Life-Threatening Bronchospasm

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Summary
While Eosinophilic Asthma is frequently underdiagnosed, COPD is often misdiagnosed. This case focusses on a COPD misdiagnosis that had life-threatening consequences. The patient was a 59-year-old, male smoker, who presented to the Emergency Department with a week’s history of increasing shortness of breath. On presentation, severe respiratory acidosis persisted acidotic despite Nebulisers, Oxygen, Steroids, and Magnesium. He was intubated for two weeks and had severe bronchospasm associated with type 2 respiratory failure. Eosinophils on admission were markedly elevated and remained so despite a week of intravenous steroids. As he missed the window for ECMO, we were advised to look at his diagnostic spirometry. Surprisingly, the spirometry done by his general practitioner, two years prior, showed Asthma not COPD. His blood eosinophils were elevated then, too. A revised diagnosis of Eosinophilic Asthma was given. Intravenous steroids were increased, and nebulised steroids were started. Soon thereafter, his condition improved, and he was stepped down from Intensive care. Hopefully, this case report increases physician knowledge of the different Asthma phenotypes and reduces incidences where correct treatment is only started during an avoidable life-threatening exacerbation.

Keywords
Eosinophilic asthma, bronchospasm, COPD

Initial management
Over the next few days, Aminophylline, Adrenaline, Magnesium and Salbutamol infusions were given. Regular intravenous hydrocortisone, antibiotics, and salbutamol nebulisers were administered. Respiratory PCR was negative for common viruses.

Despite six days of intensive bronchospasm treatment, the patient remained ventilated and in persistent type 2 respiratory failure. A referral was made to an Extracorporeal Membrane Oxygenation (ECMO) centre. It was declined, as his pH was greater than 7.2 and the cause for the elevated pCO2, his bronchospasm, was deemed reversible.

Diagnosis
On Day 9, the admission sputum was positive for Aspergillus Fumigatus, but the Aspergillus PCR and Precipitins were negative. This meant the patient was colonised by, and not sensitised to, Aspergillus. The spirometry in 2019, which showed significant air flow limitation, also illustrated a surprising degree of reversibility (Table 1). Because the eosinophil count remained unsuppressed despite a week of Hydrocortisone 50 milligrams TDS, after further discussion with the ECMO centre, the steroids were increased: 1 mg of nebulised budesonide BD and Hydrocortisone 100 mg IV TDS.

Prognosis
The following day (D10), there was a rapid deterioration with a rising pCO2 (14 kPa) and pO2 (7.6kPa) despite...
100% Inspired Oxygen. A repeat CT showed new bilateral lower lobe consolidation and pleural effusions. The tertiary centre confirmed that the patient was no longer an ECMO candidate due to prolonged invasive ventilation. They suggested proning the patient as a last resort. This was discussed between the consultants looking after the patient and the decision was not taken lightly. Shortly after proning, there was a further deterioration with an increase in pCO2 (17.15kPa).

**Case progression and outcome**

On day 12, following 16 h of proning, the patient was supinated. ABG showed vastly improved pH and pCO2. Physiotherapy led to thick secretions on suctioning and an improvement in bronchospasm. By day 15, he was breathing spontaneously. A percutaneous tracheostomy was inserted. With tracheostomy in-situ, he was stepped down to a respiratory ward, twenty-five days after entering the ICU. By day 34, he walked out the hospital with a course of prednisolone and a Trimbow inhaler (Steroid, LABA & LAMA) instead of Spiolto Respimat (LAMA & LABA).

**Discussion**

This case highlights the ease of misdiagnosing adult-onset Eosinophilic Asthma as COPD. Although the “classic” asthma patient is stereotyped as a young female with multiple allergies, De Groot et al. showed that adult-onset asthmatics with high blood eosinophils [>0.3 × 10^9 L − 1] are more often: non-atopic, middle-aged males, with fixed airflow limitation [FEV1/FVC <0.7 post-bronchodilator].

There is increasing recognition of the clinical importance of elevated eosinophils in COPD as well as

| Test                        | Result                                      |
|-----------------------------|---------------------------------------------|
| Sputum MCS                  | Aspergillus Fumigatus                       |
| Aspergillus Precipitins     | Negative                                   |
| IgE                         | 270 KU/l                                   |
| Vasculitis screen           | Negative                                   |
| Aspergillus PCR             | Negative                                   |
| Spirometry                  | FEV1/FVC ratio of 0.7                      |
|                             | FEV1 rose by 37% post-Salbutamol            |
| Echocardiogram              | Good biventricular function and a small pericardial effusion |
| Magnesium and Theophylline levels | Within normal range                      |

Asthma. Inhaled corticosteroids (ICS) have been shown to slow lung function decline^2^ causing the Global Initiative for Chronic Obstructive Lung Disease (GOLD) to recommend COPD patients with eosinophils greater than 0.3 × 10^9 L − 1 be considered for ICS.3

However, ICS-alone may be insufficient to treat severe Eosinophilic Asthma. For these patients, biological therapies targeting the Interleukin-5 (IL-5) component of the T-helper Type 2 (TH 2) lymphocyte inflammatory response have been developed. IL-5 plays a critical role in eosinophil differentiation, maturation, recruitment, and activation.4 There are currently three NICE approved biologics for severe Eosinophilic Asthma,5 Mepolizumab, Reslizumab and Benralizumab. These biologics reduce the number of eosinophils through interleukin-5 inhibition and are available on the NHS. Interestingly, a case of Mepolizumab-treated Eosinophilic Asthma has recently been published.6 Although not used in this case, sputum testing allows for improved identification of Eosinophilic driven airway inflammation, and draws associations with other biomarkers, such as blood eosinophils.7 Diagnostic sputum cell counts vary between 1 and 3%.8

In conclusion, the patient’s demographics, spirometry, and symptoms led to a near fatal misdiagnosis that caused chronic undertreatment for over a year (Table 2). Greater physician knowledge of the different Asthma phenotypes will hopefully reduce occurrences like the case described, where correct treatment (steroids) is only initiated following a life-threatening exacerbation.

**Key points**

- A label of COPD can be inaccurate
- Eosinophil counts should be noted before initiation of steroids
- Asthma has several different phenotypes
- Steroids have a role in a subset of COPD patients
- Three biologics have been approved by NICE for treating Eosinophilic Asthma

**Declaration**

**Consent:** A patient consent form was used to obtain written informed consent for us to publish this case report.

**Table 1. Results.**

| Test                        | Result                                      |
|-----------------------------|---------------------------------------------|
| Sputum MCS                  | Aspergillus Fumigatus                       |
| Aspergillus Precipitins     | Negative                                   |
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**Table 2. Blood eosinophils at time of diagnosis and admission (10^9 L − 1).**

|                      | March 2021 (Admission) | Jan 2020 | Nov 2019 (Diagnosis) |
|----------------------|------------------------|----------|----------------------|
| White cell Count     | 15.8                   | 11.9     | 10.3                 |
| [4–11 / 10^9/L]      |                        |          |                      |
| Eosinophil Count     | 1.6                    | 0.5      | 0.3                  |
| [0–0.3 / 10^9/L]     |                        |          |                      |
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