Malformations of the CNS

CNS malformations include a wide spectrum of anomalies that arise during the ontogenesis of the brain and spinal cord. They have a variable clinical picture depending on the type and extent of the defect. They are a common cause of intrauterine fetal death and also a common cause of death in children during the first year of life. Brain malformations can be the cause of epilepsy and psychomotor retardation. Dysgenesis of the cerebral cortex is one of the most common causes of epilepsy in children.

Most malformations of the CNS arise as a result of disruption of the early embryonic development of the central nervous system (CNS), through the action of external or internal noxia or genetically conditioned factors. The basis for the development of the CNS is the neural plate (a plate of thickened ectoderm), which is established around the 18th day of gestation and closes during the 3rd and 4th week to form the brain sacs and the spinal cord. The ventricular system forms in the 8th week and *the corpus callosum* in the 10th week. Other important events are: cell proliferation (division of nerve cells), cell migration, cell differentiation and cell death.

Malformations of the CNS by period of onset

Defects arising during the period of dorsal induction (3rd-4th week of gestation)

- Anencephaly; encephalocele; myeloschisis; spina bifida ; malformations of the spinal cord; malformation of the cerebellum.

Defects arising during the period of ventral induction (5th-6th week of gestation)

- Holoprosencephaly ; less severe facial dysmorphia.

Disorders of neuronal and glial proliferation (2nd-5th month of gestation)

- Microcephaly; microlissencephaly , megalencephaly, hemimegalencephaly,...

Neurocutaneous syndromes

- Tuberous sclerosis ; Hippel-Lindau disease ; Sturge-Weber syndrome

Disorders of cell migration and cortical organization

- Lissencephaly; gray matter heterotopia; schizencephaly; polymicrogyria; pachygyria

Hydrocephalus group

- Arnold-Chiari malformation ; Dandy-Walker malformation

Brain damage in the process of cellular differentiation (from the 5th month of gestation) and myelination (from the 7th month of gestation).

Dorsal induction disorders – dysraphia

The incidence of these defects in the Czech Republic in the years 1994–2010 was as follows (total incidence, i.e. births and non-births - prenatally diagnosed): anencephaly 2.75 per 10,000, encephalocele 1.14 per 10,000, spina bifida 4.09 per 10,000 live born.

Anencephaly

Anencephaly (*cranioschisis totalis*) is a congenital absence of the brain due to non-closure of the cerebral compartment of the neural tube. This defect is not compatible with life. It is often accompanied by polyhydramnios. Thanks to advances in prenatal diagnosis, this defect is almost non-existent at birth.

Encephalocele

Encephalocele is a prolapse of brain tissue into the cranial cleft, most often in the frontal or occipital regions. The tissue in the keel is often damaged. Using sonography, CT and MRI, we can determine the contents of the hernia. This malformation is often isolated, without other associated anomalies.

Spina bifida

Video in English, definition, pathogenesis, symptoms, complications, treatment. Spina bifida is a congenital spina bifida. It most often affects the lumbar and lumbar region.

Spina bifida occulta

Spina bifida occulta is a split of one or more vertebrae that does not involve the spinal cord or the spinal cord. The skin above the defect tends to be more hairy and pigmented. It is usually an asymptomatic, incidental finding, occurring in about 10% of otherwise healthy individuals. If the defect is associated with a spinal anomaly, lipoma, tethered cord syndrome, etc., it may have significant neurological symptoms, usually paraparesis of the lower limbs, sometimes with micturition and defecation disorders.

Spina bifida cystica

Spina bifida cystica is a split of the spine, in which a sac formed by the spinal cord covers (meningocele) penetrates through the defect into the subcutaneous tissue, or and spinal cord with spinal nerves (meningomyelocele).

- Meningocele

Herniation of the meningeal sheaths of the spinal cord into a cyst, usually located in the lumbosacral region. If the hernia is perforated, the child is at risk of meningitis. Neurological findings on the lower limbs may be minor.

- Meningomyelocele

Herniation of the meningeal sheaths, nerve roots and spinal cord into the dorsal cleft. 80% of meningomyeloceles are found in the thoracolumbar, lumbar and lumbosacral regions. Meningomyelocele is often associated with Chiari malformation II. type (Arnold-Chiari). There is often a significant neurological deficit - paraparesis, micturition and defecation disorders.

Myeloschisis

Myeloschisis (*rhachischisis*) is a split of the spine with exposure of nerve tissue that is not covered by skin or spinal cord sheaths. This malformation is always associated with severe spinal cord dysfunction.

Separate malformations of the spinal cord

Syringomyelia
Hydromyelia

Soubor:Anencephaly side.jpg	Soubor:Encephalocele	Soubor:Spina Bifida pelvis X-ray.jpg	Soubor:Meningomyelocele diagram.jpg	Soubor:Syringomyelia.jpg
Plod s **anencefalií**.	Batole s **encefalokélou**.	Rentgenový snímek **spina bifida occulta** v oblasti S1.	Schéma **meningomyelokély**: 1 – vak vyplněný mozkomíšním mokem, 2 – mícha.	MRI zobrazující **syringomyelii** v oblasti C6-C7; T2-vážení.

Disorders of ventral induction

Holoprosencephaly
Less severe facial dysmorphia

Disorders of neuronal and glial proliferation

This group of malformations is characterized by a reduction or, conversely, an increase in the number of cellular elements, which also have an abnormal appearance (giant neurons, balloon cells).

Microcephaly with simplified gyrification

- It arises as a result of suppression of cell proliferation.
- Findings on the brain: severe microncephaly, poor gyrification, shallow grooves, cortical layer normally thick or reduced (probably due to premature depletion of the germinal matrix).
- Clinical picture: microcephaly, abnormal neurological picture, usually refractory epilepsy from an early age.
- Autosomal recessive inheritance.

Microlissencephaly

- Findings on the brain: noticeably small brain, poor gyrification, agyria or pachygyria, distinctly thickened cortex.
- Clinical picture: microcephaly, abnormal neurological picture, epilepsy.
- Mostly autosomal recessive inheritance.

Hemimegalencephaly

- It arises as a result of excessive cell proliferation. The entire hemisphere or only part of it grows disproportionately.
- Findings on the brain: Enlargement of part or the entire hemisphere, cortical dysplasia (pachygyria, polymicrogyria), white matter abnormalities, heterotopia. Neurons have an atypical shape.
- Clinical picture: epilepsy, mental retardation, sometimes hemiparesis and hemianopsia.
- Occurrence in isolation or within genetic (neurocutaneous) syndromes (hypomelanosis Ito, neurocutaneous melanosis, naevus sebaceus syndrome, Klippel-Trenaunay,...).

Bearing cortical dysplasia type 2

- Probably the most common anomaly demonstrated in patients with refractory focal epilepsy.
- Findings on the brain: abnormal balloon cells, disturbed organization of cortical layers, increased astrocytes. Most often in pericentral areas and frontally.
- Occurrence in isolation or in patients with tuberous sclerosis .

Focal cortical dysplasia type 2 with neoplastic changes

Neurocutaneous syndromes

Sturge-Weber syndrome

Soubor:Tuberoese Sklerose 1J T2 axial2.png	Soubor:Hippel Lindau.gif	Soubor:Sturge-Weber CT.jpg
MRI mozku zobrazující subkortikální a subependymální hamartomy u pacienta s **tuberózní sklerózou**; T2-vážení, axiální řez mozkem.	Typická distribuce hemangioblastomů CNS u pacienta s **Von Hippelovou-Lindauovou chorobou**.	CT mozku zobrazující subkortikální kacifikace bílé hmoty u dítěte se **Sturgeovým-Weberovým syndromem**.

Disorders of cell migration and cortical organization

During brain development, neurons migrate from the germinal matrix to the cortex, and then their spatial arrangement and interconnection ("organization") occurs. These processes can be disturbed by endogenous (hereditary) and exogenous influences (intrauterine infections, toxins, bleeding).

Lissencephaly

Lissencephaly or "smooth brain" is a malformation in which the gyrification is completely smoothed (agyria) or only thickened, with flat and thickened gyri (pachygyria). Lissencephaly is often accompanied by heterotopia, passive enlargement of the ventricles and dysplasia of the corpus callosum. Classic lissencephaly is associated with mutations of the LIS I gene (17p13.3) or the DCX gene (locus Xq22.3). The clinical picture usually includes disturbances of vital functions, epileptic seizures (especially infantile spasms) and psychomotor retardation of various degrees.

Miller-Dieker syndrome (MDS)

- Clinical picture in newborns: low birth weight, feeding problems, frequent respiratory infections.
- Neurological picture: abnormal muscle tone (hypo- or hypertonus), psychomotor retardation, development of convulsions in infancy.
- Findings on the brain: agyria, sometimes calcifications are present.
- Typical phenotype: microcephaly, bitemporal cranial narrowing, high forehead, epicanthas, short nose with anteverted nasotrils, thin upper lip, dysplastic auricles, small chin.
- Other associated abnormalities: polyhydramnios, sacral sinus, heart defects, joint contractures, cryptorchidism in boys.
- Genetics: deletion or microdeletion of chromosome 17p13.3; LIS1 gene – has a regulatory function in the process of neuronal migration.

Isolated lissencephaly-sequence (ILS)

- Clinical picture: convulsions from an early age, delay in psychomotor development.

- Findings on the brain: a combination of agyria, pachygyria.
- Genetic background: deletion or microdeletion of chromosome 17p13.3; disruption of the LIS1 gene, which has a regulatory function in the process of neuronal migration.

X-linked lissencephaly

- It belongs to the syndrome X-SCLH/LIS (subcortical laminar heterotopia/lissencephaly).
- Phenotype in hemizygous boys: lissencephaly, epileptic seizures.
- Phenotype in heterozygous girls: subcortical striated heterotypy ("double cortex"), variously expressed mental retardation, epilepsy.
- Genetic background: deletion Xq22.3-q23, or more rarely balanced translocation X,2(q22,p21); doublecortin gene disorder, which has a regulatory function in the process of neuronal differentiation and migration.

Walker-Warburg syndrome (WWS)

- Clinical picture: congenital muscular dystrophy (with elevated CK and myogenic findings on EMG), eye abnormalities (retinal dysplasia, microphthalmia, colobomas, cataracts, glaucoma), cleft palate and lip, small penis, cryptorchidism, severe psychomotor retardation.
- Findings on the brain: "cobblestone" lissencephaly (lissencephaly with the appearance of cat heads or paving stones); absence of any cortical organization; hydrocephalus.
- Genetic basis: mutation of chromosome 9q34.1.

Gray matter heterotopia

Gray matter heteroopia is defined by the presence of clusters of normal neurons in an unusual location due to impaired migration of neurons from the germinal matrix to the cortex. It can be focal (typically subcortical or subependymal = periventricular) or diffuse (typically leptomeningeal or periventricular). Heterotopia very often occurs together with other anomalies, such as Arnold-Chiari malformation, corpus callosum dysgenesis, polymicrogyria, schizencephaly. Focal heterotopias are not a rare finding in children with certain congenital metabolic disorders that negatively affect brain development already intrauterine (e.g. nonketotic hyperglycinemia , glutaric acidemia , Zellweger syndrome , neonatal adrenoleukodystrophy).

Bilateral periventricular nodular heterotopia

- X-linked disease, rare in boys.
- Findings on the brain: nodular heterotopia of gray matter lining the lateral cerebral ventricles and protruding into their lumen.
- Clinical picture (women): epileptic seizures, mostly without neurological deficit.
- Clinical picture (hemizygous boys): combination with other anomalies, such as hypogenesis of the cerebellum, short bowel syndrome, syndactyly, frontonasal dysplasia, congenital nephrosis, disorders of hemostasis or development of the vascular system.
- Other associated abnormalities: persistent ductus arteriosus, coagulopathy, skeletal dysplasia.
- Genetic background: Xq28 mutation; disruption of the FLN1 gene, which encodes the protein filamin 1, which is important in the regulation of neuronal migration.

Polymicrogyria

Polymicrogyric cortex has an abnormal arrangement and stratification of cell layers, but is not excessive. The gyres are small, as if "baked", with shallow grooves. The image of polymicrogyria can resemble pachygyria on MRI. The polymicrogyric cortex has a normal width, its border with the white matter is uneven, abnormal gyri are visible, areas of gliosis in the adjacent white matter and enlarged subarachnoid spaces above the dysplasia. It is most often located in perisylvian and pericentral areas. It can occur focally or diffusely (bilaterally). Bilateral polymicrogyria is a sporadic defect, rarely AR inherited. It can also be caused by intrauterine CMV infection. It can also be part of the bilateral perisylvian dysplasia syndrome. Focal polymicrogyriais a very common cause of hemiparetic DMO.

Microgyria is a malformation of the brain in which the convolutions are reduced and usually supernumerary. It can affect various extensive areas - from one turn (typically the *superior temporal gyrus* in Down's syndrome) to the entire hemisphere (for example, in Arnold-Chiari malformation). It arises from damage to the immature cortex during cell migration (infection, ischemia, etc.

Schizencephaly

Schizencephaly is a brain tissue defect/cleft filled with cerebrospinal fluid, lined by gray matter and extending from the lumen of the lateral ventricle to the convexity of the hemisphere (ependymal surface of the brain through the white matter to the soft membrane), often lined by polymicrogyric cortex. These defects can be only slit-like (closed) or massive, wide gaping. They arise from a defect in a certain section of the germinal layer or from a limited destruction of an immature hemisphere. The cause can be external influences, for example the mother's medication, toxins or vascular causes. The severity of the disability is proportional to the size of the tissue defect.

Pachygyria

Pachygyria (r. *pachys tlusty* , r. *gyros* thread) is characterized by reduced hemispheres with irregular coarse threads.

In Zellweger syndrome , there are areas of micropolygyria and pachygyria on the brain, liver fibrosis and kidney cystosis are part of the defect.

Hydrocephalus group

Dandy-Walker syndrome

The classic Dandy-Walker malformation is defined as aplasia of the cerebellar vermis with a cyst in the posterior cranial fossa that communicates with IV. cerebral ventricle. The posterior cranial fossa is very spacious. More common than "true" Dandy-Walker are its variants, where we find hypoplasia of the vermis cerebella rather than complete aplasia. 90% of children have hydrocephalus .

Arnold-Chiari malformation

Chiari malformation is a heterogeneous group of four congenital anomalies of the cerebellum and brainstem.

1. Chiari malformation type I consists of herniation of the cerebellar tonsil through the foramen magnum into the space of the upper cervical spinal canal. 50-70% of patients have syringomyelia. The malformation is often asymptomatic for a long time, clinical symptoms include headaches in the occipital region, neck pain, sensory disturbances in the upper limbs, vertical nystagmus , scoliosis and manifest myelopathy. The diagnosis is most often established in children older than 2 years, the imaging method of choice is MRI. A surgical solution brings good results, its indication is usually decided by clinical symptomatology.
2. Chiari II (Arnold-Chiari malformation) is characterized by herniation of the vermis cerebellum and brainstem through the foramen magnum accompanied by "knotting" of the cervicomedullary junction. This form appears in patients with meningomyelocele, in 90% we find hydrocephalus. The diagnosis is made in childhood. In children older than 2 years, symptomatology includes apnea (central or obstructive), aspiration, stridor, nystagmus, quadriparesis. Children die from respiratory failure rather than from intracranial hypertension. The treatment is surgery, but the prognosis is not nearly as favorable as for type I.
3. Chiari III represents an encephalocele in the region of the posterior cranial fossa with evasion of the cerebellum, the lower part of the brainstem and IV. chambers.
4. Chiari IV represents cerebellar hypoplasia.

Arachnoid cysts

Arachnoid cysts are collections of MMMs that develop within the arachnoid membrane as a result of its splitting or duplication. True arachnoid cysts are congenital, but may arise secondary to infection or intracranial injury. Arachnoid cysts can increase in size over time, which explains the late manifestation of congenital cysts, but their spontaneous regression is also described. The symptomatology of arachnoid cysts is most often related to the development of hydrocephalus or intracranial hypertension , the suprasellar location of cysts can cause endocrine disorders. Arachnoid cysts are often discovered during the examination of children with headaches, convulsions, macrocephaly or ADHD . Evidence of cysts is best throughMRI with gadolinium. Cysts that cause mass effect or hydrocephalus must be neurosurgically removed.

Diagnostics

- - MRI – the most accurate imaging method.
  - CT, sonography - differentiates only gross morphological changes, has only indicative value.
  - EEG – to determine the severity of the morphological findings.
  - SPECT (single photon emission computed tomography), magnetic proton spectroscopy (1H-MRS), positron emission tomography (PET) – reflect metabolic changes in the dysplastic cortex.
  - Genetic testing.
  - Histology and histochemistry.

Links

Related Articles

- Hydrocefalus (neonatologie)
- Vrozené vývojové vady

References

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