Two girls with status asthmaticus

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Introduction

Modern advancement in asthmatic medications, improvement in asthma education and easy accessibility to medical care has made life-threatening asthma requiring mechanical ventilation infrequent in children nowadays. Two cases with status asthmaticus recently admitted to our department were presented. Both were emergency admissions from Emergency Department (ED) and they required paediatric intensive care with ventilatory support.

Case 1

A 26-month-old girl was admitted from the ED for severe asthmatic attack. She was seen by her family doctor and referred for hospital management. She had running nose the day before and developed cough and dyspnoea on the day of admission. Feeding and urine output were decreased. There was no fever, sick contact or history of foreign body choking.

She was a known asthmatic presenting as recurrent wheezing attacks during upper respiratory infections since age 1 year and had been started with inhaled steroid prophylaxis by her private doctor since the third wheezing episode. Her father suffered from allergic rhinitis while a paternal uncle had childhood asthma. There was no pet, smoker, carpet, joss stick burning in the family. Birth and perinatal history were unremarkable and there were no known food or drug allergies.

At ED, she was afebrile, tachypnoeic (breath rate 50/min), with bilateral diffuse wheezes over her chest, and tachycardic (pulse rate 190/min). Oxygen saturation measured 92% in room air, improving to 96% after given 100% oxygen. Chest X-ray showed no infiltrate or pneumothorax. She received multiple metered-dose inhalations (MDI) of salbutamol (five rounds of six 100 µg-puffs) and ipratropium bromide (one 20 µg-puff) within 1/2 hour prior to admission to our department.

On arrival at the paediatric ward, she remained tachypnoeic and tachycardic. Breath rate was 64/min and pulse rate 187/min. There was low-grade fever with body temperature 37.6°C. Air entry was fair and there were bilateral diffuse wheezes over the chest. Oxygen saturation dropped to 90% despite 100% oxygen via non-rebreathing mask. Inhalational salbutamol was continued via oxygen-driven nebulization and intravenous hydrocortisone was started. Cefotaxime was added to cover for possible pneumonia and intravenous fluid (60% normal maintenance) supplement was given as the girl was kept nil by mouth.

She remained in respiratory distress and her oxygen saturation dropped to 80% whenever she struggled and dislodged the oxygen facemask. A dose of intravenous magnesium sulphate (40 mg/kg) was given and further salbutamol was added by intravenous infusion (1.5 µg/kg/min). However, there was no significant improvement and she became tired and drowsy. Venous blood gases showed hypercapnoea (pH 7.12, pCO₂ 11.7 kPA, base excess -4). She was intubated and was put on mechanical ventilation. Immediate post-intubation arterial blood gases showed predominately respiratory acidosis (pH 7.11, pCO₂ 12 kPA, pO₂ 11 kPA, base excess -3). There was hypotension with poor peripheral circulation requiring fluid resuscitation (20 ml/kg normal saline). She was transferred to a tertiary center for paediatric intensive care. Pre-transferal Paediatric Index of Mortality 2 (PIM2) Score was -1.77, giving a predicted mortality of 14.55%.

At paediatric intensive care unit (PICU), she was put on volume-controlled ventilation under full sedation (midazolam infusion 3 µg/kg/min and fentanyl infusion 2 µg/kg/hr) and muscle paralysis (vecuronium infusion 1 µg/kg/min). Hydrocortisone, nebulized salbutamol and ipratropium bromide were continued. Intravenous salbutamol was escalated to 2 µg/kg/min and ketamine infusion (2 µg/kg/min) was started.
Azithromycin and metronidazole were given to provide additional antibiotic cover for possible chest infection and aspiration pneumonia.

Gas-trapping persisted for some time but her clinical condition gradually improved over the next day, with significant improvement in air entry. There were no major complications like severe hypoxia, pneumothorax, hypotension. Maximal pCO$_2$ was 20 kPa and maximum heart rate measured 200/min. Hypokalaemia was mild (lowest 3.16 mmol/L) and corrected with potassium supplement. She was extubated two days later and transferred to the general ward (day 5) before discharge (day 9) with budesonide MDI 400 mcg/day as prophylaxis medication.

Nasopharyngeal aspirate for influenza, parainfluenza, adenovirus and respiratory syncytial viruses were negative. Tracheal aspirate grew no bacteria and paired blood atypical pneumonia titers showed no serial changes. C-reactive protein (7.4 mg/L) was not raised. Full blood counts showed normal total white cell counts (3.99 x 10$^9$/L) but with 7% atypical lymphocytes, normal haemoglobin and platelet levels. Renal function was normal; however her liver function was deranged, with serum alanine transaminase (ALT) rising from 35 (day 2) to 3190 (day 5) IU/L, while gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), serum bilirubin, clotting profile, blood glucose and ammonia were normal. Serum antigen / antibody tests for hepatitis A, B, C were all negative but anti-viral capsid antigen IgM antibody test for Epstein-Barr virus (EBV) was positive, confirming infectious mononucleosis.

Clinically, there was no jaundice, rash, hepatosplenomegaly, lymphadenopathy, liver failure or encephalopathy. The ALT decreased to 1705 and 112 IU/L on day 8 and 18 respectively. Hepatobiliary ultrasonogram showed diffuse non-specific decreased echotexture over the periporal region. At subsequent outpatient clinic follow up, ALT returned to normal level and the hepatic inflammatory changes resolved on ultrasound reassessment three months later.

**Case 2**

An 11-year-old girl was admitted from ED for severe asthmatic attack. She had sore throat and cough two days earlier and developed dyspnoea with wheezes the day before admission. She had no fever and there was no history of recent sick contact. Prior to ED consultation, she took ten salbutamol MDI 100 µg-puffs twice but with no apparent relief.

She was a known asthmatic with eczema since toddler age. Birth and perinatal history were unremarkable and she had no known food or drug allergies. There was no family history of asthma, allergic rhinitis or eczema but the family kept a dog and both parents were smokers. She had been cared for by her family doctor all along and was put on inhaled steroid prophylaxis for the past three to four years. Drug adherence was unsatisfactory despite parental reminder; resulting in poor asthma control with wheezing attacks once every few days and she would frequently rely only on bronchodilator rescue. However, there had been no previous hospitalisation and this was her first ED attendance.

At ED, she was afebrile, tachypnoeic (breath rate 30/min) and cyanosed, with occasional wheezes over her chest. Pulse rate was 88/min and oxygen saturation measured 86% in room air, improving to 98% when given 100% oxygen. Chest X-ray showed right lower zone haziness but no pneumothorax. She was given metered-dose inhalations (MDI) of salbutamol (four 100 µg-puffs), ipratropium bromide (four 20 µg-puffs) and intravenous hydrocortisone prior to admission to our department.

When admitted to the paediatric ward, her breath rate was 24/min, pulse rate 150/min and oxygen saturation 95%. She remained in respiratory distress and air entry was fair though symmetrical. Her expiration was very prolonged and there were diffuse wheezes, suprasternal and subcostal chest insucking. Inhalational salbutamol was switched to oxygen-driven nebulization and ipratropium bromide was added. Cefotaxime and azithromycin were also commenced to cover for pneumonia. Intravenous hydrocortisone was continued and she was kept nil by mouth with supplementary intravenous fluid (90% normal maintenance) in view of marked respiratory distress.

She became progressively more tachypnoeic (breath rate 40/min) and tachycardic (pulse rate 160/min) though oxygen saturation (99% in 100% oxygen) and blood pressure (139/100 mmHg) could be maintained. Breathing further became laboured, with poor air entry and development of nearly silent chest. Intravenous
magnesium sulphate was given (loading 50 mg/kg, followed by 30 mg/kg/hr infusion) and further salbutamol was added by intravenous infusion (loading 5 µg/kg/min in first hour then 1.5 µg/kg/min). However, there was no significant improvement. Arterial blood gases showed hypercapnoea with predominately respiratory acidosis (pH 7.16, pCO₂ 9.8 kPA, pO₂ 41.6 kPA, base excess -4). She was transferred to a tertiary center for paediatric intensive care. Pre-transferal PIM2 Score was -4.44, giving a predicted mortality of 1.16%.

At PICU, she was put on bi-level positive airway pressure (BiPAP) ventilation. Nebulized salbutamol and ipratropium bromide were continued and steroid was switched to methylprednisolone. Intravenous salbutamol was escalated to 2 µg/kg/min and magnesium sulphate increased to 50 mg/kg/hr. She tolerated BiPAP ventilation and responded well to the escalated treatment. Air entry improved and respiratory distress decreased, with the maximum oxygen requirement lowered to 50%. There were no major complications like severe hypoxia, pneumothorax, hypotension. Maximum heart rate measured 130-160/min and there was no hypokalaemia. She steadily improved and could be weaned off from non-invasive ventilation the next day. She was transferred to the general ward on day 3 and discharged on day 6 with beclomethasone dipropionate MDI 200 mcg/day as prophylaxis medication.

Nasopharyngeal aspirate for influenza, parainfluenza, adenovirus and respiratory syncytial viruses were negative. Blood culture was sterile and paired atypical pneumonia titers showed no serial changes. Full blood counts, renal and liver function tests were all normal.

Discussion

Asthma is a leading chronic illness in childhood. Although new anti-asthmatic medications, modern technology advancement in drug delivery devices, structured stepwise asthma management approach, improvement in asthma education and easy accessibility to medical care have made life-threatening asthma infrequent in children nowadays, this potentially fatal presentation is still occasionally encountered in some high-risk patients. Adult studies have recognised that near-fatal asthma presents in two patterns depending on its speed of deterioration: a slow-onset group, which is characterised by gradual deterioration over days or weeks with even some transient improvement before mechanical ventilation is finally required, and a sudden-onset group, which requires mechanical ventilation within a few to 24 hours from the onset of asthmatic symptoms.1,2 The strongest risk factors identified to predict near-fatal asthma include past history of a life-threatening asthmatic episode, prior intubation and mechanical ventilation for asthma, prior admission for asthma to an intensive care unit, frequent hospitalisations (≥2) or emergency care visits (≥3) for asthma in the past year. Despite better intensive care, mortality rate remains high, particularly for those requiring mechanical ventilation, ranging from 8.3% to 22%.2,4

The two patients of status asthmaticus we described belonged to the sudden-onset group and both presented as life-threatening asthma on their first hospital attendance. While the adolescent girl in the second case was apparently an at-risk patient due to her non-adherence to prophylaxis medication, they lacked the aforementioned high-risk predictive factors for near-fatal asthma. However, paediatric studies on status asthmaticus have been limited and small-scaled, and clinicians have had difficulty identifying children at risk for potentially fatal asthmatic attacks. Western studies have found previous severe attack and non-white children with poor access to medical facility associated with the highest risk of near-fatal or fatal asthma.5,6 A few recent paediatric reviews in ethnic Chinese reported previous hospital admissions for asthma and history of non-compliance to recommended treatment were the common risk factors among patients admitted to PICU. Mortality rate ranged from 0% to 3.3% and prognosis was favourable with modern paediatric intensive care and prompt treatment.7,8

Concomitant respiratory tract infection has been one of the commonest triggering factors for asthma exacerbations. Pathogens reported included influenza and parainfluenza viruses, respiratory syncytial virus, adenovirus, rhinovirus, coronavirus, enteroviruses and atypical bacteria. Their mechanisms causing airway inflammatory response have been the focus of intense research. The immune responses may involve neutrophils, eosinophils and various
chemokines, including interleukin-8 (IL-8), intracellular adhesion molecule-1 (I-CAM-1), eosinophil cationic protein (ECP), macrophage-inhibitory-protein 1-α (MIP-1-α), and RANTES.9–13

Interestingly, infectious mononucleosis appeared to be the triggering infection for status asthmaticus in the toddler girl in the first case we presented. To our knowledge, this has not been reported before in the literature. Local reviews in Chinese children have not identified asthma exacerbation as the clinical presentation or complication of infectious mononucleosis either.14,15 Previously, EBV has been reported to be one of the major potent macrophage activators and increased serum levels of antibodies to EBV have been observed in atopic individuals.16 A recent study described the role of leukotriene pathway and its influence on T-cells during acute EBV infection in allergic asthmatics.17 Therefore, EBV is suspected to play a pathogenic role in the development of allergy.16,18 However, results of other studies19,20 have not been consistent and its precise role remains to be elucidated.

Endotracheal intubation and mechanical ventilation have been the treatment of choice for acute respiratory failure in patients with status asthmaticus. However, this may have significant complications, including barotraumas, pneumonia, airway trauma and vocal cord dysfunction. BiPAP offers an alternative non-invasive approach to mechanical ventilation that can avoid these complications. Moreover, it provides greater patient comfort, reduces sedation need, and preserves swallowing, speech and normal airway defence mechanisms. Several studies in adult populations have shown that BiPAP is a safe and effective therapy for status asthmaticus.21–24 Its application in paediatric patients was increasingly reported with promising results.25,26 Indeed, our second patient illustrated well the successful management of status asthmaticus using BiPAP in appropriately selected paediatric patients. Further prospective study is needed to improve the therapeutic strategies of this non-invasive respiratory support modality.

**Conclusion**

Two cases of status asthmaticus were presented. They were precipitated by viral illness and EBV infection appeared to be the trigger in the first case. Attention to risk factors helped in prompt recognition of life-threatening asthma. Early provision of PICU care and close monitoring contributed to favourable outcome. BiPAP obviated the need of endotracheal intubation and mechanical ventilation in the second case.

**References**

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