis with dupilumab as an add-on therapy has been reported in the literature.2 Here, we report on the significant improvement of PV with dupilumab monotherapy.

CASE REPORT

A 41-year-old woman presented with superficial bullae and crusted erosions on the scalp (Fig 1, A), chest, abdomen, back, legs, buccal and lingual mucosa (Fig 1, B), and groin. The patient reported that the lesions had been present for 4 months. Previous treatments using telemedicine and teledermatology with topical clobetasol and several courses of systemic corticosteroids over the previous 4 months had failed. The histopathologic examination showed suprabasal acantholysis with separation of the superficial epidermis overlying dermal infiltration of lymphocytes, histiocytes, and scattered eosinophils. Pro bono direct immunofluorescence studies demonstrated IgG and C3 in an intercellular pattern, confirming the diagnosis of PV. Enzyme-linked immunosorbent assay tests for anti-Dsg1 and anti-Dsg3 antibody levels were too expensive, so the patient refused. Without insurance, the patient was also unable to afford intravenous rituximab but opted for subcutaneous injections with off-label dupilumab samples. The patient received an initial 600-mg loading dose. Clinical follow-up 1 week later showed significant improvement at the scalp and other lesions. At weeks 2 and 4, the patient received 300-mg doses, with marked improvement in her quality of life. The patient had significant improvement on the scalp and trunk but had persistent oral lesions until week 5 (Fig 2). Despite the marked improvement of scalp and truncal lesions, dupilumab dosing was increased to a 300-mg weekly dose at week 5 because 1 to 2 oral lesions developed within days before the next injection. These fledgling erythematous bullae would rapidly resolve within days of each injection. By week 6, the patient’s oral lesions had cleared. She was continued on a 300-mg weekly dose.

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DISCUSSION

PV is presumed to affect genetically susceptible individuals, with a majority of patients expressing human leukocyte antigen alleles DRB1*04:02 or DQB1*05:03. The autoimmune reaction is driven by T helper 2 cells. CD4 autoreactive T cells are matured by antigen-presenting cells that present specific Dsg peptides via their human leukocyte antigen class II molecules. The CD4 cells subsequently produce IL-10 and drive the production of Dsg-specific antibodies by B cells. Nagel et al demonstrated that patients with acute PV showed higher concentrations of serum IgE and IgG4 antibodies, along with IgE deposits in the epidermis, which is a marker of a type 2 inflammation. Since dupilumab targets the IL-4 receptor, which is known to act on T helper 2 cell signaling pathways, this pathway is hypothesized to be the mechanism of action for the efficacy of dupilumab in the treatment of PV.

Although systemic corticosteroids remain the gold standard for PV treatment, patients usually require prolonged high-dose corticosteroids with associated adverse effects. Other immunosuppressive agents, such as azathioprine, mycophenolate mofetil, cyclophosphamide, and methotrexate have been used in conjunction with corticosteroids. To our knowledge, sparse data exist on the efficacy of topical corticosteroids in the treatment of PV.

Rituximab, a monoclonal antibody directed against the CD20 antigen of B lymphocytes, has been approved by the Food and Drug Administration as an intravenous infusion for moderate to severe PV. In a non-US prospective, multicenter, parallel-group, open-label, randomized trial, 46 of 90 patients with moderate to severe PV and pemphigus foliaceus were treated with intravenous rituximab plus short-term prednisone. Forty four patients were assigned to oral prednisone alone. At month 24, 41 of 46 (89%) patients assigned to rituximab plus short-term prednisone were in complete remission off-therapy versus 15 of 44 (34%) patients assigned to prednisone alone.

Dupilumab provides benefits over traditional therapies by providing a safer side effect profile. Dupilumab is also a more accessible option than rituximab, as it is a self-administered subcutaneous injection rather than an infusion center–based.

Fig 1. A, Scalp and (B) oral mucosa prior to treatment with dupilumab.

Fig 2. A, Scalp and (B) oral mucosa after 5 weeks of treatment with dupilumab.
intravenous infusion that may take hours. The dosing regimen for dupilumab typically consists of a 1,600-mg loading dose, followed by 300-mg injections every 2 weeks. In a phase 2 randomized trial of adults with eosinophilic esophagitis, weekly doses of dupilumab resulted in <6 eosinophils per high power field in 65% of patients after 12 weeks. Additionally, off-label dosage regimens of 300-mg weekly injections for the treatment of atopic dermatitis in 23 patients has been reported in the literature. The patients were reported to have improved disease control, and no adverse effects were reported.

Bullous pemphigoid is another autoimmune blistering disease characterized by antibodies to the subepidermal structural proteins, BP180 and BP230. A clinical trial evaluating dupilumab in the treatment of bullous pemphigoid is ongoing. In a multicenter case series of 13 patients with bullous pemphigoid, disease clearance or satisfactory response was achieved in 92.3% of the patients. Dupilumab monotherapy has been reported in 2 cases to significantly improve Brunsting-Perry pemphigoid, a variant of cicatricial pemphigoid characterized by involvement of the head, face, and neck with rare mucous membrane involvement.

Recently, a patient with biopsy-proven PV developed rapid progression of bullous erosions despite daily oral corticosteroid 40-mg dose of methylprednisolone. Since the patient was also infected with pulmonary tuberculosis and septic, the corticosteroid dose could not be increased and rituximab or other adjunct immunosuppressants could not be initiated. Dupilumab was added to the oral corticosteroid regimen to control the PV flare. The patient was given a 600-mg loading dose of followed by 300-mg injections every other week for 10 weeks. In the current case, dupilumab monotherapy in a patient with PV unresponsive to high-dose corticosteroids rapidly healed PV lesions. More studies are warranted to investigate the efficacy and dosage of dupilumab in the treatment of PV.

Conflicts of interest
None disclosed.

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