I. NEONATOLOGY

PERINATAL LEUKODYSTROPHY CLINICAL CASE

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Abstract

In this study the authors want to present a case of a premature newborn who presented an extremely rare disease for medical practice. Low prevalence of the perinatal leukodystrophy, the difficulty of the clinical diagnosis and the echography resemblance with other diseases of the periventricular white matter is the subjects of this presentation.

Key words: premature newborn, perinatal leukodystrophy, echography.

Introduction

Perinatal leukodystrophy is a rare cerebral disease which is part of the cerebral white matter diseases and in most of the cases starts in prenatal period. In fact this disease represents the progressive distruction of the white matter from the very proximity of the lateral ventricles. It is hard to make the difference from other affections of the white matter, especially the periventricular leukomalacia. Both diseases are characterized by initial increasing of the cerebral echogenity followed, in the next step, by the appearance of cystic formations.

In severe forms, in both affections, the area which results from white matter destruction can be ocuppied in compensation by cerebrospinal fluid leading finally to a hydrocephaly *ex vacuo.*

The progressive degeneration of the cerebral tissue, during the myelinating process is rare. Detection by MRI or transfontanellar ultrasound is difficult because normal echogenity in this period (due to high water content) is hard to differ from the pathological echogenity increasing. Therefore in this situations comparison between clinical data and ultrasound and MRI data is needed.

Case presentation

We present the case of H.A.M., female, 3 weeks old hospitalized in our department for hypotonia, rhythm and respiratory disorders, myoclonia. The new born comes from a pathological pregnancy with repeated addmitances in the hospital for bleedigs and uterine contractions. Gestational age was 31/32 weeks, birth weight 1700 g, Apgar score 7 at 1 minute and 9 at 5 minutes, born by cesarean section for breech presentation.

At birth the new born presented a generally altered state and resuscitation maneuvres were needed, also oxygen input by bag-and-mask ventilation. In early neonatal period the infant presented neonatal adaption disorders.

During the hospitalization she presented generalized hypotonia, myoclonus, nystagmus. Paraclinical investigation emphasized frequent metabolic acidosis, hydroelectrolitical disorders. The serum doseing of the immunoglobulin does not reveal Ig M increasing; genetic investigation-normal karyotype. The transfontanellar ultrasound revealed the presence of inhomogeneous, wide spread, hyperechogene formations, in parietal-occipital area (Fig.1), especially in the right side, with multiple transonic areas between 3/3mm and 11/9mm (Fig.2).

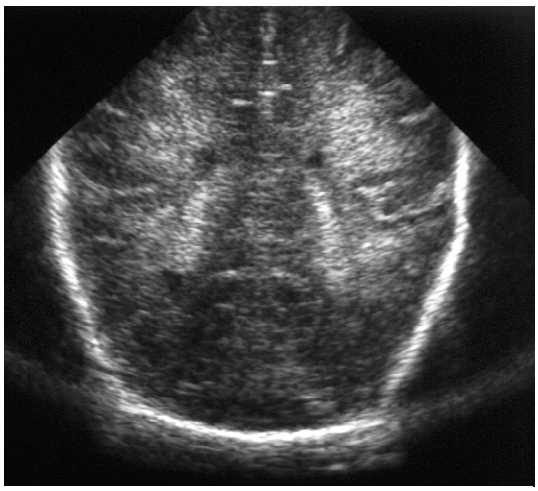

Fig.1. Iinhomogeneous, wide spread, hyperechogene formations, in parietal-occipital area.

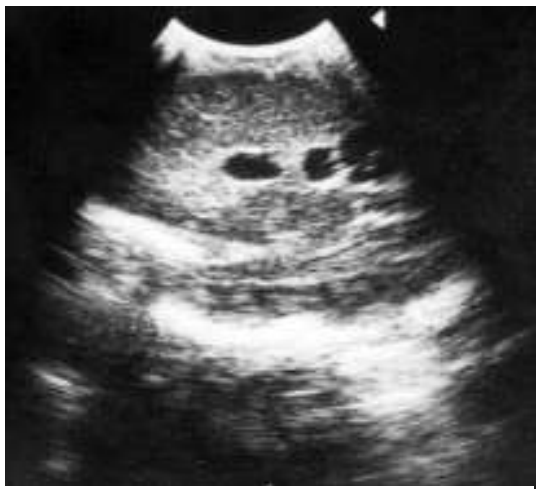

Fig.2. Mmultiple transonic areas between 3/3mm and 11/9mm.

Ventricular system had normal dimensions, with inhomogeneous hyperechogene formations, with transonic content within the bilateral lateral ventricles (Fig.3).

MRI was not performed yet, investigation being refused by the parents.

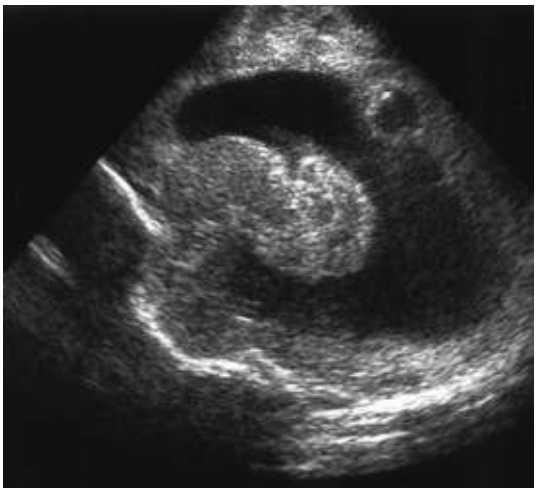

Fig.3. Ventricular system with transonic content within the bilateral lateral ventricles.

Discussion

Echographical changes of the white matter, intense increasing of echogenity, are the result of a dystrophic process of the white matter occurred especially during intrauterine life. There are multiple causes of this process and there are involved genetical, infectious, hypoxic factors, isolated or associated.

Typical placement in the white matter requires differential diagnosis with several other disorders, with early start of the white matter especially periventricular leukomalacia; in perinatal leukodystrophy these echographic densities (hyperechogenities) are placed under or above the front horns of the lateral ventricles. Typical injuries are bilateral but asymmetrical (they are symmetrical only when associated with a component of focomatosis and glyomatosis). This aspect is extremely rare in periventricular leukomalacia where the typical placement of the injury is in the very proximity of the lateral ventricles walls or at the level of lateral ventricles external angles. Another different element is the persistence of the hyperechogene injuries: in perinatal leukodystrophy the stage of the hyperechogenities lasts for month while in periventricular leukomalacia lasts 3-4 weeks. Both disorders can determine a ventriculomegaly. Revealing of the fine, granular, inside the injuries calcifications suggests a chronic intrauterine infection which can be the base of the disorder (more frequent periventricular leukomalacia, extremely rare perinatal leukodystrophy).

Both affections have a resembling clinical symptomatology: hypotonia or hypertonia, seizures, growth disorders. Therefore certain establishing of the diagnosis is difficult in the clinical stage. In the case we present the prenatal antecedents and the clinical signs led us to neurological disorder. The presence of the intense hyperechogene injuries above the lateral ventricles, the persistence of this formation also hyperechogene for a period bigger than two month led us to the suspicion of perinatal leukodystrophy.

In the literature there are presented some series of myelinating disorders (leukodystrophies), which are hard to differ, based on the clinical and imagistic data, both between themselves and from periventricular leukomalacia. Generally leukodystrophies are: lysosomal storage diseases, peroxisomal disorders and diseases caused by mitochondrial dysfunction.

Lysosomal storage diseases are characterized by accumulation in the lysosomes of several substances. Based on clinical and imagistic signs the following affections can be considered as differential diagnosis in our case:

- Krabbe disease is an autosomal recessive disorder caused by a deficiency of galactocerebroside β-galactosidase, an enzyme that degrades cerebroside, a normal constituent of myelin. The infantile forme manifests a hyperirritability, increased tonus of muscle, myoclonus, opisthotonus and nystagmus.The disease is rapidly progressive and fatal. Hyperechogene injuries are initially seen in the area of thalamus and caudate nucleus, symmetrically, and then they spread in the periventricular white matter.
- Mucopolysaccharidosis is caused by a defficiency of the various lysosomal enzymes involved in the degradation of glycosaminoglycans. Clinically and imagistically occur various degrees of hydrocephalus, atrophy and white matter changes.

The second big category of leukodystrophies is peroxisomal dysfunctions. Differential diagnosis in our case can be Zellweger syndrome named also cerebrohepatorenal syndrome, which is an autosomal recessive disorder caused by multiple enzyme defects and characterized by

neurological syndrome (hypotonia, psychomotor retardation, craniofacial dysmorphism, liver dysfunction with jaundice and cyst formations placed in renal cortical and cerebral white matter).

Leukodystrophy caused by mitochondrial dysfunctions is the third category involved in differential diagnosis of the perinatal leukodystrophy (or possible etiology). Therefore from this category we can discuss the Leigh syndrome or the subacute necrotizing encephalomyelopathy. Clinically it apears with hypotonia, psychomotor deterioration, swallowing difficulties and ataxia. Ultrasonographic hyperechogenity can be identified in early stage in the area of caudate nucleus and putamen while in the late stages hydrocephaly occurs associated with persistence of the hyperechogenic formations in the striated area.

Mitochondrial encephalopathy was met at the children with neonatal progeria syndrome (Wiedemann-Rautenstrauch): neurological injuries with antenatal debut and manifest with progressive and generalized ventriculomegaly determining degenerescence of the white matter.

Other affections which has to be differentiate with the present case are: Aicardi-Goutieres Syndrome - is a clinical entity which contains leukodystrophy with strio-cerebeloase calcification and subependymal cyst; Alexander disease with early debut manifested by macrocefaly, psychomotor retardation and seizures. Echogenity is placed mostly in the white matter of the frontal lobe.

As mentioned leukodystrophy can occur as a result of a neonatal asphyxic affection and also as a result of a genetic and metabolic disease. It is difficult to make a difference between these two types but the early start in the early neonatal period, clinical symptomatology (not so suggestive) and imagistic data led us to the perinatal leukodystrophy diagnosis from hypoxic cause. Genetic and metabolic investigations could certainly decide the diagnosis but besides the karyotype – normal - they were not performed. Besides the above mentioned regarding the placement and intensity of the lesions, we can consider that the injury from leukodystrophy is deep and affects even the middle, the gyral center while in periventricular leukomalacia there is no affection of the gyral middle of the periventricular white matter.

Conclusions

- Perinatal leukodystrophy from hypoxic cause is part of the cerebral white matter diseases with early start, most of the times in antenatal period.
- Leukodystrophy (progressive destruction of the white matter) is difficult to differentiate from the periventricular leukomalacia and also from the other types of leukodystrophia, especially in genetic and metabolic diseases.
- Differentiating from periventricular leukomalacia is made on the base of the echogenity placement, hyperechogene injury spreading and the length of the hyperecogenity stage, appearance of the cyst formations and their long persistence.

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