

OBSERVATION: CASE REPORT

Omalizumab Rescue Therapy for Refractory Status Asthmaticus

Background: Despite advances in asthma therapy, asthma mortality has remained stable in recent years (1). One reason is status asthmaticus, which can be unresponsive to initial treatment and may lead to hypercapnic respiratory failure despite maximal therapy.

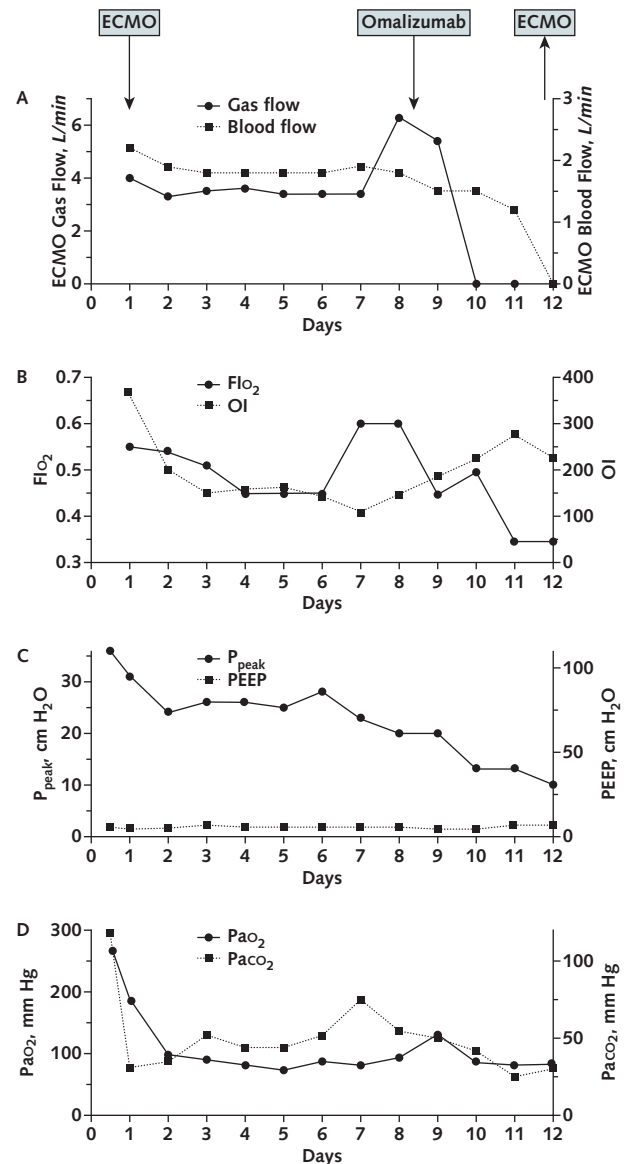
Objective: To alert clinicians to the possibility of a new rescue option for status asthmaticus.

Case Report: A 41-year-old man developed severe dyspnea while working at an outside construction site. The patient had a history of asthma with pollen allergy. He had not consulted a respiratory physician recently but had been using a short-acting β_2 -agonist inhaler several times daily for several weeks. The emergency physician who arrived at the site noted severe wheezing and intubated the patient for respiratory failure, and the patient was hospitalized.

Arterial blood gas analysis during mechanical ventilation revealed severe hypercapnic respiratory failure (PaO_2 , 267 mm Hg; PaCO_2 , 118 mm Hg; and pH, 6.95). Bronchoscopy and chest radiography excluded pneumothorax and obstruction from a foreign body or mucus. Intravenous prednisone, 1000 mg; nebulized salbutamol-ipratropium bromide; subcutaneous terbutaline; intravenous theophylline; and sedation that included intravenous ketamine were initiated for status asthmaticus. Mechanical ventilation remained difficult during the next hour, with low tidal volumes of approximately 1.0 to 1.5 mL/kg of body weight at a positive end-expiratory pressure of 5 cm H_2O with a peak inspiratory pressure of 36 cm H_2O . The patient's PaCO_2 increased to 127 mm Hg, and single-needle venovenous extracorporeal membrane oxygenation was initiated, which rapidly improved the hypercapnia.

The patient was transferred to a university hospital, where we found no signs of infection or cardiac dysfunction. Total IgE levels were elevated at 584 IU/mL (normal, < 100 IU/mL), and eosinophil levels were suppressed at less than 0.01×10^9 cells/L (normal, 0.03 to 0.44×10^9 cells/L). Allergen-specific IgE screening panels found strong sensitization (class 5) against birch and house dust mites. The event took place in mid-April when levels of birch pollen were high. We continued therapy with nebulized salbutamol-ipratropium bromide (0.5 mg of salbutamol and 2.5 mg of ipratropium bromide) 6 times daily; intravenous theophylline monitored by drug level measurement; subcutaneous terbutaline, 1 mg/d; and intravenous ketamine, 150 mg/h. We added intravenous prednisolone, 2 mg/kg daily; nebulized budesonide, 2 mg/d; oral montelukast, 10 mg/d; intravenous magnesium, 2 g over 20 minutes and then adjusted for serum magnesium levels; isoflurane via the Anaesthetic Conserving Device anesthetic delivery system (Sedana Medical) with an end-tidal concentration of 0.5%; and intermittent muscle relaxation with intravenous rocuronium. Despite this treatment, mechanical ventilation remained difficult after 1 week and the patient continued to require extracorporeal membrane oxygenation (Figure). Tracheostomy was performed on

Figure. ECMO and ventilation parameters, days 1 to 12.



A. ECMO was initiated on day 1, gas flow was discontinued on day 10, and ECMO was discontinued on day 12. B. FiO_2 and OI. C and D. The values on day 0.5 were obtained before ECMO was initiated. ECMO = extracorporeal membrane oxygenation; OI = oxygenation index; PEEP = positive end-expiratory pressure; P_{peak} = peak inspiratory pressure.

day 7 when the total IgE level increased to 780 IU/mL, and blood eosinophil levels remained undetectable. On day 8, we administered subcutaneous omalizumab, 600 mg, according to body weight and total blood IgE level as recommended by the European Medicines Agency. Ventilation began to improve, and we discontinued extracorporeal membrane oxygenation on day 10.

The patient continued to improve while receiving omalizumab every 2 weeks. He was weaned from mechanical ventilation during the next 2 weeks and had a prolonged hospital

stay for critical illness polyneuropathy. The patient was discharged to an inpatient rehabilitation facility 5 weeks after the initial event and returned home 4 weeks later after the dosage of oral prednisone was tapered to discontinuation. He has had no further attacks while receiving a high-dose inhaled corticosteroid plus an inhaled long-acting β_2 -agonist and subcutaneous omalizumab every 2 weeks. The results of lung function testing are within normal ranges, and the patient has returned to work.

Discussion: Omalizumab is indicated for IgE-mediated moderate to severe allergic asthma due to a perennial antigen that is not sufficiently controlled with an inhaled corticosteroid (according to the U.S. Food and Drug Administration) or combination therapy with a high-dose inhaled corticosteroid and long-acting β_2 -agonist (according to the European Medicines Agency). How rapidly omalizumab works is not yet established. In early trials, it improved asthma control after 16 weeks (2). A more recent trial found clinical improvement after 2 weeks of treatment (3). However, this therapy decreases the level of free IgE within hours (4). Moreover, in preclinical studies, it inhibited allergen-induced eosinophil infiltration in the lungs 30 minutes after injection and inhibited production of interleukin-4 and interleukin-5 within 6 hours (5). We began therapy with omalizumab because we hoped that it would produce clinical improvement over several weeks—we did not expect such rapid improvement. We suggest that clinicians caring for similar patients consider targeted biologic therapies guided by IgE and eosinophil levels when maximal treatment with standard options is insufficient.

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