Successful Rescue of a Child with Severe Anaphylactic Shock by Extracorporeal Membrane Oxygenation

BT Ning, CM Zhang, R Lin, YM Tang

Abstract
A 9-year and 8-month old boy suffered from anaphylactic shock induced by cefotaxime. The patient's condition deteriorated after the emergent therapy with epinephrine, high-dose of methylprednisolone and mechanical ventilation. The extracorporeal membrane oxygenation (ECMO) with V-A model was carried out successfully after 4 hours of admission to paediatric intensive care unit. The patient's conditions were getting better after ECMO application with gradual disappearance of the pulmonary oedema and haemorrhage. He was weaned from ECMO after 64 hours and extubated successfully 84 hours later.

Key words
Anaphylactic shock; Cefotaxime; Extracorporeal membrane oxygenation (ECMO)

Introduction

Cefotaxime is a third generation cephalosporin antibiotic with potent bactericidal effect, low toxicity and relatively low cost. Adverse reaction uncommon and may include skin rash, nausea, vomiting and other mild symptoms . However, severe adverse reaction such as refractory anaphylactic shock is rare.[1] We report here a 9-year and 8-month old boy suffered from anaphylactic shock induced by cefotaxime. The patient's condition deteriorated despite the use of epinephrine, high-dose of methylprednisolone and mechanical ventilation. The extracorporeal membrane oxygenation (ECMO) with V-A model has to be applied and it was able to reverse the downward clinical course after 4 hours of admission to paediatric intensive care unit (PICU). ECMO is an accepted therapeutic modality for the patient who suffered from cardiac and/or pulmonary insufficiency and failed in conventional therapy. It delivers oxygen to the tissue and organs by draining venous blood, removing carbon dioxide and adding oxygen through an oxygenator. The oxygenated blood was then returned to the circulation via a vein or artery. There are only very few reports on severe anaphylactic shock treated by ECMO in children.[2,3] Here we reported a case of intractable anaphylactic shock caused by cefotaxime and was successfully treated by ECMO.

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Case Report

A 9-year-8-month old boy weighting 39 kg was admitted to our hospital because of 2 weeks of coughing associated with recent onset of rash (2.5 hours) and haemoptysis (1 hour). The patient had history of dry cough for two weeks without shortness of breath, cyanosis, fever or rash. The cough deteriorated after treatment with Chinese herbs and azithromycin for 5 days. He was then brought to our hospital where he was diagnosed to have bronchitis and was treated

with cefotaxime and Ambroxol Hydrochloride infusion. The child experienced abrupt onset of facial rash, throat discomfort, hoarseness, vomiting, pallor after 10 minutes infusion of cefotaxime. The heart rate was 150/min, BP 80/33 mmHg and SpO_2 76%. Anaphylactic shock was diagnosed at the emergency room. First-aid measures including immediate cessation of cefotaxime infusion, bolus of volume expander with normal saline (20 ml/kg), and intravenous adrenaline twice (0.01 mg/kg). Methylprednisolone (10 mg/kg) was also added but the condition of the patient continued to deteriorate. He exhaled pinkish bubbling phlegm with facial cyanosis. Emergent tracheal intubation and ventilatory support was commenced immediately. He was diagnosed to have severe anaphylactic shock, pulmonary oedema with pulmonary haemorrhage and was admitted to PICU. He has no allergic history to penicillin but he was allergic to shrimp since infancy.

Physical examination in PICU showed that he was afebrile with tachycardia (HR: 140/min). He had hypotension and his BP was 85/35 mmHg with low SpO_2 of 72%. He was under ventilator-assisted breathing with decrease conscious level. There was no facial oedema. He had irregular respiration with coarse and moist rales diffused over the whole lung. Other organ systems were unremarkable except for the cold extremities with a capillary filling time >5 seconds.

His serial arterial blood gases and electrolytes results were showed in Table 1. Initial serum biochemical results showed total protein 51.8 g/L, albumin 31.6 g/L, GPT 61 U/L, GOT 248 U/L, ADA 61.3 U/L, Cr 121.9 μmol/L, urea 8.88 mmol/L, LDH 1271 U/L, CK 1148 U/L, CKMB 145 U/L, triglyceride 0.23 mmol/L. Complete blood count showed WBC 8.42×10^9/L,

N 62.9%, Hb 127 g/L, Plt 298×10^9/L. C-Reactive Protein: 13 mg/L. prothrombin time (PT) and activated partial thromboplastin time (APTT): 15.2 seconds and 37.6 seconds respectively. Initial chest X-ray (CXR) was compatible with acute bronchitis (not shown). Pulmonary oedema and haemorrhage were noted upon admission to PICU (Figure 1) and resolved based on the CXR 4 days later (Figure 2).

Epinephrine infusion at 1 μg/kg/min was started after admission to PICU with high dose methylprednisolone (10 mg/kg) and morphine (starting dose 0.02 mg/kg, maintenance dose 0.01 mg/kg/h). Volume expander was infused according to his circulatory status. Ventilator support was performed under SIMV mode with FiO_2 100%, respiratory frequency (R) 25/min, tidal volume (VT) 7 ml/kg, positive end expiratory pressure (PEEP) 15 cmH_2O, minute ventilation (MV) 5.0 L/min. After 2 hours of therapy, the patient's SpO_2 remained lower than 70%. The BP was also low at 85/32 mmHg with tachycardia (HR 150/min). The extracorporeal membrane oxygenation (ECMO) was commenced for cardiopulmonary support. Direct cannulation of the left femoral artery and right internal jugular vein (external jugular vein was found apparent collapse). Medtronic paediatric ECMO package (CB2503R1), MAQUET BE-PLS 2050 membrane oxygenator and a centrifugal pump system (bio-console 560) were used. VA mode of ECMO was established successfully. The key parameters of ECMO were listed as followings: centrifugal pump speed 3000 rpm, blood flow 2.5 L/min, the oxygen flow rate 2.5 L/min, FiO_2 70%. Circulation way was from the right internal jugular vein → Centrifugal pump → Membrane Oxygenation → left femoral artery. The activated coagulation time (ACT) was

Table 1 Arterial blood gas and electrolyte findings: Before the application of ECMO, the patient suffered from severe respiratory and metabolic acidosis. After half an hour of ECMO treatment, the pH, pCO_2 and pO_2 significantly improved. Ten hours later the blood gases, BE, pH, pCO_2 and pO_2 were all near normal level

	pH	pCO₂ (mmHg)	pO₂ (mmHg)	K+ (mmol/L)	Na+ (mmol/L)	Cl- (mmol/L)	ABE (mmol/L)
Before shock	7.338	37.7	102	3.3	133	106	-5.0
At emergency	6.931	85.6	56.4	3.3	139	107	-17.3
Admission to PICU	7.009	86.2	56.9	2.7	136	106	-12.6
Before membrane with 0.5 hour ECMO	7.070	51.2	56.8	3.4	137	104	-14.6
After membrane with 0.5 hour ECMO	7.207	31.6	297.0	3.7	137	105	-14.3
After 1.5 hours ECMO	7.251	31.1	285.0	2.9	138	112	-12.6
After 10 hours ECMO	7.311	30.6	139.0	3.3	136	110	-7.1

PICU=paediatric intensive care unit; ECMO=extracorporeal membrane oxygenation
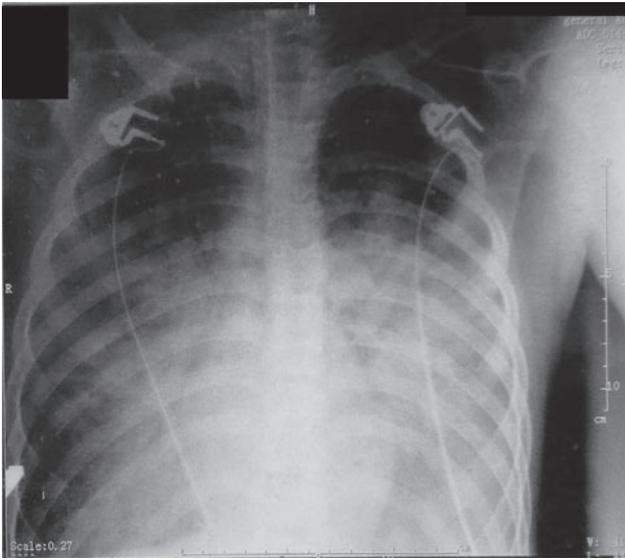
Figure 1 Chest X-ray upon admission to PICU: CXR showed diffused pulmonary infiltrates and haziness with wide range of flaky density. The heart shadow was blurred.
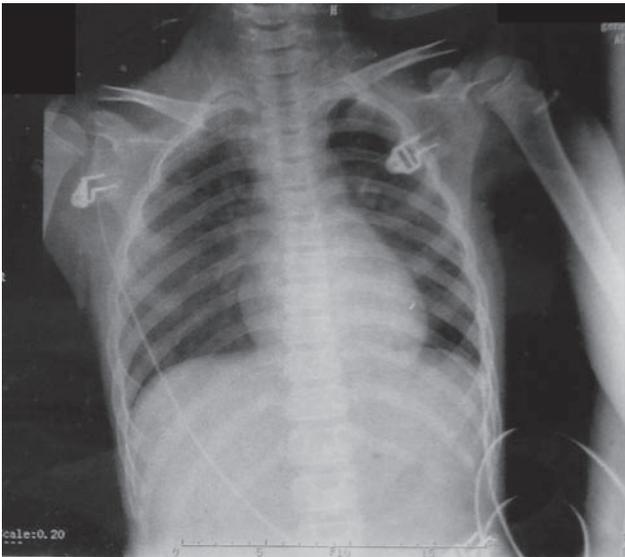
Figure 2 Chest X-ray after 4 days of therapy: CXR showed increase in lung markings but no obvious flaky shadow. There was no significant increase in the size of the heart shadow. The diaphragmatic surface was well defined with sharp costophrenic angle.

maintained between 180 and 230 seconds. The parameters of ventilator were tapered gradually. The pulmonary oedema and haemorrhage slowly resolved. He was weaned from ECMO 64 hours later and was extubated successfully 84 hours later.

Discussion

Gallelli et al[4] performed retrospective analysis of 205 cases with drug adverse reactions, the number which caused by antibiotics accounted for 44.9%. Among the 44.9%, 20.7% was related to cephalosporin, but anaphylactic shock was rarely reported. Anaphylactic shock is a severe allergic reaction involving multiple organs including the bronchial and cardiovascular system. When external antigenic substances got into the body previously sensitised, the allergen interacted with the corresponding IgE antibodies. The interaction of allergen and IgE leads to degranulation of the mast cells leading to the release of inflammatory mediators such as histamine, bradykinin, 5-HT, platelet-activating factor, etc.. These immune mediators cause systemic capillary dilatation and leakage resulting in plasma exudation. Eventually it will lead to circulatory failure due to loss of intravascular volume. In addition, due to bronchial and tracheal wall oedema, obstructive respiratory failure may develop.

The manifestations and severity of anaphylactic shock depends on the individual body response, exposure dose and time to the antigen, etc. The onset is usually very abrupt and dramatic. If there is no timely emergency treatment, the outcome can be fatal. Epineprine in the form of epipen can be life saving. Volume expander in the form of normal saline may be necessary to deal with the hypotension. Other drugs including antihistamine, steroid and arginine vasopressin have all been but their respective clinical efficacy remains uncertain due to the lack of well designed randomised double-blind evidence-based study on these aspects.[5]

ECMO is a powerful alternative to the intrinsic cardiopulmonary function of a human subject. It is effective in treating cardiac and respiratory arrest, severe acid-base electrolyte imbalance, or in rare situations, for the treatment of severe asthma, drowning, frostbite, trauma and infections.[6,7] In simple term, ECMO support can be potentially applied to all patients with potentially reversible pulmonary, cardiac or cardiopulmonary failure. The only limitation is those patients with irreversible cardiopulmonary function.[8] But the introduction

ECMO of intervention should be timely so the hypoxic-ischemic state of the body can have a chance to recovery before irreversible damage or cell death has taken place. Till now, how to decide on a timely intervention time remains a challenge. If early and appropriate support is applied before any end-organ injury caused by severe metabolic derangement or cardiac arrest, the ECMO can achieve excellent outcome. With the heparin-coated surface (HCS) technology and controlling the ACT range between 180 and 230 seconds, the ECMO can effectively reduce blood clotting or bleeding disorders. This can allow ECMO to be used in patients over a prolonged period of 1-2 weeks. The therapy related complications of ECMO include haemorrhage, thrombosis, haemolysis, renal failure, sepsis, neurological insult, distal limb ischemic and ECMO circuit system disorder. Among all these complications, haemorrhage is the commonest problem encountered. This patient developed profuse bleeding after surgical cannula installation with bleeding around the incision site. He required surgical haemostasis and blood transfusion to stabilise his condition and can continued with the ECMO treatment.[9]

The principles of successful ECMO treatment included the followings:[10] 1) timely commencement of ECMO to ensure brain oxygenation; 2) maintenance of optimal ventilator setting to reduce the pulmonary trauma or alveolar collapse; 3) appropriate clinical titration of vasoactive drugs to maintain normal cardiac workload and prevent thrombosis; 4) maintenance of ACT between 180 and 230 seconds, PT <14 seconds or APTT <80 seconds so as to prevent disseminated intravascular coagulation (DIC); 5) transfusion of fresh frozen plasma and platelets to prevent haemorrhage or thrombosis; 6) maintenance of a hematocrits level of 35-40% to warrant adequate oxygen delivery to tissues; and 7) maintenance of normal plasma colloid osmotic pressure to safeguard circulatory function and minimise tissue oedema.

During anaphylactic shock, this patient was initially treated with conventional resuscitation measures plus ventilator support for 2 hours. But the circulatory and respiratory conditions remained suboptimal. So the need of ECMO intervention was decided and carried out without too much delay. With the cooperation of surgeons, PICU doctors and extracorporeal circulation team, VA mode of ECMO was successfully established. With the ECMO support, the patient achieved significant improvement in terms of his blood pressure and SpO_2. After ECMO running for 1 hour, the ventilator requirement decreased significantly (FiO_2 from 100% to 60%, PIP 35 cmH_2O down to 31 cmH_2O,

PEEP 15 cmH_2O down to 10 cmH_2O), the need of vasoactive drugs dose also decreased at the same time. His distal extremities began to turn warm and his urine output increase. Under the ECMO support for 64 hours, the patient's condition stabilised with resolution of his pulmonary oedema and pulmonary haemorrhage (see Figure 1 and Figure 2). ECMO was withdrawn from the patient thereafter. And at 84 hours after the shock, the patient was extubated. He recovered completely after another week of hospitalisation.

Conclusion

According to the history, the boy was also allergic to shrimp. Whether the patient has multiple food or drug allergy remains to be verified. What we can conclude in this case is that based on the history and clinical manifestations, he had severe anaphylactic reaction to cephalosporin. Despite conventional treatments, he lapsed into cardiopulmonary failure and required ECMO cardiopulmonary support. Fortunately, he was able to regain his tissue and organ function subsequently without significant side effect. Therefore, in selected case of severe anaphylactic shocks, ECMO may be life saving if it is applied early.

Acknowledgement

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