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[A1]

Inflammation of CNS mimicking multifocal neoplasma. A case report

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Toxoplasmosis is one of the severest complications in AIDS. We present a patient, a male aged 44 with paresis of the right limbs, who was admitted to a neurological department in one of Warsaw's hospitals. History: 3 months of headache, weakness, body weight loss, arthralgia, diarrhoea, recurrent rashes. Head MRI revealed multiple lesions in cerebral hemispheres, brainstem and cerebellum with oedema and mass effect. The radiological conclusion was carcinoma metastases. Abnormalities in laboratory studies were as follows: lymphocytopenia, SR-140 mm/h, oesophageal candidiasis. Oncological consultation suggested a possibility of cysticercosis or toxoplasmosis which was not confirmed by laboratory tests. Anti-HIV test was positive. The patient deteriorated dramatically and died about 2 weeks after admission. AIDS was the final clinical diagnosis. Post-mortem pathological diagnosis was toxoplasma meningoencephalitis and toxoplasma pneumonia.

Conclusion: Cerebral toxoplasmosis should be considered in the case of every patient (even without HIV infection history) with non-characteristic and/or multiple ring enhancing lesions with mass effect in neuroimaging.

[A2]

Non-neoplastic focal lesions in stereotactic biopsy samples of CNS

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Stereotactic biopsy is a valuable technique that allows us to enhance the diagnostics in the case of clinically ambiguous lesions in deep, difficult locations, when a neoplasm is suspected.

155 stereotactic biopsies were carried out in 5 years (December 2000–December 2005) in the Neurosurgery Department in Katowice-Ligota. These procedures were performed under local anaesthesia, with Brain-Lab system (Leksell stereotactic frame). CTs (Hi Speed NX/i PROBE GE) and MRI (SIGNA MR/i Echospeed 1,5T GE) of the head were made. Then fusion of the images was performed in the stereotactic planning station. The material was sampled with biopsy forceps of 1.3 mm inner diameter, and the tissue was collected every 2–3 mm along the planned trajectory.

In 4 cases, areas of lower density, of unclear nature, with spaces filled with fluid, were clinically found. In 2 cases, apart from the biopsy material for cytological examination and routine paraffin-embedded slides, we were able to aspirate fluid. It was processed in a Cytospin centrifuge (by Shandon), and stained with Meyer's haematoxylin and eosin. In cytological smears, made on the basis of biopsy specimens, stained with Harris's haematoxylin and eosin, thin-walled blood capillaries and sparse larger vessels were seen. The background of the smears was "clean", or amorphic, coagulated, albuminous masses were observed. The cellular element consisted of phagocytic macrophages with foamy cytoplasm, filled with albuminous and lipid contents or with deposits of brown, haemosiderin-like substance and of sparse glia cells, with nuclear inclusions. In cytological smears made of aspirated fluid, numerous erythrocytes, a few leukocytes and sparse macrophages with haemosiderin deposits or abundant foamy cytoplasm were found. The biopsy samples were fixed, routinely processed, paraffin embedded, slides stained with Meyer's haematoxylin

and eosin, or, when needed, specifically stained. In these slides, first of all, an image of "loosened structure" of glia tissue was seen, with material "soaked with fluid", with a tendency to formation of fissures and pseudo-cystic, cavernous spaces. Small foci of coagulative necrosis, a few amyloid bodies and amorphic calcifications were seen as well. Some normal areas were found.

Diagnostic material in the remaining 2 cases consisted of cytological smears, stained with Harris's haematoxylin and eosin, made on the basis of biopsy samples and histological slides, stained with Meyer's haematoxylin and eosin, cut from routinely processed, paraffin-fixed biopsy samples. In cytological slides, thin-walled blood capillaries, morphotic blood elements, deposits of haemosiderin located in macrophages and in extracellular space, and sparse, normal and reactive astrocytes were seen. In the histological slides, glia tissue with marked oedema, degeneration, coagulative necrosis, haemorrhagic malacia, with foci of budding blood capillaries, perivascular lymphocytic inflammatory infiltrates, granulocytic infiltrates, dispersed or in fine clusters in glia tissue, haemosiderin deposits and areas of gliosis.

It was possible to diagnose post-apoplexy degenerative changes in two cases and chronic haematomas in the other two. Further observations made it possible to support the diagnoses.

The stereotactic biopsy of deeply located lesions enables us to establish diagnosis not only in tumours, but also in other, non-neoplastic lesions as well. It allows us to initiate proper treatment.

[A3]

An attempt to estimate the pleiotropic role of FAS and its ligand, FAS-L The influence of FAS and FAS-L on course of disease in gliomas of various histological malignancy, diagnosed by means of stereotactic biopsy

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The CNS tumours arise as a result of a complicated process. In one of the final stages of this process, glia cell proliferation, stimulated by growth factors, is disturbed and the glia cells avoid apoptosis. Apoptosis may be induced by extracellular factors – compounds binding to specific membrane receptors. The signal to die is transmitted by ligands to the membrane receptors, or it is transmitted directly to executive structures. The death receptors, of the Tumour Necrosis Factor superfamily (TNFSF), especially FAS (TNFRSF6, CD 95, APO-1) and their corresponding ligands, such as FAS-L (TNFSF6), are essential for this way of apoptosis. FAS pleiotropy manifests in its role in the malignancy progression of gliomas, and in its pro-apoptotic activity.

The objective of this study was to determine transcriptional activity of genes and to compare their mRNA concentrations, results of morphologic examinations and course of the disease.

The material consisted of stereotactic biopsy specimens obtained from 285 patients who have undergone stereotactic biopsy in the last 7 years in the Department of Neurosurgery in Sosnowiec. Morphologic and molecular analysis were performed on 103 cases of gliomas (30 diffused gliomas of low malignancy G2 WHO, 55 anaplastic astrocytomas G3 WHO, and 18 glioblastomas G4 WHO).

Full clinical data, cytologic examinations, routine histological examinations and immunohistochemical responses against FAS (TNFRSF6) and FAS-L (TNFSF6) were analyzed. A pattern of the material processing for the molecular analysis was developed. In this analysis, concentrations of mRNA of FAS (TNFRSF6) and of FAS-L (TNFSF6) were examined by means of RT-QPCR (Taq-Man) method with ABI-PRISM 7700 sequence detector. Then, the course of the disease (defined as stagnation, recurrence of the process or death) was compared to the strength of immunohistochemical responses against FAS (TNFRSF6) protein and FAS-L (TNFSF6) protein, and to the number of mRNA molecules encoding these proteins in 3 groups of diffuse gliomas.

We found that cytological smears fixed in pure alcohol, dried and not stained yield enough mRNA to perform molecular analyses to determine the number of mRNA molecules per cell. Analyzing the clinical data, morphological findings, immunohistochemical

responses with antibodies against FAS (TNFRSF6) and FAS-L (TNFSF6) and number of mRNA molecules encoding these proteins in diagnosed material, we found that transcriptional activity of genes encoding FAS (TNFRSF6) and FAS-L (TNFSF6) is better correlated with the course of the disease than strength of immunohistochemical reaction against FAS and FAS-L proteins. Our findings enable us to claim that assessment of activity of some genes may be considered as a valuable additional marker in the diagnosis and prognosis of diffuse astrocytomas of various grades of malignancy.

[A4]

Receptors for glutamate and ischaemic preconditioning

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Preconditioning to ischaemia by a brief episode of sublethal insult induces tolerance to the subsequent lethal ischaemic insult. Literature data indicate that hypothermia and inhibition of NMDA receptors both inhibit induction of ischaemic tolerance. In our studies we examined the effect of MK-801 on induction of ischaemic tolerance in different temperature conditions.

It is known that activation of group one of metabotropic glutamate receptors (mGluR I) sets up stimulating effects on neurons. Therefore antagonists of group I metabotropic glutamate receptors may inhibit excessive stimulation in the nervous system and prevent neurodegeneration.

However, the involvement of mGluRs I in the induction of ischaemic tolerance is unknown. In this study we tested the effect of antagonists of mGluR1 and mGluR5 – EMQMCM and MTEP respectively.

In all experiments the model of forebrain ischaemia on Mongolian gerbils was used. Drugs were administered i.p., 1 hour before preconditioning ischaemia at dose 3 mg/kg – MK-801 and 5 mg/kg – EMQMCM and MTEP.

Tolerance to 3 min ischaemia was induced 48 hours earlier by 2 min preconditioning ischaemia.

Animals pretreated with antagonist of NMDA receptor were heated or allowed to undergo spontaneous regulation of temperature. Gerbils treated with antagonists of mGluRs I were kept in normothermia. Brain temperature was measured with telemetry equipment.

Loss of CA1 pyramidal neurons was assessed 14 days after 3 min ischaemia.

Ischaemic preconditioning reduced neurodegeneration from about 70–90% to 20–50% in normothermic gerbils, but failed to induce tolerance in heated animals pretreated with MK-801. We speculate that the inhibitory effect of MK-801 on induction of ischaemic tolerance described by other authors could be evoked by hypothermia.

Administration of EMQMCM and MTEP also did not inhibit induction of ischaemic tolerance. Control of brain temperature showed that MTEP withdrew the postischaemic hyperthermia, while EMQMCM induced short-term hypothermia.

Our data indicate that mGluRs I do not play an essential role in the induction of ischaemic tolerance in the gerbil's brain.

[A5]

The level of homocysteine in neurodegenerative diseases

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Homocysteine (Hcy) metabolism is part of a biochemical reaction involved in one-carbon metabolism. In physiological conditions folate is a cofactor in one-carbon metabolism, during which it promotes the remethylation of Hcy to regenerate methionine. Folate deficiency has been implicated in cardiovascular diseases and, more recently, it has been shown to contribute to many neurological and psychiatric disorders including dementia, Alzheimer's disease (AD), Parkinson's disease (PD), depression and schizophrenia.

Furthermore, recently papers have indicated that an increased plasma homocysteine level has been shown to be a strong, independent risk factor for the development of dementia and AD, and L-dopa treatment PD patients.

The aim of the study was to determine of the level of homocysteine in plasma from AD and PD patients, and in controls with the HPLC/EC (high-pressure liquid chromatography system with electrochemical detection) method.

38 AD patients (36–85 years) and 98 PD patients (34–81 years) (71 PD patients were treated with L-dopa, 27 PD patients not treated with this drug), and 50 controls (22–76 years) were studied.

The level of Hcy in plasma of AD patients ($p<0.01$) and PD patients ($p<0.001$) was significantly higher than in controls. The level of this amino acid was markedly higher after 63 years as well ($p<0.01$). The concentration of Hcy increased after L-dopa treatment in PD patients compared to controls ($p<0.001$) and PD patients untreated with L-dopa ($p<0.05$). The changes of plasma Hcy concentration related to the duration of treatment were observed. The highest level of Hcy in PD patients was in the first five years of L-dopa treatment; then it tended to be lower in subsequent years.

Our results showing a significant increase in Hcy plasma levels both in AD and PD patients support the view that chronic high plasma levels of homocysteine may have deleterious effects on brain function and neuronal survival. Furthermore, L-dopa pharmacotherapy of PD patients can modify the concentration of Hcy related to the duration of this drug's use.

[A6]

Expression of latent HSV-1 and CMV in brains of senile and demented patients

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HSV-1 remains in a latent form in 80–90% of the population. Some peripheral neurons continue to harbour infection for the lifetime of the host. Herpes simplex virus type-1 (HSV-1) was proposed as an environmental risk factor for APOEε4 positive Alzheimer's disease (AD) patients. The potential role of HSV-1 and other Herpes viruses in AD pathology is still a matter of controversy.

The main purpose of the study was to examine HSV-1 and CMV latent infection in brains of demented and senile patients.

Brain expression of replicated viruses was investigated in 13 cases including 5 AD patients, 2 other types of dementia and in 6 patients with other neurological diseases. In all cases infection of the central nervous system was excluded. To study expression of latent HSV-1 and CMV ABC immunohistochemistry was performed. Cortical layer and adjacent white matter were analyzed under the light microscope.

The present study revealed HSV-1 and CMV immunopositive cells in different regions of the brains in demented and senile patients. In most cases nuclear expression of viruses was observed. On the basis of our results latent infection of HSV-1 and CMV was confirmed within the brains by immunohistochemistry.

[A7]

Enterogenous cyst of spinal cord – a case report

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A 13-year-old boy presented with severe neck pain induced by a mild trauma.

Overnight, he developed left-sided hemiparesis and Brown-Sequard syndrome.

Imaging studies revealed congenital defect of the cervico-thoracic vertebrae and edematous--haemorrhagic lesion of the spinal cord at the C6-D2 level. Due to the progressive clinical picture, he underwent laminotomy at the C6-D1 level and excision of an intramedullary cyst filled with haemolysed blood.

Microscopic evaluation revealed gastric mucosa. Definitive diagnosis was "enterogenous cyst with intramedullary haemorrhage and proliferative reaction".

An enterogenous cyst acts as a slow-growing tumour, causing a progressive mass effect and compression of adjacent structures. An additional noxious factor is proteolytic cyst content (gastric juice), leading to chemical myelitis.

[A8]

Focal cerebral lesion in a patient with plasmocytoma

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A 48-year-old woman was admitted to the Neurosurgical Department with symptoms of facio-brachial hemiparesis increasing for several months. The patient had diabetes type I; at admission she was alert, with hyperleukocytosis but without hyperpyrexia. For more than a year she had been treated due to a plasmocytoma localized in the lumbar region of the spine and 5 months before she finished chemotherapy, staying in remission. The patient had also undergone amputation of the uterine cervix due to high grade dysplasia.

Cerebral CT showed a focal hypodense contrast enhancing lesion in the right fronto-parietal region, surrounded with oedema. Radiologically a brain abscess or metastatic tumour was diagnosed.

A diagnostic stereotactic biopsy was performed. The fluid material was aspirated and sent for bacteriological and pathological analyses. Microscopically the material consisted of necrotic debris, purulent exudates and fragments of fungal hyphae consistent with Aspergillus. Bacteriologically Aspergillus fumigatu species was diagnosed, and analyses for anaerobic bacteria were negative.

The cerebral aspergilloma in the presented case developed based on the coincidence of diabetes and decreased immunity in the course of oncological treatment.

[A9]

Ischaemic lesions of the spinal cord suggesting neurologically and radiologically neoplastic process

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We present three patients aged 45 (patient 1), 47 (patient 2) and 50 (patient 3) with increasing neurological problems for several weeks (1), months (3) and three years (2). The patients were admitted to the clinics with paraparesis and sphincter dysfunction (1,2,3), with pain (1) and sensory deficits (3). MRI of the spinal cord showed segmental enlargement with infiltration at corresponding levels – thoracic (1), thoraco-lumbar (2) and cervical (3). Pathological lesions were hyperintense in T2 and PD sequences and in two cases did not show any contrast enhancement. In patient 2 intraspinal mass was contrast enhancing in its distal part. Radiologically in all cases the neoplastic intramedullary process was suggested.

The patients were operated on in the Neurosurgery Department for decompression and diagnostic biopsy. The lesions were partially removed. In clinical observation stable clinical amelioration was achieved in patients 1 and 2, but in case 3 it was transient, with concomitant remission and aggravation of symptoms. The pathological examination of biopsy material excluded the neoplastic process. Ischaemic changes, selective necrosis, demyelination, oedema and vascular changes were found. The blood vessels presented arteriosclerosis and wall thickening, and in patient 2 perivascular scanty lymphocytic infiltrates were visible.

Radiological and clinical differential diagnosis between vasogenic myelopathy and intramedullary

tumour can create serious difficulties and surgical biopsy is necessary for the final diagnosis.

[A10]

8-oxo-2'-deoxyguanosine in neurodegenerative diseases

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Oxidative stress has been shown to be involved in the pathogenetic mechanisms of many neurodegenerative disorders. The central nervous system is particularly exposed to free radical injury, given its high metal content, which can catalyze the formation of oxygen free radicals, and the relatively low content of antioxidant defences. Several studies show markers of oxidative damage – lipid peroxidation, protein oxidation, DNA oxidation and glycoxidation markers – in brain areas affected by neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD).

Oxygen free radicals cause peroxidation and subsequent DNA lesions such as the oxidative modified nucleoside 8-oxo-2'-deoxyguanosine (8-oxo2dG).

Furthermore, symptomatic treatment of PD patients with L-dopa may add to the oxidative load and play a role in disease progression.

The aim of the study was to determine the level of 8-oxo2dG in peripheral lymphocytes from AD and PD patients, and in controls with HPLC/EC/UV (high--pressure liquid chromatography system with electrochemical and UV detection) method.

38 AD patients (36–85 years) and 98 PD patients (34–81 years) (71 PD patients were treated with L-dopa, 27 PD patients not treated with this drug), and 50 controls (22–76 years) were studies.

The level of 8-oxo2dG in lymphocytes of AD patients ($p<0.001$) and PD patient ($p<0.05$) was significantly higher than in controls. The marker of oxidative damage to DNA was insignificantly higher between 22 and 76 years. Furthermore, oxidative modification of guanine in DNA (8-oxo2dG) was markedly higher ($p<0.01$) after treatment with L-dopa compared to the controls. The highest level of 8-oxo2dG was in PD patients after ten years of L-dopa treatment.

Our findings indicate that neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease generate oxidative stress and pharmacotherapy of L-dopa in PD can modify level of oxidative DNA damage.

[A11]

8-α-oxoguanine DNA glycosylase isoform transcript content in Alzheimer's disorder

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Reactive oxygen species (ROSs) are highly reactive and may oxidize macromolecules in cells such as proteins, lipids and DNA. ROSs cause modifications of bases and sugar components of DNA, which result in mutations and breaks of the DNA chain.

8-α-oxoguanine DNA glycosylase (OGG1) is a main DNA repair enzyme that excises 8-oxo-2'-deoxyguanosine (8-oxo2dG) from DNA. This enzyme exists in the three different isoforms OGG1a, OGG1b and OGG1c. 8-oxo2dG is one of the crucial lesions produced in DNA by ROSs. It has been postulated that decrease in expression of OGG1 leads to accumulation of DNA damage and mutations. Damage to genomic DNA may result in death of the central nerve cells, which can be associated with Alzheimer disease. DNA damage may also be involved in formation of mutations that result in malignant transformation of cells and development of other hereditary diseases.

Using reverse transcription and real-time quantitative PCR analysis (RQ-PCR) we analyzed the expression of OGG1 transcript isoforms in peripheral blood mononuclear cells (PBMCs) of patients with Alzheimer's disease and the control group.

PBMCs from patients and controls were isolated by centrifugation over Ficoll-Hypaque (density 1.077 g/cm^3). Total RNA was isolated according to the method of Chomczyński and Sacchi. RNA integrity was confirmed by denaturing agarose gel electrophoresis, and the concentration was quantified by measuring the optical density (OD) at 260 nm. RNA samples were treated with DNase I, and reverse-transcribed into cDNA using oligo-dT primers. RQ-PCR was conducted in a Light Cycler real-time PCR detection system by Roche Diagnostics GmbH (Mannheim, Germany) using SYBR® Green I as detection dye, and target cDNA was quantified using the relative quantification method. The quantity of investigated transcript in each sample was standardized by either β-actin or calculated per million cells.

We observed a decrease of OGG1a, OGG1b isoforms and increase of OGG1c transcripts in patients compared to the control PBMC. However, we did not find statistically significant differences in levels of these transcripts between patient and control groups.

Our observation may suggest that OGG1c isoform may play a more significant role in mechanisms of DNA repair in Alzheimer's diseases. However, this investigation requires an increase in the number of patients and controls to determine the precise role of OGG1 isoforms in Alzheimer's disease.

[A12]

Focal blood-brain barrier changes in white matter following experimental brain ischaemia

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Brain ischaemia is a neurodegenerative disease that affects cognition, behaviour and function. In these types of functional changes white matter lesions, which are seen in the subcortical and periventricular areas, have been implicated in the neuropathogenesis. Periventricular white matter lesions are referred to as leukoaraiosis. Leukoaraiosis have been found in the brains of patients with Alzheimer's disease and stroke. This type of injury is responsible for cognitive impairment in the aging population, too. In this situation we will explore the role and impact of ischaemia on brain white matter neurodegeneration in the context of possible development of Alzheimer's disease pathology. Because it is not clear whether the blood-brain barrier (BBB) in white matter is altered following brain ischaemia-reperfusion injury in long--lived animals we take into consideration investigation of ischaemic BBB changes. In view of the potential chronic effects of various extravasated substances on the development of white matter neurodegenerative injury we will discuss the possibility of influence of chronic ischaemic BBB disruption on Alzheimer's-type cognitive impairment. Additionally we will focus on the question of whether or not the neuropathological mechanism(s) observed in ischaemic white matter changes is the same as that observed in Alzheimer's disease. Using female Wistar rats, BBB dysfunction [1], distributions of amyloid precursor protein (APP) around BBB vessels [2] and platelet pathology [3] were examined in white matter after 10 min brain ischaemia [4] with 1-year survival. Rat brains were perfusion fixed for light and electron microscopic analysis [1]. Permeability alterations of BBB were random, spotty and dispersed and dominated periventricularly. At the same time we noted perivascular C-terminal of APP deposits surrounding BBB vessels, forming perivascular cuffs. Peroxidase extravasations and C-terminal of APP staining involved BBB vessels. Our study revealed numerous platelet aggregates of varying sizes in- and outside BBB vessels. Platelet aggregates such as BBB changes and C-terminal of APP deposits were focal, random and dispersed. C-terminal of APP deposits and platelet aggregation/pathology correlated very well with BBB insufficiency. Chronic BBB changes and platelets in the perivascular space with cytotoxic fragments of APP accumulation may be involved in the gradual maturation of injurious process in ischaemic white matter leading over a lifetime to severe and progressive dementia. Progressing damage of the white matter after ischaemia may be caused not only by degeneration of axons of neurons destroyed during ischaemic injury, but also by pathological changes in BBB vessels with deposition of cytotoxic fragments of APP. We further examined the role of cerebral ischaemia-reperfusion injury with an alternative hypothesis that proposes that repetitive microischaemic-reperfusion insults may form the

basis for development of chronic neurodegenerative disorders such as Alzheimer's disease. This process may occur by increasing the sensitivity of ischaemic neurons and white matter to amyloid formation and aberrant APP processing. On the other hand brain ischaemia provides a bridge between experimental and clinical research that greatly facilitates the interpretation of complex disease processes i.e. in Alzheimer-type dementia. Thus our data support that cardiac arrest in rats represents a good model to study the effect of β-amyloid peptide, confirming that brain ischaemia may be of help to get more insights into the mechanisms leading to the onset and progression of Alzheimer's disease. The profile of white matter neuropathology that is observed in brain ischaemia shares a commonality with the same changes in the Alzheimer's disease brain.

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[A13]

What is it with the penumbra?

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The low effectiveness of human ischaemic stroke therapy means that the penumbra – a risk zone or therapeutic window – is constantly at the centre of attention of many investigators. Many clinical and experimental studies of the penumbra using neuroimaging, histopathological, immunocytochemical, biochemical and electrophysiological methods have been performed. The penumbra is observed not only in some cases with focal brain ischaemia but also in brain and spinal cord trauma and in some cases of subarachnoid haemorrhage. Within this dynamic zone of recurrent depolarization, PET investigations revealed metabolic disturbances, but morphological and neurochemical studies indicated that neurons and astrocytes in the penumbra are able to synthesize various neuroprotective factors. Some of these factors were also found in regions distant from the infarction. Findings obtained from the above investigations perhaps will contribute to extracorporeal synthesis of neuroprotective factors generated by CNS cells and their application in protection of cells within the penumbra.

[A14]

Pineal glial cysts. Report of three cases with diverse clinical pattern

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Glial pineal cysts are benign, mostly asymptomatic lesions that are found incidentally in brain MR imaging or at autopsy studies. Symptomatic cysts of the pineal gland are less common findings and those requiring surgical excision must be distinguished from the neoplastic cystic lesions occurring in the pineal region, such as pineocytoma, low-grade astrocytoma or teratoma.

In this report we present 3 examples of pineal glial cysts, which were diagnosed histopathologically in patients presenting varied clinical pattern. The material for study was obtained in one asymptomatic

case at autopsy from a 69-year-old man who died of ruptured aneurysm of the aorta and in two cases at surgery from young persons. The first surgical case was a 19-year-old girl suffering with severe headaches and the second case was a 17-year-old boy with suspicion of a pineal tumour in MRI. In all cases histopathological and immunohistochemical examination of the specimens revealed a characteristic pattern of cystic structures surrounded by dense fibrillar glial tissue and in part by pineal parenchyma and fibrous capsule, consistent with non-neoplastic pineal glial cysts.

[A15]

Mitochondrial encephalopathies in differentiation of multifocal changes in the brain. Case report of MELAS

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Mitochondrial encephalopathies (ME) are a multisystem disease caused by mutations in the mitochondrial DNA (mtDNA) or mutations in nuclear DNA producing deletions/depletions in mtDNA. In the brain most ME usually cause scattered or diffused foci of necrosis and cavitation, spongy vacuolation, gliosis and mineralizations.

We report a 28-year-old female patient with a normal perinatal and psychomotor development history until the age of 14, when hypoparathyroidism appeared. At the age of 17 intermittent migraine-like headache, transient pareses/hemiparesis and transient amblyopia were observed, followed by epileptic seizures. After some years, dementia, mixed aphasia, cortical deafness and blindness developed.

In a period of 10 years, neuroimaging examination successively revealed: calcification of bilateral basal ganglia, ischaemic foci in the cortex and white matter of occipital, parietal and frontal lobes as well as cerebellar atrophy. In order to exclude infectious disease, multiple sclerosis and neoplasmas, a brain biopsy was performed at the age of 21 years. The biopsy specimens were histochemically, immunohistochemically and electron microscopically examined, which suggested sudanophilic leukoencephalopathy but did not confirm the diagnosis.

The patient was clinically diagnosed with MELAS syndrome, based on the case history and the clinical picture. Later, molecular examination was also performed.

The diagnosis was confirmed by postmortem neuropathological examination in light and electron microscopy. Necrotic foci of various ages not corresponding to arterial perfusion territory were visible. In many structures there was also mineralization in and around the walls of vessels, sometimes with thickening of the affected vessels and spongy vacuolation of cerebral and cerebellar white matter. Electron microscopy revealed proliferation and pleomorphism of mitochondria in neurons and axons and an increased number of mitochondria within cells of vessel walls.

The authors suggest that in differentiation of multifocal changes in the brain, mitochondrial encephalopathies should also be taken into consideration.

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