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CASE REPORT

Cytomegalovirus Infection Associated With Atypical Bronchopulmonary Dysplasia In A Preterm Neonate: A Case Report

*Zurina Zainudin[1], Aisha Fadhilah Abang Abdullah[1], Dg. Zuraini Sahadan[2].

[1] Department of Paediatric, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia
[2] Department of Paediatric, Hospital Serdang, Jalan Puchong, 43400 Serdang, Selangor.

ABSTRACT

Cytomegalovirus (CMV) is frequently isolated from neonates. Symptomatic infection is only apparent in 10% of affected babies with particular predilection for the reticuloendothelial and central nervous system. Isolated respiratory system involvement is rarely encountered. We report a case of a premature 32 weeks infant who required prolonged oxygen dependency and treated for bronchopulmonary dysplasia. The diagnosis of CMV pneumonitis was only discovered after detection of CMV DNA in the bronchoalveolar lavage. A high level of clinical awareness is crucial as a definite diagnosis and treatment will significantly alter the morbidity and the cost of therapy.

Keywords: Cytomegalovirus infection, cytomegalovirus pneumonitis, atypical bronchopulmonary dysplasia

***Correspondence Author:**
Zurina Zainudin,
Email: zaizurina@upm.edu.my
Tel: +603-89472610/2619
Fax: +603-89489369

INTRODUCTION

Prolonged oxygen dependency in a neonate beyond the 28th day of life and/or 36 weeks corrected gestational age is customarily suggestive of bronchopulmonary dysplasia (BPD) [1]. It was first described in 1967 by Northway et al. in a group of premature infants who developed chronic lung disease after receiving ventilation and supraphysiologic oxygen for acute respiratory distress syndrome. With the advanced in perinatal care, clinical characteristic of BPD has evolved. Unlike the classical BPD, infants from the post-surfactant era presented with milder pulmonary sequelae that occur without preceding history or after recovery from respiratory distress syndrome. This is often referred to as an atypical BPD [1]. The association between cytomegalovirus (CMV) infections with BPD has rarely been reported and this is the first reported case from our country. This report deals with a premature infant who has acquired isolated CMV pneumonitis manifested as atypical BPD.

CASE HISTORY

A premature infant was born at 32 weeks of gestation following prolonged rupture of chorioamniotic membrane. Mother had received 2 doses of antenatal steroids and completed a course of tablet erythromycin. The baby weighed 1950gm, measured 43cm in length and had cranial perimeter of 30cm at birth. He had mild respiratory distress but other systemic examination was unremarkable. Chest radiograph was normal, haematological indices were within normal limit (total white cell count 22,500/μL with 70% neutrophils, 20% lymphocytes, platelet 356,000/mm3) and blood sample was sterile. He was treated as presumed sepsis with a combination of intravenous crystalline penicillin-gentamycin and remained stable on air.

After an initial period of improvement, he developed nosocomial pneumonia at day 6 of life requiring high flow nasal cannula support. Antimicrobial therapy was upgraded as per unit's protocol. Unfortunately he remained tachypnoeic and dependent on oxygen therapy of 2L/min via nasal cannula until day 28 of life. Serial chest radiograph revealed bilateral lungs hyperinflation with presence of interstitial opacities (Figure 1). Reassessment of haematological and acute phase protein demonstrated no abnormalities. Both

mycoplasma and chlamydia serology were negative and microbiological study from blood and nasopharyngeal aspirates specimen failed to identify significant pathogen. Inhaled corticosteroid was added to his therapy for the possibility of BPD. However he made minimal progress despite satisfactory weight gain.

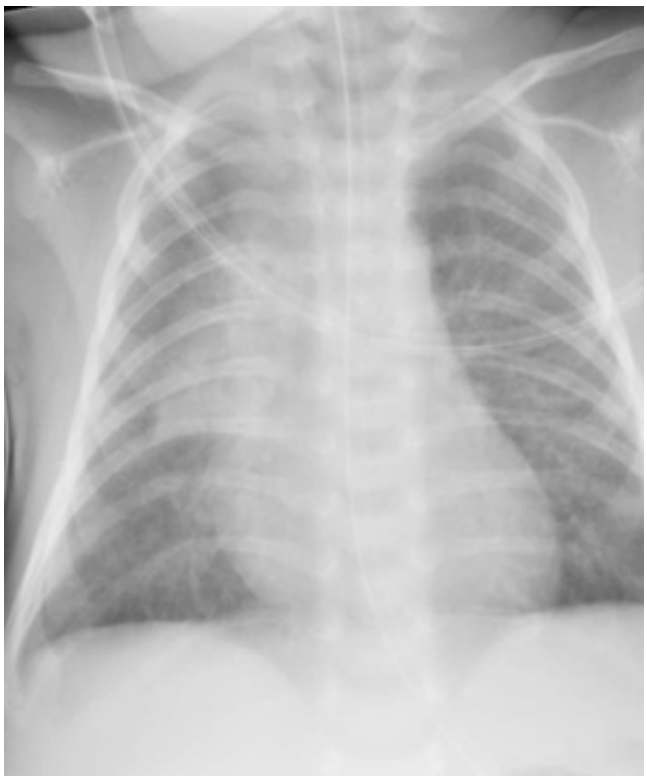

Figure 1. CXR at day 28 of life showed generalised hyperinflation with reticular opacities

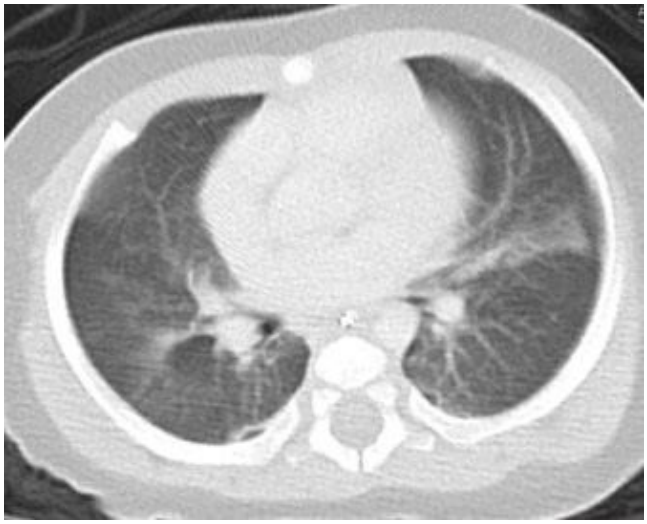

Figure 2. Axial HRCT showing patchy ground glass changes with underlying fibrotic scarring at right and left upper lobe with irregular interlobular septal thickening at 4th week of IV Ganciclovir

At day 65 of life, he developed another episode of worsening respiratory distress requiring non-invasive ventilator support for 2 days. Repeated nasopharyngeal aspirate isolated multi-resistant *Acinetobacter baumannii, Escherichia coli* and *Klebsiella pneumoniae* consecutively. Antimicrobial therapy was tailored towards the aetiological agent however no noticeable clinical improvement observed. Further evaluation was performed including diagnostic flexible bronchoscopy which disclosed a normal airway anatomy with evidence of infection on the right airways. Bronchoalveolar washings were negative for *Mycobacterium tuberculosis*, respiratory syncytial virus, adenovirus, human metapneumovirus, influenza virus, parainfluenza virus and candida albicans., However the polymerase chain reaction (PCR) for CMV was positive with 499copies/mL. Serology, urinary and pharyngeal CMV were negative. Cranial ultrasound and ophthalmic assessment showed no calcification or chorioretinitis. Maternal CMV IgG serology was detected but IgM was negative. Computed tomography of the thorax revealed area of patchy ground glass changes with underlying fibrotic scarring (Figure 2).

He was commenced on intravenous ganciclovir (12mg/kg/day) for 5 weeks following which his respiratory symptoms resolved and was successfully weaned off oxygen. Bronchoalveolar fluid analysis was negative for CMV on day 28th of treatment. He was discharged at 4-month-old and continued to do well on follow up.

DISCUSSION

Cytomegalovirus (CMV) is frequently isolated from neonates and majority of them are asymptomatic [2]. Infection is clinically apparent in only about 10% of cases with reticuloendothelial and central nervous system involvement, occasionally with systemic illnesses, features the typical presentation [2]. Isolated pulmonary involvement as seen in our patient is rarely the only manifestation of CMV infection in neonates.

CMV pneumonitis is more likely to develop following aspiration of the infected cervical secretion at birth or as a result of postnatally-acquired disease. Even though the latter is very rare in term infants, serious disease is relatively common in premature babies because of their immature immune system and lack of protection from passive transfer of maternal antibodies that occur mostly in the third trimester [2]. Isolation of CMV from the bronchoalveolar lavage at 3 month of age in conjunction with the existence of maternal CMV IgG serology instead of IgM strongly suggest the latter route of transmission in our case.

The role of CMV in the development of BPD is still unclear. Deposition of CMV in the lung tissues may trigger an immunopathogenic response resulting in

diffuse interstitial pneumonitis with significant reduction in surfactant production giving rise to symptoms of respiratory insufficiency and radiographic appearance of diffuse bilateral interstitial infiltrates [3]. In premature infants, symptoms are often severe and frequently persist for months with subsequent development of bacterial infections necessitate artificial ventilatory support and increased oxygen administration.. Alternatively the direct effects of CMV on the lung parenchyma causing diffuse necrotising pneumonitis and fibrosis have also been attributed to the development of BPD [3]. The affected infants may present with prolonged oxygen dependency without preceding history of respiratory distress consistent with the clinical definition of atypical BPD as seen in our case.

Although lack of clinical research evidence on the therapy of CMV infection in neonates, ganciclovir is increasingly being used to treat symptomatic infants [2]. It is administered in infants with severe organ disease such as pneumonitis or those with central nervous system involvement to improve the neurodevelopmental and auditory outcome. Favourable response had been observed in our patient without apparent adverse effects similar to previously reported cases [4,5]. The potential benefits of intravenous immunoglobulin have been suggested by some investigators however there were no randomized trials to assess its efficacy [2].

CONCLUSION

This report highlights the possible implication of CMV infection in a preterm infant. Clinically it may resemble BPD or prolonged its course and can be fatal. A definite diagnosis and treatment will significantly alter the morbidity and the cost of therapy.

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