

Early Postnatal Seizures in a Neonate with Wolf–Hirschhorn Syndrome

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Abstract

Keywords

- ▶ Wolf–Hirschhorn syndrome
- ▶ seizure
- ▶ neonate
- ▶ persistent pulmonary hypertension

Background Wolf–Hirschhorn syndrome (WHS), which is characterized by a typical facial appearance, growth retardation, mental retardation, seizures, and congenital cardiac defects, has an estimated incidence of 1 per 50,000 births.

Case We report a case of a low birth weight neonate with WHS and seizures, as well as persistent pulmonary hypertension in the early neonatal period. Apgar scores were 6 (1 minute) and 8 (5 minutes) with evident retraction. After admission to the neonatal intensive care unit, the patient had tonic–clonic seizures with epilepticus 30 minute after birth. Although the seizures were uncontrollable, continuous thiopental administration was effective for seizure mitigation.

Conclusion Neonatal seizures with WHS occur rarely. This is the first case report on seizures just after birth in a neonate with WHS.

Wolf–Hirschhorn syndrome (WHS) causes a typical facial appearance, growth retardation, developmental delay, and seizures, as well as congenital cardiac defects.¹ It has an estimated incidence of 1 per 50,000 births.² Deletion of the terminal band of the short arm of chromosome 4 with a breakpoint at the 4p15–4p16 region is the most common genetic abnormality causing WHS. Although WHS-associated seizures typically occur from 3 to 23 months after birth³ and only a few case reports of neonatal seizures with WHS exist. Furthermore, there have been no case reports of seizures just after birth in a neonate with WHS. Here we report the case of a low birth weight neonate presenting with WHS and seizures just after birth, as well as persistent pulmonary hypertension in the early neonatal period.

Case Report

The patient's mother was a 34-year-old woman (gravida 0, para 0) with no history of disease. During pregnancy, fetal ultrasonography performed at the gestational age (GA) of 26 weeks at another general hospital indicated fetal growth

retardation, and therefore the mother was transferred to our prenatal care center. Tests for toxoplasma, cytomegalovirus, rubella, herpes, and human immunodeficiency virus yielded negative results. Fetal ultrasound performed at the GA of 27 weeks showed a ventricular septal defect, with normal fetal brain development; preliminary maternal amniocentesis at the GA of 27 weeks showed 46, XY, del (4)(p15.2).

At the GA of 37 weeks, an elective cesarean section was performed. The patient was a male with a birth weight of 1,738 g (standard deviation [SD]: –3.0), height of 43.5 cm (SD: –1.9), and head circumference of 28.2 cm (SD: –3.2). Apgar scores were 6 (1 minute) and 8 (5 minutes) with evident retraction breathing. Positive pressure ventilation with a mask and bag was started immediately. After admission to the neonatal intensive care unit, the patient developed epilepticus with tonic–clonic seizures at 30 minute after birth. The patient required mask bagging and oxygen supplementation and had apnea; therefore, tracheal intubation using a 2.5-mm endotracheal tube was performed and synchronized intermittent mechanical ventilation was started. A venous line and a peripheral intravenous (IV) catheter line were inserted and diazepam (0.3 mg/kg, two doses) was

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intravenously administered. For uncontrolled seizures, phenobarbital (15 mg/kg, one dose) and midazolam (0.1 mg/kg, two doses) were administered, but the seizures stopped only after thiopental administration (3 mg/kg, two doses) 1 hour after birth. There were no intracranial hemorrhage, hypoglycemia, electrolyte imbalance, metabolic abnormality, and infection. Chest radiography showed respiratory distress syndrome. Oxygenation was temporarily improved after endotracheal administration of Surfacten (120 mg/kg; Tokyo-Tanabe Co. Ltd., Tokyo, Japan). However, oxygenation worsened with relapse of seizure and pulmonary hemorrhage. A maintenance thiopental infusion (3 mg/kg/hour) was started and the seizures stopped. A fraction of inspired oxygen of 100% was required; cardiac ultrasonography revealed mild tricuspid regurgitation and a right-to-left shunt of the patent ductus arteriosus, and we diagnosed neonatal persistent pulmonary hypertension. Therefore, high-frequency oscillatory ventilation and nitric oxide inhalation (20 ppm) was started.

The clinical course during the early postnatal period is shown in ►Fig. 1. After the maintenance thiopental infusion was started, ultrasonography showed that the ejection fraction worsened and the blood pressure decreased. Dobutamine (3 µg/kg/minute) and dopamine (3 µg/kg/minute) were therefore administered, but the blood pressure did not elevate sufficiently. We considered that the hypotension was attributable to the maintenance thiopental administration. On day 5, the thiopental infusion was stopped and the blood pressure increased from day 6. There was no seizure recurrence.

As shown in ►Fig. 2A, amplitude-integrated electroencephalogram (aEEG) recording after maintenance thiopental infusion showed the suppression of electrical activity, as

previously described.⁴ On day 7, electrical activity improved (►Fig. 2B). Nitric oxide inhalation was stopped on day 12, and the patient was extubated on day 34. Antiepilepsy prophylaxis with sodium valproate was administered from day 35. There were no abnormal electroencephalogram findings at 3 months old. The patient is now aged 5 months and has not had any further seizures.

Discussion

Neonatal seizures occur in approximately 1.8 to 3.5 cases per 1,000 live births.⁵ The most common cause is hypoxic-ischemic encephalopathy, which accounts for approximately two-thirds of all neonatal seizures.⁶ Other causes include intracranial hemorrhage, central nervous system infection, cortical development malformations, and metabolic disturbances such as hypoglycemia and hypocalcemia. Neonatal seizures presenting with congenital anomalies are a rare occurrence.

Battaglia et al reported that seizures occurred in 95.8% (46/48) of 48 children with WHS,⁷ with seizures starting at the ages of 3 to 23 months and having a peak incidence at 9 to 10 months. However, in 2003, another study on WHS showed that neonates aged between 1 day and <1 month had tonic-clonic seizures and were treated with phenobarbital.⁸ Thus, seizure onset in WHS can occur in the neonatal period; however, to our knowledge, this is the first case report on early postnatal seizures in a neonate with WHS.

For the treatment of seizures and epilepsy in WHS, phenobarbital and sodium valproic acid are typically used. In the present case, phenobarbital, midazolam, and diazepam were ineffective, but thiopental was effective. Thiopental is often

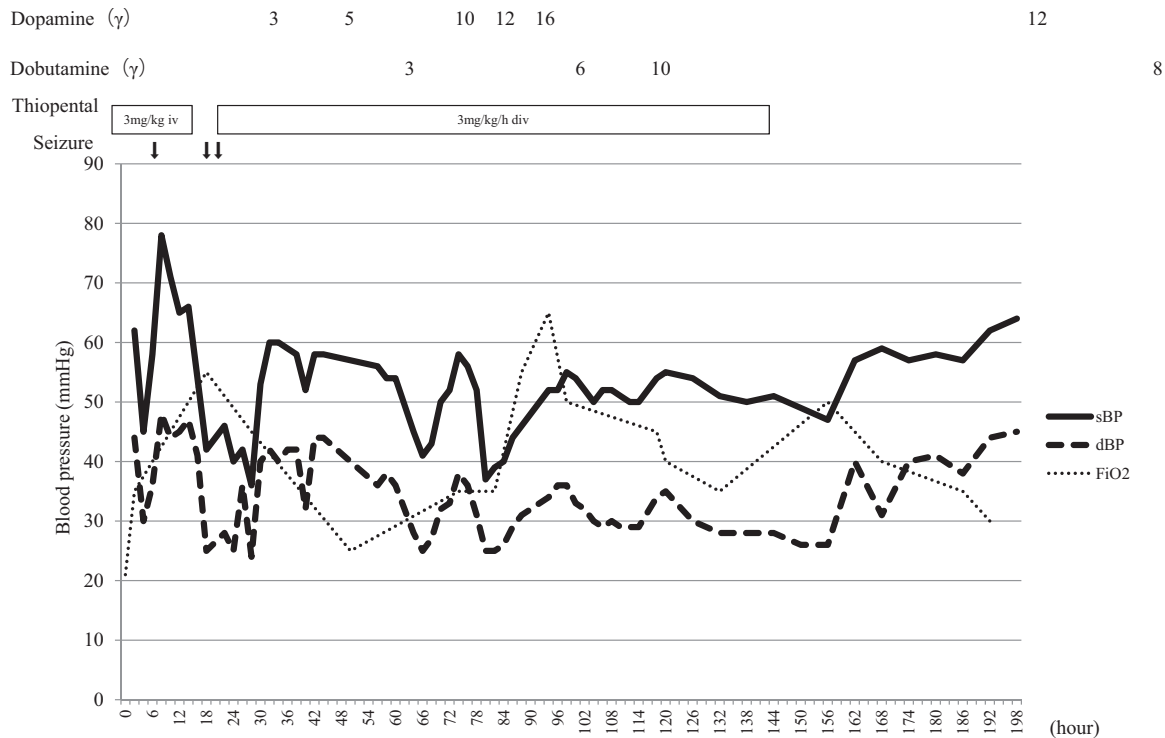


Fig. 1 Clinical course in the early postnatal period. dBP, Diastolic blood pressure; FiO₂, fraction of inspired oxygen; sBP, systolic blood pressure.

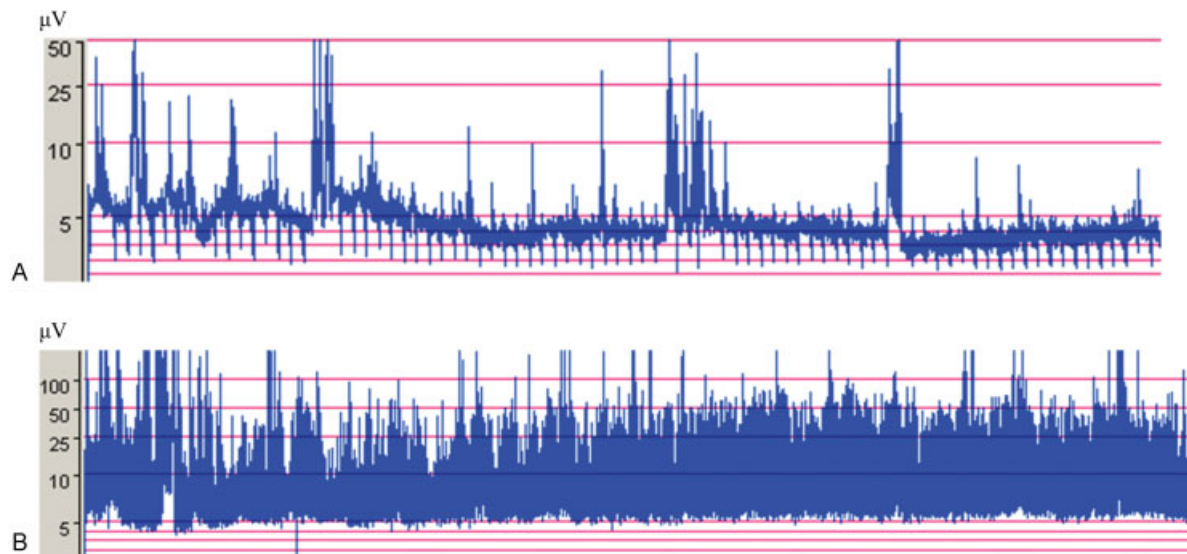


Fig. 2 Abnormal amplitude-integrated electroencephalogram findings caused by maintenance thiopental administration. (A) Immediately after maintenance thiopental administration on day 0. (B) 3 days after thiopental administration was stopped.

administered to children with uncontrollable seizures.⁹ Bonati et al reported that thiopental was effective in phenobarbital-resistant neonatal seizures. They administered high-dose thiopental (10 mg/kg IV) in nine severely asphyxiated neonates (body weight: 1,120–3,750 g; GA: 33–41 weeks) and observed mild hypotension and EEG suppression.⁴ Other reports concerning thiopental administration in neonates and children (loading dose: 10–15 mg/kg; maintenance infusion: 0.75–5 mg/kg/hour) indicated no major side effects such as severe hypotension. Although the total thiopental dose (1–3 mg/kg/hour over 3 days) administered was low, as shown in ►Figs. 1 and 2, the present case also showed mild hypotension and aEEG suppression with the continuous administration of thiopental.^{9–11}

Scher et al reported seizures in neonates who experienced peripartum asphyxia that resulted in persistent pulmonary hypertension.¹² WHS is rarely associated with persistent pulmonary hypertension. The patient in our case did not have peripartum asphyxia; however, from the clinical course, it was considered that persistent pulmonary hypertension might be caused by seizures. Furthermore, we speculated that in this case, hypotension was caused not only by thiopental but also by pulmonary hypertension.

In summary, neonatal seizures with WHS are a rare occurrence. However, in all cases of WHS after birth, there exists a possibility of seizures in the early neonatal period. Therefore, prenatally diagnosed neonates with WHS should be delivered in a maternity hospital with a type 3 neonatal unit capable of treating neonatal seizures.

Conflict of Interest

The authors declare that they have no competing interests.

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