

TISSUE DYSPLASIAS OF BRAIN HEMISPHERES OF PREMATURE FETUSES AND NEWBORNS IN BELARUS

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ABSTRACT

In 20 years after the Chernobyl disaster problems of low dose radiation are persistent in Belarus. Radio induced genes mutations of somatic cells and gametes can lead to different pathological conditions e.g. tissue dysplasias. The aim of the present study was a morphological description and systematization of tissue dysplasias of brain hemispheres of premature fetuses and newborns with gestational age 22-36 weeks. Paraffin sections of citoarchitectonical fields 4, 10 and 17 were stained with haematoxylin and eosin, LFB, antibodies to β III-tubulin and GFAP. Tissue dysplasias of brain hemispheres were characterized and systematized. It was established that tissue dysplasias of brain hemispheres were divided into 3 groups: heterotopias, dissynchronias and hypoplasia. It was shown that some of them can be developed in postnatal period. A new form of neocortical tissue dysplasia was revealed – «honeycomb structure» of neocortex which is characterized of irregular distribution of neurons and glia in the cortical plate.

Keywords: Brain Hemispheres, Tissue Dysplasias, Newborn

Introduction

In 20 years after the Chernobyl disaster problems of low dose radiation are persistent in Belarus. Because of the Chernobyl disaster the fouling factor of our non-nuclear country was exceeded twice as much as the fouling factor of both Ukraine and Russia. The almost whole territory of Belarus was contaminated, and every inhabitant was under an influence of radiation of different intensity.

Unlike established clear patterns of correlations between high doses of radiation and pathophysiological responses, the results of influence of low doses of radiation, as a rule, do not appear immediately. Pathophysiological effects of low doses of radiation accumulate gradually and finally manifest it by clinical symptoms after a few years and even decades. It was established that

- the minimal threshold of doses of radiation which can not cause gene mutations is absent;

- primary damage of genes can be increased by the reduplication mechanism of vital functions of gene structures.

Effects conditioned by the combination of influence of low doses of radiation and other anthropogenic factors can developed faster and can be more prominent. Radio induced gene mutations of gametes can lead to different pathological conditions in descendants, including metabolic and immune diseases, congenital malformations e.g. tissue dysplasias. Tissue dysplasias are etiological and morphological heterogeneous congenital malformations of development of cells and tissues. Tissue dysplasias are divided into two main groups: Geterotopias – displacement of cells from the place of its normal localization within the edges of one organ (e.g. brain); Disssinchronias – congenital abnormalities of the rate of tissue development with anomalies of cell differentiation and maturing. The biological role of tissue brain dysplasias is very wide – from the absence of an influence on the psychomotor status of a person to the development of different brain diseases e.g. epilepsy.

This study is the part of the large long-time comparative investigation of congenital malformations in children born in Belarus before and after Chernobyl disaster.

The aim of the present study was a morphological description and systematization of tissue dysplasias of brain hemispheres of premature fetuses and newborns at the gestational age of 22-36 weeks.

Material and Methods

Clinical details. Post-mortem brains of 72 newborns at the gestational age of 22-36 weeks suffering from IVH grade 1 (n = 23), grade 2 (n = 31) and grade 3 (n = 18) were examined. Brain malformations, intracranial birth injures and meningoencephalitis were excluded. All newborns were normally formed; their birth weight and birth height fit with standards. There were 56 boys (78.6%) and 66 girls (21.4%) in a group.

For comparison post-mortem brains of 31 normally formed fetuses at the similar gestational age were investigated. The fetuses died from acute asphyxia because of total premature detachment of placenta. IVH grade 1 was revealed in 24 cases, grade 2 – in 7 cases. There were 23 boys (76.7%) and 8 girls (23.3%) in group. IVH grade was diagnosed accordingly criteria of International Nosotaxy-12:

Grade 1 – subependimal hemorrhages;

Grade 2 – subependimal and intraventricular hemorrhages;

Grade 3 – subependimal, intraventricular and periventricular hemorrhages.

All autopsies were realized from 2001 to 2005 year. The delay between death and post-mortem examination was 15.3 ± 0.9 hours.

Traditional histological methods. Formalin-fixed and paraffin-embedded sections of the citoarchitectonical fields 4 (motor cortex center), 10 (cortex center higher nervous activity), 17 (visual cortex) and brain periventricular areas stained with haematoxylin and eosin, Nussle stain and luxol fast blue – modified Kluver's method.

Immunohistochemistry. Immunohistochemistry was performed with primary antibodies against β III-tubulin – marker of both immature and mature neurons and glial fibrillary acid protein (GFAP) – marker of astroglia.

The results are presented as the mean \pm standard error in mean. For statistical analysis the program package STATISTICA 6.0 was used. The results of statistical tests were only recorded as significant if $p < 0.05$.

Results and Discussion

Based on the results of investigations the systematization of tissue brain hemispheres dysplasias adapted to the perinatal and neonatal periods of ontogenesis has been developed.

Systematization of tissue brain hemispheres dysplasias

➤ **Neocortex.**

Dissynchronias: Lamination delay (Persistence of the cells complexes; Non-division a layer into sub layers; Delay of the neocortex lamina growth); Delay of neurons maturing; Neurons with two nucleuses; Embryonic dividing cells; Persistence of the granular subpial layer; Accelerated reduction of the granular subpial layer; Persistence of the Cajal-Retzius cells; Accelerated reduction of the Cajal-Retzius cells; Myelinization delay.

Heterotopias: Heterotopias of neurons within the limits of cortical plate; Leptomeningeal heterotopias of neurons; Heterotopias of single pyramidal neurons or/and their groups in white matter (more mature heterotopic pyramidal neurons in white matter in compare with pyramidal neurons of the 5 layer of the corresponding cytoarchitectonic field; dystopic gyri); Abnormalities of the neurons orientation; Papillae of Retzius – protrusions of the 3 layer to the molecular layer; Irregular distribution of the neurons and glia in the neocortical area with abnormalities of cytoarchitecture and lamination in the form of «honeycomb structure» of the citoarchitectonical field.

➤ **White matter.**

Dissynchronias: Myelinization delay.

Hypoplasia.

➤ **Ependyma of the lateral ventricles and germinative matrix.**

Heterotopias: Subependymal pseudoglands; Protrusions of the germinative matrix in the lateral ventricles cavity.

Dissynchronias: Persistence of the polystichous ciliated epithelium; Delay of the germinative matrix reduction (Delay of the cells reduction; Delay of the vessels reduction); Acceleration of the germinative matrix reduction.

Distribution of the tissue brain hemispheres dysplasias of fetuses and newborns is presented in the table.

Frequency of the tissue brain hemispheres dysplasias of fetuses and newborns at the gestational age of 22-36 weeks

Dysplasia	Number of observations, % (X±m%)	
	Fetuses (n=31)	Newborns (n = 72)
Neurons with two nucleuses	16 (51,0±9,0)	20 (27,8±5,3)*
Embryonic dividing cells	3 (9,7±5,3)	3 (4,2±2,4)
Persistence of the granular subpial layer	–	4 (5,6±2,7)
Accelerated reduction of the Cajal-Retzius cells	–	10 (13,9±4,1)
Leptomeningeal heterotopias of neurons	–	1 (1,4±1,3)
Heterotopias of pyramidal neurons of 5 th layer in 4 th layer.	17 (54,8±8,9)	35 (48,6±5,9)
Heterotopias of pyramidal neurons of 5 th layer in 6 th layer.	11 (35,5±8,6)	18 (25,0±5,1)
Heterotopias of pyramidal neurons of 5 th layer in 2 th layer	–	5 (6,9±3,0)
Heterotopias of single pyramidal neurons in white matter	28 (90,3±5,3)	65 (90,3±3,5)
Abnormalities of the orientation of the neurons of 5 th layer	23 (74,2±7,9)	56 (77,8±4,9)
Papillae of Retzius	13 (41,9±8,9)	20 (27,8±5,3)
«Honeycomb structure» of the citoarchitectonical field	8 (25,8±7,9)	8 (11,1±3,7)
Combination of papillae of Retzius and «honeycomb structure» of the citoarchitectonical field	8 (25,8±7,9)	8 (11,1±3,7)
Subependymal pseudoglands	7 (22,6±7,5)	36 (50,0±5,9)
Protrusions of the germinative matrix in the lateral ventricles cavity	–	12 (16,7±4,4)*
Delay of the germinative matrix reduction	–	9 (12,5±3,9)
Acceleration of the germinative matrix reduction	–	7 (9,7±3,5)

* p<0,05

A new form of neocortical tissue dysplasia was revealed – the «honeycomb structure» of neocortex which is characterized of irregular distribution of neurons and glia in the cortical plate (Fig. 1). A permanent combination of the «honeycomb structure» and papillae of Retzius is the indication of the common cause of their pathogenesis.

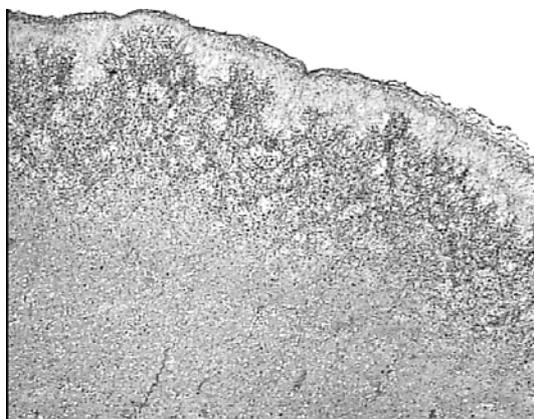


Fig. 1. *The «honeycomb structure» of neocortex and papillae of Retzius*

It was established that in premature newborns some heterotopias (leptomeningeal heterotopias, subependymal pseudoglands, protrusions of the germinative matrix in the lateral ventricles cavity), dissynchronias and hypoplasia can develop postnatal.

Obtained results are evidence of high frequency of tissue brain hemispheres dysplasias in fetuses and newborns. Many endogenous (gene mutations) and exogenous (hypoxia, infections, toxins, low dose radiation) factors to a variable degree influence on pre-natal ontogenesis of embryo and fetus. Moreover, brain of premature newborn has a nonoptimal for postnatal life structural and functional organization and also heightened sensibility to different effects. Pathological, adaptive and compensatory processes in the newborn's central nervous system can lead to the development of tissue brain hemispheres dysplasias.

Conclusions

Systematization of tissue brain hemispheres dysplasias is useful for the both practicing physicians and scientists as it leads to a better conceptual understanding of the disorders and their pathogenetic relationships. The systematization can help to describe properties and degree of brain development in both norm and pathology conditions.

The next part of our work will be the investigation of brains of both fetuses and newborns which were born in 1984-1985 years and in 1986-1989 years in Minsk and the Gomel region. We are going to compare the structure and frequency of tissue brain hemispheres dysplasias before and after the Chernobyl disaster and to establish the role of radiation in the development of these malformations.