

Successful Treatment of Refractory Status Asthmaticus With Omalizumab.

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Case report

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Abstract

The presented case demonstrates the efficacy of omalizumab as a rescue therapy of refractory status asthmaticus associated with high IgE levels. Omalizumab should be considered in patients with status asthmaticus unresponsive to standard treatment.

Background

Mortality due to bronchial asthma has gradually declined since the introduction of inhalational corticosteroids in the late 1980s, but it has plateaued since 2006.¹ Refractory status asthmaticus is the cause of rare cases of in-hospital death due to acute bronchial asthma. Here, we report the case of a patient with refractory status asthmaticus requiring extracorporeal membrane oxygenation who was successfully treated with omalizumab, a humanized recombinant monoclonal anti-IgE antibody.

Case Report

A 25-year-old woman with a history of pollen allergy and bronchial asthma presented with severe shortness of breath preceded by several weeks of worsening symptoms after starting a new job in a textile warehouse. The patient had been inhaling ipratropium/fenoterol several times a day over the past few weeks and had undergone two courses of antibiotic treatment for suspected bronchitis but had not used inhaled corticosteroids.

Upon admission, she was tachypneic and complained of dry cough and breathlessness. Clinical examination revealed wheezing and tachypnea with prolonged expirium. Chest X-ray was normal. Status asthmaticus was diagnosed, and a standard treatment with nebulized salbutamol and intravenous methylprednisolone was initiated. The patient was admitted to the intensive care unit, and nebulized ipratropium/fenoterol, intravenous magnesium sulfate, terbutaline and theophylline were added to the therapy. A trial of noninvasive ventilation was carried out, but it was not effective. Ten hours after admission, the patient was intubated because of exhaustion and mechanical ventilation was initiated. Terbutaline was replaced with intravenous adrenalin, which had only a moderate effect on ventilation. Regardless of intensive bronchodilator therapy, deep sedation, muscle paralysis and an aggressive ventilatory regimen, the condition of the patient was deteriorating into severe respiratory acidosis. Therefore, support with venovenous extracorporeal membrane oxygenation (ECMO) was initiated. The respiratory acidosis was rapidly corrected and $p_a\text{CO}_2$ normalized (Figure). We continued treatment with methylprednisolone (1000 mg for 3 days, 60 mg from day 4), intravenous terbutaline, continuous magnesium sulfate and theophylline. Oral montelukast and intravenous bisuleptin was added. Inhaled sevoflurane with an end-tidal concentration of 2.5% was added to ketamine and sufentanil sedation for its bronchodilatory effect. Ribavirin, cefotaxime and clarithromycin were administered for 2 days until viral and bacterial lung infection was ruled out.

Echocardiogram and chest X-ray were normal, microbiological examination of tracheal aspirate including viral and bacterial PCR was negative. Her total IgE level was hugely elevated at 2087 kIU/L, with strong positivity of specific IgEs against several inhaled allergens.

On day 8, ventilation showed no signs of improvement despite the treatment and the patient was still requiring full ECMO support. We administered 600 mg of omalizumab subcutaneously according to the patient's body weight of 55 kg and IgE level. We saw the first improvement in ventilation parameters after 90 min. In the next 12 h after omalizumab administration, the patient's tidal volumes increased from 100 ml to 500 ml, minute ventilation increased from 1 L/min to 5 L/min, and ECMO gas flow could be stopped. On the next day, ECMO was disconnected. A 5-day course of meropenem was started for ventilator-associated pneumonia. Ventilation continued to improve, and the patient was weaned from sedation and mechanical ventilation and extubated on day 10. Two weeks after the first dose, a second dose of omalizumab was administered. The patient was discharged home on day 25. Her asthma has been well controlled since the hospital discharge. Oral prednisone was tapered to discontinuation, and the patient has been treated with a high-dose inhaled beclomethasone/formoterol fixed combination, oral montelukast and levocetirizine. No additional dose of omalizumab was required.

Discussion

To the best of our knowledge, this is the second published case report of omalizumab treatment for a patient with refractory status asthmaticus.

Omalizumab is a humanized recombinant monoclonal anti-IgE antibody indicated for adults and pediatric patients 6 years of age and older with moderate to severe persistent asthma, a positive skin test or in vitro reactivity to a perennial aeroallergen, and whose symptoms are inadequately controlled with inhaled corticosteroids. It is not currently indicated for the relief of acute bronchospasm or status asthmaticus.⁷ However, the decision to administer omalizumab in the unapproved indication of status asthmaticus was supported by several facts. First, the patient had been fully dependent on ECMO for 7 days, with no signs of improvement despite therapy. Second, a case of successful use of omalizumab in a patient with refractory status asthmaticus and a high IgE level has been previously reported.³ Third, the patient had strong polyvalent atopic sensitization, and there is evidence supporting the efficacy of omalizumab in other IgE-mediated diseases such as chronic spontaneous urticaria, allergic rhinitis, nasal polyposis and food allergy, regardless of IgE level⁴. Cases of successful and safe treatment of pruritic bullous pemphigoid, severe atopic dermatitis or rare hyperimmunoglobulin-IgE syndrome, where the IgE level commonly reaches 2000–5000 IU/L, have also been reported,⁵ as well as the successful use of omalizumab in cases of bronchial asthma with IgE levels higher than 700 IU/L.⁶ Therefore, we believed that the potential benefit of omalizumab outweighed its possible side effects.

The course of our case was very similar to the previously published case report,³ with a remarkably fast and significant effect of omalizumab on ventilatory status. The first effect on ventilation was seen within

hours. Bronchial spasm completely resolved within 12 hours after the administration of omalizumab, and the patient's ventilatory status normalized on the next day. The patient was extubated a few days later.

Conclusion

The presented case and the previously published report showed that omalizumab was very effective in treating refractory status asthmaticus and the administration of omalizumab changed the seemingly unfavorable outcome of these patients. No side effects were noted. Therefore, we believe that omalizumab should be considered in status asthmaticus patients with high IgE levels and refractory to standard treatment. Although severe cases of acute asthma exacerbation unresponsive to standard therapy are rare, a future small clinical trial of omalizumab in an acute setting should be considered.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Patient's written consent to publication of information about them was obtained and is available upon request.

Availability of data and materials: Data are available upon request.

Competing interests: The authors declare no conflict of interest.

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Figures

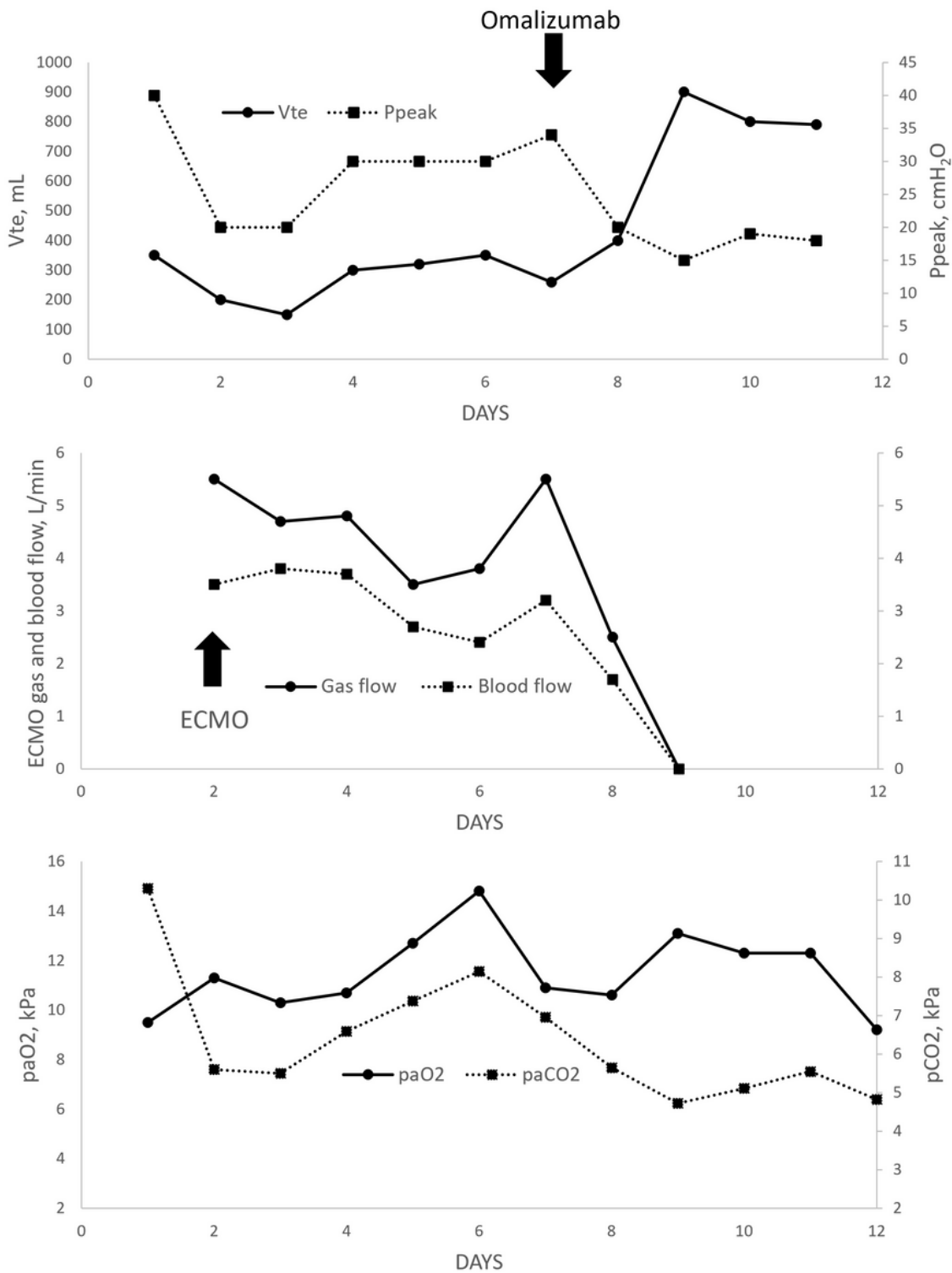


Figure 1

ECMO and ventilation parameters. Arrows show ECMO initiation on day 1 and omalizumab administration on day 7. Tidal volume and minute ventilation significantly improved within 24 hours after omalizumab administration, ECMO was stopped on day 9. The patient was extubated on day 11. ECMO, extracorporeal membrane oxygenation; Ppeak, peak inspiratory pressure; Vte expiratory tidal volume.