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SHORT COMMUNICATION

Severe adenovirus pneumonia requiring extracorporeal membrane oxygenation support — Serotype 7 revisited

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KEYWORDS
Extracorporeal membrane oxygenation;
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Summary
Introduction: Adenovirus causing severe fatal pneumonia has been well described in infants, children, and patients with immunocompromised function, but reports in previously healthy adults are rare. We report 3 cases of severe adenovirus pneumonia in whom conventional mechanical ventilation failed and required extracorporeal membrane oxygenation support.
Methods: Retrospective case records review of 3 patients admitted to the medical intensive care unit, Singapore General Hospital, a tertiary care university-affiliated hospital, with severe adenovirus pneumonia requiring extracorporeal membrane oxygenation support from February to March 2013.
Results: All 3 patients were previously healthy immunocompetent adults from the community with negative HIV serology. Duration prior to development of respiratory failure requiring intubation and invasive mechanical ventilation was 2, 8 and 3 days. Veno-venous extracorporeal membrane oxygenation (ECMO) support as rescue ventilation was instituted in all 3 patients after 2, 16, and 5 days of conventional mechanical ventilator support. Duration on ECMO support was 16, 22, and 9 days and mechanical ventilation was 18, 62, and 19 days respectively. Length of stay in intensive care unit was 18, 68, and 21 days, and length of stay in hospital was 20, 70, and 31 days respectively. Two of the 3 patients died.

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Conclusion: The mainstay of treatment for patients with severe adenovirus pneumonia is still supportive, with the use of antivirals not apparently effective. Whilst ECMO support for rescue ventilation may be considered, the outcomes do not appear as promising as other viral pneumonias, mirroring that previously described in the paediatric population.

Introduction

Adenovirus causing severe fatal pneumonia has been well described in infants, children, and patients with immunocompromised function, but reports in previously healthy adults are rare. We report 3 cases of severe adenovirus pneumonia in whom conventional mechanical ventilation failed and required extracorporeal membrane oxygenation (ECMO) support.

Methods

Retrospective case records review of 3 patients admitted to the medical intensive care unit, Singapore General Hospital, a tertiary care university-affiliated hospital, with severe adenovirus pneumonia requiring ECMO support from February to March 2013. Patients were considered for ECMO based on a set of criteria used by our centre — age below 65 years, good premorbid status, and presented with a PaO2:FiO2 ratio <60 secondary to severe pneumonia despite optimal conventional mechanical ventilation for over 6 h.

Veno-venous ECMO was performed for all 3 patients. The common femoral veins were cannulated percutaneously using the Seldinger technique. Venous blood was drained from the inferior vena cava using a long 19 F or 21 F cannula in one common femoral vein and returned to the venous system via the contralateral femoral vein using a short 17 F cannula after passing through the oxygenator. A centrifugal pump was used to drive the circuit flow. Flow rates were adjusted to achieve adequate oxygenation.

Results

Age of the 3 patients was 38, 62, and 32 years, and BMI was 21.5, 25.6, and 34.7 kg/m^2 respectively. Two were male of Chinese ethnicity, the third was an Indian female. One of the 3 patients was a smoker. Duration of symptoms prior to presentation was 6, 4, and 4 days. Cough and fever were present in all 3 patients, with a highest temperature of 39, 38.7, and 40 °C respectively. One patient had associated rhinorrhea, another had diarrhoea, and both manifested rhabdomyolysis. None of the patients presented with dyspnoea or sorethroat. All 3 patients were previously healthy immunocompetent adults from the community with negative HIV serology. Total white cell counts were within the normal range (4.71, 5.8, and 9.4 $\times$ 10^9/L) but 2 of the 3 patients manifested mild lymphopenia. Inflammatory marker CRP was markedly raised although procalcitonin was only mildly elevated. All 3 patients had adenovirus PCR isolated using the Seegene Anyplex II RV16 Detection Assay (Seegene, Korea) — 2 from endotracheal tube aspirates and 1 from throat swab. Genotyping revealed adenovirus serotype 7 for all 3 patients. Bronchoscopy with bronchial washings was performed in the 3 patients to exclude any viral and/or bacterial co-infections and none were detected. Empiric broad-spectrum antibiotics were initially administered but deescalated when microbiology results were available.

Duration prior to development of respiratory failure requiring intubation and invasive mechanical ventilation was 2, 8, and 3 days. Veno-venous ECMO support as rescue ventilation was instituted in all 3 patients after 2, 16, and 5 days of conventional mechanical ventilator support. One patient required inotropic support prior to ECMO implantation but none were on renal replacement therapy. Duration on ECMO support was 16, 22, and 9 days and mechanical ventilation was 18, 62, and 19 days respectively. The 3 patients' oxygenation response to ECMO is shown in Table 1.

Two patients were treated with antiviral medications — one with oseltamivir and the other with cidofovir. Both patients demised despite maximal support. The third patient received 3 days of intravenous immunoglobulin and was discharged home after 31 days in hospital. None of the patients were given steroid therapy. Length of stay in intensive care unit was 18, 68, and 21 days, and length of stay in hospital was 20, 70, and 31 days respectively.

Discussion

Severe adenovirus disease affecting a previously healthy adult host is rare and reports scarce. Sporadic cases of severe pneumonia from adenovirus in healthy adults have been published — serotype 4 [1,2], serotype 7 [3], and more recently serotype 14 [4]. Outbreaks of severe respiratory illness caused by adenovirus serotype 14 in the community [5] and Air Force training facility [6] have also been described. An older paper described an outbreak in a mental care centre from serotype 35 [7]. Clinical presentation of our 3 patients were very similar to a previous review, where cough and high fever were dominant symptoms and progression to dyspnoea and acute respiratory failure occurring within days [8].

Despite the advances in intensive care, overall mortality from severe acute respiratory failure remains high at 66% [9,10]. Extracorporeal membrane oxygenation was first clinically introduced in 1972 as a means of cardiopulmonary support for patients with potentially reversible cardiac and/or respiratory failure in whom maximal conventional ventilator strategies have been exhausted. It's use is most established in the neonatal and paediatric

Table 1 Oxygenation response to veno-venous extracorporeal membrane oxygenation support.

		Pre ECMO	D1	D5	D10	D15	Pre ECMO explant	Post ECMO explant
Patient 1								
ECMO manufacturer/model: Terumo, Capiox SP								
Conventional Vent settings	FiO2	1.0	1.0	1.0	0.8	1.0		
	PEEP	12	8	20	18	18		
PaO2		50	51	75	52	[a]		
ECMO FiO2			1.0	1.0	0.8	1.0		
Patient 2								
ECMO manufacturer/model: Maquet, Rotaflow								
Conventional Vent settings	FiO2	1.0	0.8	0.6	0.7	0.6	0.6	1.0
	PEEP	18	12	16	16	16	10	12
PaO2		41	80	93	102	60	57	69
ECMO FiO2			1.0	1.0	1.0	0.6	0.5	
Patient 3								
ECMO manufacturer/model: Maquet, Rotaflow								
Conventional Vent settings	FiO2	1.0	0.5	0.6	0.4		0.4	0.5
	PEEP	16	8	12	12		12	10
PaO2		51	107	63	70		70	74
ECMO FiO2			1.0	1.0	0.8		0.8	

[a] No blood gas was taken.

population in whom viral pneumonia accounts for 25% of all respiratory failure cases necessitating ECMO with an overall survival of 60% [11]. Unfortunately a primary diagnosis of adenovirus pneumonia often requires prolonged ECMO support and portends the poorest survival of 25% [12]. The use of ECMO in adult respiratory failure is more controversial with previous randomized controlled studies failing to demonstrate an improved outcome with ECMO support [13,14]. More recent studies have suggested that careful patient selection is crucial to outcome, with isolated viral pneumonia demonstrating the highest survival rates of 78% with ECMO [15,16]. The H1N1 influenza pandemic led to a resurgence of interest in the feasibility of adult ECMO support with studies showing an overall in-hospital mortality of 28% [17]. We could find only one previous publication of ECMO support for severe adenovirus pneumonia in an adult heart transplant recipient [18]. Our report suggest that ECMO support for rescue ventilation in patients with severe adenovirus pneumonia may improve outcome, although overall mortality remains high.

Conclusion

More than 40 years after the first description of adenovirus serotype 7 causing fatal pneumonia in 3 healthy military trainees [3], we report 3 previously healthy adults with severe adenovirus serotype 7 pneumonia in whom conventional mechanical ventilation failed and required ECMO support. The mainstay of treatment is still supportive, with the use of antivirals not apparently effective. Despite the advances in intensive care, 2 of our 3 patients died. Whilst ECMO support for rescue ventilation may be considered for patients with severe adenovirus pneumonia, the outcomes do not appear as promising as other viral pneumonias, mirroring that previously described in the paediatric population [12].

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