Case Report

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Early Leukapheresis Depletion in an Ex-Premature with Severe Acute Respiratory Distress Syndrome Due to Bordetella Pertussis and Coronavirus Infection

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Keywords
Pediatric · Bordetella pertussis · Infant · Acute respiratory distress syndrome · Intensive care · Pulmonary hypertension · Hyperleukocytosis · Leukapheresis

Abstract
We describe a 2 weeks corrected gestational age infant admitted in pediatric intensive care unit (PICU) for severe acute respiratory distress syndrome (ARDS) associated to *Bordetella pertussis* and Coronavirus infection. He developed leukocytosis as soon as ARDS required intubation and aggressive mechanical ventilation: hence he underwent 3 early therapeutic leukapheresis treatments in order to avoid the worsening of related cardiopulmonary complications, according to recent literature on pertussis infection in infants. The infant was discharged from PICU healthy.

Introduction

The association of life-threatening cardiopulmonary complications and hyperleukocytosis is an actual challenge for intensivists who deal with infants with severe *Bordetella pertussis* infection in pediatric intensive care. In current literature, we can find case reports and retrospective evaluation among critical care infants and pertussis-related hyperleukocytosis, often reporting the use of leukapheresis as a life-saving weapon to overcome extreme situation in patient with multi-organ failure. We suggest its application early and effectively to avoid such critical and poor outcome-related complications.

Case Report

We report a case of critical pertussis in a 2-month-old boy who developed a leucocytosis treated with early leukapheresis depletion.

A 2 weeks corrected gestational age old boy, weighing 3.5 kg, with history of prematurity (35 weeks), jaundice, and hypocalcemia, was admitted to the Emergency Department of Bambino Gesù Pediatric Hospital for dyspnea and cough. A diagnosis of bronchiolitis was made, the patient was not hospitalized, and a therapy with inhaled corticosteroids was given.

After 5 days, the patient developed lethargy and inappetence at home, so he was brought to the emergency department again: he had stridor and abdominal retractions, a chest X-ray showed bilateral pulmonary infiltrates and lung hyperinflation.

Blood tests showed high white blood cell (WBC) count 35,000 (N 10,320 U/L; L 19,250 U/L), Hb 13.7 g/dL, total bilirubin 1.87 mg/dL (direct bilirubin 0.48 mg/dL).

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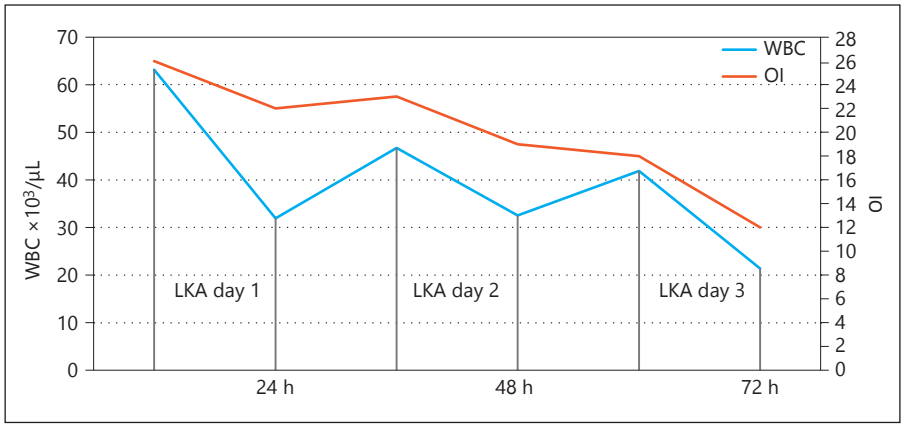

Fig. 1. Leukapheresis daily treatment with WBC count and OI trend. WBC, white body cell; LKA, leukapheresis day; OI, oxygenation index.

The patient was admitted to the pediatric ward, started a therapy with clarithromycin and high flow nasal cannulae, but after 2 days, he showed worsening of his respiratory distress. The patient was transferred to pediatric intensive care unit and put in helmet continuous positive airway pressure, but had whooping cough attacks with cyanosis and bradicardia and after <12 h due to severe hypoxic respiratory failure he was intubated and mechanical ventilation (IPPV; FiO2 = 1; PEEP = 8) was started; after intubation his oxygenation index was 26. His brain scan was normal. Real-time PCR for *Bordetella pertussis* and viral PCR for coronavirus OC43 were both positive.

At this point, his WBC was 63,000/μL and echocardiogram was made and, though there were no signs of pulmonary hypertension, according to recent literature we performed promptly a leukapheresis [1, 2].

The patient underwent 3 procedures of leukapheresis with the aim to reduce the number of leucocytes and avoid cardiopulmonary complications [3].

The procedures were performed daily with Spectra Optia Cell Separator, the first 2 procedures with MNC procedure (collection of mononucleats) the third one with CMNC procedure (continuous collection of mononucleats). These 2 procedures are different because while in MNC the separation of cells is based on the specific gravity and on the dimension of the cells, in CMNC (not in double cycle), the separation is only based on the specific gravity of the cells. In all the 3 procedure as anticoagulation it was used ACD-A with a ratio AC:blood of 1:18 and a bolus of heparin 25,000 UI/kg for each procedure. Considering the extreme low weight of the patient (3.5 kg), it was always performed blood prime with 1 unit of irradiated PRBC. The CVC was an Arrow bilumen 4Fr, length 5 cm that permitted a speed of 10 mL/min.

A median of 862.6 mL of whole blood (range 788–900 mL) corresponding to 2.4 blood volume has been processed (range 2.2–2.5). The procedures had a mean duration of 83 min (range 80–90 min), the mean volume of ACD-A used was 50.3 mL (range 46–53 mL), and in each procedure a volume of 36 mL was removed. Considering the initial blood cell counts with a great number of PMN, the separator interface was always set at the collection of mononucleats' line.

The end point of the procedures was always the number of WBC reached from 63,150 to 31,940/μL with the first procedure, from 46,700 to 32,510/μL with the second procedure, from 41,840 to 21,380/μL with the third procedure (Fig. 1). All the 3 procedures were well-tolerated hemodynamically by the infant. During the procedures, the patient underwent repeated venous ABG and ACT which were always normal.

The patient was safely extubated after 11 days of mechanical ventilation, put in Helmet continuous positive airway pressure for 3 days and high flow nasal cannulae for 4 days, and then discharged to the infectious pediatric disease ward.

We decided to perform leukapheresis only on the basis of WBC count (>50,000/μL) although the echocardiography was negative for pulmonary hypertension. In fact, according to the pathophysiologic hypothesis of leukosequestration (WBC aggregates in lung microvasculature in the autopsy reports), when pulmonary hypertension occurs, it is highly associated to fatal complications and leukoapheresis at this point could be ineffective to avoid them [4, 5].

Romano et al. [6] described a 3-month-old infant with severe pertussis, hyperleukocytosis, and pulmonary hypertension who underwent double volume exchange transfusion successfully. Rowlands et al. [7] reported an actual fall in mortality rate from 44 to 10% among infants with critical pertussis undergone leukodepletion by exchange transfusion. We can find other case reports of successful exchange transfusion and leukapheresis to reduce leukocytosis and improve outcome among severe pertussis in infants, with Lashkari et al. [8], Martinez et al. [9], Onoro et al. [10], Donoso et al. [11], Taffarel et al. [12].

The current literature is clear to be aware of leukocytosis associated to high mortality rate among fulminant pertussis in infants. To date, despite the actual lack of complete knowledge about the exact molecular pathogenetic pathway, the early removal of leukocytes by leukapheresis may have the role for avoiding and preventing the activation of the immunological cascade due to the effects of pertussis toxin [13]. The post-portem findings in fulminant pertussis have been described as necrotizing bronchiolitis, extensive damage to the alveolar epithelium, tenacious airway secretions, and leukostasis with pulmonary vessels fulfilled with leukocytes without well-organized thrombi, all factors contributing to increased pulmonary vascular resistance, hypoxemia, and intractable cardiac failure in fulminant pertussis.

This neonate was a premature and the association of *Bordetella pertussis*, rising leukocytosis, and Coronavirus infection put him in a life-threatening clinical situation according to his oxygenation index 26.

Our experience confirms the feasibility of leukapheresis depletion also in ex-premature, and its early providing may be lifesaving in order to avoid cardiopulmonary complications *Bordetella pertussis* related [14].

Acknowledgment

There are no acknowledgments to declare.

Statement of Ethics

This case report complies with the guidelines for human studies, and the research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. In the manuscript, parents or guardians have given their written informed consent to publish their case (including publication of images). The study protocol was approved by the institute's committee on human research.

Disclosure Statement

On behalf of the authors, the correspondent author declares that authors have no conflict of interest and no financial relationships relevant to this article to disclose.

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Author Contributions

L.A. and E.R. promoted early LKA, drafted, and reviewed the manuscript. A.M. drafted the manuscript and performed early LKA. G.L., S.L., and G.D.P. performed early LKA. R.B. and S.P. reviewed the manuscript.

References

1 Sawal M, Cohen M, Irazuzta JE, Kumar R, Kirton C, Brundler MA, et al. Fulminant pertussis: a multi-center study with new insights into the clinico-pathological mechanisms. Pediatr Pulmonol. 2009 Oct;44(10):970–80.

2 Kuperman A, Hoffmann Y, Glikman D, Dabbah H, Zonis Z. Severe pertussis and hyperleukocytosis: is it time to change for exchange? Transfusion. 2014 Jun;54(6):1630–3.

3 Assy J, Séguéla PE, Guillet E, Mauriat P. Severe neonatal pertussis treated by leukodepletion and early extra corporeal membrane oxygenation. Pediatr Infect Dis J. 2015 Sep;34(9):1029–30.

4 Kazantzi MS, Prezerakou A, Kalamitsou SN, Ilia S, Kalabalikis PK, Papadatos J, et al. Characteristics of Bordetella pertussis infection among infantsand children admitted to paediatric intensive care units in Greece: A multicentre, 11-year study. J Paediatr Child Health. 2017 Mar;53(3):257–62.

5 Cherry JD, Wendorf K, Bregman B, Lehman D, Nieves D, Bradley JS, et al. An observational study of severe pertussis in 100 infants ≤120 days of age. Pediatr Infect Dis J. 2018 Mar;37(3):202–5.

6 Romano MJ, Weber MD, Weisse ME, Siu BL. Pertussis pneumonia, hypoxemia, hyperleukocytosis, and pulmonary hypertension: improvement in oxygenation after a double volume exchange transfusion. Pediatrics. 2004 Aug;114(2):e264–6.

7 Rowlands HE, Goldman AP, Harrington K, Karimova A, Brierley J, Cross N, et al. Impact of rapid leukodepletion on the outcome of severe clinical pertussis in young infants. Pediatrics. 2010 Oct;126(4):e816–27.

8 Lashkari HP, Karuppaswamy S, Khalifa K. Pertussis-related hyperleukocytosis: role of hyperhydration and exchange transfusion. Clin Pediatr (Phila). 2012 Oct;51(10):987–90.

9 Martinez M, Rochat I, Corbelli R, Tissières P, Rimensberger PC, Barazzone-Argiroffo C. Early blood exchange transfusion in malignant pertussis: a case report. Pediatr Crit Care Med. 2011 Mar;12(2):e107–9.

10 Oñoro G, Salido AG, Martínez IM, Cabeza B, Gillén M, de Azagra AM. Leukoreduction in patients with severe pertussis with hyperleukocytosis. Pediatr Infect Dis J. 2012 Aug;31(8):873–6.

11 Donoso AF, Cruces PI, Camacho JF, León JA, Kong JA. Exchange transfusion to reverse severe pertussis-induced cardiogenic shock. Pediatr Infect Dis J. 2006 Sep;25(9):846–8.

12 Taffarel P, Bonetto G, Haimovich A. [Severe pertussis, progression and exchange transfusion as an alternative treatment. Case reports] [in Spanish]. Arch Argent Pediatr. 2012 Aug;110(4):327–30.

13 Ronco C, Reis T, De Rosa S. Coronavirus epidemic and extracorporeal therapies in intensive care: si vis pacem para bellum. Blood Purif. 2020, Epub ahead of print.

14 Ronco C, Ricci Z, Husain-Syed F. From multiple organ support therapy to etracorporeal organ support in critically lll patients. Blood Purif. 2019;48(2):99–105.