PREMATURITY – A RISK FACTOR FOR CEREBRAL PALSY

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Abstract

The progress made in neonatal medicine led to a better survival rate of premature newborns of smaller and smaller gestational ages, which also led to a greater risk of complications such as cerebral palsy, whose incidence is increased to 1.5-5.6 per 1,000 live births among premature infants. The risk factors associated with prematurity in producing cerebral palsy are multiple. Of these, the most common are: corioamniotitis, fetal malpresentations, birth asphyxia, periventricular leukomalacia, intracranial haemorrhage, hypoxic-ischemic lesion. The clinical-etiological forms encountered are spastic hemiplegia, spastic tetraplegia, spastic diplexia and extrapyramidal dyskinesia. Prognosis is severely affected by the presence of epilepsy, deafness, hallucinations, strabismus, mental retardation (30-50%), attention deficit and autism. It is appreciated that 25% of patients with cerebral palsy have walking disorders. Cerebral palsy is considered a serious condition with immediate and long term sequelae that affects quality of life and social integration.

Key words: prematurity, cerebral palsy, risk factors

Introduction

Although the term cerebral palsy (CP) was first described more than a century ago, it still is a a very present subject due to its relatively high incidence among premature newborns [1].

First symptoms in the newborn and infant period are atypical, this is why some authors state that the diagnosis can be established only after the age of 3 (or 5 according to other authors) [2]. This is the case because of the association of also mental retardation in 30-50% of patients with CP and recurrent seizures (even epilepsy) in 50-60% of cases, signs that are not specific for CP [3].

Embriogenesis

The progress made in neonatal medicine led to a better survival rate of premature newborns of smaller and smaller gestational ages, which also led to a greater risk of complications. A rapid review of the principal stages of brain development may lead to a better understanding of the pathogenesis of the disease:

- 3-4 weeks of gestation – neurulation
- 2-3 months of gestation – development of the prosencephalon
- 3-4 months of gestation – neurogenesis
- 3-5 months of gestation – neuronal migration
- From the 5th month of gestation – organization of the cerebellum
- from birth to years – myelination [4].

Epidemiology

A prevalence of 1,5 – 5,6 of 1000 premature newborns [5] and 2 – 2,5 of 1000 term newborns is estimated [6]. Multiple studies show a higher risk of cerebral palsy among premature newborns (37-38 weeks of gestation), but also among postterm newborns (over 42 weeks of gestation) in comparison to full term newborns (40 weeks of gestation) [5]. Taking this into account, studies show that lesions that occur before 20 weeks of gestation can lead to neuronal migration disorders, lesions that occur betwen 26-34 weeks of gestation can lead to periventricular leukomalacia and those that occur between 34-40 weeks of gestation lead to focal or multifocal cerebral lesions [4,6].

The high incidence of CP among preterm newborns can be explained through the circulatory particularities, respectively the termination of the fetal cerebral circulation with periventricular white matter hypoperfusion. This leads to hemorrhagic lesions of the germinal matrix and/or periventricular leukomalacia. It is widely known that at 26-34 weeks of gestation, the periventricular white matter, especially at the exterior angles of the lateral ventricles, is the most vulnerable area [7,8].

Risk factors

From an etiologic point of view there are multiple risk factors associated to prematurity in producing CP. It is considered that 70-80% of cases appear mostly due to association of prenatal conditions and lesions. Studies show a correlation between an Apgar Score <5 and the high incidence of the disease [9].

The most frequently incriminated prenatal risk factors are: previous miscarriages, maternal mental retardation, maternal disease such as seizures, thyroid disorders, hypertension, maternal exposure to toxins (mercury), first trimester bleeding, multiple pregnancies [8,9].

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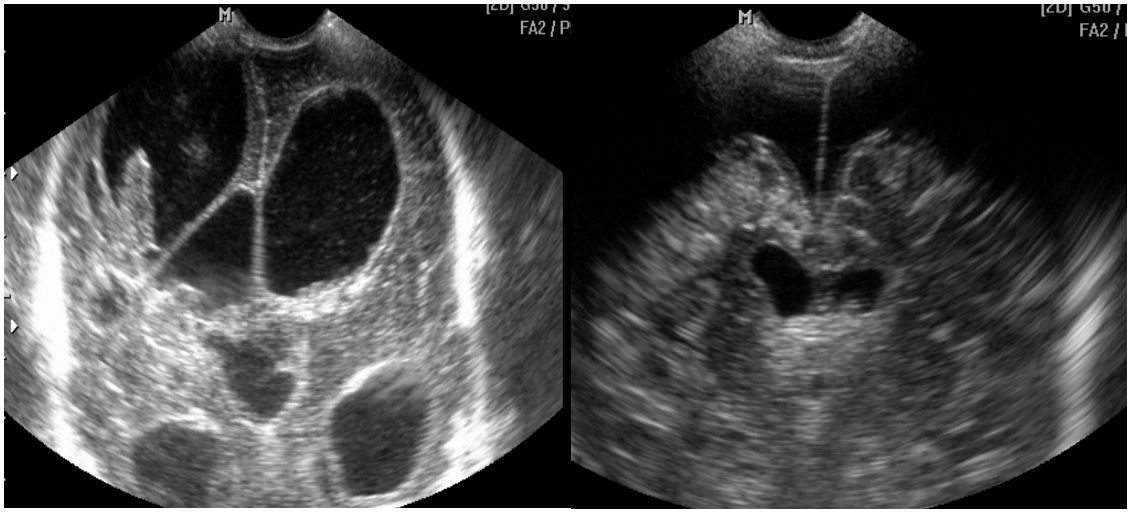

Fig. 1 and 2. Posthemorrhagic porencephaly and cerebral atrophy.

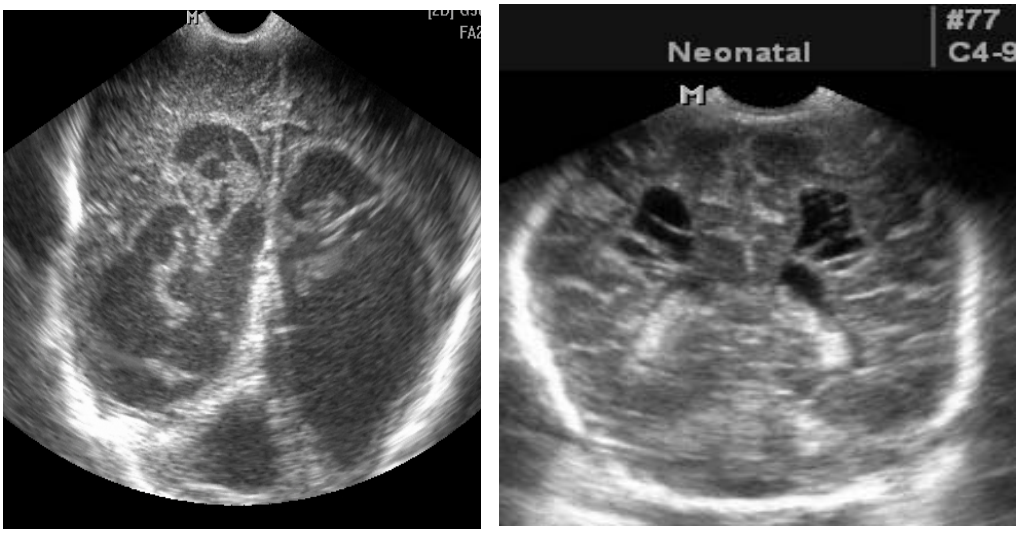

Fig. 3 and 4. Periventricular leukomalacia and severe peri/intraventricular hemorrhage (grade IV)

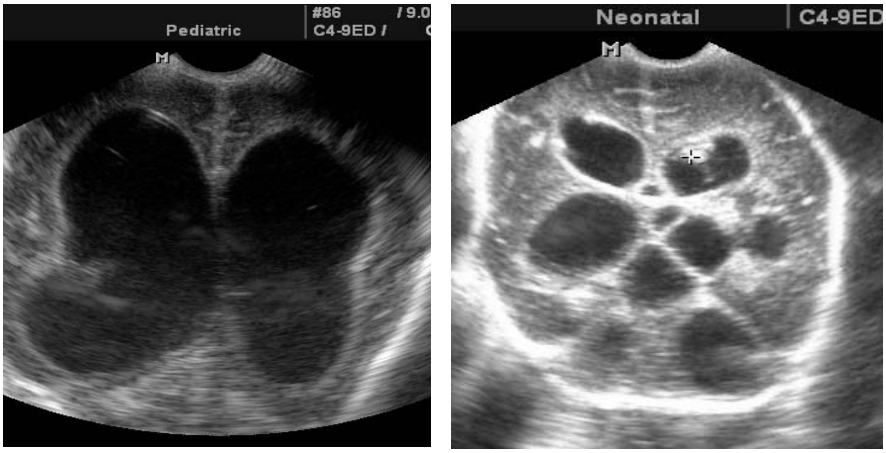

Fig. 5 and 6. Hydrocephaly and multicystic encephalomalacia.

The most common prenatal risk factors are: prematurity, chorioamnionitis, fetal malpresentations, birth asphyxia. In less than 10% of the cases, birth asphyxia cand be considered a cause of CP even if it occurs on a malformative background, growth restriction, severe maternofetal infections. Even in these cases, the classic diagnostic criteria for birth asphyxia have to be present: Apgar Score <4 at 5 minutes, fetal bradycardia, metabolic acidosis, multiple organ failure due to tissue hypoxia and early imaging changes [10].

Postnatal risk factors are also involved in the development of CP: periventricular leukomalacia (preterm newborns), intracranial hemorrhage, hypoxic ischemic lesion (meconium aspiration, pneumothorax), infections (meningitis, encephalitis, severe congential pneumonia), persistent fetal circulation (pulmonary hypertension of the newborn at term), nuclear jaundice [11].

Clinico-etiological forms

Spastic hemiplegia

The most frequent cases are congenital (70 – 90%) and only 10-30% of aquired causes [12].

It can be unilateral (the middle cerebral artery's teritory being the most frequent affected) and affect especially the left side (2 times more frequent than the right). From a neuropathologic point of view this type of lesion is produced on the basis of posthemorrhagic porencephaly (Figure 1), cerebral atrophy (Figure 2) and periventricular leukomalacia of the preterm newborns (Figure 3) [4].

Spastic diplegia

Is a controversial disease from an etiological point of view, especially for newborns at term. Among preterm newborns, periventricular leukomalacia and severe peri/intraventricular hemorrhage (grade IV) are most frequently involved. (Figure 4) [4].

Spastic tetraplegia

A severe form of cerebral palsy, that appears due to prenatal causes in 50% of cases, perinatal in 30% and postanatal causes in 30% of cases [5]. From a neuropathologic point of view the most common causes are: hydrocephaly (Figure 5), diffuse cortical atrophy, multicystic encephalomalacia – isolated or communicating with the ventricular system (Figure 6).

Extrapyramidal dyskinesia

Not so frequent in the common medical practice. Nuclear jaundice was the most frequent cause, but it's incidence decreased significantly. Other causes are: hypoxic-ischemic injury, prematurity, some cerebral degenerative diseases. Some cases caused by high bilirubin concentrations (without nuclear jaundice) are cited in specialized literature [10].

Hypoxic-ischemic lesions of the basal nuclei and talamus are more frequent among the term newborns than premature newborns [4].

Evolution and prognosis

Short term outcome is determined by the complication rate. The most common complications are: gastroesophageal reflux with aspiration pneumonia (sometimes with acute respiratory failure), absent or insufficient sucking and deglutition reflex, chronic constipation (even occlusion), chronic pulmonary disease (BPD – broncho-pulmonary dysplasia) [6].

Long term prognosis is severely affected by the presence of: epilepsy, deafness, halucinations, strabismus, mental retardation (30-50%), attention deficit, autism. 25% of the patients with cerebral palsy have walking disorders and 25% are severely affected and in need of intensive medical care [13].

Conclusions

1. Cerebral palsy is a serious condition, with immediate and long term sequelae that affect quality of life and social integration.
2. It is more frequent among preterm and postterm newborns. The most incriminated risk factors affect these age groups.
3. From a neuropathologic point of view, the most common lesions that cause cerebral palsy are: periventricular leukomalacia, intraparenchymal hemorrhage, cerebral atrophy, porencephaly, and hydrocephaly.

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