Unusual presentation of more common disease/injury

Congenital cytomegalovirus infection associated with development of neonatal emphysematous lung disease

Bridget Helen Staunton,¹ David Crabbe,² Catherine Cullinane,³ Dominic Smith⁴¹Acute Assessment Unit, Hull and East Yorkshire Hospitals NHS Trust, Hull, UK;²Department of Paediatric Surgery, The Leeds Teaching Hospitals NHS Trust, Leeds, UK;³Department of Histopathology, The Leeds Teaching Hospitals NHS Trust, Leeds, UK;⁴Department of Paediatrics, York Teaching Hospital NHS Foundation Trust, York, UK**Correspondence to** Dr Bridget Helen Staunton, bridget.staunton@nhs.net**Summary**

A 26-week-gestation infant developed cystic lung changes which required lobar resection at 6 weeks of age. Lung histology showed cytomegalovirus (CMV) inclusion bodies. The authors present the radiology and histology images of this case and review the literature regarding congenital CMV infection and cystic lung disease. Lung disease caused by CMV is typically a diffuse pneumonitis. This is the first reported case of congenital CMV infection causing emphysematous lung disease to develop in the neonatal period. The case raises awareness of CMV as a possible cause of cystic lung lesions in newborns.

BACKGROUND

Cytomegalovirus (CMV) is a common congenital infection and we report a manifestation that is not well known. This is relevant to the investigation and management of infants with cystic lung lesions. The infant required surgical and antiviral treatment.

CASE PRESENTATION

A female infant was admitted to the neonatal intensive care unit after delivery at home at 26 weeks gestation following spontaneous onset of rapid labour. Birth weight was 965 g. Examination showed normal morphology

and signs of respiratory distress. Intermittent positive pressure ventilation was initiated and surfactant was administered.

The baby's mother had attended for antenatal care. Ultrasound scanning at 20+6 and 23+4 weeks gestation showed polyhydramnios. No obvious cause for the hydramnios was apparent. Fetal echocardiography had been performed during the pregnancy because of a family history of transposition of the great arteries. This echocardiogram was normal.

Maternal blood was sent on the day of delivery to screen for congenital infection. The results were consistent with recent primary infection with CMV, with positive CMV IgG antibody and positive CMV IgM antibody. CMV IgG avidity was reported as moderate.

The initial chest radiograph was consistent with respiratory distress syndrome (figure 1). The baby was ventilated for 5 days and then extubated to continuous positive airway pressure support (CPAP).

CMV infection was confirmed by PCR testing of the baby's urine on day 1 of life. Blood tests from the baby showed the presence of CMV IgM. CMV IgG was not detected. Other than jaundice, for which phototherapy was started on day 1, there were no clinical features of CMV infection. The clinical picture at this stage was of respiratory distress syndrome typical for a baby born at 26 weeks gestation. No antiviral treatment was initiated.

By day 44 the baby was tolerating low flow oxygen (0.02 l/min) via nasal cannulae. On day 49 she became tachypnoeic, her oxygen requirements increased (0.3 l/min) and she began to have apnoeic episodes.

INVESTIGATIONS

A chest radiograph was taken on day 51 because of the baby's new respiratory symptoms. This showed lobar emphysema involving the left upper lobe associated with mediastinal shift (figure 2).

Figure 1 Chest radiograph on day 1 showing changes consistent with hyaline membrane disease.

Figure 2 Chest radiograph on day 51 showing lobar emphysema involving the left upper lobe with mediastinal shift and collapse of the left lower lobe.

Figure 3 Operative photograph showing the emphysematous lung herniating out of the thoracotomy.

On day 52 the baby was taken to the operating theatre. Bronchoscopy was normal. A left thoracotomy was performed to reveal an emphysematous upper lobe (figure 3). A left upper lobectomy was performed. One week later the baby was self ventilating in air with a normal respiratory rate.

Histological examination of the resected lung was consistent with pulmonary and interstitial emphysema associated with a CMV pneumonitis. There was no evidence of underlying cystic anomaly. CMV inclusions were seen both in the alveolar cells and within the alveolar sacs (figure 4).

TREATMENT

Antiviral therapy was initiated in view of the histological findings. Oral valgancyclovir at a dose of 30 mg twice daily was given for 6 weeks.

OUTCOME AND FOLLOW-UP

The baby responded well to lobectomy and antiviral chemotherapy. She was discharged on day 89 weighing 2.29 kg and with head circumference 33.8 cm at 39+2 weeks corrected gestation.

Figure 4 Emphysematous lung with dilated alveoli and CMV inclusions in alveolar cells to right of centre, note one has typical owl's eye nucleus (H&E x200).

Follow-up was arranged with viral load and neutrophil count monitoring at fortnightly intervals. Blood viral load fell from 151 000 copies per millilitre on day 65, to 8591 copies per millilitre on day 90, and viral copies were not detected on day 97. The neutrophil count was 0.5, 1.5, 1.8 and $1.0 \times 10^9/l$ when measured at fortnightly intervals during this period. The initial low level was a source of concern when initiating valgancyclovir treatment; however, no adverse effects from the treatment were seen and the baby remained asymptomatic.

At 6 weeks post-term corrected age she was developing and growing well, with weight between the second and ninth centiles and head circumference just above the 50th centile. Chest, abdominal and neurological examinations were normal. She remains under follow-up by ophthalmology, audiology and paediatrics.

DISCUSSION

CMV is the most common congenital viral infection in developed countries. A meta-analysis by Dollard *et al* found a birth prevalence of 0.7%. 12.7% of these infants were symptomatic at birth.¹

The cytopathic effect of CMV produces enlarged cells with intranuclear and cytoplasmic inclusions, which may give the cells an 'owl's eye' appearance. The effects of CMV can be found in virtually every human cell type. Infected lung sections show a multi-focal distribution in the alveolar walls, alveolar spaces and interstitium.²

Neonatal lung disease linked to CMV infection can take a variety of forms. Pneumonitis is well recognised, usually occurring at 1 to 4 months of age. This was observed by Preece *et al* in six out of 50 children with congenital CMV infection. These children developed an afebrile pneumonitis characterised by tachypnoea and hyperinflation.³ In 1976 two infants with CMV pneumonitis were described by Whitley *et al*.⁴ The literature contains only a small number of case reports describing lung disease in neonatal CMV infection. One case describes early severe neonatal lung involvement with pulmonary hypertension resulting from recurrent maternal CMV infection.⁵

Regarding cystic or emphysematous lung disease in CMV infection, two previous reports exist. Bradshaw *et al*

describe an infant born at 30 weeks who, after initial negative serology, acquired CMV infection postnatally. On day 19 the baby developed multi-cystic lung disease in the left upper lobe and right perihilar region. No antiviral therapy was given and this infant showed gradual clinical improvement and substantial resolution of the cystic changes.⁶ Carrol *et al* report a case of congenital lobar emphysema which was diagnosed antenatally. This infant went on to have a left upper lobectomy. Histological examination of the excised tissue revealed features consistent with congenital lobar emphysema as well as mild interstitial inflammation and CMV inclusion bodies.⁷

Congenital lobar emphysema develops due to partial obstruction of the lobar bronchus leading to air trapping. Obstruction may be caused by intrinsic abnormalities of the bronchus, or by external compression such as from a bronchogenic cyst or abnormal blood vessel. Lobar emphysema of infancy features alveolar distension rather than destruction. This is different to emphysema of later life which is defined by enlargement of the air spaces due to breakdown of their walls.

Lobar emphysema is an uncommon disease of infancy. Serological evidence of CMV infection in this baby and the presence of CMV inclusion bodies in the lung implicate the virus. The initial chest radiographs did not show focal changes and it is likely that the lobar emphysema developed postnatally as a result of CMV infection. As Carrol *et al* have previously postulated, CMV pneumonitis leading to inflammation and obstruction in the bronchial tree may result in the development of congenital lobar emphysema. Where this occurred in this preterm infant she responded well to lobectomy and antiviral chemotherapy.

Learning points

- CMV infection may underlie emphysematous lung disease in infants.
- The emphysematous lung lesion may develop during antenatal or neonatal life.
- It is appropriate to measure CMV serology for infants with emphysematous lung disease.

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Competing interests None.

Patient consent Obtained.

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