Intraventricular Hemorrhage (IVH) — Causes and Treatment

Intraventricular hemorrhage within the subependymal germinal matrix is a disease that is significantly more common in premature infants, especially those born before the age of 32 weeks of gestation. Infants with intraventricular hemorrhage are usually asymptomatic but might develop non-specific symptoms and signs of anemia. Hypotonia, coma, seizures, and death can occur in more severe cases of intraventricular hemorrhage. Cranial ultrasonography is the diagnostic modality of choice for establishing the diagnosis and for follow-up. Treatment mainly consists of cardiovascular and respiratory support, surgical intervention for posthemorrhagic hydrocephalus and the use of acetazolamide to treat progressive hydrocephalus.

Overview
Pre-term delivery is associated with several complications that can be life-threatening or can cause long-term disability and sequelae in the patient. Periventricular hemorrhage and intraventricular hemorrhage are one common acquired lesion of the central nervous system that specifically affects premature infants.

The condition is characterized by hemorrhage into the intraventricular space and the periventricular white matter. Involvement of the periventricular white matter is associated with long-term disability due to the proximity of the lesion to the motor tracts.

**Epidemiology of Intraventricular Hemorrhage in Premature Newborns**
The most important risk factors for intraventricular hemorrhage in newborns are **very low birth weight** and **delivery at a gestational age that is less than 35 weeks**. The estimated incidence of intraventricular hemorrhage in premature newborns can range between 20 to 50%.

Intraventricular hemorrhage in premature infants is associated with **significant mortality** with an estimated mortality rate that can be as high as 50%. The most important risk factor for increased mortality is the extent of hemorrhage. Patients with low-grade hemorrhage have the lowest mortality rate of around 5%.

Differences in the incidence of intraventricular hemorrhage between males and females were not observed; however, recent studies of **indomethacin prophylaxis** for intraventricular hemorrhage in premature babies have shown improved efficacy in male infants.

Intraventricular hemorrhage is more common in neonates born before the 32nd week of gestation. Most cases of intraventricular hemorrhage occur within the first 72 hours of life, but some cases of hemorrhage can happen as late as 7 days post-delivery; therefore, screening programs for intraventricular hemorrhage in premature infants have been recommended to continue until the age of one week.

**Risk factors**

- Extreme prematurity.
- Hypotension, hypothermia, metabolic acidosis, thrombocytopenia.

**Pathophysiology of Intraventricular Hemorrhage in Premature Newborns**

Intraventricular hemorrhage originates from the **fragile retefemale like a capillary network** that supplies the subependymal germinal matrix.

The **subependymal germinal matrix** is responsible for the neuronal proliferation, neuroblasts division, and neuronal cell migration into the cerebral parenchyma within the developing brain of the fetus. **Neuronal proliferation** usually ceases at the age of 20 weeks of gestation and **glial cell proliferation** is finished by 32 weeks of gestation.

After 32 weeks, the subependymal germinal matrix has almost completely regressed which explains why intraventricular hemorrhage is much more common in premature newborns who are born before 32 weeks of gestation.

The anatomical classification of the location and extent of the intraventricular hemorrhage is important for prognostic concerns. **Grade I periventricular or intraventricular hemorrhage** is defined as subependymal and germinal matrix hemorrhage.
Grade II is the same as grade I but with the extension of hemorrhage into the lateral ventricles but without ventricular enlargement.

Grade III hemorrhage is associated with ventricular enlargement.

Grade IV hemorrhage involves the cerebral parenchyma and is not confined to the subependymal and germinal matrix.

The most important pathogenic mechanism of periventricular hemorrhage and intraventricular hemorrhage in premature newborns is loss of autoregulation. Premature infants with pulmonary disease are more prone to impaired cerebral blood flow and pressure autoregulation, which explains the increased incidence of intraventricular hemorrhage in this subgroup of patients.

Additionally, birth, tracheal suctioning and the use of intravascular fluids for resuscitation are also known to alter cerebral blood flow and intracranial pressure in premature infants who have poorly developed cerebral blood flow autoregulation.

This mechanism of impaired autoregulation and increased cerebral blood perfusion in the fragile capillaries of the germinal matrix is thought to be responsible for grades I, II and III hemorrhages. Grade IV hemorrhage is caused by cerebral infarction due to increased venous pressure.

The most likely cause of increased cerebral venous pressure is the ongoing hemorrhage from the germinal matrix into the lateral ventricles and the enlargement of the ventricles, which can cause venous engorgement. The term periventricular hemorrhagic infarction can be used interchangeably with grade IV hemorrhage.

Due to the destruction of the motor tracts by the hemorrhagic incident, infants who survive usually have cerebral palsy. The involvement of the cortex can result in seizures and/or mental retardation.

Posthemorrhagic hydrocephalus usually happens in surviving infants and is caused by decreased absorption of the cerebrospinal fluid and obstruction of the cerebrospinal fluid circulation.
Clinical Presentation of Intraventricular Hemorrhage in Premature Newborns

Premature babies are usually sick and intraventricular hemorrhage is rarely associated with any significant changes in the clinical picture of the infant.

Due to the relatively large ratio of the head to the body of the infant and the ability of the head to expand, infants with intraventricular hemorrhage might develop symptoms and signs of anemia. Pallor, increased capillary refill time or shock can be observed.

Infants with severe intraventricular hemorrhage might develop metabolic or respiratory acidosis, apnea, hypotonia, and stupor. The newborn might go into a coma. The fontanels are usually full and firm to palpation due to the increased intracranial pressure. Seizures might happen in a minority of the patients. Children with grade III and IV hemorrhage might die and the diagnosis might be confirmed only on autopsy.

Diagnostic Workup for Intraventricular Hemorrhage in Premature Newborns

Laboratory investigations are rarely useful in infants with intraventricular hemorrhage unless the hemorrhage is severe enough to cause metabolic acidosis or respiratory acidosis. Lymphocytosis and lymphopenia have been observed in infants with intraventricular hemorrhage.

Imaging studies are the mainstay diagnostic tool for the screening, confirmation, and follow-up of intraventricular hemorrhage. Premature newborns, especially if less than 30 weeks of gestation, should undergo cranial ultrasonography at the age of one week postnatally. Cranial ultrasonography should be repeated at 36 to 40 weeks postmenstrual age in all premature babies.

If at any time point, the diagnosis of intraventricular hemorrhage is confirmed by cranial ultrasonography, follow-up serial ultrasonographies are indicated. Follow-up serial ultrasonographies should be repeated on a weekly basis looking for progression of hemorrhage and the development of posthemorrhagic hydrocephalus.

Computed tomography scanning and magnetic resonance imaging have a limited role in the diagnosis of intraventricular hemorrhage because of the excellent sensitivity and specificity of cranial ultrasonography.
Treatment of Intraventricular Hemorrhage in Premature Newborns

Infants with intraventricular hemorrhage might have hemorrhagic shock, metabolic disturbances and/or respiratory distress; therefore, cardiovascular and respiratory support is indicated.

Anemia and metabolic acidosis can happen in infants with severe intraventricular hemorrhage. In that case, acute correction of anemia with blood transfusions might be needed. Serial lumbar puncture has been shown to be ineffective in the prevention of progressive hydrocephalus.

Infants who develop late or progressive hydrocephalus should receive acetazolamide which decreases the production of the cerebrospinal fluid. Posthemorrhagic hydrocephalus might require a ventriculoperitoneal or ventriculosubgaleal shunt placement.

Indomethacin prophylaxis was shown to improve the cognitive profile of infants who develop intraventricular hemorrhage, especially males, but not the motor function outcome. This effect was preserved and still observed until school-age.

References


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