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Case Report

'Near-Fatal' Asthma; A New Approach in Treatment

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Abstract

A 49 year-old male was admitted at the intensive care unit because of respiratory failure due to near fatal asthma. Phenotyping showed high serum eosinophilic counts even during prednisolone treatment. Because of lack of response, off-label mepolizumab was administered. Serum eosinophilic counts dropped significantly and the patient recovered successfully. This case report shows the importance of precision medicine during the treatment of near fatal asthma. Due to early recognition of the asthma phenotype and the use of biologicals, further deterioration could probably been prevented.

Keywords: *Asthma; Phenotype; Biologicals*

Abbreviation

ER: Emergency Room

Introduction

Asthma is a common heterogeneous inflammatory disorder of the airways. Although there is an increasing knowledge of pathogenesis and treatment, there are still patients who do not respond to initial therapy and are at risk of progression to acute respiratory failure. This case report shows the importance of recognition the asthma phenotype in a patient with near fatal asthma.

Case Presentation

A 49 year-old male presented to the emergency room (ER) with shortness of breath and persistent productive cough of non-purulent sputum. There was no documented medical history and no medication use (especially no NSAID usage). Several days earlier he visited his general practitioner where he was treated for possible new diagnosed asthma with an inhaled corticosteroid and b-agonist. On presentation to the ER, auscultation of the lung revealed a prolonged and wheezing expiration. Respiratory rate of 30/min was measured with an oxygen saturation of 94% on 5L/min of oxygen. He was hemodynamically stable and additional investigation ruled out underlying infectious causes. Full blood count showed increased absolute eosinophils of 1.30 x 10^9/L (< 0.30 x 10^9/L).

Despite of immediate administration of 50mg prednisolone and bronchodilation with salbutamol-ipratropium nebulizer, the patient remained tachypnoeic with signs of respiratory failure (pH 7.28 (7.35 - 7.45) and pCO_2 7.1 kPa (4.7 - 6.4 kPa)). More b2-agonist and magnesium were given intravenously and admission to the intensive care unit followed. Therapy with noninvasive positive pressure ventilation failed. Because of severe hypoxia and a persistent respiratory acidosis, combination of invasive mechanically ventilation and partial extracorporeal membrane oxygenation was initiated.

High serum eosinophilic counts (2.21 x 10^9/L) persisted even after 5 days of prednisolone treatment. Since the total IgE count was only mild elevated (423 kU/L, normal 0 - 100 kU/L) and the inhaled allergen tests showed online mild sensitization for house dust mites, the asthma was categorized as an eosinophilic phenotype. Therefore, additional treatment with mepolizumab 100 mg subcutaneously was administered (at time of case presentation the only available humanized monoclonal antibody IL-5) together with high dose of prednisolone. The following day improvement was noticeable and he could be extubated successfully. Serum eosinophil count dropped to 0.12 (< 0.30 x 10^9/L). A combination of long acting B2 agonist and inhaled corticosteroid was started. Because the patient recovered successfully well the oral prednisolone was tapered over a period of 3 months.

Discussion

Asthma is a reversible increase in airway obstruction due to smooth muscle contraction, mucus secretion and airway inflammation with edema. Asthma can be divided in phenotypes based on cellular inflammation patterns: eosinophilic (allergic and non-allergic), non-eosinophilic (neutrophilic type 1, type 17 and paucigranulocytic) and mixed granulocytic inflammation [1-3]. Cellular pathway and treatment are described in table 1.

Asthma subtype	Cellular pathway	Biomarkers	Treatment*
Eosinophilic			
Allergic	T helper 2 cells are triggered by allergens and produce IL-4, IL-5 and IL-13	Sputum or blood eosinophilia high total IgE or IgE levels to allergens IL-4, IL-5 and IL-13 High FeNO	Good response to steroids Anti-IgE, Anti-IL-4/13
Non-Allergic	Innate lymphoid cells are triggered by pollutants, microbes, mold or NSAID usage and produce IL-5 and IL-13	Sputum or blood eosinophilia low IgE IL-5 and IL-13 High FeNO	High doses of steroids are often necessary Anti-IL-4/5/13
Non- Eosinophilic			
Type 1, Type 17	T helper 1 or 17 cells are triggered by pollutants, oxidative stress or microbes and produce IL8, IL-17 and IL-23	IL-8, IL-17, neutrophils	Poor response to steroids Possible response to macrolide therapy
Paucigranulocytic	Non-inflammatory epithelial reaction to pollutants or oxidative stress	-	-
Mixed granulocytic	T helper 1, 2 and 17 are all involved	All mentioned above	poor response to therapy

Table 1: *Asthma phenotypes based on cellular inflammation patterns.*
**Treatment for all asthmatic patients indifferent of their phenotypes includes B2-agonists and anticholinergic nebulization following GINA-guidelines.*

The difference between near fatal asthma and severe asthma is the need for mechanical ventilation or ICU admission and hypercapnia (> 6.5 kPa) [4,5]. In patients with a near fatal asthma, a significant limitation in gas-flow occurs due to dynamic hyperinflation caused by airway narrowing and high respiratory rates which increases work of breathing. Hypercapnic respiratory failure develops due to inadequate alveolar ventilation and hypoxemic failure due to shunting.

First line of therapy in the immediate management includes oxygen suppletion, B2-agonists -anticholinergic nebulization and corticosteroids. In case of insufficient clinical response intravenous magnesium sulphate and intravenous B2-agonists could be administered. Deterioration to respiratory failure should be recognized early. Arterial blood gas analysis and peak flow measurements are easy accessible tools which can be useful as objective measurements of response to therapy. If despite of aggressive treatment respiratory failure develops, intubation with mechanical ventilation is required [6-8].

Because of new insights in the pathophysiology of asthma, personalized medicine has been developed. Current treatment strategies includes anti-IgE monoclonal antibodies to inhibit IgE-mediated inflammation reactions and anti-cytokine therapy (mainly anti-IL-5 and IL-4/IL13) to target the specific cytokines involved in the inflammation cascade. This case presentation describes a late onset non allergic eosinophilic asthma. Therefore he received humanized monoclonal antibody IL-5 which decreases the recruitment of eosinophils and thereby reduces the airway inflammation caused by this cellular pathway [9,10]. Although the use of biologicals is already an add-on treatment strategy for specific phenotypes in severe asthma in daily practice, usage in critical care medicine has not been described before.

Conclusion

This case report shows the importance of precision medicine in a critically ill patient. Due to early recognition of the asthma phenotype in patients, further deterioration can probably been prevented. The use of biologicals in a critical care setting is new and could be a useful approach to treat ongoing respiratory failure and prevent death in eosinophilic asthma. More research is needed to investigate this hypothesis.

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