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[A1]

Malformations of cortical development in children: clinical manifestation, neuroimaging and neuropathology in selected cases

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Cerebral cortical development could be divided in three steps: cellular proliferation, neuronal migration and organization. Based on known pathologic, genetic and neuroimaging features a classification for malformations of cortical development was proposed by Barkovich in 2001, updated in 2005. Malformations of the cerebral cortex development (MCCD) often demonstrate epileptic seizures and delay in psychomotor development. About 20–40% of children with epilepsy are drug-resistant and there is a large paediatric population requiring epilepsy surgery operations.

In our work we performed clinical analysis of 68 children with MCCD treated in our hospital between 2000 and 2006. In our work to consider type of MCCD we used the updated classification scheme proposed by Barkovich et al. We analyzed epilepsy, gestational and perinatal history, initial symptoms, time to establishing full diagnosis and neurodevelopmental/IQ status. In our results we found that despite similar clinical manifestation neuropathological basis could be significantly different and vice versa, children with nearly identical neuropathological findings could have completely different neurological and radiological symptoms. Children with drug-resistant epilepsy are potential candidates for neurosurgical treatment; especially lesionectomies in such cases could be very promising in terms of epilepsy management and quality of life as well.

[A2]

Familial Westphal variant of Huntington's disease. Report of the clinical abnormalities

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Huntington's disease (HD) is the most common autosomal dominant neurodegenerative disease of the central nervous system. The main clinical symptoms in adults are mood changes, choreic movements and progressive cognitive decline. Juvenile HD known as Westphal variant (Wv-HD) presents with significantly different signs characterized mainly by rigidity, myoclonus and seizures often causing diagnostic problems.

We present a patient with Wv-HD in the third generation of women. Our patient, a 24-year-old woman, presented with severe global rigidity, flexed posture,

slight intention tremor of the left extremities, severe speech difficulties recognized as dysarthria and dysphasia, seizures, choreic movements and higher cognitive decline. Her mother and grandmother suffered from juvenile HD and presented with the same symptoms. Analysis of the gene revealed two alleles containing 16 and 70 repeated CAG. Magnetic resonance imaging showed dilatation of the anterior horns of the lateral ventricles, thinned cortical layer of the frontal lobes and small ferrum deposits within basal ganglia.

The reported patient is a very rare case, who presents with typical signs of juvenile HD, but with atypical onset of the disease with choreic movements. Moreover, our report is probably the first description of inherited Wv-HD among three generations of women.

[A3]

Encephalopathy with vanishing white matter

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Introduction: Progressive encephalopathies constitute a heterogeneous group of CNS diseases, with different phenotypic features even in the definite diseases. Except genetically determined disorders with identified mutation and with definite enzymatic block or storage material, there are disorders whose aetiology cannot be found.

The clinical data: the presented patient was a female child of young non-consanguineous parents, with no history of neurodegenerative diseases. Development was affected from early infancy; the girl was able to walk with help when 2 years of age at the bright base. Expressive speech was delayed and deafness was suspected. The first neurological examination when she was 2 years old revealed ataxia; intellectual development was below the normal range. The progressive course of ataxia was accompanied by pyramidal signs, at the beginning left-sided, then generalised with seizures. Microcephaly, dystrophy, bulbar signs, recurrent vomiting developed late in the disease and optic atrophy with maculopathy as well. Death occurred when she was 3 years old due to cardio-respiratory insufficiency in the course of pyelonephritis and sepsis.

MRI: a significant portion of the white matter and especially the frontal hemispheres were involved in the process, hypointensive in T1 time and FLAIR and in part with reticular formation, hyperintensive in T2 time.

EMG: no features of myopathy and neuropathy

Other tests: mitochondrial and peroxysomal disorders were excluded, organic acidoses, protein metabolism disturbances, akantocytosis, adrenoleukodystrophy and storage disorders as well.

Neuropathologic examination: diffuse damage to the white matter with cystic formation. Diagnosis: Childhood ataxia with CNS hypomyelination/vanishing white matter disease (CACH/VWM).

Discussion: Cystic formations of CNS are characteristic for van der Knaap disease (encephalopathy with cerebellar/pyramidal syndrome) with macrocephaly and slow clinical course.

CACH/VWM is diagnosed in the lack of a specific marker, using clinical (acute clinical course, disabled after 2 years of being ill, and death in the first decade of life) and radiological criteria. A helpful tool is MR spectroscopy with the lack of NAA, choline and creatine signal, and the increase of lactate and glucose signal. The cerebrospinal fluid examination revealed increased level of glycine. The disease is genetically heterogeneous; linkage to a region at chromosome 3q27 was found, but routine examinations and prenatal examinations are not available. This familial disease has been known for at least 20 years and has been identified in several populations. However, the most severe course was detected in the Indian population, especially Cree Indians in North America and known as "Cree leukoencephalopathy" with onset between 3 and 9 months and death at about 21 months. In the clinical picture of the described cases ataxia was the most important feature. Hypotonia, seizures, blindness and microcephaly developed later on.

[A4]

Histopathologic features of hemimegalencephaly – a case report

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Hemimegalencephaly is a severe disease of the brain in which one can observe marked enlargement and dysplastic changes in one hemisphere. Clinical signs of the condition are contralateral hemiparesis, severe epilepsy and mental retardation, which are mostly resistant to pharmacotherapy and thus secondarily disabling. Early hemispherectomy can lead to seizure reduction or withdrawal, which can reduce the damage caused by the disease and functional compensation by the next hemisphere.

We present the case of a 5-month-old girl with severe pharmacoresistant epilepsy, who underwent functional hemispherectomy due to a severe case of hemimegalencephaly.

Incomplete resection of the frontal lobe fibres led to seizure replenishment, which led to anatomical hemispherectomy. This committed a seizure withdrawal and partial regain of clinical status.

Pathologic findings revealed disarray of cortical lamination with large bizarre neurons and balloon cells with abundant pale eosinophilic cytoplasm, loss of grey-white matter differentiation, neuronal heterotopia and gliosis.

Hemimegalencephaly may be considered as a diffuse form of focal cortical dysplasia type II.

[A5]

Is focal cortical dysplasia type IIB the focal form of tuberous sclerosis complex?

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Objectives: Focal cortical dysplasia (FCD) type IIB is a malformation of cortical development characterized by presence of balloon cells. These cells share phenotypic features of giant cells found in Tuberous Sclerosis Complex (TSC), but the relationship between FCD type IIB and TSC is not established.

Methods: The panel of antigens, including hamartin, tuberin, mTOR, pS6K, pAkt, pErk, NSE, GFAP and nestin, was studied under the confocal microscope in two FCD IIB and two FCD I cases. The specimens were obtained from patients operated on for intractable epilepsy, who did not manifest clinical symptoms of TSC. Normal brain tissue was used as the control group.

Results: We found loss of tuberin and hamartin expression as well as strong immunoreactivity for mTOR, pS6K, pAkt, and pErk in both FCD type IIB lesions. Cortical balloon cells in these samples were NSE-positive, whereas most subcortical giant cells were labelled with GFAP. In FCD type I and normal brain tissue, tuberin and hamartin were detected, and immunoreactivity for mTOR, pS6K, pAkt, and pErk was subtle. Nestin expression in all samples was weak or absent.

Conclusions: Loss of TSC1 and TSC2 products expression as well as enhanced mTOR pathway immunoreactivity suggest that FCD type IIB may present focal form of TSC.

[A6]

Faulty position of cerebellar cortical neurons as sequel of disturbed neuronal migration

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During normal development of the cerebellum neurons migrate from the place of origin to the place of residence in the correct laminar position within the cerebellar cortex. The cerebellar cortical neurons have dual origin. The young neuronal cells from the ventricular zone migrate in a radial direction to form the layer of Purkinje cells. Another set of neuroepithelial cells migrate along the pial surface to form a secondary germinal matrix, the external germinal (granular) layer. The cells in this layer retain the capacity to divide and many of the daughter cells are destined to form the internal granular layer.

We present a morphological picture of cerebellar cortex malformation in two cases (age 26 and 34 gestational weeks). Both our cases presented pathology of the vessels within meninges, which were abnormal, cavernous, thin-walled. Vasculomeningeal proliferation fused with the underlying external granular layer. In the cerebellar tissue multiple cavities with a network of meningeal tissue and embedded pathological vessels were observed. Cavities were surrounded by widely scattered granule cells. Large granule cell clusters and abnormal pericavital aggregations of the external granule cells disturbed normal cortical lamination. Disorientation of Purkinje cells was stated. Calbindin-immunoreactive Purkinje cells aligned in fragments of monolayer between granule cells. They were embedded in the granule neuron mass forming a monolayer or improper arranged clusters. The normal layered pattern of the cerebellar cortex was disorganized. Interlamellar and interfolial fusion was stated. The folia were coupled together. The folial cerebellar pattern was completely obliterated.

The presented cases represent a spectrum of morphological changes which are the consequence of aberrant migration. The meningeal vessel pathology, affected meningoglial network led to over-migration of granule external neurons through a defective glial limiting membrane. Disturbance of proliferation of external granule cells caused in consequence abnormal development and increase of granule cells. Granule cells are potent regulators of Purkinje cell development and enhance survival and dendritic development of these neurons. The abnormal aggregation of external granule cells affected the misorientation of Purkinje cells, disturbed the arrangement of Purkinje cell settlement and dendritic tree orientation. The directed migration of the external granule cells to their destination underneath the Purkinje cell layer is guided by and is dependent upon glial processes of the Bergmann glial cells. Defect of the glial limiting membrane (Bergmann glial end feet contact the meningeal cells) led to anomalous formation of an internal granular layer.

A cascade of disturbances can be stated in the presented cases. Against the background of vascular pathology affecting the meningoglial network the migration pathways were disrupted. The defective movement of neurons and their faulty maturation resulted in abnormal neurogenesis, disturbances of cortical layering, and defects of cerebellar folia formation.

[A7]

Clinical aspects of agenesis of corpus callosum and associated brain abnormalities

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Background: The corpus callosum is the major neopallial connection between the two cerebral hemispheres. Hypoplasis or agenesis of corpus callosum (ACC) can be an isolated malformation of the central nervous system (CNS), and may be associated with other CNS malformations or abnormalities of other organs.

Aim of the study: The objective of this study was to investigate coexistence of agenesis of the corpus callosum (ACC) with other developmental disorders of the central nervous system (CNS), as well as compare the clinical manifestations of isolated ACC with those of ACC accompanied by other defects of the CNS.

Material and method: The analyzed group included 30 children diagnosed with ACC, aged 4 months to 15 years, 10 girls and 20 boys, who were treated within clinical departments of the Medical University of Gdansk within the last 3 years.

Results: In 13 children (43%) ACC was an isolated defect of the nervous system, while in 17 others (57%) ACC coexisted with other defects of the CNS (e.g. holoprosencephaly, hydrocephalus, distension of the subarachnoid cisterns, arachnoid cysts, neuroblast migration disorders, cerebellar defects). In some of the patients with ACC there were also developmental defects of other organs present: they were diagnosed with Apert syndrome, Toriello-Carey syndrome, Aicardi syndrome. In one child the clinical picture corresponded to the VATER sequence. One boy was found to have mosaic ring chromosome 7, and one other boy had microdeletion of chromosome 22 (CATCH syndrome).

Conclusion: Estimation of ACC is particularly important for wider diagnostics of the CNS and also for providing examinations of other organs. Diagnosis

of other developmental defects of the CNS coexisting with ACC implies more severe clinical manifestations.

[A8]

Cortical dysplasias – common neuropathological changes in intractable temporal epilepsy

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Cortical dysplasias represent a well recognized cause of medically intractable epilepsy exhibiting distinct clinical, neuroradiological and histopathological findings. The classification of various types of cortical dysplasias has evolved in the last 10 years. The currently established classification confirms two major groups of structural abnormalities referred to as focal cortical dysplasia (FCD). FCD type I represents only subtle cortical dislamination, whereas the common FCD type II is characterized by cortical dislamination accompanied by evident neuronal cytopathology. FCD type II is further subdivided into FCD type IIA with dysmorphic, bizarre neurons in grey and/or white matter and FCD type IIB (Tylor-type) with presence of dysmorphic neurons and so-called "balloon cells" similar to those observed in tuberous sclerosis.

We demonstrate the neuropathological characteristics of surgically resected tissue from 21 patients affected by intractable seizures. The majority of neurosurgical specimens revealed histopathological hallmarks of focal cortical dysplasias (FDC) type II, especially FCD type IIA with aberrant architectural organization of the neocortex and adjacent white matter accompanied by dysmorphism of neurons. Characteristic histopathological findings include diffuse or focal disorganization of cortical layers with neuronal dislamination, blurring of the grey-white junction and occurrence of large, dysmorphic neurons in the deep cortex and white matter. The "balloon cells" typical for FCD type IIB (Taylor type) were evidenced in 3 patients. Other histopathological abnormalities consisted of aggregates of immature neurons, increased number of neurons in the molecular layer, numerous ectopic neurons in white matter, presence of pial glio-neuronal tissue, reactive cortical astrogliosis, calcifications and/or chronic inflammation. So-called dual pathology with combination of FCD and hippocampal sclerosis is recognized in numerous cases.

[A9]

Ectopic cerebellum in anterior cranial fossa. Report of a unique case associated with skull congenital malformations and epilepsy

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Heterotopic cerebellar tissue located outside its normal anatomical position has been sporadically reported. The presence of a totally isolated, well-organized ectopic cerebellar mass is extremely exceptional. We present a unique case of an isolated, well-differentiated ectopic cerebellum located in the anterior cranial fossa in a 25-year-old woman with hypertelorism, skull deformation and a long-standing history of epileptic seizures. Magnetic resonance imaging revealed a mass lesion at the base of the frontal lobes with no apparent connections to the adjacent brain structures. The normal cerebellum was also present in its typical infratentorial location. The lesion was covered by thin, densely packed folia resembling the surface of the cerebellar hemispheres. The mass lesion was completely resected.

Histologically, the cerebellar cortex was composed of well-differentiated external molecular, Purkinje cell, and internal granular cell layers. The deeper part of white matter displayed the features of neuroglial, hamartomatous-like abnormalities. There were numerous neuronal and/or glial heterotopias

ranging from single dysplastic neurons to well--circumscribed clusters of neuronal and/or glial cells surrounded by neuropil. Some large neurons looked like mature ganglion cells, Purkinje cells, or dentate neurons. Large irregular islands of heterotopic tissue displaying well-differentiated cerebellar cortex could also be seen. Other parts of the ectopic cerebellum revealed loosening of tissue with dispersed glioneuronal elements. The ectopic brain tissue may arise from disturbed migration of primitive pluripotent stem cells during embryogenesis.

The presented case of cerebellar ectopia associated with skull congenital malformations exhibited multiple dysontogenetic abnormalities. To our knowledge, this is the first report of totally isolated, well-differentiated ectopic cerebellum in the anterior cranial fossa accompanied by skull deformation and epilepsy.

[A10]

Correlation of neuroradiological, electroencephalographic and clinical findings in cortical dysplasias in children

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Cortical dysplasias (CD) are defined as circumscribed malformations of cortical development. They result from impairment of neuronal proliferation, migration and differentiation. CD is a common pathological substrate in patients with early-onset childhood epilepsy and/or developmental delay as well as neurological signs. Recognition of the importance of cortical dysplasias has been shown in many studies when introducing the structural MRI. The following study was performed in order to correlate the neuroimaging findings with the electroencephalographical and clinical picture of children with cortical dysplasias.

Materials and methods: 46 patients with the presence of CD features in MRI were identified. There were 18 female and 28 male patients. The age ranged from 3 months to 12 years (mean age = 6.2, median age = 3.1). The objectives of the study were explained to the parents or legal representatives of children when possible and also informed consent was obtained. Multiple EEG recordings as well as detailed clinical analysis of all patients were performed. Statistical analysis was conducted in order to correlate the type of CD with clinical outcome and electrophysiological findings

Results: There were 31 patients with focal dysplasias, 6 with schizencephaly, 4 with heterotopias, 3 lissencephaly and 2 with band heterotopia. 80% presented epilepsy (60% of them drug-resistant). Additionally, we tried to elucidate the clinical characteristics of epilepsy. In 75% of epilepsy patients the electroencephalographical changes correlated with anatomical localization of CD. 74% of patients were mentally retarded and 30% had focal neurological deficits.

Conclusions: There were no correlations between the type of CD and the severity of the clinical picture, especially the level of mental retardation and presence of drug-resistant epilepsy. Different age at epilepsy onset and various responsiveness to antiepileptic drugs in the majority of patients may reflect different dynamics in epileptogenicity of the underlying CD.

[A11]

Disturbances in central nervous system development in a rat model of familial amyotrophic lateral sclerosis

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In a rat model of familial ALS (fALS), we observed a group of rats in which clinical symptoms and signs non-characteristic for transgenic animals appeared at various age. The presence of such abnormalities indicated the possibility of damage – possibly in the course of foetal development – to structures different than the ones described previously in the model.

The material was composed of five Dowley--Spraque fALS rats arising from 3 litters; two

animals, one transgenic (tg+) and one wild (tg–), were at the age of 24 days; one tg– rat was at the age of 43 days and two at the age of 67 days (both tg+). The animals revealed symptoms and signs of damage to the CNS; they ran all around, had hyperextension of nucha, fell laterally and demonstrated movements resembling smacking. Two of them did not have a considerable part of the tail.

Histopathological and immunohistochemical investigations showed: disturbed cell migration in the form of dysplasia in the new cortex (cerebrum and cerebellum), developmental abnormalities involving ependyma with the presence of tannicytes and the ventricular system (especially the third ventricle), irregular shape of the dentate nucleus and the presence of radial glial fibres.

Features of delayed and abnormal ontogenic development of the CNS manifested as (1) disturbances in cell migration and (2) axial malformations belonging to the group of dysraphia. The abnormalities were observed in the transgenic as well as wild rats. Our observations confirmed the results of research performed by Kirby et al. (2005) suggesting that mutated SOD1 gene in the rat model of fALS influences many genes including genes important during development.

Conclusions: 1. In animals from the rat fALS model, abnormalities in CNS development may appear, 2. Developmental abnormalities involve process of migration and dysraphic malformations, 3. In rats, the presence of both types of abnormalities developing in different ontogenic periods indicates that a mutated SOD1 gene may influence the whole animal ontogenesis.

[A12]

Surgical treatment of children with refractory epilepsy due to malformations of cortical development

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Malformations of cortical development may be associated with drug-resistant partial epilepsy suitable for surgical therapy. Focal cortical dysplasias represent the main group of malformations of cortical development, but there are also other types of alterations. Defining candidacy for surgical therapy and tailored resection requires thorough pre-surgical evaluation so that the approach will be individualised for each patient. We present our series of 52 patients with malformation of cortical development selected from 160 consecutively operated paediatric patients. Within this group encompassing different types of malformation of cortical development, including polymicrogyria (two patients), hemimegalencephaly (one patient) and focal cortical dysplasia (twenty patients) the largest group was 29 individuals with benign tumours DNT and ganglioglioma associated with FCD.

All patients underwent scalp EEG and video-EEG. Magnetic resonance imaging represented the indispensable premises for planning surgery and tailoring resection. Magnetic resonance imaging was helpful in 92% of patients with MCD, while signal alterations were present in all other cases. The best outcome was observed in patients with temporal FCD: 69% seizure-free (Engel class I) and 84% with tumours and dysplasia after at least 1 year of follow-up.

[A13]

Brain and cerebellar hemidysplasia in a case with ipsilateral body dysplasia (suspicion of CHILD syndrome)

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CHILD syndrome is an acronym for congenital hemidysplasia with ichthyosiform nevus and limb defects. This is an X-linked dominant disorder affecting females with early lethality in hemizygous males. The clinical features there are congenital hemidysplasia with ichthyosiform erythroderma and ipsilateral hypoplasia of limbs and other parts of skeleton as well as defects of the brain, heart, kidney

and lung. The cause of CHILD syndrome is mutation in the *NSDHL* (*steroid dehydrogenase-like protein gene*) gene at Xq28, which affects cholesterol biosynthesis. We report a female premature newborn with left side body hemidysplasia and ipsilateral defects of the skin, visceral organs and brain. It was second twin gestation (one embryo died at 6 gestational weeks); the pregnancy was terminated at 29 weeks of gestation because of multiple foetus malformations. Newborn evaluation after birth revealed hypoplasia of the left part of the body with hypoplasia of the ipsilateral part of the skull, eye, arm and leg. There were absent ipsilateral palmar dermatogliphs, alopecia on half of the head, pale coloration of the skin of trunk with sharp midline. Echocardiography showed left heart hypoplasia without mitral and aortal valves defects. Brain ultrasonography showed hypotrophy of the left brain hemisphere with large cyst communicated with lateral ventricle and agenesia of corpus callosum. The cerebellum had abnormal structure. The child died after one day of life. CHILD syndrome was suggested after clinical evaluation of multiple congenital malformations with hypoplasia of the left part of the body.

General autopsy showed hypoplasia of the left side of the face and body, hypoplasia of the left heart atrium and ventricle, unilobar left lung with narrowing of the ipsilateral pulmonar artery, hypoplasia of the left kidney and adrenal. Microscopic structure of the inner organs was normal. Gross neuropathological evaluation showed asymmetry of brain, cerebellum and brain stem with normal for age development and size of right side structures and hypolplasia of left one. The left brain hemisphere showed lissencephalic appearance, in some places with cobblestone surface. A large cavum inside hemisphere was present without connection with right lateral ventricle. The brain pallium in the left hemisphere was 5–7 mm wide. There was only a small connection of the central structures of both brain hemispheres in the basal part of basal ganglia and brain stem. Microscopical evaluation showed normal for age structure and development of the right structures of the brain. The left brain hemisphere showed bizarre cortical and basal ganglia dysplasia; there were diffuse neural heterotopias in the submeningeal space, mainly on the basal surface. In the left part of the brain stem there was no cortical tract. Left cerebellar hemisphere also had dysplastic structure with large heterotopic focuses in the white matter – it looked like the cerebellar cortex was invaginated into the inner part of the cerebellum. Karyotype from peripheral blood leukocytes was normal – 46, XX. DNA for molecular investigations was isolated from cultured skin. Sequence analysis of the coding exons of SNDHL and EBP gene was performed. In the NSDHL gene missense mutation c. 1046A >G; p. Y 349C was detected. This mutation affects an amino acid which is highly conserved from yeast to man and therefore it could cause the phenotype of the reported child.

[A14]

Malformations of the brain in a foetus with compound heterozygosity for two PAX6 mutations

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PAX6 is an important transcription factor and master regulator of eye development. In addition to causing aniridia, PAX6 haploinsufficiency can result in anomalies of the CNS, such as absence or hypoplasia of the anterior commissure [1,2], polymicrogyria and absence of pineal gland [2]. We report findings on a malformed foetus whose parents were aniridic (both sporadic cases). Molecular analysis revealed compound heterozygosity for two PAX6 mutations. The parents were not consanguineous, and neither had any family history of poor vision or any other ocular conditions. CT scan of the brain in the parents showed aplasia of the pineal gland, hypoplasia of corpus callosum and of the anterior commissure. Ultrasonography of the foetus performed at 25 weeks' gestation revealed gross intracranial malformation described as "possible schizencephaly". Absence of the eyes (suspected anophthalmos or microphthalmos) was also reported. Cytogenetic examination in cultures of amniocytes showed normal female karyotype of the foetus. The pregnancy was terminated at 25 weeks' gestation. The stillborn female foetus weighted 458 g, its length was 36 cm,

head circumference was 23 cm. The general autopsy showed: fused palpebral fissures, apparent absence of the eyes, very small rudimentary nose with very narrow nostrils, and a high arched palate. Palmar contraction of both wrists was observed. No malformations of the inner organs were reported. Postmortem X-ray showed proportional shape of the skull, but the brain was very small, filling only 1/3 of the cranial cavity; above the brain there was a large collection of fluid. The brain hemispheres comprised loosely joined global structures of brain tissue. The corpus callosum was absent and the midline fissure of the brain was wide. Olfactory bulbs, optic nerves, chiasm and tracts were absent. The brain stem and the cerebellum were small, but the spinal cord was normal in shape and size. Frontal sections of the brain confirmed irregular structure of the hemispheres, absence of corpus callosum, and small, ill-shaped lateral ventricles. In the posterior of the brain bilateral fissures connected the lateral ventricles with the submeningeal space. The third ventricle was normal in shape. Basal ganglia were indistinguishable within masses of germinal matrix. The thalamus was the only clearly recognizable basal structure. Microscopic evaluation revealed as a most striking feature an enormous amount of germinal matrix both in the inner part of the hemispheres and on the surface of the hemispheres and in the submeningeal space. The structure of the cerebral cortex was irregular, with a paucity of neural cells, and in some regions abnormally large neurons could be seen in the superficial cortical layers. The white matter was difficult to discern with regions showing hypercellularity or paucity of glial cells or nests of germinal cells. The thalami seemed to be of normal structure (not evaluated in detail). Several small cysts lined with ependymal cells, with small patches of choroid plexus, were seen on the surface of the cerebral hemispheres. The cerebellum showed marked dysplastic changes: small convolutions, irregular structure of the cortex layers, with paucity of inner granular cells and many heterotopic foci in the white matter, but some parts of the cerebellum were structurally normal. The structure of the brain stem and spinal cord was normal, except the absence of the pyramidal tracts. Myelination status of the spinal cord corresponded to the gestational age of the foetus. Conclusions: Micrencephaly with signs of disturbed proliferation, migration and differentiation of brain cells was observed. The spinal cord was not affected, except for the absence of pyramidal tracts – a consequence of malformed brain hemispheres. The myelencephalon and thalamus were spared, in contrast to the severely affected neocortical structures. Similar brain malformations in newborn with compound heterozygosity for two different PAX6 mutations were first described by Glaser et al. in 1994 [3].

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[A15]

Application of PCA method in characterization of metabolic changes in patients with progressive encephalopathies

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Introduction: The present study combines MRS and pattern recognition (PR) method – the principal components analysis (PCA) that revealed to be useful in metabonomics and complex biological data analysis. The objective of this study was to evaluate whether PCA could visualize the metabolic differences between encephalophatic patients' spectra and normal ones without spectra resolving.

Materials and methods: Principal Component Analysis was applied to 100 1H NMR *in vivo* spectra acquired in 20 patients with brain encephalopathies and in 20 healthy persons.

The whole-body 2T MRI/MRS system (Elscint 2T Prestige) equipped with a standard head coil and operating at a proton resonance frequency of 81.3

MHz was used (the PRESS pulse sequence parameters: TR 1500 ms, TE 35 ms and 100 acquisitions and the voxel volume: 1.5x1.5x1.5 cm^3).

The NMR spectra were analyzed in the range from 0 to 4.2 ppm and the number of spectral points was 256. Prior to the analysis the spectra were centred in order to remove any relative shifts.

The PR analyses were performed using STATISTICA version 7.1, StatSoft, Inc. 2005 equipped with the multivariate exploratory techniques. The Varimax factor rotation technique was used to maximize the variance of the loadings. Four principal components have been adopted as effectively representing the major variations in the data.

Two data sets were investigated: the first set consisted of the unresolved encephalopahatic patients' and the normal spectra and the second one comprised only the encephalopahatic patients' spectra in order to find any possible clustering in this heterogeneous group.

The loading factors were interpreted in terms of markers of biochemical changes.

Results and discussion: *In vivo* 1H MRS is a non-invasive tool to investigate brain metabolism; however the spectra deconvolution is time-consuming and frequently provides ambiguous results. The PCA analyses of the studied groups show distinct clustering of the encephalopahatic patients' and the normal spectra – the characteristic spectral range falls between 1.3–1.95 ppm, whereas the PCA analyses of the encephalopahatic patient group alone reveal the clustering of the spectra obtained in patients with urea cycle defect.

Conclusion: Application of PCA to the unresolved NMR spectra consisting of a large number of interrelated variables results in reduction of the dimensionality of the data, while retaining the variation present in the data set. PCA is a fast and useful method of automatic NMR spectra differentiation.

[A16]

Polymicrogyria as cerebral cortical dysgenesis in one of a pair of monozygotic twins

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Introduction: Polymicrogyria belongs to aetiologically heterogenic cerebral cortical dysgenesis. It can be due to genetic factors with different patterns of inheritance or/and acquired factors (e.g. due to intrauterine anoxia/ischaemia or intrauterine infection). The time of its development is 12–27 weeks of gestation.

Rationale: To present a case of cerebral cortical dysgenesis (polymicrogyria) in one of a pair of monozygotic twins.

Case report: The 14-year-old girl is the child of unrelated parents. She was born after pregnancy complicated by partial amniorrhea (during 5th month) by cesarean delivery as the second twin. Apgar's score was 10. Her mental development is above average level. Praxis of left hand was revealed in neuropsychological examination. From the 10th year of age she suffered from partial epileptic seizures successfully treated with valproid acid. MRI scans revealed unilateral polymicrogyria in the right frontal-parietal region. The patient's sister is healthy with high IQ and normal MRI brain images.

Conclusion: Occurrence of cerebral cortical dysgenesis in only one child of a set of monozygotic twins points to a complex relationship between genetic and environmental factors contributing to development of the central nervous system.

[A17]

Cerebral childhood and adolescent X-linked adrenoleukodystrophy. Clinical presentation and laboratory studies in five cases

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X-linked adrenoleukodystrophy (X-ALD) belongs to primary leukoencephalopathies with metabolic defect in peroxisomal membrane transporting protein *ABCD1* leading to accumulation of saturated very long-chain fatty acids (VLCFA) $C_{24:0}$ and $C_{26:0}$ in plasma, brain and adrenal cortex. The diagnosis of X-ALD patients is based on the detection of increased VLCFA levels, particularly $C_{24:0}/C_{22:0}$ and $C_{26:0}/C_{22:0}$ ratios in serum. The ALD gene has been mapped to the terminal segment of the long arm of the X-chromosome (Xq28 locus). X-ALD is considered to be very rare. It occurs worldwide at 0.5–3.3 in 100,000 males. The classification of different phenotypes of X-ALD is based on the age of onset and the organs principally affected. Of the several clinical phenotypic forms of X-ALD, 30–40% of children under 10 years present the childhood – onset cerebral form. Adolescent cerebral X-ALD with onset between 11–21 years occurs much less often.

Three boys of childhood onset cerebral X-ALD at the age of 5, 7 and 7.5 years and two of juvenile cerebral form of the disease aged 11 and 12 years were presented. We based our diagnosis on a clinical picture and a range of diagnostic procedures including neuroradiological, neurophysiological and biochemical tests. In all patients a rapidly progressive spasticity, ataxia and mental deterioration were found. Seizures appeared in four of them. Additionally visual and hearing impairment was observed in three patients. Adrenal insufficiency was also diagnosed in our cases. MR revealed demyelination located mainly bilaterally in the parieto-occipital areas. All patients showed involvement of parieto-occipital lobes, optic radiation and splenium of the corpus callosum. Abnormalities in VEP, BAEP and SEP (from median and tibial nerve stimulation) parameters were found in all patients. The clinical diagnosis in every case was confirmed by the significantly elevated concentration of VLCFA measured in plasma in comparison to normal values.

Abstracts
Index of authors