OMCR

Oxford Medical Case Reports, 2021;4,113–114

doi: 10.1093/omcr/omaa029
Case Report

CASE REPORT

Dupilumab: a new contestant to corticosteroid in allergic bronchopulmonary aspergillosis

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Abstract

Allergic bronchopulmonary aspergillosis (ABPA) is a disease characterized by severe disability with recurrent wheezing and shortness of breath. The current recommended therapy is daily oral corticosteroids +/− oral antifungal therapy. Despite this, many patients continue to have severe symptoms, and others require fairly high daily oral corticosteroid dosing to achieve control, which in turn may induce the well-known effects of long term steroid use. The anti-interleukin drugs have been reported to help improve daily symptoms and reduce steroid requirements. Much of the literature highlights the benefit of omalizumab. We present a case of dupilumab as add-on therapy in a patient with ABPA, which allowed us to reduce daily steroid dosage.

INTRODUCTION

Allergic bronchopulmonary aspergillosis (ABPA) is characterized by an exaggerated Th-2 response to colonized *Aspergillus fumigatus*, resulting in increased production of interleukin (IL)-4, IL-5, IL-10 and IL-13 [1]. Prolonged administration of oral corticosteroids (OCSs), to suppress this immunologic cascade, is associated with significant side effects. Monoclonal antibodies have been successfully employed to suppress the Th-2 response in severe asthma and may have a place in the armamentarium of medications used for ABPA, due to shared pathways, but this has not been extensively studied [2]. We present a case of ABPA, where use of Dupilumab, a monoclonal antibody against IL-4Rα, resulted in successful de-escalation of steroids.

CASE REPORT

A 60-year-old female with ABPA presented with exacerbation of dyspnea and an h/o steroid-induced adverse reactions, i.e. pathological fractures and osteoporosis. She was also on triple inhaler therapy, theophylline and zafirlukast. Immunoglobulin E (IgE) was 1267 IU/ml, sweat chloride was positive, CFTR was negative, *A. fumigatus* antibodies were positive. Prolonged taper of OCS improved her symptoms and decreased IgE level to 463 IU/ml. However, further de-escalation of prednisone resulted in relapse of symptoms. Addition of voriconazole resulted in decrease in IgE, but prednisone reduction was still not achievable below 20 mg daily, and she developed steroid-induced myopathy. Omalizumab was added but it resulted in a hypersensitivity reaction. Dupilumab was initiated at a dose of 300 mg subcutaneously every 2 weeks, which dramatically improved her symptoms and quality of life. IgE decreased to 79 at 4-month follow-up and she is now tapered to prednisone 5 mg on alternate days.

DISCUSSION

Production of IL-4 and IL-13 induces IgE isotype switching, increased mast cell expression and other biologic activities, which are central to the pathogenesis of allergic diseases [3]. Dupilumab is currently the only approved biologic that targets the IL4/13 pathway. The data on the benefit of

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Received: November 19, 2019. **Revised:** February 18, 2020. **Accepted:** April 17, 2020

anti-interleukin antibody therapy in the management of ABPA is sparse. Most of the literature is confined to case reports of its efficacy. The following studies are the largest to date looking at this issue. A Cochrane review included just one randomized double-blind study with an $n = 14$ comparing a daily dose of 600 mg omalizumab or placebo as add-on therapy to twice daily itraconazole and daily OCSs for 6 months [2]. The study was terminated early due to inability to recruit participants and showed no clear benefit. A retrospective multicenter observational study of 32 patients with heterogeneous treatment strategies showed no clear benefit of omalizumab. A total of 56% of patients were on OCSs while 78% had received antifungals at the time of initiation of omalizumab [4]. A separate case review of 116 patients with asthma and ABPA demonstrated improvement in symptoms and reduction in the steroid dose with addition of omalizumab with asthma control test score increasing from 11.37 ± 6.2 to 18.53 ± 9.5 ($P = 0.01$). Approximately one-third of the patients were able to discontinue prednisone while the others reduced the prednisone dose to $\leq$90% of the initial dose. The patients ranged from age 7 to 76 years with an average total IgE level of 1901 and mean baseline FEV1 values of 21–115% predicted. A total of 99% of patients previously had treatment failure using systemic steroids +/− antifungal therapy. The mean period of omalizumab use was 13.4 months [5]. In the era of molecular engineering, our case demonstrates a clinical application of a targeted therapy as step up therapy to reduce the daily dosage of OCSs needed to achieve control in APBA. A large randomized study is needed to confirm the efficacy of the anti-interleukin drugs in the management of ABPA, the optimal dosing intervals, identify the subgroup of patients who are likely to benefit from this therapy and the optimal duration of therapy.

ACKNOWLEDGEMENTS

There are no acknowledgements.

CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest expressed by any of the authors.

FUNDING

There was no funding for this paper.

ETHICAL APPROVAL

No ethical approval was required.

CONSENT

Informed consent was secured from the patient and is stored with our offices per the journal guidelines and is available on request.

GUARANTOR

O'Neil Green, MD, will be the guarantor for this article.

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