

## CEREBRAL MALFORMATIONS ASSOCIATED WITH MACROCRANIA – CLINICAL AND PARACLINIC DIAGNOSIS

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### Abstract

Precocious determination of positive diagnosis in the presence of macrocrania, confirmed by the increase of the cranial perimeter with more than 2 percentiles and by the dilation of the ventricular system, visualized with the help of ultrasounds.

The study was carried out retrospectively on a one year period (2008) in the Newborn and Infant care Clinique from “Louis Turcanu“ Children Hospital, on a number of 11 hospitalized premature newborn children, selected based on clinical and imagistic criteria.

The incidence of the cerebral malformations was of 1.21 percent, the most frequent malformative types being the craniovertebral dysraphisms: five cases.

Rapid-evolving hydrocephalia was the death cause for the associated cerebral malformations. The most frequent malformative types were the craniovertebral dysraphisms, which presented a complete clinical and imagistic picture.

**Key words:** macrocrania, the craniovertebral dysraphisms, hydrocephalia, premature.

### Introduction

Myelomeningocele represents the most severe form of dysraphism involving the vertebral column and occurs with an incidence of 1/4000 live births.

The cause of myelomeningocele is unknown, but as with all neural tube closure defects, a genetic predisposition exists; the risk of recurrence after one affected child increases to 3-4% and increases to 10% with two previous abnormal pregnancies. Nutritional and environmental factors undoubtedly have a role in the etiology of myelomeningocele as well. Folate is intricately involved in the prevention and etiology of neural tube defects (dysraphism).

This condition produces dysfunction of many organs and structures, including the skeleton, skin, and gastrointestinal and genitourinary tracts, in addition to the peripheral nervous system and the central nervous system. A myelomeningocele may be located anywhere along the neuraxis, but the lumbosacral region accounts for at least 75% of the cases. The extent and degree of the neurologic deficit depend on the location of the myelomeningocele, as well as the associated lesions. Newborns with a defect in the

midlumbar region typically have a saclike cystic structure covered by a thin layer of partially epithelialized tissue.

Remnants of neural tissue are visible beneath the membrane, which may occasionally rupture and leak cerebrospinal fluid.

### Material and method

The positive diagnosis was confirmed by the increase of the cranial perimeter and by the imagistic methods. The cranial ultrasonography was used as a method for diagnosis and the estimation of prognosis. The MRI was used for diagnosis confirmation and determination of the time of the surgical intervention.

The study was carried out retrospectively on a one year period (2008) in the Newborn and Infant care Clinique from “Louis Turcanu“ Children Hospital, on a number of 11 hospitalized premature newborn children, selected based on clinical and imagistic criteria.

Out of the group of 11 premature newborns with frequent cerebral malformations, 5 cases presented craniovertebral dysraphism, 4 cases presented hydrocephalia secondary to intraventricular hemorrhage, and 2 cases deceased due to hydrocephalia secondary to intraventricular hemorrhage and meningoencephalitis.

The following parameters were observed: gestational age, weight at birth, antepartum and perinatal pathology, increase of the cranial perimeter, dilation of the ventricular system, observed by ultrasonography and MRI.

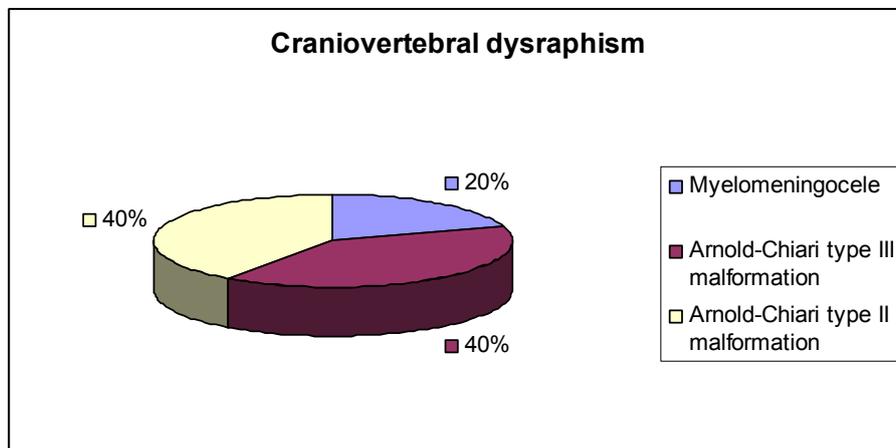
### Results

The incidence of the cerebral malformations was of 1.21 percent, the most frequent malformative types being the craniovertebral dysraphisms: five cases ( 45.45 percent). Thus the following were associated: the myelomeningocele – one case ( 20 percent), Arnold-Chiari type III malformation – two cases ( 40 percent), Arnold-Chiari type II malformation – two cases ( 40 percent) (Graphic 1, fig 1, fig 2.). The corpus callosum agenesis was observed in three of these cases (fig 3.). One case of these presented meningoencephalocele, holoprosencephaly and the Arnold-Chiari type III malformation.

In all of these cases the gestational age varied between 36 and 37 weeks of gestation.

The weight at birth varied between 2470 and 3100 grams.  
Antepartum and perinatal pathologies were present in all cases.

The increase of the cranial perimeter was observed in all cases (Graphic 2).



Graphic 1. Craniovertebral dysraphism.

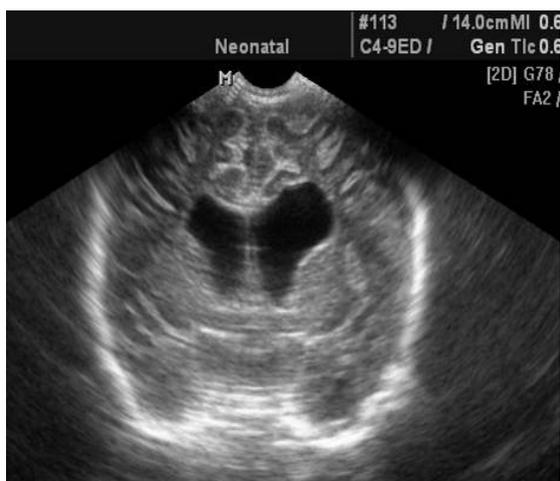


Fig.1. Median coronal scan. Mild hydrocephalus in association with a type II Chiari.

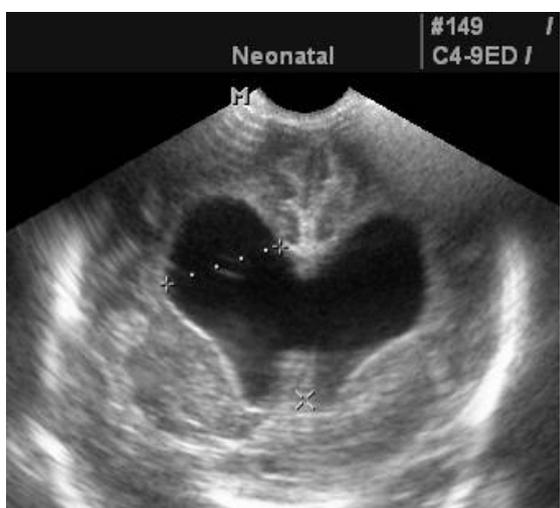


Fig.2. Median coronal scan. Severe hydrocephalus in association with a type II Chiari.

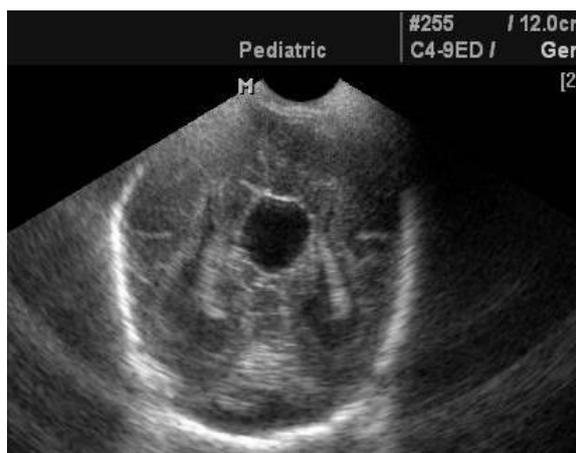
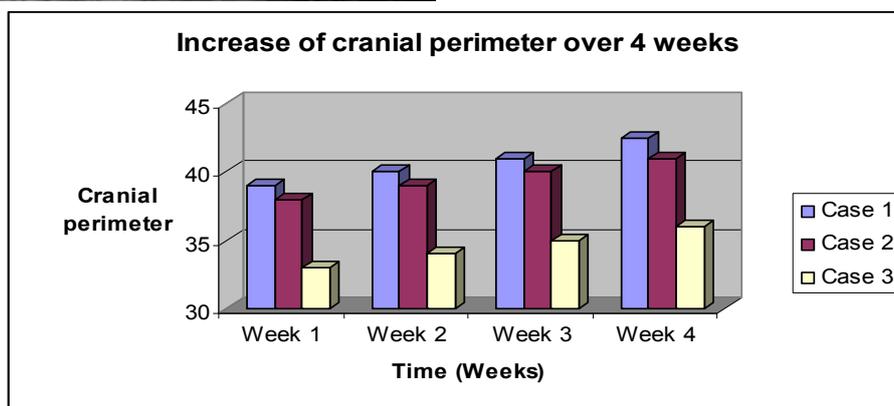


Fig.3 Posterior coronal scan. The corpus callosum agenesis. Hypertrofia of cavum septum pellucidum.



Graphic 2. Increase of Cranial perimeter over 4 weeks.

The clinical signs were the classic ones of hydrocephalia to which the following were associated: neonatal seizures, paresis, inferior member paralysis, respiratory and cardiac rhythm disturbances.

Cerebral imagistics was utilized for the assessment of ventricular dilatation and the degree of compression of the cerebral tissue (fig3).

Although the therapeutic intervention was fast, the ventricular-peritoneal drainage valve was mounted in five cases (fig.4) and the specific anticonvulsive and ethiopathogenic medication was administered, the mortality rate was still high 18,18 percent). Four cases presented a favorable evolution, with the ventricular dimensions stabilized.



Fig.4. Sagittal scan. Severe hydrocephalus. The ventricular-peritoneal drainage valve.

### Discussions

Examination of the infant shows a flaccid paralysis of the lower extremities, an absence of deep tendon reflexes, a lack of response to touch and pain, and a high incidence of

lower extremity deformities (clubfeet, subluxation of the hips).

Infants with myelomeningocele typically have an increasing neurologic deficit as the myelomeningocele

extends higher into the thoracic region. Patients with a myelomeningocele in the upper thoracic or the cervical region usually have a very minimal neurologic deficit and, in most cases, do not have hydrocephalus.

Hydrocephalus in association with a type II Chiari defect develops in at least 80% of patients with myelomeningocele. The possibility of hydrocephalus developing should always be considered, no matter what the spinal level. Ventricular enlargement may be indolent and slow growing or may be rapid, causing a bulging anterior fontanel, dilated scalp veins, setting-sun appearance of the eyes, irritability, and vomiting associated with an increased head circumference. About 15% of infants with hydrocephalus and Chiari II malformation develop symptoms of hindbrain dysfunction, including difficulty feeding, choking, stridor, apnea, vocal cord paralysis, pooling of secretions, and spasticity of the upper extremities, which, if untreated, can lead to death. This Chiari crisis is due to downward herniation of the medulla and cerebellar tonsils through the foramen magnum.

Surgery is often done within a day or so of birth but can be delayed for several days (except when there is a cerebrospinal fluid leak). Evaluation of other congenital anomalies and renal function can also be initiated before surgery. After repair of a myelomeningocele, most infants require a shunting procedure for hydrocephalus. If symptoms or signs of hindbrain dysfunction appear, early surgical decompression of the medulla and cervical cord is indicated.

In utero surgical closure of a spinal lesion has been successful in a few centers. Preliminary reports suggest that there may be preservation of motor function with better motor outcomes as well as a lower incidence of hindbrain abnormalities and hydrocephalus. This suggests that the defects may be progressive in utero and that prenatal closure may prevent the development of further loss of function. In utero diagnosis is facilitated by maternal serum alpha-fetoprotein screening and by fetal ultrasonography.

For a child who is born with a myelomeningocele and who is treated aggressively, the mortality rate is 10-15%. At least 70% of survivors have normal intelligence, but learning problems and seizure disorders are more common than in the general population. Because myelomeningocele is a chronic handicapping condition, periodic multidisciplinary follow-up is required for life. Renal dysfunction is one of the most important determinants of mortality.

Holoprosencephaly is a developmental disorder of the brain which results from defective cleavage of the prosencephalon and inadequate induction of the forebrain structures. The abnormality, which represents a spectrum of severity, is classified into three groups: lobar, semilobar, and lobar, depending on the degree of the cleavage abnormality.

Facial abnormalities including cyclopia, cebocephaly, single central incisor tooth, and premaxillary agenesis are common in severe cases, because the prechordal mesoderm that induces the ventral prosencephalon is also responsible for induction of the median facial structures. A lobar

holoprosencephaly is characterized by a single ventricle, an absent falx, and fused basal ganglia. Care must be taken not to overdiagnose based on ventricular abnormalities alone. Evidence of noncleaved midline brain structures is the critical element.

Affected infants have high mortality rates; some live for years. The incidence of holoprosencephaly ranges from 1/5000 to 1/16000. A prenatal diagnosis can be confirmed by ultrasonography after the 10<sup>th</sup> week of gestation for more severe types. The cause for holoprosencephaly is usually not identified, although there appears to be an association with maternal diabetes.

Agenesis of the corpus callosum consists of a heterogeneous group of disorders that vary in expression from severe intellectual and neurologic abnormalities to the asymptomatic and normally intelligent individual. The corpus callosum develops from the commissural plate that lies in proximity to the anterior neuropore. An insult to the commissural plate during early embryogenesis causes agenesis of the corpus callosum. When agenesis of the corpus callosum is an isolated phenomenon, the patient may be normal, whereas individuals with neurologic symptoms, including mental retardation, microcephaly, hemiparesis, diplegia and seizures, have associated brain anomalies due to cell migration defects, such as heterotopias, microgyria, and pachygyria (broad, wide gyri) in addition to the absence of the corpus callosum. The anatomic features are best depicted on MRI or CT scan and show widely separated frontal horns with an abnormally high position of the third ventricle between the lateral ventricles. MRI precisely outlines the extent of the corpus callosum defect. Absence of the corpus callosum may be inherited as an X-linked recessive trait or as an autosomal dominant trait. The condition may be associated with specific chromosomal disorders, particularly 8-trisomy and 18-trisomy.

Hydrocephalus is not a specific disease; rather, it represents a diverse group of conditions that result from impaired circulation and absorption of cerebrospinal fluid or, in the rare circumstance, from increased production by a choroids plexus papilloma.

Causes of hydrocephalus:

1. Communicating: achondroplasia, basilar impression, benign enlargement of subarachnoid space, choroid plexus papilloma, meningeal malignancy, meningitis and posthemorrhagic.

2. Noncommunicating: aqueductal stenosis (infectious, X-linked), Chiari malformation, Dandy-Walker malformation, Klippel-Feil syndrome, mass lesions (abscess, hematoma, tumors and neurocutaneous disorders, vein of Galen malformation, Walker-Warburg syndrome).

3. Hydranencephaly: holoprosencephaly, massive hydrocephalus and porencephaly.

Obstructive or noncommunicating hydrocephalus develops most commonly in children because of an abnormality of the aqueduct or a lesion in the 4<sup>th</sup> ventricle.

Nonobstructive or communicating hydrocephalus most commonly follows a subarachnoid hemorrhage, which is usually a result of intraventricular hemorrhage in a premature infant.

The clinical presentation of hydrocephalus is variable and depends of many factors, including the age at onset, the nature of the lesion causing obstruction, and the duration and rate of increase of the intracranial pressure. In an infant, an accelerated rate of enlargement of the head is the most prominent sign. In addition, the anterior fontanel is wide open and bulging, and the scalp veins are dilated. The forehead is broad, and the eyes may deviate downward because of the impingement of the dilated suprapineal recess on the tectum, producing the setting-sun eye sign. Long-tract signs including brisk tendon reflexes, spasticity, clonus (particularly in the lower extremities), and Babinski sign are common owing to stretching and disruption of the corticospinal fibers originating from the leg region of the motor cortex. Irritability, lethargy, poor appetite, and vomiting are common manifestations. Serial measurements of the head circumference indicate an increased velocity of growth. A foreshortened occiput suggests Chiari malformation.

Chiari malformation consists of two major subgroups. Type I typically produces symptoms during adolescence or adult life and is usually not associated with hydrocephalus. Patients complain of recurrent headache, neck pain, urinary frequency and progressive lower extremity spasticity. The deformity consists of displacement of the cerebellar tonsils into the cervical canal. Although the pathogenesis is unknown, a prevailing theory suggests that obstruction of the caudal portion of the 4<sup>th</sup> ventricle during fetal development is responsible. The type II Chiari malformation is characterized by progressive hydrocephalus with a myelomeningocele. This lesion represents an anomaly of the hindbrain, probably due to a failure of pontine flexure during embryogenesis, and results in elongation of the 4<sup>th</sup> ventricle and kinking of the brainstem, with displacement of the inferior vermis, pons, and medulla into the cervical canal. Approximately 10 % of type II malformations produce symptoms during infancy, consisting of stridor, weak cry, and apnea, which may be relieved by shunting or by posterior fossa decompression. Plain skull radiographs show a small posterior fossa and a widened cervical canal. CT scanning with contrast and MRI display the cerebellar

tonsils protruding downward into the cervical canal and the hindbrain abnormalities. The anomaly is treated by surgical decompression.

Therapy for hydrocephalus depends on the cause. Medical management, including the use of acetazolamida and furosemide, may provide temporary relief by reducing the rate of cerebrospinal fluid production, but long-term results have been disappointing. Most cases of hydrocephalus require extracranial shunts, particularly a ventriculoperitoneal shunt (occasionally a ventriculostomy suffices). The major complications of shunting are occlusions (characterized by headache, papilledema, emesis, mental status changes) and bacterial infections (fever, headache, meningismus), usually due to *Staphylococcus epidermidis*. With meticulous preparation, the shunt infection rate can be reduced to less than 5%. The results of intrauterine surgical management of fetal hydrocephalus have been poor, possibly because of the high rate of associated cerebral malformations in addition to the hydrocephalus.

Prognosis depends on the cause of the dilated ventricles and not on the size of the cortical mantle at the time of operative intervention, except in cases in which the cortical mantle has been severely compressed and stretched. Hydrocephalic children are at increased risk for various developmental disabilities. The mean intelligence quotient is reduced, particularly for performance tasks, as compared with verbal abilities. Many children have abnormalities in memory function. Visual problems are common (strabismus, visual field defects, optic atrophy with decreased acuity secondary to increased intracranial pressure).

### Conclusions

Rapid-evolving hydrocephalia was the death cause for the associated cerebral malformations. The most frequent malformative types were the craniovertebral dysraphisms, which presented a complete clinical and imagistic picture.

The incidence of the cerebral malformation was 1.21 percent, out of which 45.45 percent were craniovertebral dysraphisms and 36.36 percent were hydrocephalia secondary to intraventricular hemorrhage.

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