

## Letters

## Omalizumab treatment in a child with severe asthma and multiple steroid-induced morbidities

Allergic asthma, the most common type of asthma, is mediated by the release of proinflammatory mediators that occurs after the allergen binds to IgE on the surface of effector cells.<sup>1</sup> Omalizumab is a recombinant humanized monoclonal antibody that blocks the interaction between IgE and mast cells.<sup>2</sup> Omalizumab therapy significantly decreases the incidence of asthma exacerbations; improves the control of symptoms, such as wheezing, breathlessness, and nighttime awakenings<sup>2</sup>; improves asthma-related quality of life<sup>3</sup>; and reduces both oral and inhaled corticosteroid doses.<sup>1,2</sup> This last benefit is obviously favorable because long-term corticosteroid treatment can cause harmful adverse effects.

In the United States and Canada, omalizumab is indicated for adults and adolescents (12 years and older) with moderate-to-severe persistent asthma who have a positive skin test result or in vitro reactivity to a perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids. European regulatory authorities have approved its use in children aged 6 to 11 years, but the US Food and Drug Administration has not, citing cardiovascular safety as an issue.<sup>4–6</sup> However, several studies have shown that treatment of childhood asthma (ages 6–12 years) with omalizumab is safe and effective, reducing the requirement for inhaled corticosteroids and protecting against exacerbations.<sup>6–8</sup>

Our 9-year-old patient had severe allergic asthma that had led to multiple emergency department visits to the Children's Hospital of Eastern Ontario and intensive care unit admissions. Skin prick testing revealed that he was significantly allergic to dust mites, trees, grass, cats, and dogs. Baseline IgE level was 1,337 IU/mL; allergen specific IgE concentrations were not measured. His measured forced expiratory volume in 1 second (FEV<sub>1</sub>) was 80% of best predicted (Figure 1). Before his visit to our clinic, his treatment regimen included inhaled corticosteroids since the age of 3 years, a leukotriene inhibitor, and frequent courses of oral prednisone. On average, the patient experienced 6 to 8 exacerbations per year during which he received prednisone 30 mg/d for 10 days. However, in the year before initiation of omalizumab therapy, he was prescribed a daily prednisone dose of 40 mg/d for 8 months. This was titrated slowly to a daily prednisone dose of 2.5 mg, which he continued to take until omalizumab therapy was started. As a result of the high doses of prednisone, he developed complications of steroid use, including adrenal insufficiency. Investigations of back pain noted that he had developed compression deformities of the anterior aspect of T5 and T6. Bone mineral density (BMD) measurement at L1–L4 revealed diminished bone mass, a z score of –0.9, and a femoral neck BMD of 4.1 SDs below the mean. Total body BMD, excluding the head, demonstrated a z score of –1.3 at its nadir.

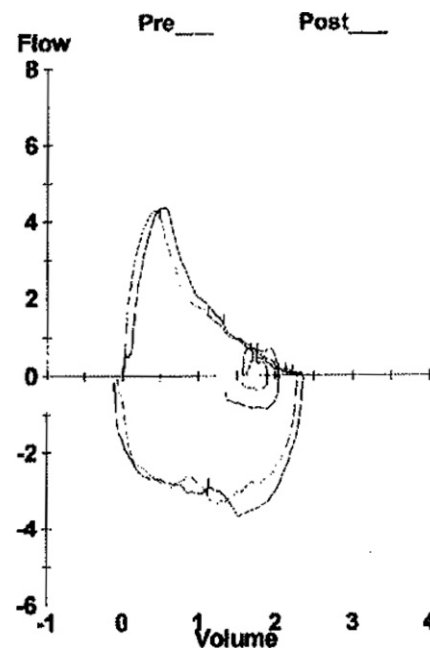


Fig. 1. Flow-volume loop when forced expiratory volume in 1 second (FEV<sub>1</sub>) was 80% predicted.

Because of the presence of corticosteroid-induced adverse effects, a decision was made to treat the patient with omalizumab. Because he was younger than 12 years, approval for treatment was obtained from Health Canada. The chosen dose of 375 mg every 2 weeks was based on his weight and IgE level. His prednisone dose of 2.5 mg/d was discontinued, and alternate therapy with hydrocortisone was given until his adrenal insufficiency was adequately treated. Omalizumab was well tolerated. Spirometry (performed monthly in triplicate), serum cortisol levels, BMD scans, and patient's quality of life were used to monitor the clinical response to treatment.

Eleven months after omalizumab treatment, the patient was able to decrease his total inhaled corticosteroid dose from 800  $\mu$ g/d before treatment to 200  $\mu$ g/d after treatment. His FEV<sub>1</sub> increased from 80% of predicted to 106% of predicted. His morning serum cortisol level increased from 12 nmol/L before treatment to 215 nmol/L afterward (reference range, 185–624 nmol/L). Total hip BMD increased from 0.626 to 0.686 g/cm<sup>2</sup>. L1–L4 BMD increased from 0.638 to 0.740 g/cm<sup>2</sup>. Quality of life was measured with the Pediatric Asthma Quality of Life Questionnaire, which looks at standardized activities using a 7-point

scale, with a score of 1 representing the greatest impairment and a score of 7 representing no impairment. Our patient's quality-of-life score increased from 4.7 before treatment to 7 after treatment. Most importantly, he no longer required oral corticosteroid treatment and has not had any asthma exacerbations since beginning treatment.

Omalizumab therapy can eliminate steroid dependency and permit resolution of adverse effects of long-term steroid use. Omalizumab itself has not been shown to cause serious adverse effects when compared with placebo.<sup>7,8</sup> We do not promote the off-label use of omalizumab in general, but in selected pediatric patients such as ours with serious steroid-induced complications, the risk-benefit ratio may fall in favor of its use.

Caroline Rizk, MD\*

Alicia Ring, RPN†

Stephanie Santucci, RN†

Ian MacLusky, MD, FRCPC\*

Jacob Karsh, MD, FRCPC\*

William H. Yang, MD, FRCPC, FAAAAI\*†

\*University of Ottawa

Ottawa, Ontario, Canada

†Allergy and Asthma Research Centre  
Ottawa, Ontario, Canada

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