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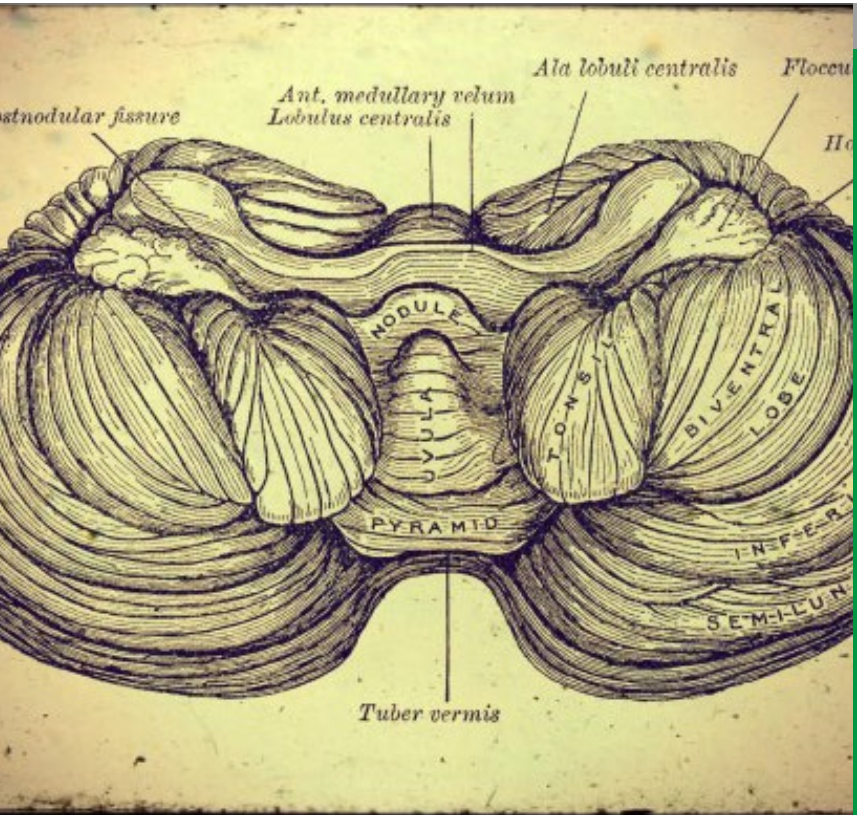
Neurodevelopmental consequences of massive cerebellar bleeding in a preterm infant



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Title figure:
Anatomy of the cerebellum
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INTRODUCTION

Cerebellar injury is a common complication in preterm infants. The impact on future development and the risk for severe impairment depends on the size and location of the cerebellar hemorrhage as well as additional intracranial abnormalities. We describe the case of a preterm female infant with a large cerebellar bleeding and report the results of her follow-up assessments at 3, 12 and 24 months.

This premature female infant was born by Cesarean section at 26 2/7 weeks of gestation with a birth weight of 550 g (P 5 – 10). Pregnancy had been complicated by intrauterine growth restriction. A fetal MRI performed at 21 6/7 weeks to evaluate a suspected enlarged 4th ventricle had shown normal brain structures. A full course of antenatal corticosteroids for fetal lung maturation had been administered three days prior to delivery because of pathological umbilical cord blood flow. Two days later a Cesarean section was performed due to maternal HELLP syndrome.

The postnatal course was complicated by respiratory distress syndrome and the development of bilateral pneumothoraces and pulmonary interstitial emphysema. The girl had to be ventilated for the first 23 days of life (DOL). She developed moderate bronchopulmonary dysplasia and was supported with CPAP and high-flow nasal cannula for the first 116 days of life, requiring supplemental oxygen until DOL 114. In addition, the infant developed sepsis resulting in low blood pressures requiring the administration of adrenalin and dopamine between DOL 4 – 11.

She also developed retinopathy of prematurity stage III in the right and stage II in the left eye. A persistent ductus arteriosus was treated with indomethacin and paracetamol but remained patent until discharge.

Cranial ultrasounds were performed on a regular basis. On DOL 5, bilateral periventricular / intraventricular hemorrhages grade III and a large right-sided cerebellar hemorrhage were detected (Fig. 1). Due to increasing ventricular dilatation lumbar puncture was performed twice on DOL 7 and 12. Subsequently, ventricular size decreased and remained stable, and no shunt had to be placed.

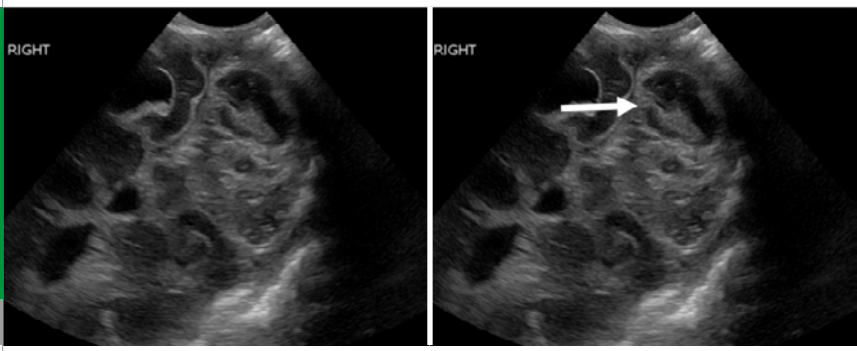

Fig. 1

Cranial ultrasound imaging through the mastoid fontanel on DOL 16 demonstrating extensive destruction of the right cerebellar hemisphere (arrow).

A cranial MRI performed at a corrected post-menstrual age of 42 weeks showed significant destruction of the right cerebellar hemisphere with partial involvement of the vermis (Fig. 2, 3). Hemosiderin deposits could be detected in the capsula interna, nucleus caudatus and both lateral ventricles indicating previous hemorrhages.

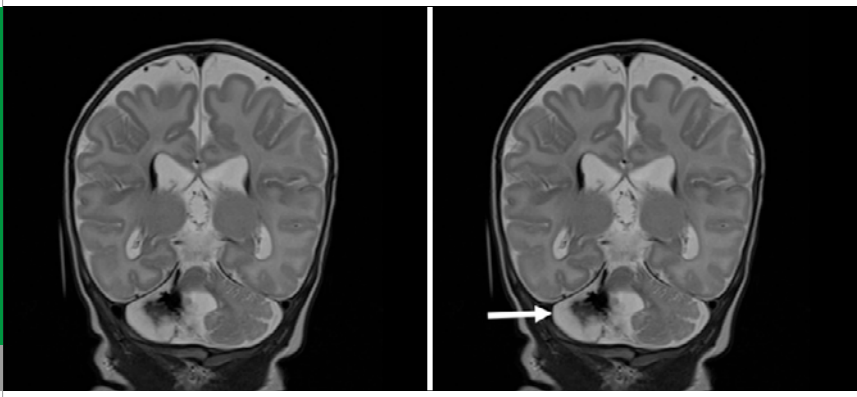

Fig. 2

T2-weighted MRI at 42 postmenstrual weeks (coronal view) showing massive destruction of the right cerebellar hemisphere (arrow); in addition, there is hemosiderin staining in both lateral ventricles and borderline enlargement of the intra- and extracerebral CSF spaces.

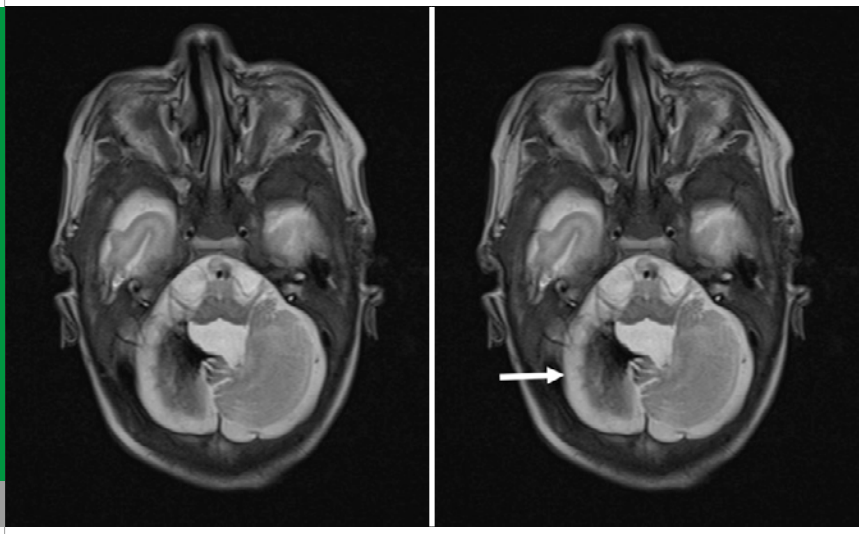

Fig. 3

T2-weighted MRI at 42 postmenstrual weeks (axial view) showing massive destruction of the right cerebellar hemisphere (white arrow).

On DOL 122 (corrected age of 43 4/7 weeks), the girl was discharged home. Neurological examination before discharge showed normal findings for gestational age, except for abrupt spontaneous movements. Physiotherapy had been started during the hospital stay and was continued after discharge.

The girl underwent routine neurodevelopmental follow-up assessments for children born at less than 30 weeks of gestation at the Child Development Center of University Children's Hospital Zurich at 3, 12 and 24 months respectively. Due to myopia and strabismus she was also seen regularly by ophthalmologists.

At a corrected age of 3 months, delayed gross motor development with poor head control and muscular hypotonia of the trunk and hypertonia of the extremities without asymmetry were recognized. Analyses of General Movements showed an abnormal pattern with abrupt movements. However, fidgety movements could be detected.

During the follow-up assessment at 12 months corrected age, the mother reported delayed acquisition of motor milestones. The girl had learned to turn at 8.5 months corrected age and had started to crawl at 11 months corrected age. She had started to grasp at 8 months corrected age, preferring the left hand. At the time of examination, the girl

was not able to sit independently and showed truncal instability when held. She could crawl and could get into a standing position when supported. Movement quality was abrupt.

The results of the Bayley III (Bayley Scales of Infant Development-Third Edition; German Version) showed developmental delay with a cognitive composite score of 65. The language composite score was 87 (norm composite score 100±15 respectively, norm scaled score 10±3) and the motor composite score was 89 (fine motor scaled score 10, gross motor scaled score 7). At this point, early intervention therapy was started.

At 24 months corrected age, the mother reported that the girl had learned to walk independently at 22 months corrected age, but her gait was very unsteady and ataxic; during the examination the girl could not yet run. There was significant microcephaly (Fig. 4). Examination of fine motor function revealed tremor and dyscoordination with a left-hand preference. A diagnosis of ataxic cerebral palsy affecting the right side more profoundly was made. The Bayley III revealed a global developmental delay with a cognitive composite score of 55, a language composite score of 78 and a motor composite score of 70.

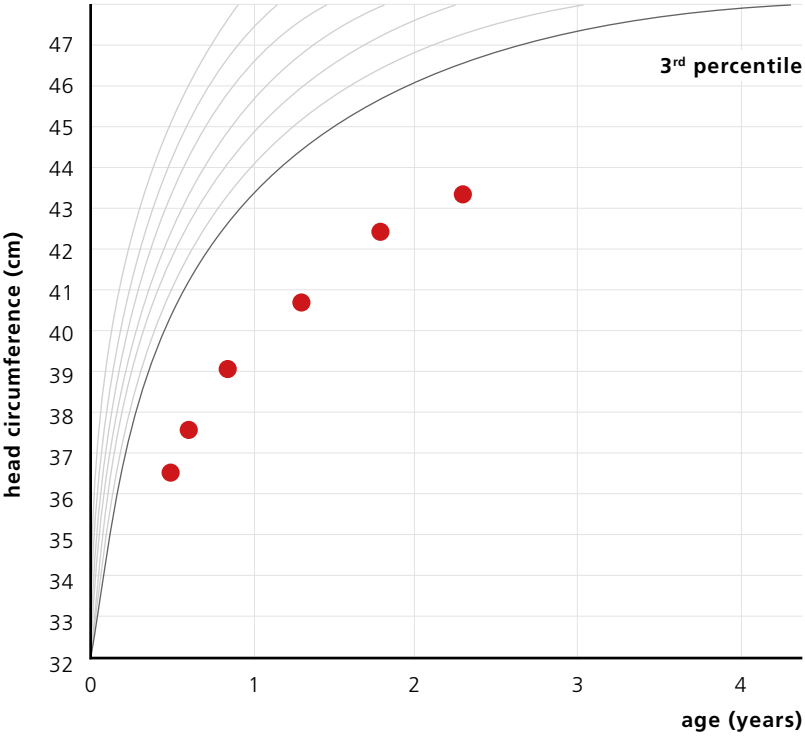

Fig. 4

Growth curve of the head circumference demonstrating severe microcephaly.

DISCUSSION

Cerebellar hemorrhage is a relatively common complication in very preterm infants and can vary from punctate bleedings to massive destruction of the hemisphere(s) (1). Larger bleedings can normally be detected in the neonatal period with cranial ultrasound examination through the anterior fontanelle. The approach via the posterior fontanelle and the mastoid window, however, is more sensitive. Nevertheless, smaller hemorrhages and punctate bleedings can be hard to detect via ultrasound and MRI can be superior to cranial ultrasound in such cases (2).

Depending on the imaging technique, the incidence of cerebellar hemorrhage in children born at less than 32 weeks of gestation varies ranging from 2.2 % to 19 % (3). Aside from lower gestational age and lower birth weight, the use of inotropic agents, treated PDA and thrombocytopenia are independent risk factors for the development of cerebellar hemorrhages (4).

The cerebellum plays an important role in motor function. More recently, it has become more evident that it also plays an important role in other developmental domains such as language and cognition (5) and thus, when injured, can cause long-term neurodevelopmental disabilities (1). The severity of neurodevelopmental impairment depends on the size, the location of the cerebellar injuries, as well as the presence of additional supratentorial abnormalities.

Infants with small bleedings usually show little or no neurodevelopmental sequelae (6), whereas infants with large bleedings and/or involvement of the vermis are at high risk for severe impairments of cognition, motor, langue and behavioral development (Table) (7).

Type and/or location of cerebellar hemorrhage	Number of patients	Incidence of severe impairment reported in the literature
Vermis involvement	15	87 – 93 %
Large hemorrhage	111	46 – 82 %
Punctate bleeding	15	13 – 20 %
Bilateral hemorrhage	6	17 %
Unilateral hemorrhage	42	24 – 43 %

Table
Overview of the reported incidence of severe impairment among 128 preterm infants with different types of isolated cerebellar hemorrhages (adapted from Hortensius et al.) (7).

In the CHOPIn Study (a multicenter study on Cerebellar Hemorrhage and Outcome in Preterm Infants), Boswinkel et al. (8) described the outcome of 177 preterm infants with cerebellar hemorrhage. The risk for an abnormal outcome at two years of age increased with the size of the injury. Punctate bleedings were defined as bleedings < 4 mm, limited bleedings > 4 mm but less than 1/3 of the hemisphere and massive bleedings if more than 1/3 of the hemisphere was involved. If at least one of the outcome parameters (neurological examination, Bayley scales of infant development III (BSID-III) or Griffiths Mental Development Scales Revised (GMDS), Child Behaviour Checklist) was

abnormal, this was considered an abnormal composite outcome. Amongst children with a punctate cerebellar hemorrhage an abnormal composite score was found in 39 % of cases, in comparison to children with massive injury where the probability for an abnormal composite score was as high as 67 %. Infants with massive bleeding and vermis involvement were at highest risk for unfavorable outcome and always showed an abnormal composite score. Comprehensive data about the long-term outcome after cerebellar hemorrhage in preterm infants at school age is thus far lacking.

CONCLUSION

Cerebellar hemorrhage is a well-known complication in preterm children. Massive cerebellar bleeding with vermis involvement carries the highest risk for poor neurodevelopmental outcome. Early detection and a better understanding of the mechanisms leading to cerebellar hemorrhage are needed to prevent severe long-term sequelae.

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