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Near fatal asthma: Acute effect of omalizumab in paediatric patient undergoing extracorporeal carbon dioxide removal ($ECCO_2R$)

Davide Colombo*; Alessia Guzzo; Federico Merlo; Michele Battista; Cristina Orsatti; Gianmaria Cammarota; Roberta Nicali; Alessandro Fiocchi; Stefano Cusinato

***Corresponding Author: Davide Colombo**
Anesthesia and Intensive Care Department, SS. Trinità Hospital ASL Novara, Novara, Italy.
Email: davide.colombo@med.uniupo.it

Abstract

Objective: Severe status asthmaticus not responsive to therapy are not a prerogative of severe asthma. We report the case of a severe status asthmaticus refractory to medical therapy, undergoing Invasive Mechanical Ventilation (IMV) and extra-corporeal carbon dioxide removal ($ECCO_2R$). Since it was life-threating situation, the equip decided to administer off-label Omalizumab, a drug with an anti-IgE action.

Data synthesis: After the drug administration patients clinically improved, White Blood Cell (WBC) count in Broncho-Alveolar Lavage (BAL) decreased rapidly and the patient can be weaned from $ECCO_2R$ and IMV. Finally, patient was discharged from ICU to hospital ward and then to home.

Conclusion: Off-label use of Omalizumab provided a fast WBC reduction in BAL and fast recovery in a paediatric severe status asthmaticus refractory to all treatment.

Abbreviations

BGA: Blood Gas Analysis; $ECCO_2R$: Extra Corporeal Carbon dioxide Removal; ED: Emergency Department; ICU: Intensive Care Unit; NIV: Non-Invasive Ventilation; OTI: orotracheal intubation; SABA: Short-Acting Beta2 selective adrenergic Agonists.

Introduction

Severe asthma is a life-threatening condition that is particularly challenging in patients who do not respond to conventional therapy [1]. In critically ill patients admitted with severe asthma, Invasive Mechanical Ventilation (IMV) is often required to stabilize the respiratory status. Anaesthetic medical drugs in combination with Extracorporeal Carbon Dioxide Removal System ($ECCO_2R$) are well-described rescue therapies used to treat patients suffering from severe status asthmaticus [1].

In particular, the use of extracorporeal carbon dioxide removal system ($ECCO_2R$) has been proposed as a bridge therapy to curb hypercapnia and acidosis [8-10].

The medical treatment of asthmatic access does not involve the use of biological drugs, which are usually used for its prevention. Among them, omalizumab is an approved drug used for IgE-mediated moderate-to-severe asthma that is refractory to high-dose inhaled corticosteroids and long-acting beta2 agonist [11]. In addition, omalizumab is not indicated for the relief of acute bronchospasm or status asthmaticus [12].

We report a case of severe asthma refractory to conventional and rescue therapies in a pediatric patient, in whom omalizumab was effectively used to revert the life-threatening condition.

Patient information

A 17-year-old boy with a history of allergic asthma treated with on-demand SABA presented to our emergency department with severe acute asthma exacerbation. He had previously suffered from a few asthma attacks, requiring, in one case, hospital admission.

Clinical findings and diagnostic assessment

The boy presented to our ED with hypoxemic Acute Respiratory Failure (ARF) after 12 hours of asthma exacerbation managed at home with oral steroids and a salbutamol Metered-Dose Inhaler (MDI). In the ED, he received maximal high-dose nebulized salbutamol, intravenous methylprednisolone, nebulized epinephrine, intravenous magnesium sulphate and O_2-therapy, without any benefits. After 24 hours from the symptoms' presentation, he was finally admitted to the ICU. On ICU admission, the patient presented with increased work of breathing (respiratory rate 35/minutes; use of inspiratory accessory muscles), inability to speak, orthopnea, and mild hypercapnia on blood gas analysis (BGA): pH 7.36, paO_2 92 mmHg, $paCO_2$ 43 mmHg, and HCO_3- 24 mEq/L. Thus, Invasive Mechanical Ventilation (IMV) after Orotracheal Intubation (OTI) was performed (V_T 560 mL; RR 9 bpm; I/E 1:7; PEEP 0, FiO_2 50%).

Timeline and therapeutic interventions

On day 1, immediately after OTI, severe respiratory acidosis (pH 7,27; $PaCO_2$ 56 mmHg; PaO_2 101 mmHg; HCO_3- 26 mEq/L) was observed at BGA in combination with a high airway resistance, significant gas trapping, and a high time constant (τ)(airway resistance 59 $cmH_2O/L/s$; PEEPi 12 cm H_2O; τ 17s). With the aim of facing off hypercarbia and respiratory acidosis, veno-venous $ECCO_2R$ was started [13].

Once a high flow 13.5 French dual lumen catheter (MAHURKAR ™, Covidien™, Minneapolis, USA) was placed in the left femoral vein under ultrasound guidance, veno-venous $ECCO_2R$ was started (PrismaLung+, Baxter - Deerfield, IL), and the operational parameters of veno-venous $ECCO_2R$ were set as follows: a blood flow of 450 mL/min and a sweep gas flow of 10 L/min. Pre -and post-filter blood gas analyses showed a ΔCO_2 of 32.1 mmHg corresponding to 71.1% of the total CO_2 extraction. Systemic anticoagulation was initiated using unfractionated heparin (mean, 1617± 295 IU/h) to maintain an aPTT of 71.1 ± 26.8 seconds. Bronchodilation was supported by continuous infusion of ketamine and inhaled sevoflurane.

On day 2, pH was compensated for by a slight increase in bicarbonate levels and a sensitive reduction in $PaCO_2$ levels due to $ECCO_2R$ (pH 7.37; $PaCO_2$ 48 mmHg; PaO_2 102 mmHg; HCO_3^- 28.6 mEq/L). I.v. theophylline and magnesium sulphate were also added. Chest radiography was performed, and pneumothorax was excluded.

On day 3, airway resistance reached its maximum value in the presence of persistent gas trapping and a high τ (airway resistance 130 $cmH_2O/L/s$; $PEEP_{TOT}$ 10 cm H_2O; τ 37 s). A rebound in the total IgE level was observed (2421 UI/mL). Film array respiratory panel analyses conducted on the bronchoalveolar lavage (BAL) assay excluded major infections.

On day 4, the BGA was as follows: pH, 7.37; $PaCO_2$ 59 mmHg; PaO_2, 70 mmHg; and HCO_3, 34 mEq/L. Bronchospasm was still clinically present with audible inspiratory and expiratory wheezing, confirmed by severe alterations in respiratory mechanics (R 125 cm $H_2O/L/s$; PEEPi 9.2 cm H_2O; τ 30.5 s).

Owing to the lack of a clinically relevant impact and the risk of renal injury induced by prolonged administration, sevoflurane was discontinued [14]. The day after, in consideration of the severe status of asthmaticus refractory to all the medications employed, an allergology specialist was consulted (AF) and the off-label administration of omalizumab was commenced. A single dose of Omalizumab 900 mg was injected subcutaneously, according to body weight and IgE level [12].

BAL was sampled before omalizumab administration for the following three days. Leukocyte count data are shown in Figure 1. The leukocyte count gradually decreased over the next 3 days. Figure 1 depicts how airway resistance decreased soon after omalizumab administration, suggesting its efficacy for clinical improvement. The reduction in white blood count (WBC) in BAL fluid supports this hypothesis (Figure 1). The patient's respiratory condition progressively improved within 2 days of omalizumab administration; therefore, theophylline and magnesium sulphate were discontinued.

On day 7, as mechanical measurements improved (R 21 cm $H_2O/L/s$; PEEPi 2 cm H_2O; τ 6.5 s), RR increased to 12 bpm, while maintaining a good gas exchange (pH 7.41, $PaCO_2$ 48 mmHg, PaO_2 73 mmHg, HCO_3- 31.3 mEq/L).

On day 8, due to further improvements in ventilatory mechanics, $ECCO_2R$ and ketamine were also discontinued. The $ECCO_2R$ treatment lasted 185 h, with the $ECCO_2R$ membrane cartridge replaced every 72 h. Therefore, weaning from IMV was initiated until extubation on day 9. Immediately after extubation, the patient was assisted by non-invasive ventilation (NIV) with neurally adjusted ventilatory assist (NAVA) (Servo-U, Getinge, Sölna, SW) [15,16] via an oro-nasal mask. In the absence of muscular fatigue or dyspnea, NIV was rapidly discontinued. The $ECCO_2R$ catheter was removed 24 h after spontaneous breathing, without any complications. The patient was monitored in the ICU for 72 h and then discharged to the medical ward. On day 18, the patient was discharged without any further exacerbation of in-hospital asthma.

Outcomes and follow-up

Asthmatic status lasted several days, and the patient remains deeply sedated, paralyzed and mechanically ventilated with continuous VV-$ECCO_2R$ in absence of complications. After extubation, he

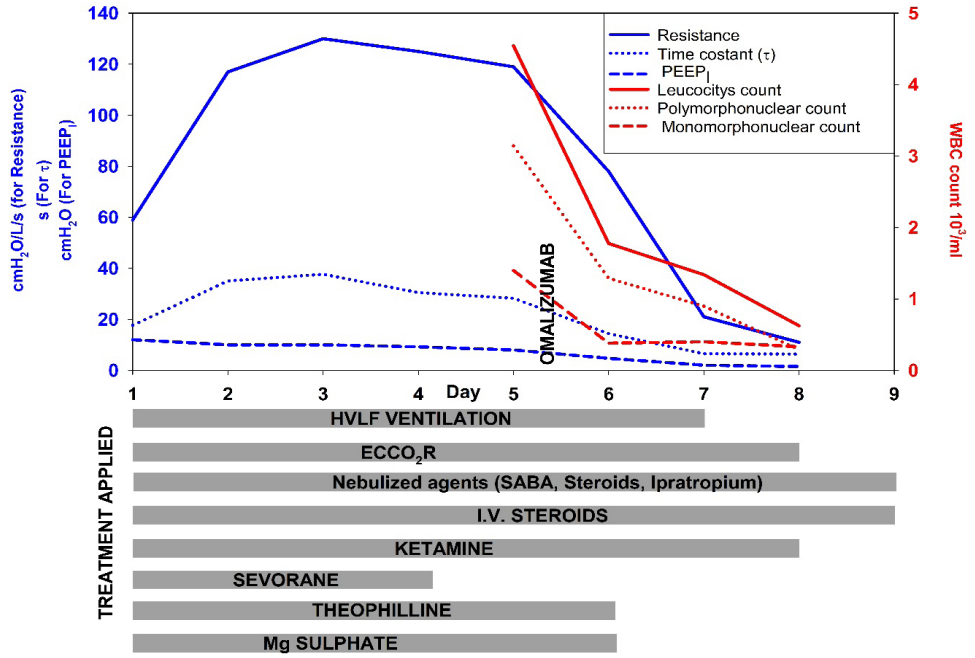

Figure 1: Respiratory mechanics, white blood cell (WBC) count in bronchoalveolar lavage (BAL), and treatment applied over time. In particular, on the Y-axis, resistance (cmH_2O/L/s), time constant (s), and total positive end expiratory pressure [PEEPTOT] (cmH_2O); on the right Y-axis: Total leukocyte count (n/ml), Polymorphonuclear count (n/ml), and Monomorphonuclear count (n/ml); under the x-axis, the treatment applied and their duration in bar format.

started his new chronic therapy with a long-acting bronchodilator (beclomethasone/formoterol spray), oral montelukast, and was finally referred to a specialized center for the administration of omalizumab.

The administration of Omalizumab provided respiratory mechanic improvement and reduction of WBC in BAL.

Discussion

The humanized monoclonal anti-IgE antibody omalizumab rapidly neutralizes free IgE [17] and inhibits IgE receptor binding by steric inhibition [18]. To our knowledge, its use in acute asthma exacerbations has not been described in pediatric patients. Our clinical observations suggest that omalizumab might be useful in the critical context of refractory asthma Ig-E mediated.

Our patient did not respond to any standard medical treatment, including oxygen, inhaled SABA, inhaled short-acting muscarinic antagonists, systemic glucocorticoids, magnesium sulphate [19,20] and theophylline [21,22].

When intubation and mechanical ventilation became necessary, intravenous ketamine and inhaled sevoflurane were added as second-line therapies [4,6]. Mechanical ventilation carries the risk of serious complications due to dynamic hyperinflation, such as barotrauma and hemodynamic instability [23]. As bronchospasm is associated with prolongation of the respiratory system τ, due to expiratory flow limitation and increased flow resistance, slower emptying of alveoli may result in significant gas trapping (PEEPi) [24]. The interventions aimed at minimizing the increase in PEEPi, including a low respiratory rate with

normal or slightly increased tidal volume (HVLR high volume low-rate ventilation) and a reduced I/E ratio, were, in turn, responsible for hypercapnia and respiratory acidosis worsening [25].

The use of $ECCO_2R$ allowed for the reduction of tidal volume and minute ventilation, limiting lung overinflation and gas trapping. However, we were unable to wean the patient from this supportive therapy, which cannot be applied for prolonged periods [8,26]. Off-label use of omalizumab was then considered and administered.

The reduction of symptoms, the disappearance of signs of inflammation in BAL, and the normalization of ventilation parameters occurred rapidly in the 48 hours following the introduction of omalizumab, suggesting a potential cause-effect relationship.

According to its prescribing information, Omalizumab "is not indicated for the relief of acute bronchospasm or status asthmaticus" [12]. It is also explicitly not indicated "for other allergic conditions". Despite this, after the publication of clinical cases [27] and case series [28] indicating its efficacy, it is currently being studied as a treatment for food allergies in prospective trials [29]. This report suggests that omalizumab administration could play a role in acute asthmatic attack in a selected population.

Asthma exacerbations can be fatal. Data from the WHO Mortality Database estimated that global asthma mortality in the 5-34-year age group did not decrease appreciably from 1993 to 2006 [30,31]. Specifically, in Italy, mortality has reduced from 0.19 deaths per 100.000 people in 1993 to 0,06 per 100.000 people in 2006 [30], but in developed countries, we are now experiencing signals of upward rebound in mortality [32,33]. According to data from the US, asthma exacerbation rates among children <18 years old with current asthma decreased from 62% in 2001 to 48% in 2014 but increased in 2016 to 54% [34].

Conclusions

Our case suggests that the combination of $ECCO_2R$ delivered via a dialysis machine and omalizumab may be an effective treatment option for status asthmaticus in the young population. In addition, these treatments can also be safely applied in secondary hospitals to avoid potentially harmful transportation, thus contributing to reduced mortality from NFA in pediatric patients.

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References

1. Leatherman J. Mechanical Ventilation for Severe Asthma. Chest. 2015; 147: 1671-1680.

2. Racca F, Montagnini L. Acute Asthma Exacerbations in Children: From Emergency Room to Intensive Care Unit Management. Practical Trends in Anesthesia and Intensive Care. 2019; 2020: 83-103.

3. Goyal S, Agrawal A: Ketamine in status asthmaticus: A review. Indian J Crit Care Med. 2013; 17: 154-161.

4. Vaschetto R, Bellotti E, Turucz E, Gregoretti C, Corte FD, et al. Inhalational anesthetics in acute severe asthma. Curr Drug Tar-

gets. 2009; 10: 826-832.

5. Schutte D, Zwitserloot AM, Houmes R, de Hoog M, Draaisma JM, et al. Sevoflurane therapy for life-threatening asthma in children. Br J Anaesth. 2013; 111: 967-970.

6. Ruszkai Z, Bokrétás GP, Bartha PT. Sevoflurane therapy for life-threatening acute severe asthma: a case report. Can J Anaesth. 2014; 61: 943-950.

7. Weber T, Schiebenpflug C, Deusch E. Inhalational sevoflurane in severe bronchial obstruction unresponsive to multipharmacologic therapy: a case report. F1000Research. 2012; 1.

8. Lobaz S, Carey M. Rescue of Acute Refractory Hypercapnia and Acidosis Secondary to Life-Threatening Asthma with Extracorporeal Carbon Dioxide Removal (ECCO2R). Journal of the Intensive Care Society. 2011; 12: 140-142.

9. Cooper DJ, James Cooper D, Tuxen DV. Extracorporeal Life Support For Status Asthmaticus. Chest. 1994; 106: 978-979.

10. Baker A, Richardson D, Craig G. Extracorporeal Carbon Dioxide Removal (ECCO2R) in Respiratory Failure: An Overview, and where Next? Journal of the Intensive Care Society. 2012; 13: 232-237.

11. Rees PJ. Review: omalizumab reduces exacerbation and steroid use in chronic asthma. Evidence-Based Medicine. 2007; 12: 11-11.

12. Website.

13. Combes A, Auzinger G, Capellier G, du Cheyron D, Clement I, et al. ECCOR therapy in the ICU: consensus of a European round table meeting. Crit Care. 2020; 24: 490.

14. Stabernack CR, Eger EI, Warnken UH, Förster H, Hanks DK, et al. Sevoflurane degradation by carbon dioxide absorbents may produce more than one nephrotoxic compound in rats. Can J Anaesth. 2003; 50: 249-252.

15. Colombo D, Cammarota G, Bergamaschi V, De Lucia M, Corte FD, et al. Physiologic response to varying levels of pressure support and neurally adjusted ventilatory assist in patients with acute respiratory failure. Intensive Care Med. 2008; 34: 2010-2018.

16. Navalesi P, Colombo D, Cammarota G. Neurally adjusted ventilatory assist. New Developments in Mechanical Ventilation. 2012; 116-123.

17. Luu M, Bardou M, Bonniaud P, Goirand F. Pharmacokinetics, pharmacodynamics and clinical efficacy of omalizumab for the treatment of asthma. Expert Opin Drug Metab Toxicol. 2016; 12: 1503-1511.

18. Pennington LF, Tarchevskaya S, Brigger D, Sathiyamoorthy K, Graham MT, et al. Structural basis of omalizumab therapy and omalizumab-mediated IgE exchange. Nat Commun 2016; 7: 11610.

19. Reddel HK, FitzGerald JM, Bateman ED, Bacharier LB, Becker A, et al. GINA 2019: a fundamental change in asthma management: Treatment of asthma with short-acting bronchodilators alone is no longer recommended for adults and adolescents. Eur Respir J. 2019; 53.

20. Wechsler ME. 2020 Updated Asthma Guidelines: Intermittent inhaled corticosteroids and long-acting muscarinic antagonists for asthma-the latest NAEPP guidelines are SMART! J Allergy Clin Immunol. 2021; 147: 1640-1642.

21. Dalabih A, Harris ZL, Bondi SA, Arnold DH. Contemporary Aminophylline Use for Status Asthmaticus in Pediatric ICUs. Chest. 2012; 141: 1122-1123.

22. Banasiak NC. Childhood Asthma Practice Guideline Part Three: Update of the 2007 National Guidelines for the Diagnosis and Treatment of Asthma. Journal of Pediatric Health Care. 2009; 23: 59-61.

23. Demoule A, Brochard L, Dres M, Heunks L, Jubran A, et al. How to ventilate obstructive and asthmatic patients. Intensive Care Medicine. 2020; 46: 2436-2449.

24. Laher AE, Buchanan SK: Mechanically Ventilating the Severe Asthmatic. J Intensive Care Med. 2018; 33: 491-501.

25. Georgopoulos D, Kondili E, Prinianakis G. How to set the ventilator in asthma. Monaldi Arch Chest Dis. 2000; 55: 74-83.

26. Mikkelsen ME, Joseph Woo Y, Sager JS, Fuchs BD, Christie JD, et al. Outcomes Using Extracorporeal Life Support for Adult Respiratory Failure due to Status Asthmaticus. ASAIO Journal. 2009; 55: 47-52.

27. Arasi S, Mennini M, Cafarotti A, Fiocchi A. Omalizumab as monotherapy for food allergy. Curr Opin Allergy Clin Immunol. 2021; 21: 286-291.

28. Fiocchi A, Artesani MC, Riccardi C, Mennini M, Pecora V, et al. Impact of Omalizumab on Food Allergy in Patients Treated for Asthma: A Real-Life Study. J Allergy Clin Immunol Pract. 2019; 7: 1901-1909.e5.

29. Website.

30. Ebmeier S, Thayabaran D, Braithwaite I, Bénamara C, Weatherall M, et al. Trends in international asthma mortality: analysis of data from the WHO Mortality Database from 46 countries (1993-2012). The Lancet. 2017; 390: 935-945.

31. Wijesinghe M, Weatherall M, Perrin K, Crane J, Beasley R, et al. International Trends in Asthma Mortality Rates in the 5- to 34-Year Age Group. Chest. 2009; 135: 1045-1049.

32. Vianello A, Caminati M, Crivellaro M, El Mazloum R, Snenghi R, et al. Fatal asthma; is it still an epidemic? World Allergy Organ J 2016; 9:42.

33. Fiocchi A, Valluzzi R, Dahdah L. Zero tolerance for asthma deaths in children. J Pediatr. 2020; 96: 403-405.

34. Zahran HS, Bailey CM, Damon SA, Garbe PL, Breysse PN, et al. Vital Signs: Asthma in Children-United States, 2001-2016. MMWR Morbidity and Mortality Weekly Report. 2018; 67:149-155.

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Authors Information: Davide Colombo[1,2]*; Alessia Guzzo[1,3]; Federico Merlo[1,4]; Michele Battista[5]; Cristina Orsatti[6]; Gianmaria Cammarota[7]; Roberta Nicali[8]; Alessandro Fiocchi[9]; Stefano Cusinato[5]

[1]Anesthesia and Intensive Care Department, SS. Trinità Hospital ASL Novara, Novara, Italy.

[2]Health Science Department, Piemonte Orientale University, Novara, Italy.

[3]Anesthesia and Intensive Care Residency Program, Piemonte Orientale University, Novara, Italy.

[4]C.R.I.M.E.D.I.M. - Research Center in Disaster and Emergency Medicine, Piemonte Orientale University, Novara, Italy.

[5]Dialysis and Nephrology Dept., SS. Trinità Hospital ASL Novara, Novara Italy.

[6]Territorial Pediatrician, Arona, Italy.

[7]Dipartimento di Medina e Chirurgia, Università degli Studi di Perugia, Perugia Italy.

[8]Out-patient Pneumonology Division, ASL Novara, Novara, Italy.

[9]Translational Research in Pediatric Specialities Area, Division of Allergy, Bambino Gesù Children's Hospital, IRCCS, Piazza Sant'Onofrio, Rome, Italy.

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