Cytomegalovirus (CMV) is the most common cause of congenital infection. Fetal CMV infection is transmitted in utero via the placenta resulting in congenital infection. Ten to 15% of infected neonates show obvious clinical features at birth (1). Congenital CMV infection may present several nonspecific manifestations, although pneumonitis is considered a rare manifestation (2–4). Ganciclovir and valganciclovir, the most commonly used antiviral drugs for the treatment of symptomatic congenital CMV infection, have been shown to be beneficial for hearing and developmental outcomes (5,6). Although the response to treatment with anti-CMV drugs has been evaluated in immunocompetent children with acquired CMV pneumonitis, treatment response remains unclear in congenital CMV pneumonitis (7). We report a case of congenital CMV infection manifesting as respiratory distress because of pneumonitis, where CMV genome load measurement was beneficial for evaluating treatment response.

A female neonate was delivered to a 32-year-old gravida 2, para 2 mother by cesarean section without asphyxia. The mother was Japanese living in Japan and had not received any formal prenatal care. Her past medical history and infectious disease screening tests were unremarkable. The weight, length, and head circumference of the neonate were 3,070 g (mean + 0.8 SD), 46.2 cm (mean − 0.9 SD), and 34.2 cm (mean + 0.9 SD), respectively. We estimated the gestational age as 38 weeks by Dubowitz scoring. Vital signs and physical examination were normal on the day of birth, but we initiated oxygen inhalation on day 4 because of mild tachypnea and decreased oxygen saturation. Chest radiograph revealed a reticular pattern in both lung fields (Fig. 1). Chest computed tomography was also performed (Fig. 1), and she was diagnosed as having congenital pneumonitis. Laboratory data on day 4 showed a white blood cell count of 12,590/μL (reference value 9,100–34,000/μL), hemoglobin 15.4 g/dL (reference value 15.0–24.0 g/dL), platelets 1.5 × 10^5/μL (reference value 129/μL, reference value < 15/μL) predominated by lymphocytes (129/μL), and increased protein (146 mg/dL, reference value < 0.8). The neonate was diagnosed with meningoencephalitis with pleocytosis (131/μL, reference value < 15/μL) predominated by lymphocytes (129/μL) and increased protein (146 mg/dL, reference value < 120 mg/dL) in the cerebrospinal fluid although the CMV genome was not detected in the cerebrospinal fluid. Chorioretinitis was also diagnosed in both eyebounds on fundoscopy. She was diagnosed as

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having symptomatic congenital CMV infection. Intravenous ganciclovir therapy was started on day 12 at a dose of 6 mg/kg/dose twice daily for 6 weeks. Respiratory function improved gradually after administration of ganciclovir, and we stopped the oxygen inhalation therapy on day 23 (Fig. 2). Improvement of the chorioretinitis was confirmed on day 19. The automatic auditory brainstem response was normal. Magnetic resonance imaging on day 55 revealed some white matter lesions in both frontal lobes, but these signs improved at follow-up investigation 8 months later. We also measured the CMV genome load in the blood and urine (Fig. 2) (9). No side effects of ganciclovir were observed during treatment, and she was discharged on day 62. There has been no deterioration of respiratory function and chorioretinitis for 2 years. Neurodevelopment and audibility are normal at age 2 years.

The present case highlights 2 important clinical issues. First, congenital CMV infection can present with pneumonitis manifesting as neonatal respiratory distress. Second, CMV genome load measurement may be useful to evaluate treatment response to ganciclovir therapy in congenital CMV infection.

CMV pneumonitis is estimated to occur in fewer than 1% of infants with congenital CMV infection and can be more frequent and severe in immunocompromised pre-term neonates than immunocompetent term neonates (3). Congenital CMV pneumonitis may persist for several months and result in the development of bronchopulmonary dysplasia (BPD), a chronic lung disease defined by
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oxygen requirement either at 28 postnatal days or 36 weeks postmenstrual age (10). Coclite et al. (3) suggested that CMV infection in neonates may play an indirect role in BPD by causing increased exposure to other causative factors such as secondary bacterial pneumonitis, a requirement for oxygen inhalation, and mechanical ventilator support. In addition, persistent CMV infection may also cause diffuse necrotizing pneumonitis with fibrosis leading to BPD not only in immunocompromised or preterm infants, but also in immunocompetent or term infants. Based on these perspectives, early diagnosis of and intervention for congenital CMV pneumonitis are important to prevent the development of BPD. Furthermore, only a few cases of severe congenital CMV pneumonitis requiring mechanical ventilation have been reported although there is no case presenting mild respiratory distress (11–14). We considered that the positive CMV-IgM of the mother and the neonate suggested CMV infection had occurred later in pregnancy, and this factor may explain why the neonate had congenital CMV infection with mild respiratory distress.

The benefit of measuring the CMV genome load to evaluate the treatment response to ganciclovir therapy has not been well reported; however, it may be helpful. Morillo-Gutierrez et al. (15) reported that periodic viral load testing is important to identify emerging resistant strains of CMV during antiviral therapy. In the present case, intravenous ganciclovir therapy appeared to have been clinically effective. In addition, the CMV genome was not detected in the blood on day 25, 13 days after starting ganciclovir therapy. The CMV genome load in the urine decreased gradually, and the reduction appeared to be correlated with the improvement in respiratory function. CMV genome load in the urine decreased to 614 copies/mL at the end of the 6-week treatment period and did not increase after treatment was completed. A viral load increase was observed in the blood after the completion of ganciclovir therapy; however, we did not treat this because this rebound increase of CMV genome load has been reported previously and exacerbation of clinical findings was not observed (16). We assumed that the decline in CMV viral load in the blood and urine reflected a favorable response to treatment. Furthermore, a sufficient reduction of the CMV genome load in urine may be an important indicator for evaluating completion of treatment.

Congenital CMV infection can present with pneumonitis manifesting as respiratory distress, and early diagnosis and intervention are important to prevent the development of BPD. Clinicians should consider congenital CMV infection as a differential diagnosis for neonates presenting with respiratory distress. We suggest that the CMV genome load be monitored during antiviral therapy and regarded as an indicator of response to treatment. Further studies are needed to clarify the usefulness of CVM genome load measurement for the treatment of congenital CMV infection.

Conflicts of interest None to declare.

REFERENCES