DOI: JCDR/2012/3880:1905

Case Report

Neonatology Section

Persistent Oxygen Dependency in Preterm Newborn: Beyond Bronchopulmonary Dysplasia

SMITA RAMACHANDRAN, BHANU KIRAN BHAKHRI, VIKRAM DATTA

ABSTRACT

Background: Respiratory tract infections can mimic bronchopulmonary dysplasia (BPD) in clinical and radiological findings.

Methods: Description of the clinical course of an affected newborn. Reports of similar observations from the literature have been discussed.

Results: A 32 week, preterm female who weighed 1260 grams at birth had multiple morbidities (E Coli sepsis, congenital pneumonia, anaemia and patent ductus arteriosus) during the first 3 weeks of life. The baby continued to be oxygen dependent beyond 4 weeks of life despite improvement in other clinical parameters and was diagnosed to be having BPD. Investigations revealed the evidence of cytomegalovirus pneumonitis, which showed clinical and radiological resolution following ganciclovir therapy.

Conclusion: The atypical presentation of BPD and the persistent respiratory distress warrants ruling out coexisting respiratory tract infections like CMV, as a timely diagnosis and treatment can tremendously alter the morbidity and cost of therapy in these babies.

Key Words: Bronchopulmonary dysplasia, Cytomegalovirus pneumonitis, Ganciclovir

INTRODUCTION

Management of a preterm newborn with bronchopulmonary dysplasia (BPD) can be a challenge for the treating neonatologist. Adequate attention needs to be paid to comorbidities like infections of the respiratory tract, which can sometimes mimic the presentation of BPD or unduly prolong the course of the existing BPD [1].

CASE REPORT

A preterm female was delivered to a second gravida mother at 32 weeks of gestation by caesarean section due to foetal distress. The antenatal period was uneventful and the serology for intrauterine infections including cytomegalovirus (CMV) was non-reactive. The mother had received 2 doses of antenatal steroids. The baby's birth weight was 1260 grams and no active resuscitation was required by the baby at birth. She was admitted in the neonatal unit in view of her very low birth weight.

During the first 3 weeks of her life, the baby was managed for multiple problems viz. E Coli sepsis which required antimicrobials and inotropic support, pneumonia which required mechanical ventilation, anaemia which required three packed red cell transfusions and patent ductus arteriosus. In view of the multiple risk factors, the prophylaxis for BPD was given to the baby in form of vitamin A 5000 U thrice weekly, intramuscular, starting from day 16 till 28 days of life, salbutamol aerosol nebulisation and periextubation dexamethasone.

At 28 days of life, she was diagnosed to be having BPD in view of the continued oxygen dependency. The examination was unremarkable except for the anaemia and the palpable spleen. However, as the oxygen dependency persisted till the 8th week of life despite adequate weight gain, further investigations were planned. CT scan of the chest showed a ground glass appearance which was suggestive of BPD [Table/Fig-2a] with bilateral basilar posterior infiltrates. The laboratory evaluation revealed sterile blood cultures and no evidence of fungal sepsis, blood loss, marrow suppression or intravascular haemolysis. In view of the multiple red blood cell transfusions, a possibility of acquired CMV infection was also considered. The serological marker (IgM) for CMV was detectable and PCR which was subsequently done was positive for CMV in the baby's urine. This was followed by an ophthalmological evaluation and ultrasound of the cranium. Both were normal.

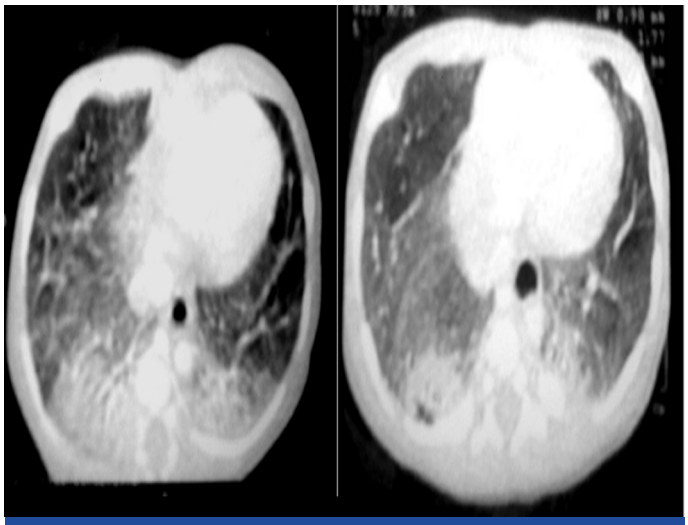
In view of the possible CMV pneumonitis, intravenous ganciclovir was started on Day 60 of life (10 mg/kg 12 hrly for 6 weeks). While on Ganciclovir, the baby was monitored for blood cell counts and liver functions twice weekly. Within a week of initiating the therapy, the baby started showing a favourable response in terms of a decreased FiO2 requirement and she was weaned off from oxygen after 2 weeks of therapy. The baby gained weight steadily and achieved all the milestones which were appropriate for her postnatal age. The CT scan which was done after the successfully completed treatment, showed a marked resolution of the reticular infiltrates [Table/Fig-2b], which was consistent with the improved clinical condition. A BERA was planned at discharge and the baby was followed up till 6 months of age. She is doing well with satisfactory growth and development and no respiratory symptoms.

DISCUSSION

The diagnosis of BPD is currently based on the need for supplemental oxygen for at least 28 days after birth, and its severity

Identified viral agent	Study
Cytomegalovirus	Sawyer MH et al, 1987 [4]
	Suzumura H et al, 1996 [7]
	Brayer C et al, 2004 [5]
	Koklu E et al, 2009 [10]
	Present Case, 2011
Respiratory Syncytial Virus	Carpenter TC et al, 2004 [1]
Adenovirus	Faden Het al, 2005 [11]

[Table/Fig-1]: Viral agents implicated for pneumonia mimicking as Bronchopulmonary dysplasia



[Table/Fig-2a $ 2b]: Axial view of CT scan chest showing widespread reticular shadows suggestive of interstitial fibrosis; b) Resolution of the infiltrates after 6 weeks of Gancyclovir therapy

is graded according to the respiratory support which is required at 36 post-menstrual weeks [2].

With the better survival of premature newborns, numerous preventive measures have been recommended in such babies with risk factors for developing BPD [2]. Immaturity and growth retardation are the major risk factors for the development of BPD. Sepsis, chorioamnionitis, fluid overload, patent ductus arteriosus (PDA) and surfactant deficiency contribute to the pathogenesis of the disease [3]. Several viral agents have been implicated for prolonging the course of BPD in preterm newborns [Table/Fig 1]. Though an association between CMV and BPD has been established in previous studies, the symptomatic resolution following therapeutic interventions has rarely been reported [4,5]. The reported incidence of the roentgenographic evidence of BPD is significantly greater in the CMV-infected infants (75%) than that in the controls (38%) [4] CMV may induce pathological changes like interstitial pneumonitis and fibrosis, which are similar to that which are seen in BPD [6]. The CMV infection in very low birth weight newborns may present with prolonged oxygen dependency, hyperinflation and reticular opacities in the chest roentogram, a picture which is consistent with BPD [7].

Ganciclovir is the most commonly used antiviral therapy in all the symptomatic CMV infected patients [8]. Ganciclovir is indicated in viral sepsis syndrome, pneumonitis, thrombocytopaenia, retinitis, oesophagitis and colitis [9]. CMV infection with BPD results in a longer hospital stay and a longer respiratory support requirement and it can be fatal if it is left untreated [6]; hence, ganciclovir is given in active pneumonitis. A favourable response is usually observed within 2-3 weeks of initiating the ganciclovir therapy. Brayer reported a rapid regression of the symptoms in a preterm baby with CMV pneumonia which manifested clinically and radiologically like BPD, while on gancyclovir therapy [5]. In our patient, the clinical and radiological improvement was evident after 2 weeks and 6 weeks of initiating the antiviral therapy respectively. To the best of our knowledge, the resolution of the radiological findings by gancyclovir therapy in CMV pneumonitis which manifested as BPD is being reported for the first time.

The presentation of BPD has rarely been reported in newborns with congenitally acquired CMV infection, with positive titres of CMV IgM in the mother, thus indicating the mode of transmission. [5,10,11].

CONCLUSION

Infections like CMV should be ruled out in preterm newborns with an aberrant course of BPD, since the CMV infection can mimic BPD in the clinical presentation or prolong the course of the coexisting BPD. A timely diagnosis and the institution of antiviral therapy can alter the morbidity and the cost of therapy in these patients.

REFERENCES

[1] Carpenter TC, Stenmark KR. Predisposition of infants with chronic lung disease to respiratory syncytial virus induced respiratory failure: a vascular hypothesis. *Paediatr Infect Dis J.* 2004 Jan;23(1 Suppl): S33-40.

[2] Laughon MM, Smith PB, Bose C, Mathew M. Laughon. Prevention of bronchopulmonary dysplasia. Semin Fetal Neonatal Med. 2009 Dec;14(6):374-82. *Epub* 2009 Sep 6.

[3] Farstad T, Bratlid D, Medbø S, Markestad T. Norwegian Extreme Prematurity Study Group. Bronchopulmonary dysplasia- prevalence, severity and predictive factors in a national cohort of extremely premature infants. *Acta Paediatrica* 2011;100:53-58.

[4] Sawyer MH, Edwards DK, Spector SA. Cytomegalovirus infection and bronchopulmonary dysplasia in premature infants. *Am J Dis Child* 1987;141:303-05.

[5] Brayer C, Bony C, Salles M, Sampériz S, Pilorget H, Attali T, et al. Bronchopulmonary dysplasia and cytomegalovirus pneumonia. *Arch Paediatr* 2004;11(3):223-25.

[6] Hsu ML Cheng SN, Huang CF, Jan CI, Fan HC, Wang CC, et al. Perinatal cytomegalovirus infection which was complicated with pneumonitis and adrenalitis in a premature infant. *J Microbiol Immunol Infect.* 2001;34(4):297-300.

[7] Suzumura H, Sakurai K, Kano K, Ichimura T. Chronic respiratory failure following an acquired cytomegalovirus infection in a very low birthweight infant. *Acta Paediatr Jpn*. 1996;38(6):677-80.

[8] Capretti MG, Lanari M, Lazzarotto T, Gabrielli L, Pignatelli S, Corvaglia L et al. Very low birth weight infants who were born to cytomegalovirus-seropositive mothers were fed with their mothers' milk: a prospective study. *J Paediatr*. 2009 Jun;154(6):842-8.

[9] Demmler GJ. Congenital cytomegalovirus infection treatment. *Paediatr Infect Dis J*. 2003Nov;22(11):1005-6.

[10] Koklu E, Karadag A, Tunc T, Altun D, Sarici SU. Congenital cytomegalovirus infection which was associated with severe lung involvement in a preterm neonate: a causal relationship? *Eur J Paediatr*. 2009 Nov;168(11):1409-12.

[11] Faden H, Wynn RJ, Campagna L, Ryan RM. Outbreak of adenovirus type 30 in a neonatal intensive care unit. *J Paediatr.* 2005 Apr;146(4):523-7.

AUTHOR(S):
1. Dr. Smita Ramachandran
2. Dr. Bhanu Kiran Bhakhri
3. Dr. Vikram Datta

PARTICULARS OF CONTRIBUTORS:
1. Senior resident
2. Assistant Professor
3. Professor

Institution to which this study is associated with:
Division of Neonatology, Department of Paediatrics, Lady Hardinge Medical College & Associated Hospitals, New Delhi, India.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Bhanu Kiran Bhakhri,
Assistant professor,
Department of Pediatrics, Lady Hardinge Medical College,
Shaheed Bhagat Singh Marg, New Delhi 110001, India.
phone: +919818735574
E-mail: drbhanu04@yahoo.co.in

DECLARATION ON COMPETING INTERESTS:
No competing Interests.

Date of Submission: **Jun 10, 2011**
Date of Peer Review: **Aug 22, 2011**
Date of Acceptance: **Oct 10, 2011**
Date of Publishing: **May 01, 2012**