

# Intracranial hemorrhage associated with medulla oblongata dysplasia in a premature infant

## A case report

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### Abstract

**Rationale:** Medulla oblongata dysplasia is an extremely rare form of neurodevelopmental immaturity in premature infants. Intracranial hemorrhage in premature infants may be closely related to neurodevelopmental immaturity.

**Diagnoses:** We report a female premature infant who succumbed to intracranial hemorrhage caused by medulla oblongata dysplasia.

**Patient concerns:** The infant was born at 31 weeks gestation. The onset manifestation was symptomatic epilepsy associated with subependymal hemorrhage.

**Interventions:** Levetiracetam and sodium valproate were administered. During the hospitalization, hydrocephalus developed and the intracranial hemorrhage aggravated.

**Outcomes:** The infant died on day 171 after birth.

**Lessons:** Early identification and prompt treatment should be emphasized. Clinicians should be aware of this condition, as it can potentially cause neonatal intracranial hemorrhage.

**Abbreviations:** AIFD = Acute Intrapartum Fetal Distress, PI = Premature infant, PS = Pulmonary Surfactant, sEH = Subependymal Hemorrhage.

**Keywords:** case report, infant, intracranial hemorrhage, medulla oblongata dysplasia, neonate

## 1. Introduction

Intracranial hemorrhage is a major contributor to morbidity and mortality in premature infants. It is found at autopsy in approximately 50% to 70% of all infant death cases.<sup>[1]</sup> The causes of intracranial hemorrhage in newborns are multifactorial and vary with gestational age. Birth trauma and asphyxia are the 2 most common etiological factors.

Other relatively infrequent factors include inherited or acquired coagulopathies, congenital arteriovenous malformations, aneurysms, vascular neoplasms, hypertension associated with coarctation of the aorta, and vitamin K deficiency.<sup>[2–6]</sup> Additionally, intracranial hemorrhage in premature infants may be closely related to neurodevelopmental immaturity.<sup>[7]</sup>

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The development and maturation of the central nervous system is a complex, age-dependent dynamic process. Neonatal medulla oblongata dysplasia is an extremely rare developmental anomaly. Due to its low morbidity rate, the natural courses and clinical progression of medulla oblongata dysplasia are still poorly understood.

Herein, we report a female premature infant who succumbed to intracranial hemorrhage caused by medulla oblongata dysplasia.

## 2. Case report

The study was approved by the ethics committees of Beijing Friendship Hospital, Capital Medical University. Written informed consent was obtained from the patient's legal guardians.

This female infant was born to a gravida 4 para 2 mother at 31<sup>+3</sup> weeks of gestation. A diagnosis was made of fetal distress, cesarean scar, concomitant uterine fibroids, and nuchal encirclements of the umbilical cord (3 cycles). Thus, a cesarean delivery was performed.

Intraoperatively, III-degree amniotic fluid contamination was noted, whilst the umbilical cord and placenta were all normal. The Apgar score was 9/10 (cry, 1 point) at 1 minute, 9/10 (cry, 1 point) at 5 minutes, and 10/10 at 10 minutes. The birth weight was 1135g. An endotracheal intubation was performed immediately after birth, and intratracheal instillation of pulmonary surfactant (poractant alfa; 240 mg) was administered.

The neonate was referred to the neonatal intensive care unit with pressurized oxygen supply. Physical examination showed lack of blood perfusion in the perioral and nasion areas;

nevertheless, there was no abnormality of respiratory rhythm, skin rash, jaundice, bleeding spots, or convulsion. Further examination revealed a temperature of 36.0°C, respiratory rate 50 breaths/min, pulse 126 beats/min, and blood pressure 48/29 mm Hg. The bregma was flat and soft, with an area of approximately 10 mm × 10 mm. The simple gestational age assessment was consistent with the 31-week gestation. Auscultation of the chest revealed coarse crackles, and there was no cardiac souffle. The abdomen and extremity examinations were all normal. The swallowing, sucking, embrace, and grasp reflexes were all incomplete.

The following diagnoses were suspected: severe pneumonia; disseminated intravascular coagulation; bronchopulmonary dysplasia; mediastinal emphysema; symptomatic epilepsy; fungal infection; gastrointestinal bleeding; severe anemia; hepatic function impairment; renal function impairment; severe hydrocephalus; conjunctivitis; corneal epithelial lesion; thrombocytopenia; hypoxemia; hyperglycemia; hyponatremia; patent foramen ovale; growth retardation; and medulla oblongata dysplasia.

After birth, the neonate was treated with mechanical ventilation including continuous positive airway pressure and bilevel positive airway pressure, and she developed severe infection. Multiple antimicrobials were applied, including augmentin, cefoperazone/sulbactam, piperacillin/tazobactam, meropenem, vancomycin, fluconazole, and azithromycin. Additionally, we used low-molecular weight heparin to regulate the coagulation function, etamsylate for hemostasis, omeprazole for gastric acid suppression, and glutathione with glucuronolactone for maintaining the hepatic function.

On day 13, the neonate was fed with breast milk; nevertheless, the sucking and swallowing reflexes were poor, and citricoline and nasogastric feeding were administered. Cranial ultrasound showed cerebral dysplasia. On day 38, laboratory examination of heel blood showed phenylketonuria. On day 44, cranial ultrasound revealed subependymal hemorrhage. On day 45, hydroxylase- and biotin-related gene tests were normal. Additionally, high-resolution chromosome examination and exome sequencing revealed no abnormality.

On day 57, the infant developed epileptic seizures, and levetiracetam and sodium valproate were administered. The ocular fundus examination showed bilateral retinal hemorrhage. The infant was treated with recombinant human erythropoietin injection to promote bone marrow hematopoiesis. On day 102, repeated cranial ultrasound showed subependymal hemorrhage and ventriculomegaly.

On day 166, the vital signs of the infant were stable; gastrostomy and ventriculoperitoneal shunt were recommended, which her parents refused and the infant was discharged. Five days later, the infant died.

### 3. Discussion

In this case, no chromosome abnormalities were found, and the preterm infant primarily manifested as symptomatic epilepsy, bulbar paralysis with neurological function impairments (especially, dysphagia), and growth retardation. The death of this infant was attributed to intracranial hemorrhage and hydrocephalus associated with medulla oblongata dysplasia. The limitation of this study was the absence of radiological (computed tomography or magnetic resonance imaging) or pathological (autopsy) evidence.

Premature birth is associated with variable short-term and long-term complications.<sup>[5,8]</sup> These complications are closely and

negatively associated with gestational age; generally, the earlier an infant is born, the higher the risk and severity of complications. Short-term complications mainly include multi-organ functional disturbances.<sup>[9]</sup>

The most common premature complication is difficulty breathing due to immaturity of the respiratory system. In infants with bronchopulmonary dysplasia, apnea may be the prominent clinical manifestation. When the infant's lungs lack surfactant, the lungs cannot expand and contract normally and the infant usually develops respiratory distress syndrome. In the current case, we performed an endotracheal intubation immediately after birth, and used intratracheal instillation of pulmonary surfactant (poractant alfa). During hospitalization, no apnea was observed.

Cardiac defects are also common complications in premature infants. The most frequent cardiac problems are patent ductus arteriosus and hypotension. The former refers to a persistent opening between the aorta and the pulmonary artery, which often leads to fetal outcomes. Hypotension may be multifactorial and can result in neonatal cardiogenic shock.<sup>[10]</sup>

Another common developmental anomaly in premature neonates is central nervous system dysplasia.<sup>[1,5,8]</sup> This condition can involve the cerebrum, the cerebellum, and the brain stem as well. The most common manifestations of central nervous system dysplasia are intracranial hemorrhage and hydrocephalus. Most hemorrhages are mild and resolve with little neurological sequelae, while severe hemorrhage can cause permanent brain injury. Hydrocephalus usually necessitates an operation to relieve accumulation of cerebrospinal fluid.

Medulla oblongata dysplasia is an exceedingly rare form of central nervous system developmental abnormality. The medulla oblongata contains the cardiac, respiratory, digestive, vomiting, and vasomotor centers, and therefore is crucial to the regulation of autonomic functions including breathing, heart rate, and blood pressure. In the current case, the premature infant presented with tachypnea, tachycardia, and hypotension, especially, the swallowing reflex was incomplete, suggesting that the medulla functions were impaired.

Other relatively infrequent complications include thermoregulation abnormalities, gastrointestinal dysfunctions, anemia, metabolic disturbances, and immune system problems.<sup>[8]</sup> In the current case, we used multimodal mechanical ventilation for maintaining the blood oxygen level and multiple antimicrobials for treating the severe infection. Additionally, we applied low-molecular weight heparin to regulate the coagulation function, etamsylate for hemostasis, omeprazole for gastric acid suppression, glutathione with glucuronolactone for maintaining the hepatic function, and recombinant human erythropoietin injection to promote bone marrow hematopoiesis.

All the above complications can be life threatening, and early identification and prompt treatment should be emphasized.

### 4. Conclusion

We report herein a case of neonatal intracranial hemorrhage associated with medulla oblongata dysplasia. Medulla oblongata dysplasia is an extremely rare form of neurodevelopmental immaturity in premature infants. Clinicians should be aware of this condition, as it can potentially cause neonatal intracranial hemorrhage.

### Author contributions

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