Hydrocephalus Pathogenesis

Hydrocephalus constitutes a complex neurological condition of heterogeneous origin characterized by excessive cerebrospinal fluid (CSF) accumulation within the brain ventricles. The condition may dangerously elevate the intracranial pressure (ICP) and cause severe neurological impairments. Pharmacotherapies are currently unavailable and treatment options remain limited to surgical CSF diversion, which follows from our incomplete understanding of the hydrocephalus pathogenesis.

Molecular studies on the pathogenesis of hydrocephalus have provided a means to improve the treatment and follow-up of patients with hydrocephalus [1].

Over this past century, the majority of hydrocephalus cases have been explained by functional or anatomical obstructions to bulk cerebrospinal fluid flow. More recently, hydrodynamic models of hydrocephalus have emphasized the role of abnormal intracranial pulsations in disease pathogenesis.

The classic understanding of hydrocephalus as the result of obstruction to bulk flow of CSF is evolving to models that incorporate dysfunctional cerebral pulsations, brain compliance, and newly characterized water-transport mechanisms.

Karimy et al. reviewed the molecular mechanisms of CSF secretion by the choroid plexus epithelium, the most efficient and actively secreting epithelium in the human body, and provide experimental and clinical evidence for the role of increased CSF production in hydrocephalus. Although the choroid plexus epithelium might have only an indirect influence on the pathogenesis of many types of pediatric hydrocephalus, the ability to modify CSF secretion with drugs newer than acetazolamide or furosemide would be an invaluable component of future therapies to alleviate permanent shunt dependence. Investigation into the human genetics of developmental hydrocephalus and choroid plexus hyperplasia, and the molecular physiology of the ion channels and transporters responsible for CSF secretion, might yield novel targets that could be exploited for pharmacotherapeutic intervention [2].

Terminal deletion of chromosome 6q is a rare chromosomal abnormality associated with intellectual disabilities and various structural brain abnormalities.

Iwamoto et al. presented a case of 6q terminal deletion syndrome with unusual magnetic resonance imaging (MRI) findings in a neonate.

The neonate, who was prenatally diagnosed with dilation of both lateral ventricles, was born at 38 weeks of gestation. MRI demonstrated abnormal membranous structure continuing to the hypertrophic massa intermedia in the third ventricle that had obscured the cerebrospinal fluid pathway, causing hydrocephalus. G-band analysis revealed a terminal deletion of 6q with the

karyotype 46, XY, add(6)(q25.3) or del(6)(q26). He underwent ventriculoperitoneal shunt successfully, and his head circumference has been stable.

6q terminal deletion impacts the molecular pathway, which is an essential intracellular signaling cascade inducing neurological proliferation, migration, and differentiation during neuronal development. In patients with hydrocephalus in association with hypertrophy of the massa intermedia, this chromosomal abnormality should be taken into consideration. This case may offer an insight into the hydrocephalus pathogenesis in this rare chromosomal abnormality [3].

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3)
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