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Periventricular Leukomalacia: Overdiagnosis and Differential Diagnosis

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Abstract

In the medical literature and practice occurs overdiagnosis of the PVL, assignment to it of various forms of destruction of the white matter of the cerebral hemispheres of the brain. Three types of existence "cerebral leukomalacia": 1) periventricular leukomalacia (PVL), 2) diffuse leukomalacia (DFL) and 3) subcortical leukomalacia (SCL). In addition, there is a multicystic encephalomalacia (ME) - hypoxic damage and infectious origin with the capture of the cortex and subcortical brain structures. There are white matter lesions without its full Necrosis - telencephalic gliosis (TG). We must also bear in mind the existence of periventricular pseudocysts, periventricular hemorrhagic infarction and intracerebral hemorrhage in the white matter of the cerebral hemispheres of the brain. This is the primary group of hypoxic-ischemic lesions of the white matter of the brain hemispheres Clinicians should not overestimate the findings of neuroimaging experts who are not 100% correct.

Keywords: *Periventricular Leukomalacia; Classification; Newborn; Diffuse Leukomalacia; Hypoxic-Ischemic Lesions; Differential Diagnosis; Overdiagnosis of HVL*

Abbreviations

PVL: Periventricular Leukomalacia; DFL: Diffuse Leukomalacia; SCL: Subcortical Leukomalacia; ME: Multicystic Encephalomalacia; TG: Telencephalic Gliosis; MRI: Magnetic Resonance Imaging; CP: Cerebral Palsy

Periventricular leukomalacia (PVL) is one of the most well-studied forms of white matter damage in newborn babies, has its own etiology, pathogenesis, morphology and clinic. Special monographs devoted to PVL have been published [1,2]. The history of PVL study [2] began with the studies of J. M. Parrot, which published the first drawing of PVL in 1873, continued in the works of German authors called "encephalodystrophy" and other scientists called "necrosis" and "infarction" of white matter of the brain, and then established itself in works of French, American, Russian, Japanese and other scientists called "periventricular leukomalacia". Morphologists have developed a classical understanding of PVL, according to which PVL is ischemic necrosis of periventricular zones of white substance of cerebral hemispheres. For the "classical" PVL are characterized by 2 main features: 1) the presence of foci of necrosis (often coagulating) white matter of the brain, 2) the location of foci in the periventricular zones of the lateral ventricles. However, in recent decades, the blurring of classical ideas about PVL has begun, due to poor knowledge of the various forms of lesions of the white matter of the cerebral hemispheres. The existing neurosonographic classification of De Vries L.S. (1992), in which 4 stages of PVL is isolated, plays its negative role in this destruction of classical ideas about PVL [3,4]. In fact, all authors of scientific papers that rely on this classification in their clinical studies examine not only PVL, but also other lesions of white matter in the brain, that is, they are engaged in overdiagnosis of PVL. This classification leads to overdiagnosis of PVL. The first stage in the classification (increased echogenicity (echodencity, echotexture), existing for more than 7 days) does not at all indicate the presence of necrosis in the brain substance, with PVL may be absent. Stage 4 (common cysts, including subcortical) does not belong to PVL, as it is characteristic for other forms of the white matter damage of the brain - subcortical leukomalacia (SCL) and diffuse leukomalacia (DFL).

The results of numerous own studies of deceased fetuses and newborns [5,6] allow us to conclude about the existence of 3 types of "cerebral leukomalacia": 1) PVL, 2) DFL and 3) SCL. These are different forms of damage to the white matter of the brain, having a different etiology, pathogenesis, clinic and prognostic consequences. For DFL, widespread necrosis of white matter of the brain, which periventricular and central parts of the cerebral hemispheres are involved with the transition to subcortical areas. All the diffuse cystic lesions of the white matter of the brain described in the literature, located predominantly in the central regions of the centrum semiovale and extending even into the subcortical regions, are not PVL, but DFL [7-9]. DFL is more often observed in deeply premature infants and children with extremely low body weight (less than 1000g). Classical PVL is more typical for "late premature babies" [10], with a birth weight of 2001 - 2500g; in this weight group, the PVL frequency was 31.6%, and in the group of the dead weight of 1001 - 1500g - 13.3% [1,2,6]. M. Dambska [11] rightly notes that there are two samples of lesions of white matter in the brain: 1) classical periventricular coagulation necrosis and 2) diffuse periventricular colliquative necrosis of the centrum semiovale. PVL and DFL are different forms of lesions of white matter in the brain. For DFL colliquated necrosis with common cysts of the centrum semiovale is characteristic, and for PVL - coagulation necrosis and small cysts in periventricular areas of the cerebral hemispheres. Only with severe lesions these cysts can spread to the central parts of the white matter of the cerebral hemispheres. In addition, the classification in question may include another independent hypoxic-ischemic brain lesion – multicystic encephalomalacia (ME) [6,12].

The development of modern nosology of cerebral lesions in the perinatal period should be accompanied by the isolation of individual forms of lesions, but the use of this classification leads to the fact that virtually any lesions of the white matter of the large hemispheres by neurosonographic researches experts will refer to PVL, which is incorrect. PVL, DFL, SKL and ME lead to infantile cerebral palsy (CP), but this does not mean all these lesions are PVL. Magnetic resonance imaging (MRI) is considered more accurate in the diagnosis of the PVL, however, in children with Stage 1 MRI, diagnosed with MRI, normal neuropsychiatric development is observed [13]. In large groups of studies, it was found that children with the first stage of PVL in 85% of cases have no clinical and neurological consequences [14]. These data also indicate the overdiagnosis of PVL in these childrens, since PVL is characterized by the appearance of foci of necrosis with the destruction of nerve fibers, which necessarily leads to clinical consequences. A number of neuroimaging specialists understand responsibility for the correct diagnosis of brain damage, avoid overdiagnosis, write about insufficient information in MRI [15], or simply write about cystic or non-cystic forms of white matter lesions of the brain [16].

There are numerous publications about the antenatal detection of cysts in the brain hemispheres [17-19] with their erroneous reference to PVL. Identified cysts could be attributed to ME or other forms of brain damage. PVL rarely occurs in childbirth [2], but there is no evidence of antenatal origin of PVL. If, however, any damage to the brain, any cysts, is attributed to PVL, then this is an example of a typical overdiagnosis of PVL. It is very likely that the cysts found in the lateral corners of the anterior horns of the lateral ventricles [19] are subependymal pseudocysts, another type of brain damage in fetuses and newborns [3,6], which is not related to PVL.

Some authors in their studies rightly come to the conclusion that there are lesions of white matter in the brain without cysts and without glial foci [18,20], but for some reason they are referred to PVL, which contradicts the essence of this brain injury. Without necrosis, there is no PVL. Therefore, it is necessary to recognize the existence of other lesions of the white matter of the brain, to develop a new nosology, but not to refer them to PVL. This is a white matter damage to the brain, like telencephalic gliosis (TG) [6], which other authors call "perinatal telencephalic leukoencephalopathy" and "white matter gliosis" [21-24]. TG leads to a cognitive deficit, can be accompanied by some atrophy of white matter in the brain, an expansion of the lateral ventricles of the brain, does not lead to CP. The isolation of TG is extremely important, as some clinicians believe that PVL can exist without brain necrosis, and PVL is defined as "necrosis and/or brain gliosis" [20], which cannot be accepted. Without foci of necrosis (cysts, gliosis scar), there is no PVL. Gliosis usually exists around the foci of PVL (the so-called diffuse PVL component), accompanied by PVL. Gliosis exists around any other foci (inflammation, trauma, hemorrhage), accompanies them. If, however, gliosis exists without necrosis, then this brain damage, other than PVL, is TG. It is extremely important to distinguish nosological forms of lesions of the white matter of the cerebral hemispheres, among which PVL is one of the forms. Hypoxic-ischemic damage to white matter in the brain can be limited to the damage to glial cells, especially oligodendrocytes,

by the so-called "incomplete necrosis," and can lead to the destruction of axons and vessels (complete necrosis). For PVL, SKL and DFL, complete necrosis, paresis and paralysis are characteristic, and for TG - incomplete necrosis, the syndrome of minimal brain dysfunction and cognitive deficits.

Place PVL among other brain lesions can be represented in the following table.

Complete necrosis of white matter of the cerebral hemispheres	Cerebral Leukomalacia	Periventricular leukomalacia
		Diffuse leukomalacia
		Subcortical leukomalacia
Incomplete necrosis of white matter in the cerebral hemispheres	Telencephalic gliosis	
Necrosis of the cortex, white matter, subcortical formations	Multicystic encephalomalacia	
Intrauterine malformation	Subependymal pseudocyst	
Circulatory disorders	Periventricular hemorrhagic infarction	
	Intracerebral hemorrhage	
	Cerebral infarction	

Conclusion

In the medical literature and practice, there is the overdiagnosis of PVL, attributing to it various forms of damage to the white matter of the cerebral hemispheres. In the International Statistical Classification of Diseases 10th Revision there is no PVL, but there is "cerebral leukomalacia" (code P91.2). In our opinion, this general concept does not clearly reflect the nature of brain damage. Among cerebral leukomalacia, at least three forms can be distinguished: 1) PVL, 2) SCL and 3) DFL. For the "classical" PVL are characterized by 2 main features: 1) the presence of foci of necrosis (often coagulating) white matter of the brain, 2) the location of foci in the periventricular zones of the lateral ventricles. For DFL, widespread necrosis of white matter of the brain, which periventricular and central parts of the cerebral hemispheres are involved with the transition to subcortical region. PVL and DFL are different forms of lesions of white matter in the brain. In addition, there are lesions without complete necrosis of the brain, which we call "telencephalic gliosis", and other authors - "perinatal telencephalic leukoencephalopathy" or "gliosis". In differential diagnosis, it is also necessary to take into account the existence of such lesions of white matter in the cerebral hemispheres, such as ME, periventricular hemorrhagic infarcts, intracerebral hemorrhages and subependymal pseudocysts. Clinicians should not be overestimated data imaging studies. Clinicians do not need to overestimate the findings of neuroimaging studies and the conclusions of specialists.

Conflicts of Interest

Do not exist.

Financial Interest

Do not exist.

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