

Reslizumab in an invasively ventilated patient with acute respiratory failure

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Clinical Implications

- Reslizumab should be considered as rescue therapy in patients with acute respiratory failure due to eosinophilic asthma.

TO THE EDITOR:

Targeted asthma therapies have resulted in an improvement of asthma control but not mortality.¹ Despite good evidence regarding the safety and efficacy of anti-IL5/IL5R antibodies for patients with severe eosinophilic asthma, there are no data on their safety or efficacy when used as rescue therapy in patients with acute respiratory failure due to asthma-chronic obstructive pulmonary disease (COPD) overlap (ACO).^{2,3}

A 53-year-old female patient diagnosed with COPD 5 years prior was referred to our severe asthma clinic in July 2018 because of rapid disease progression in the previous 6 months despite multiple systemic corticosteroid and antibiotic treatments. The patient is a chronic smoker (approximately 40 pack-years) with a family history of asthma. She had no history of nasal polyps. The medication consisted of inhaled high-dose corticosteroids, long-acting muscarinic antagonists, long-acting β -agonists, and oral corticosteroids (OCS, 25 mg prednisolone/day). At the time of initial presentation post-bronchodilator (BD), pulmonary function testing (PFT) showed a severe obstructive lung disease with a forced expiratory volume after 1 second (FEV₁) of 960 mL (33% predicted), an FEV₁/forced vital capacity ratio (Tiffeneau index) of 28.3%, and a total lung capacity of 6.69 L (123% predicted). One PFT with pre- and post-BD values from the previous year showed a reversibility of 440 mL (40%). Fraction of exhaled nitric oxide was 54 ppb. When presenting at our outpatient clinic peripheral blood eosinophils were 260/ μ L despite OCS. In the previous 6 years, values of 300/ μ L or greater had been documented 9 times with maximum values reaching 600/ μ L. Semiquantitative sputum cytology showed a modest eosinophilic inflammatory infiltrate (<5%). Her history, PFT, and laboratory tests support that she has ACO with a component of late-onset severe eosinophilic asthma. She was considered for anti-IL5 antibody treatment, and an appointment for re-evaluation was scheduled.

Two months later the patient was admitted to the ICU of another hospital with acute hypercapnic respiratory failure (pO₂ 84 mm Hg, pCO₂ 200 mm Hg, pH 6.8). She was immediately intubated, and cardiopulmonary resuscitation had to be performed for 2 minutes. Auscultation revealed a silent chest. The ventilator's flow-time diagram showed massive obstruction. Initially administered medication included

standard sedation protocols, vasoactive drugs, and anti-obstructive drugs including high-dose corticosteroids. Five hours after intubation, blood gas analysis (BGA) showed moderate hypercapnia (pO₂ 81 mm Hg, pCO₂ 61 mm Hg, pH 7.25) with a fraction of inspired oxygen of 0.21, and a reduction of ventilation support to moderate levels was possible. Regardless, the patient remained highly obstructive and an early weaning was not possible. On the basis of our previous observations of reslizumab recipients showing marked clinical and PFT improvements within 24 hours after administration, we recommended reslizumab (3 mg/kg) intravenously that she received on day 3. The therapy was tolerated well. Within a day there was a perceived clinical improvement. Less than 24 hours after administration the patient was switched to spontaneous breathing, successfully extubated a day later, and subsequently transferred to the regular ward of our specialized pulmonology department. Thirteen days after intubation, BGA was satisfactory while breathing room air and the patient was discharged. PFT performed 13 days after the onset of acute respiratory failure showed severe obstruction (600 mL FEV₁) with massive reversibility (660 mL and 111%). Reslizumab is being administered every 4 weeks while tapering OCS. So far there have been no exacerbations since, and the treatment is tolerated well.

A recent publication reported the first use of omalizumab as rescue therapy in an invasively ventilated patient with severe allergic asthma.⁴ This is the first published case describing the use of reslizumab in acute respiratory failure. The main limitation is that we cannot exclude the possibility that the patient would have improved without reslizumab. However, the coincidence of a significant clinical improvement with the reslizumab application supports our interpretation of a reslizumab effect. Another novelty in this case is that the patient has both severe eosinophilic asthma and COPD, a patient group for which there is not yet much evidence regarding the use of monoclonal antibodies. More cases have to be collected, but we believe that in selected patients (high likelihood or confirmed diagnosis of eosinophilic airway disease and no other contraindications for monoclonal antibody administration) reslizumab can be considered safe and possibly efficacious as a rescue medication in critically ill patients by or in cooperation with very experienced centers.

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