Respiratory Medicine Case Reports 28 (2019) 100869

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

A case report of severe hypothermia complicated by acute respiratory distress syndrome

C. Vahdatpour[a,*], A. Sussman[a], T. Mahr[b]

[a] Department of Medicine, Pennsylvania Hospital, University of Pennsylvania Health System (UPHS), Philadelphia, PA United States
[b] Pulmonary, Allergy, and Critical Care Division, Department of Medicine, Pennsylvania Hospital, University of Pennsylvania Health System (UPHS), Philadelphia, PA United States

ARTICLE INFO

Keywords:
Hypothermia
Acute respiratory distress syndrome

ABSTRACT

Acute respiratory distress syndrome has not been a described complication of hypothermia. Causes of hypothermia are commonly associated with alcohol abuse and infection, both of which could lead to acute respiratory distress syndrome. We present a case of severe hypothermia complicated by acute respiratory distress syndrome in a young immunocompetent male treated successfully with mechanical intubation and venovenous extracorpeal membrane oxygenation. Risk factors for known causes of acute respiratory distress syndrome included a witnessed aspiration event and RSV pneumonia. On review of the literature, severe hypothermia has been found to cause pulmonary edema in post-mortem studies, but acute respiratory distress syndrome has not yet been recognized as a known complication. Our case highlights that acute respiratory distress syndrome may be multifactorial in etiology and related to complications of severe hypothermia.

1. Introduction

Severe hypothermia can present with complications that increase risk for acute respiratory distress syndrome (ARDS). ARDS has several known etiologies and is generally identifiable on clinical history and physical exam. We present a case in a young healthy male who developed ARDS from a multifactorial etiology, and we propose that severe hypothermia was a contributor to his ARDS physiology.

2. Case description

A 29-year-old male with past medical history notable for depression and alcohol abuse presented to the emergency department on a late winter evening via ambulance after being found unresponsive in his basement.

The morning of his presentation, his housemate found him on the cold basement floor and thought the patient was still asleep from his previous night. It was noted that the patient had spent the previous night drinking alcohol and had unintelligible speech prior to returning home. When his housemate returned home in the evening, the patient was found in the same position, unresponsive, and cold. Emergency services were called.

Initial vitals revealed a temperature of 24.9 °C, pulse 46 beats per minute, blood pressure 60/37, oxygen saturation 92% on room air, and respiratory rate 16 breaths per minute. Physical exam was notable for: listless appearance with a GCS of 7, dry mucus membranes, bradycardia that was irregularly irregular, and bibasilar coarse breath sounds bilaterally. Arterial blood gas on arrival demonstrated pH < 7.0, $pCO_2$40 mmHg, pO_2 104 mmHg, and lactate 8.5 mmol/L on 100% FIO2.

Due to progressive tachypnea during his ED course and altered mental status, he underwent rapid sequence intubation for airway protection. Following rapid sequence intubation, the patient experienced a moderate to large emesis that was non-bloody and non-bilious. Warmed fluid boluses were given, and he was covered with a forced air warming blanket system.

Chest radiograph 17 minutes after intubation revealed bilateral patchy opacities (Fig. 1). EKG demonstrated bradycardia, atrial fibrillation, and Osborn waves (Fig. 2). Initial laboratory data was significant for white blood cell count 5.2 thousand/μL, potassium 3.0 mmol/L, carbon dioxide 18 mmol/L, creatinine 1.72 mg/dL, glucose 201 mg/dL, anion gap 17, negative troponin, and creatinine kinase 594 U/L. His ethanol level was 135 mg/dL, and urine drug screen was otherwise negative.

He was warmed at a rate of 3° per hour over the course of 7 hours continuing active external and core rewarming. He was additionally started on broad-spectrum antibiotics, as there were concerns for compounding aspiration pneumonia and septic shock. His hypotension

* Corresponding author. Department of Medicine, Pennsylvania Hospital, 800 Spruce St., Philadelphia, PA, 19107, United States.
E-mail address: cyrus.vahdatpour@pennmedicine.upenn.edu (C. Vahdatpour).

https://doi.org/10.1016/j.rmcr.2019.100869
Received 4 March 2019; Received in revised form 28 May 2019; Accepted 28 May 2019
Available online 29 May 2019

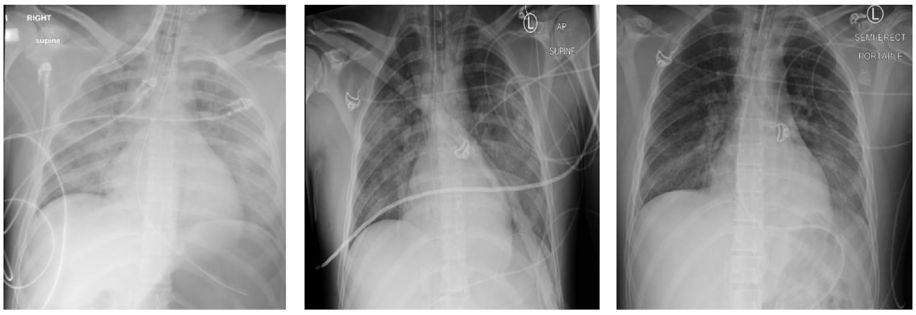

Fig. 1. Chest radiography over clinical course.

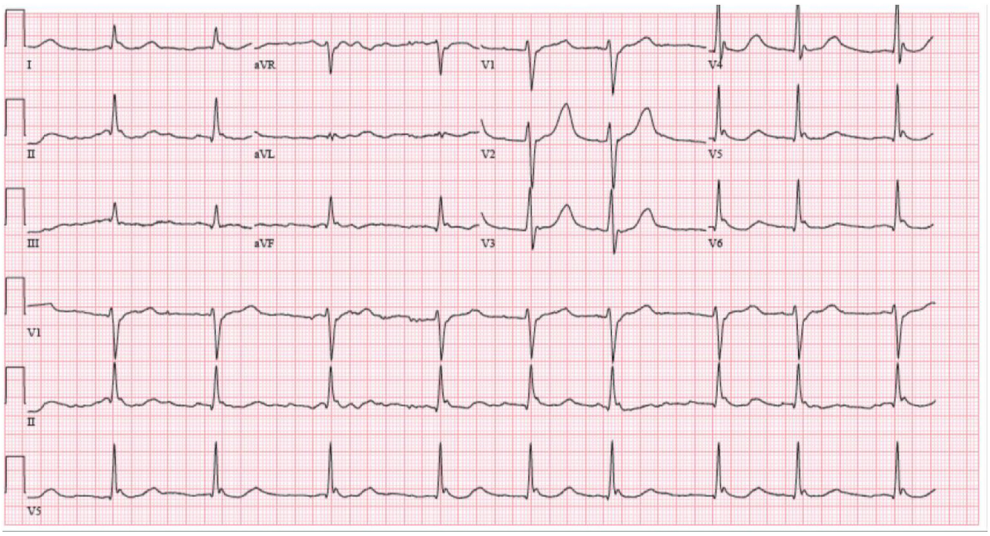

Fig. 2. Patient EKG on admission.

on admission was addressed with aggressive warm fluid boluses, norepinephrine, and vasopressin.

Early in his course of rewarming, his arterial oxygen saturation quickly declined (Table 1). Flolan initiation, lung recruitment maneuvers, and BiLevel ventilation were attempted to improve oxygenation with little improvement. Despite high BiLevel settings (RR 10, P_{high} 32, P_{low} 0, inspiratory to expiratory ratio 9:1, and FiO_2 100%), his PaO_2 was 40's-50's. Transthoracic echocardiogram revealed a hyperdynamic left ventricle without valvular or ventricular abnormality. 40 mg IV furosemide was administered with great response (3.8 L urinary output over 6 hours).

Table 1
ABG trend after admission.

Approx. Hours from Admission	Arterial pH	Arterial PaCO2 (mmHg)	Arterial PaO2 (mmHg)	SPO2%	HCO3- (mmol/L)
0	7	40	104	94	16.8
1	7.1	40	42	76	12.4
2	7.13	45	54	70	15
4	7.17	45	48	90	16.4
11	7.38	38	215	100	22.5
12	7.41	36	520	100	22.8
14	7.4	38	147	100	23.5
17	7.4	35	132	100	21.7
19	7.38	35	119	100	20.7
24	7.38	40	151	100	23.3

Trend of arterial blood gas values over time from admission to 24 hours after admission. Inspiratory oxygen saturation was monitored via forehead pulse oximeter. Each value was unchanged when corrected for body temperature. The patient was cannulated and placed on venous-venous extracorporeal membrane oxygenation therapy approximately 9 hours after initial admission time.

Once his bladder temperature reached 29.4 °C, he began to follow simple commands and required fentanyl for sedation for ventilator synchrony. Given his improved neurological status and persistent hypoxia in the setting of ARDS, he was considered to be a venovenous extracorporeal membrane oxygenation (VV-ECMO) candidate. Prior to ECMO cannulation, his BiLevel settings were RR 10, P_{high} 28 and P_{low} 0, inspiratory to expiratory ratio 9:1, and FiO_2 100%. He was cannulated early in the morning and started on VV-ECMO. Quickly after initiation, his blood gases normalized, and CXR findings improved (Fig. 1). He was decannulated 1.5 days later. He was extubated one day after ECMO decannulation.

Respiratory viral panel obtained on admission was subsequently found to be RSV-A positive. No other revealing culture data was noted. He completed treatment for possible aspiration pneumonia and was discharged to home on room air 1 week after initial presentation.

3. Discussion

ARDS is an inflammatory process associated with acute lung injury that results in: reduced capillary integrity, diffuse pulmonary edema that is not fully explained by left heart disease, and impaired lung compliance. Clinically ARDS is defined by a known insult that is temporally associated with hypoxia, bilateral radiographic pulmonary infiltrates, and a PaO_2/FiO_2 ratio < 300 on PEEP of > 5 mmHg [1]. Cautious interpretation of ABGs are important when determining the severity of ARDS because hypothermia increases the solubility of oxygen and carbon dioxide within the blood [2]. The partial pressure of oxygen may be falsely elevated and would explain a discrepancy between the severity of a low oxygen saturation in comparison with a less

severe partial pressure of oxygen. Infection and aspiration are common causes of ARDS and are discussed individually. To date, severe hypothermia has not been described as a direct etiology in the development of ARDS.

3.1. RSV as a cause of ARDS

RSV causing ARDS in the pediatric population is well described. RSV pneumonia has also been linked to ARDS in the elderly, immunocompromised, those with cardio-pulmonary pathologies, and alcohol use disorder [3,4]. Disease severity has been associated with lower levels of serum neutralizing antibody and nasal IgA [5]. Neither of these two investigations is routinely collected during hospital admission regardless of disease severity at presentation. In the immunocompetent young adult, RSV has rarely been described as a cause of ARDS [6,7].

3.2. Aspiration as a cause of ARDS

Aspiration results from impaired swallowing, allowing oral and/or gastric contents to enter the lung [8]. Aspiration has a spectrum of clinical consequences that include chemical pneumonitis, aspiration pneumonia, and ARDS. Macro-aspiration may lead to chemical pneumonitis when there are both large volume and acidotic gastric contents (usually with a pH < 2.5) [8]. Chemical pneumonitis is accompanied by sudden onset dyspnea, hypoxemia, tachycardia, and examination findings of diffuse wheezes or crackles. Aspiration-induced lung injury is caused by inflammatory mediators, which include pro-inflammatory cytokines (i.e tumor necrosis factor), chemokines (i.e interleukin-8), and neutrophil recruitment [8]. Alcohol use increases the risk for aspiration events by impaired consciousness, weakened cough reflex, and reduced pulmonary ciliary mobility of foreign products.

Chest radiograph is generally abnormal and characteristic of ARDS in 16.5% of patients with witnessed aspiration. ARDS from aspiration is more likely with shock physiology [8]. One case report described a young healthy male requiring 12 days of ECMO after an aspiration event during endotracheal intubation for a surgical procedure, leading to ARDS [9].

3.3. Hypothermia-induced ARDS

There are case reports on patients with non-cardiogenic pulmonary edema secondary to hypothermia [10–12]. Pulmonary edema may be a consequence of hypothermia itself and/or as a complication of the rewarming phase. It is important to consider that in patients with hypotension from hypothermia, pulmonary edema may be a consequence of volume resuscitation during rewarming. This consequence may even be found in young patients with normal cardiac function. Post-mortem CT scans in patients who died from hypothermia have demonstrated pulmonary edema [13]. High immunohistochemical expressions of matrix metalloproteinase 9 have been identified in one post-mortem study on patients with hypothermia-induced pulmonary edema [14]. While pulmonary edema is described, all ARDS criteria have not yet been described in the literature to be regarded as a complication of hypothermia.

3.4. ECMO in ARDS

The CESAR trial found ECMO to be useful in patients with ARDS, but it did not show superiority over conventional ventilation [15]. CESAR highlighted the value of lung protective ventilation and ECMO in combination during refractory respiratory failure. The EOLIA trial found that there was no statistical benefit to ECMO versus conventional ventilation [16]. With the exception of inhaled Flolan, our case did not incorporate the additional recruitment maneuvers (i.e high frequency oscillation ventilation, paralytic agents, proning, or almitrine infusion) used by clinicians in the EOLIA trial.

3.5. With consideration to the presented case

In our case, it is very likely that his hypothermia was severe enough to cause pulmonary edema-which lead to reduced pulmonary compliance and hypoxia. It is unclear if his hypothermia alone caused ARDS as he could have aspirated prior to presentation. We feel this was less likely as his oxygen saturation was 92% on admission. He did have a witnessed aspiration event during intubation. No study to date has described how quickly an aspiration event may cause chemical pneumonitis findings on chest radiography, and in our case this was seen within 17 minutes after the aspiration event.

RSV was unlikely to contribute significantly as he was not immunocompromised and without chronic cardio-pulmonary disease. It is more likely that his ARDS was multifactorial due to a chemical pneumonitis and from complications related to hypothermia.

ECMO has been used in cases of severe hypothermia as a rewarming technique in patients with cardiac arrest [17]. Although its use for rewarming did not apply in our case, it would be sensible to consider when other interventions have failed in patients who present with refractory hypothermia.

Our patient's rapid improvement on VV-ECMO is unclear. Perhaps it reflects restoration of his pulmonary capillary integrity that was compromised as a result of his hypothermia or during aggressive rewarming. Additionally, his prompt recovery may suggest that he was already in the process of recovery prior to initiation of VV-ECMO. Possible pathophysiology contributing to ARDS in hypothermia would include the aberration of the capillary endothelial cell size in combination with compromised integrity of their intercellular junctions/clefts. Quick resolution after re-establishing normal temperature may suggest that the pathophysiology is a temporary structural deviation that is rapidly reversible. We would encourage more investigation to define mechanisms in impaired pulmonary capillary integrity and the increased susceptibility towards pulmonary edema in patients with hypothermia.

4. Conclusion

The etiology of ARDS is typically known and management is directed at addressing the underlying cause and providing hemodynamic support. We present a case that is multifactorial and suggests hypothermia as a new contributing factor. It is unclear if hypothermia-associated ARDS is due to altered pulmonary capillary integrity, a risk associated with current rewarming strategies, or a combination of the two. More investigation is needed on the pathophysiology and management complications in hypothermia.

Declaration of interests

None of the above authors have any conflicts of interest to declare. None of the above authors have any funding to declare during the production of this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100869.

References

[1] Acute Respiratory Distress Syndrome: the Berlin Definition. JAMA [Internet] 2012 [cited 2019 Feb 24]; 307Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2012.5669.

[2] A. Bacher, Effects of Body Temperature on Blood Gases. Appl. Physiol. Intensive Care Med, [Internet] Springer Berlin Heidelberg, Berlin, Heidelberg, 2006 [cited 2019 May 15]. pp. 33–36Available from: http://link.springer.com/10.1007/3-540-

37363-2_9.
[3] S.M. Simet, J.H. Sisson, Alcohol's effects on lung health and immunity, Alcohol Res. Curr. Rev. 37 (2015) 199–208.
[4] E.E. Walsh, Respiratory syncytial virus infection, Clin. Chest Med. 38 (2017) 29–36.
[5] E.E. Walsh, A.R. Falsey, Humoral and mucosal immunity in protection from natural respiratory syncytial virus infection in adults, J. Infect. Dis. 190 (2004) 373–378.
[6] Y.-H. Luo, C.-Y. Huang, K.-Y. Yang, Y.-C. Lee, Inhaled ribavirin therapy in adult respiratory syncytial virus-induced acute respiratory distress syndrome, Arch. Bronconeumol. Engl. Ed. 47 (2011) 315–317.
[7] M.H. Zaroukian, G.H. Kashyap, B.B. Wentworth, Respiratory syncytial virus infection: a cause of respiratory distress syndrome and pneumonia in adults, Am. J. Med. Sci. 295 (1988) 218–222.
[8] L.A. Mandell, M.S. Niederman, Aspiration pneumonia, in: D.L. Longo (Ed.), N. Engl. J. Med. 380 (2019) 651–663.
[9] W.A. Wetsch, F.A. Spöhr, J. Hinkelbein, S.A. Padosch, Emergency extracorporeal membrane oxygenation to treat massive aspiration during anaesthesia induction. A case report: emergency ECMO for massive aspiration, Acta Anaesthesiol. Scand. 56 (2012) 797–800.
[10] C.F. Morales, P.J. Strollo, Noncardiogenic pulmonary edema associated with accidental hypothermia, Chest 103 (1993) 971–973.
[11] D. Otto, M. Franke, J.F. Madden, Hypothermia accompanied by noncardiogenic pulmonary edema: a case report, Del. Med. J. 68 (1996) 499–502.
[12] P. Perich, L. Tuchtan, C. Bartoli, G. Léonetti, M.-D. Piercecchi-Marti, Death from hypothermia during a training course under “extreme conditions”: related to two cases, J. Forensic Sci. 61 (2016) 562–565.
[13] W. Schweitzer, M. Thali, G. Giugni, S. Winklhofer, Postmortem pulmonary CT in hypothermia, Forensic Sci. Med. Pathol. 10 (2014) 557–569.
[14] Q. Wang, T. Ishikawa, T. Michiue, B.-L. Zhu, D.-W. Guan, H. Maeda, Molecular pathology of pulmonary edema in forensic autopsy cases with special regard to fatal hyperthermia and hypothermia, Forensic Sci. Int. 228 (2013) 137–141.
[15] G.J. Peek, F. Clemens, D. Elbourne, R. Firmin, P. Hardy, C. Hibbert, H. Killer, M. Mugford, M. Thalanany, R. Tiruvoipati, A. Truesdale, A. Wilson, CESAR: conventional ventilatory support vs extracorporeal membrane oxygenation for severe adult respiratory failure, [Internet], BMC Health Serv. Res. (2006) [cited 2019 Feb 28]; 6Available from: https://bmchealthservres.biomedcentral.com/articles/10.1186/1472-6963-6-163.
[16] ECMO for severe acute respiratory distress syndrome, N. Engl. J. Med. 379 (2018) 1090–1093.
[17] K. Sawamoto, S.B. Bird, Y. Katayama, K. Maekawa, S. Uemura, K. Tanno, E. Narimatsu, Outcome from severe accidental hypothermia with cardiac arrest resuscitated with extracorporeal cardiopulmonary resuscitation, Am. J. Emerg. Med. 32 (2014) 320–324.