Folia Neuropathologica

# Abstracts from XVI Conference of Polish Association of Neuropathologists "Neuropathology close to clinical practice"

November 6th, 2010, Warsaw

## [A1]

### Diagnostic dilemmas in biopsy of brain demyelinating and inflammatory changes

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Demyelinating and inflammatory changes may mimic neoplastic tumours of the brain. Some demyelinating processes that take the form of an expansive lesion are called "tumefactive" and in these cases biopsy of the brain may be necessary. Also some inflammatory conditions of the brain (apart from abscesses which obviously behave very much like tumours) may sometimes demand biopsy to exclude tumour.

In such cases interpretation of biopsy material is especially difficult and must be very cautious. The neuropathologist has to take into the consideration not only microscopic changes but also neuroimaging, biochemical data and the clinical picture. The authors present important issues of the biopsy diagnostics of such lesions in the examples of three chosen cases. Case 1 is of an 18-year old girl with a juxtaventricular lesion, presenting with abrupt but partially transient hemiplegia. Case 2 is a 37-year old man with an extremely large parieto-occipital lesion with symptoms of disease (including optic neuritis), which appeared two years earlier. Case 3 is a boy with 8-year history of the disease and a lesion involving in the later stages almost the entire, but only one brain hemisphere. The patient underwent biopsy of the brain twice and in both of them there were unspecific but severe inflammatory changes.

In the two first cases biopsy material was quite similar and suggested tumefactive demyelination. The third case remains an enigma and one of the diagnostic options is Rasmussen's encephalitis.

The authors present these cases as examples of utmost difficulty as well as responsibility in diagnosing tumefactive demyelination and unspecific inflammation of the brain.

## [A2]

### Expression of 8-oxoguanine DNA glycosylase 1 (OGG1) and apoptotic proteins in the brain of a double transgenic mouse model of Alzheimer's disease

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Alzheimer's disease (AD) is one of the most important neurodegenerative disorders and is characterized by deposition of senile plaque, and neurofibrillary tangles in the brain, which may cause generation of free radicals. Reactive oxygen species are highly reactive and may oxidize macromolecules in cells such as proteins, lipids and especially nucleic acids (DNA) and cause several base or sugar modifications in the structure of DNA, leading to strand breaks in the DNA chain. OGG1 is a main DNA repair enzyme that excises 8-oxo-2'-deoxyguanosine (8-oxo2dG) from DNA. 8-Oxo2dG is one of the crucial lesions produced in DNA by oxygen radical-forming agents. It was postulated that decreased expression of OGG1 may lead to higher background mutation frequency and could increase the DNA damage risk. DNA damage may induce apoptosis in wild-type p53-expressing cell. Bcl-2 is an anti-apoptotic protein, which prevents caspase-3 activation through an interaction with Apaf-1. It is neuroprotective against apoptotic cell death caused

by amyloidogenic peptides. Bcl-2 family gene expression regulation is not completely understood in AD.

The aim of the study was to analyse the level of OGG1 and Bcl-2, and Bax proteins, and active caspase-3 in the brain of a double transgenic mouse model of Alzheimer's disease. The studies were performed on 6-8-month-old female mice of B6.Cg-Tg(APP695)3DBo Tg(PSEN1dE9)S9Dbo/J strain (Jackson Lab., USA). Brains of animals were isolated and divided into 3 structures: cerebral grey matter (GM), subcortical white matter (WM) and cerebellum (C). The level of OGG1 and Bcl-2, and Bax proteins was determined with Western Blot method, and study of active caspase-3 was performed with immunohistochemistry technique.

Our studies showed that the level of OGG1 protein was similar in all analysed structures of the brain of experimental animals but little high was in GM. Nevertheless, in GM the level of Bax protein and Bax: Bcl-2 ratio were the highest. However, in M experimental animals the level of OGG1 protein and Bax: Bcl-2 ratio were the lowest.

Moreover, in all analysed structures of the brain of experimental animals appear cells with active caspase-3.

Our study in the mouse model of AD indicated that in the brain of experimental mice, Bcl-2 family proteins and active caspase-3 may be involved in aetiopathology of AD, and OGG1 protein no protect before increased level of pro-apoptotic protein, Bax.

## [A3]

### Capillary vessel involvement in CADASIL

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**Introduction:** CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is a generalized angiopathy manifesting clinically as migraine with aura, progressing dementia and recurrent ischaemic strokes. Lately, in CADASIL patients disturbed vasoregulation, reduced cerebral blood flow in the white matter and diffuse hyperintensities within white matter on MRI images were observed. CADASIL is connected with mutations in the *NOTCH 3* gene but the underlying pathomechanisms linking *NOTCH 3* mutations with morphological changes and clinical symptoms are still unknown. The disease is characterized by degeneration and loss of vascular smooth muscle cells (VSMC) in small resistant arteries and arterioles. Since the receptor protein encoded by the *NOTCH 3* gene is expressed not only on VSMC but also on pericytes in capillaries, microvessels can be a target for the pathological process in CADASIL.

**Material and methods:** On tissues from autopsy brains and skin-muscle biopsies of 12 CADASIL patients morphological examination of capillary vessels in light, fluorescent and electron microscopy was performed. Routine histological stains and immunohistochemical reactions with antibodies against fibronectin to study microvessel permeability were applied. The control material was composed of tissues from 6 brains and skin-muscle biopsies of patients without diseases involving the CNS.

**Results:** In ultrastructural examination pericytes were less numerous than in the control material, shrunken, and revealed features of degeneration similar to changes observed in VSMC. Their cytoplasm contained numerous vacuoles, vesicular structures and complexes of enlarged pathological mitochondria. Degenerative changes were also observed within endothelial-pericytic junctions. Near the pericyte cell membrane numerous deposits of granular osmiophilic material (GOM) were found. Examination of capillary endothelial cells revealed their degeneration, selective death or swelling leading to narrowing or occlusion of the capillary lumen. Pathological endothelial changes were visible mainly in microvessels with pericyte degeneration. The immunohistochemical reaction revealed fibronectin immunoreactivity around microvessels in the cerebral white matter, suggesting their increased permeability.

**Conclusions:**

1. In CADASIL not only VSMC but also pericytes and, probably secondarily, endothelial cells are damaged.
2. Since pericytes are responsible for regulation of contractility in capillaries, their degeneration can be associated with defective vasomotor reactivity observed in CADASIL.
3. Degeneration of pericytes and endothelial cells can lead also to increased microvessel permeability

and disturbances in cerebral microcirculation, resulting in the dispersed white matter damage characteristic for the disease.

## [A4]

### The comparison of different ways of induction of experimental allergic encephalomyelitis (EAE)

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The aim of the study was to compare the way of induction of experimental allergic encephalomyelitis (EAE).

In the basic model female Lewis rats, six weeks old, were used for experiments. Induction of EAE was made by injection of guinea pig spinal cord 50% homogenate with complete Freund adjuvant (CFA) 1 : 1 and mycobacterium tuberculosis 4 mg/ml into hind pads 100 μl each. On the same day pertussis toxin was given intraperitoneally. After 12 days post immunisation (dpi) rats revealed neurological symptoms evaluated on a five-grade scale as follows: 0 – no symptoms, 1 – limp tail, 2 – hind leg weakness and incontinence, 4 – paraplegia & weight loss, 5 – death. Histological studies showed inflammatory foci in the periventricular area in the brain and the spinal cord in the acute phase of EAE as well as in the chronic phase. Looking for induction-specific oral tolerance to myelin oligodendrocyte glycoprotein (MOG), we used this neuropeptide (MOG35-55) to evoke EAE. We followed the original procedure to inject a mixture of peptide (70 μg) with complete Freund adjuvant with *Mycobacterium tuberculosis*, followed by pertussis toxin injection the same day. After 12 days post immunisation local inflammatory symptoms in the hind pad were expressed (functio laesa), but neurological symptoms were minimal (limp tail). In the brain and spinal cord there were no inflammatory foci. We tried to change the proportion of volume of MOG to CFA from 1 : 1 to 1 : 0.5 and to 1 : 1.025 to 1 : 0.125 but without the expected effect.

## [A5]

### Molecular analyses in Creutzfeldt-Jakob disease

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There are no non-invasive tests allowing for definite *premortem* diagnosis of Creutzfeldt-Jakob disease (CJD). 14-3-3 protein in the cerebrospinal fluid (CSF) is the only biochemical marker included in the diagnostic criteria for CJD approved by the WHO. Testing for 14-3-3 protein has been performed in the Department of Molecular Pathology and Neuropathology, Medical University of Lodz since 2003, along with genetic analyses of the polymorphic *PRNP* codon 129. To date, we have analysed CSF samples from 28 patients initially diagnosed as probable sporadic CJD cases, 101 possible, and 98 non-likely CJD patients. Additionally, 12 CSF samples from patients diagnosed for other neurological diseases, not conducted with prions, were included in the analysis. Among 28 probable CJD cases, 25 were positive for 14-3-3 protein; 11 of 14-3-3-positive and 1 negative patient were definitely neuropathologically confirmed as CJD cases. Protein 14-3-3 was also detected in 37/101 possible (12 of which were subsequently confirmed as definite cases), 10/98 non-likely CJD, and 3/12 other neurological diseases. False positive results were found in CSF samples from patients with encephalitis, CNS tumour and subarachnoid haemorrhages. Our findings indicate that the test for 14-3-3 protein is useful only when considered in an appropriate clinical context, together with other diagnostic criteria. A positive result in patients who do not meet the criteria for possible CJD is more likely to be a false positive one. *PRNP* codon 129 analysis performed in 44 probable and possible CJD cases positive for 14-3-3 protein revealed a proportion typical for CJD: 64% Met/Met, 20% Val/Val, and 16% Met/Val genotypes. Genetic analyses are useful for identification of the molecular subtype of the disease and can aid the diagnostics of patients suspected of variant CJD as all clinical vCJD cases known to date have been Met/Met homozygotes.

## [A6]

### Changes in astrocytes of rat brain during the course of experimental autoimmune encephalomyelitis

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Multiple sclerosis is one of the most frequent causes of neurological disabilities in young adults. During the course of MS progressively developing plaques of demyelination are observed, with oligodendrocyte and axonal death. Experimental autoimmune encephalomyelitis (EAE) is the best known and frequently used model of MS. Recently, investigations concerning pathological mechanisms in MS/EAE are focused on the role of astroglial cells. Astrocytes not only maintain an extracellular milieu optimal for neuronal function, but also influence neuronal cells' properties. Thus, dysfunctional astrocytes may play an active role in neurodegenerative axonal damage being the source of potentially toxic substances such as glutamate and ATP. The aim of this study was to investigate changes in astrocytes in rat brain during the course of experimental autoimmune encephalomyelitis using microscopic and biochemical techniques. We observed very early activation of astroglia, which took place in an asymptomatic phase of the disease. Starting from day 4 post immunization, we noticed the enhanced expression of astroglial markers – GFAP, S100b, and also connexin 43, which builds hemichannels and tight junctions channels – relative to the control animals. Changes in the expression of the main glutamate transporter, GLT-1, were also observed. Parallel to the activation, pathological changes in cerebellar astrocytes were seen in microscopic study which were described as clasmatodendrosis. As astroglia are the main source of glutamate and ATP which under pathological conditions may be released through the connexin hemichannels, P2X7R and the reversed transporter system, we conclude that these cells may be involved at a very early stage in the progression of symptoms in the brain of diseased animals.

## [A7]

### The influence of the extent of surgical resection of glioblastoma on survival. Preliminary results

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**Objective:** Treatment of glioblastoma still remains a challenge for neuro-oncology. The main goal of surgical treatment of patients with this highly malignant primary brain tumour is radical removal of the tumour without causing neurological deficits. However, according to published literature, it remains unclear whether the extent of surgical resection influences survival. Therefore, the aim of this study was to assess the influence of degree of glioblastoma resection on survival time. The author also analysed other factors influencing survival and quality of patients' life.

**Material and methods:** The study is based on a prospective protocol. All consecutive patients with neuropathologically proved glioblastoma were enrolled in the study. Patients underwent either gross total resection, partial resection or biopsy of the tumour. All patients were given the same postoperative adjuvant therapy. Every tumour was assessed by means of semi-automatic volumetry based on enhanced T1 MRI preoperatively and postoperatively. The patients were followed up until death. Survival times were recorded and analysed in relation to the extent of resection and other clinical factors. The patients who died in the 30-day perioperative period were excluded from the study. Survival analysis was performed using Kaplan-Meier product limit estimators, and the variables patient age, gender, neurological status, location and volume of the tumour, and extent of resection were included in the analysis.

**Results:** This is the first part of the study. It includes data of 30 patients enrolled between June 2007 and December 2009. There were 20 males and 10 women, with mean age 58.5. In this group preoperative volume of the tumour was < 50 $cm^3$ in 16, 50-100 $cm^3$ in 12, and > 100 $cm^3$ in 2 patients respectively. The mean extent of resection of the tumour was 77% (range 0% [biopsy] – 100% [total resection]). The mean survival was 346 days, range 77-933 days. The statistical analysis showed no statistically significant correlation between surgical resection and survival time ($p < 0.05$).

**Conclusions:** Despite there being some trend that more radical resection of glioblastoma prolongs survival, there is a lack of strong statistical evidence to support this hypothesis.

## [A8]

### Microglia in gliomas

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**Introduction:** Microglia are considered the immune cells of the brain. Microglial cells were shown to be present in astrocytic tumours, although the findings of correlation between microglia and tumour grade were inconsistent. In this study we evaluated the extent of tumour infiltrating microglia in astrocytic and oligodendroglial tumours.

**Material and methods:** The extent of tumour infiltrating microglia was determined in 50 samples of supratentorial gliomas (30 astrocytomas and 20 oligodendrogliomas) using immunohistochemistry. Antibodies against CD68 and Iba1 were used. Immunostaining results were assessed semi-quantitatively.

**Results:** Expression of both microglial markers was significantly higher in astrocytomas than in oligodendrogliomas ($p$ = 0.002 for Iba1 and $p$ = 0.016 for CD68). There was a statistically significant difference in microglial infiltrate assessed using Iba1 and CD68 between low- (WHO grade II) and high-grade (WHO grade III and IV) astrocytomas with $p$ values of 0.015 for Iba1 and 0.0002 for CD68. Kaplan-Meier survival analysis showed that glioma patients with high Iba1 expression had significantly shorter overall survival than those with low Iba1 expression (log rank, $p$ = 0.015). There was a similar trend for CD68 expression (log rank, $p$ = 0.074). The two microglial stains were highly correlated ($r^2$ = 0.689).

**Conclusions:** Microglial cells are less abundant in oligodendrogliomas than in astrocytomas and microglial infiltration is an adverse prognostic factor. Further studies are needed to determine whether microglia could be therapeutically modulated in high-grade gliomas.

## [A9]

### Proliferative activity in all subtypes of glioblastoma

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**Introduction:** Glioblastoma is the most malignant (G4) and the most frequent primary brain tumour in adults. It accounts for 60-75% of astrocytic tumours with a peak incidence at between 45 and 75 years of age. According to the 2007 WHO classification of the central nervous system the tumour has two variants: giant cell glioblastoma and gliosarcoma. Proliferative activity in glioblastoma is usually prominent.

**The purpose** of the study was to answer the question: Are there any differences between values of the proliferative index MIB-1 of small cell glioblastoma, giant cell glioblastoma and gliosarcoma?

**Material and methods:** Surgical specimens from 60 patients operated on in the Department of Neurosurgery of the Medical University of Lublin between 1996 and 2009 were formalin-fixed, paraffin-embedded, stained with H&E and diagnosed according to the WHO classification as follows: glioblastoma – 20 cases; giant cell glioblastoma – 20; gliosarcoma – 20. Next, 3-µm-thick sections were immunostained using MIB-1 monoclonal antibody and MIB-1 proliferative index (MIB-1 PI) was calculated. For each diagnostic group: number of cases, mean, standard deviation, standard error of the mean, minimum, maximum, and 95% confidence interval for the mean were calculated. Analysis of variance (ANOVA) was used to test the hypothesis that mean values of MIB were equal for each diagnostic group.

**Results:** The mean values of MIB-1 PI were as follows: glioblastoma – 25.7% (14.7-43.7%); giant cell glioblastoma – 21.7% (4.9-39.7%) and gliosarcoma – 27.2% (12.5-46.9%), but there were no statistically significant differences of the MIB-1 PI mean value between diagnostic groups.

**Conclusions:** We observed that proliferative activity shows great regional variation and is the most prominent in gliosarcoma. In giant cell glioblastoma it was much lower but there were no significant differences in MIB-1 PI between subtypes of glioblastoma in our study.

## [A10]

### The role of electron microscopy in the diagnosis of CADASIL syndrome

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Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is a systemic vascular disorder caused by mutations in the Notch3 gene located on chromosome 19. Morphologically, the presence of granular osmiophilic material (GOM) in thickening of vessel walls is the main pathological finding in electron microscopy. The Notch3 gene has 33 exons but CADASIL mutations exist in exons 2-24 which encode the extracellular domain of the Notch3 receptor.

To date, over 170 different mutations in 2-24 exons have been reported. However, more mutations exist in exons 2-6. The diagnosis of CADASIL may be confirmed by genetic testing. Theoretically, screening of 23 exons is the gold standard for the diagnosis of CADASIL with sensitivity close to 100%. From the practical point of view, genetic screening of 23 exons is expensive, time consuming and not feasible for most laboratories. On the other hand, genetic testing of a limited number of exons may frequently be insufficient to find Notch3 mutations. Moreover, in some countries genetic testing for CADASIL diagnosis is not performed.

Ultrastructural investigations of different extracerebral biopsies from patients present an alternative method for confirming CADASIL diagnosis. Although clinical manifestations are only cerebral, morphological changes in vessels, including the presence of granular osmiophilic material, are also present in other organs, e.g., muscles, kidneys and skin. In CADASIL, electron microscopy shows GOM deposits consisting of a specific ultrastructural feature pathognomonic for this disease.

In the present study, the ultrastructural examination of the skin and muscle biopsies derived from 7 patients revealed lesions of blood vessels typical of CADASIL. A thorough electron microscopy analysis showed extracellular granular osmiophilic material located close to the cellular surface of vascular smooth muscle cells (VSMCs), as well as pericytes in capillaries and between degenerated VSMCs or in their indentations in numerous vessels. GOM at the ultrastructural level revealed a characteristic picture and it can be easily distinguished from other non-specific granular debris present in some other diseases.

GOM specificity is 100%, which means that this structure is pathognomonic for CADASIL. However, in different reports the sensitivity of GOM examination in electron microscopy ranges from 45 to 100%. It was postulated that GOM detection by electron microscopy is only useful when positive. Our experience and that of other authors suggest that a small size of the examined specimens and the focal localization of GOM deposits are the major causes of such great differences in sensitivity.

The results of our study show that a thorough ultrastructural analysis of a sufficiently large number of vessels significantly enhances the sensitivity of GOM detection. Moreover, in our opinion and in the opinion of some other authors, additional biopsies should be examined if we fail to find GOM in the first biopsy.

Electron microscopy and genetic testing are still the gold diagnostic standard in CADASIL.

## [A11]

### Soft tissue perineurioma of retroperitoneum – an incidental finding in an 80-year-old man

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Soft tissue perineurioma is a rare peripheral nerve sheath tumour with perineural cell differentiation. Soft tissue perineuriomas are typically not associated with nerve and usually develop in the subcutaneous tissue of the extremities and trunk in adults. The grading system of perineuriomas ranges from benign (WHO grade I) to malignant (WHO grades II and III).

The 80-year-old patient had undergone left side hemicolectomy due to adenocarcinoma of the large intestine. Among lymphatic nodes of retroperitoneal adipose tissue, a lesion composed of cream cystic nodules measuring from 0.3 to 0.7 cm in diameter was found. The tumour was well circumscribed but not

encapsulated, the cut surface white-grey and myxoid. Histologically, the tumour was composed of multiple pseudo-onion structures consisted of spindle cells with strikingly thin cytoplasmic processes arranged in lamellae. Their nuclei were elongated and the nucleoli inconspicuous. No mitoses were found. The tumour was hypocellular, with scant stroma conferring loose myxoid appearance. Immunohistochemically, the tumour cells were epithelial membrane antigen (EMA) and vimentin positive, whereas they lacked S100, CD34 and p53. Axons in the centre of pseudo-onion bulbs were S100 positive.

In the differential diagnosis schwannoma, neurofibroma, MPNST and myxoma were taken into consideration. On the basis of histological and IHC data, the diagnosis of benign soft tissue perineurioma (WHO I) was made. To our best knowledge this is the fifth case reported in the retroperitoneal location.

## [A12]

## Immunolocalization of receptor for advanced glycation end-products (RAGE) and amyloid beta peptides in human choroid plexus and ependyma after cardiac arrest

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The close relationship between Alzheimer's disease (AD) and alternations in the bidirectional transport of amyloid-beta peptides (Aβ) across the blood-brain barrier (BBB) has been recently documented. This barrier is located in endothelial cells of brain capillaries and expresses the receptors and transporters that enable Aβ transport. The receptor for advanced glycation end-products (RAGE) mediates influx of Aβ to the brain from the circulating blood, whereas amyloid-beta efflux transport is supported by low-density lipoprotein receptor-related protein 1 (LRP-1). Because localization of these receptors in other brain barriers is not known, in the present study we examined RAGE and LRP-1 in the choroid plexus (blood – cerebrospinal fluid barrier) and in the ventricular ependyma (cerebrospinal fluid – brain barrier). This study was performed on 32 patients (54-78 years of age) affected by severe ischaemia due to cardiac arrest. These patients were resuscitated but they died a few days or a few weeks afterwards. The age-matched controls included patients who died immediately after cardiac arrest. Since aging and severe ischaemia are known risk factors for developing Alzheimer's disease, we also assessed immunolocalization of amyloid-beta peptides in the brain, choroid plexus and ependyma of all our patients.

The battery of antibodies generated against different antigenic domains of LRP-1, RAGE and Aβ was purchased from Santa Cruz Laboratory (USA). The immunohistochemical and immunocytochemical reactions were evaluated respectively in light or electron microscopes.

In brains of the oldest patients who died 3-4 months after resuscitation the heaviest accumulation of amyloid-beta peptides was found. These peptides formed numerous deposits of different type as diffuse and senile plaques, brain vessel wall deposits and Aβ-immunopositive infiltrations around numerous brain vessels and in subependymal brain regions. In the choroid plexus, Aβ-peptides were found within blood vessels, in the basement membrane and in large vacuoles of epithelial cell cytoplasm. The content of these vacuoles underwent progressive digestion leaving in some cells a denser peripheral part of this material which formed rings or rolls. In all epithelial cells of the choroid plexus and in ependymal cells RAGE receptors were found. They were precisely located in the fragments of cell membrane that were connected with the basement membrane or with the ventricular surface of the brain. Antigens of LRP-1 receptors were not found.

The results of our study confirmed the previous observations that RAGE receptors participate in the clearance of amyloid-beta peptides from the circulating blood. RAGE mediates transport of these peptides across the blood – cerebrospinal fluid barrier located in the epithelial cells of the choroid plexus. RAGE operating in ependyma binds amyloid-beta peptides from the cerebrospinal fluid and transports them into the brain through the cerebrospinal fluid – brain barrier. Taken as a whole, all our results reinforce the hypothesis that the RAGE receptor is a potential drug target in Alzheimer's disease.

## [A13]

### Primary and secondary clear-cell brain tumours

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Clear cell morphology is seen in different types of primary brain tumours, metastases, and certain non-neoplastic disorders. The most common clear cell brain tumours include oligodendroglioma, central/extraventricular neurocytoma, clear cell variant of ependymoma clear cell meningioma, haemangioblastoma, and metastatic clear cell carcinoma. Moreover, clear cell features can sometimes be observed in regions of other primary brain tumours such as pilocytic astrocytoma, dysembryoplastic neuroepithelial tumour (DNT) with oligodendrocyte-like elements, glioblastoma with small cell or oligodendroglial component, diffuse astrocytoma, pineocytoma, rosette-forming glioneuronal tumour (RGNT), paraganglioma, pituitary adenoma, germinoma, and primary CNS lymphoma. Occasionally, some non-neoplastic disorders such as demyelinating processes or cerebral infarct with foamy macrophages might mimic tumours of clear cell histology. All these lesions exhibit similar morphological characteristics and ought to be considered in the differential diagnosis. This is particularly important in small biopsy materials obtained by stereotactic and endoscopic biopsies. The critical histological diagnosis of clear tumours requires a spectrum of immunohistochemical staining. In some cases the evidence of ultrastructural features of astroglial, ependymal, meningothelial or epithelioid differentiation might be helpful for identifying cell histogenesis. Both clinical and neuroradiological data are also important, especially in diagnosis of small surgical samples.

## [A14]

### Lipomatous differentiation in astroglial tumour

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Lipomatous transformation of tumour cells into mature adipocyte-like cells in primary neuroectodermal tumours of the central nervous system is encountered only occasionally. More often focal lipidization occurs in neuronal tumours including cerebellar liponeurocytoma. In the literature only a few cases of low-grade astroglial tumours with advanced lipidization have been reported.

We present an example of advanced lipomatous changes in a low-grade astroglial tumour. The tumour was seen on MRI as a relatively well-circumscribed lesion in the right temporal lobe in a young patient with drug-resistant, intractable epilepsy. The tumour was highly cellular and composed mainly of pleomorphic astroglial cells. A few Rosenthal fibres and occasional eosinophilic granular bodies or hyaline droplets were seen. Focally, the tumour tissue contained neoplastic cells of neuronal origin. Numerous cells exhibited various amounts of fat droplets. Some neoplastic cells with cytoplasm completely filled with large lipid droplets closely resembled mature adipocytes. Mitosis, necrosis and vascular proliferation were absent. The reticulin fibres were limited to blood vessels. Neoplastic cells revealed a low proliferation potential with very low MIB-1 labelling index. Immunohistochemically, the astroglial cells exhibited diffuse expression of GFAP and S100 protein. Some cells revealed immunoreactivity of NSE, Neu-N and synaptophysin.

Our case demonstrates extensive lipomatous transformation in a low-grade astroglial tumour with neuronal component.

## [A15]

### Tumours of the pineal region with papillary features – diagnostic dilemma

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The pineal gland is a region typical for localization of various neoplasms including tumours with papillary histological features. So-called papillary tumour of the pineal region (PTPR) is a rare neoplasm included in the 2007 WHO classification of brain tumours. The differential diagnosis of this neoplasm is often difficult because both primary and secondary papillary lesions of the pineal region ought to be considered, including parenchymal pineal tumour, papillary ependymoma, papillary meningioma, choroid plexus papilloma and metastatic papillary carcinoma.

We report three cases of PTPRs with various histological features, i.e. vessels covered by several layers of uniform columnar to cuboidal tumour cells, distinct papillae covered by layers of polymorphous cells with atypical, hyperchromatic nuclei or solid cellular areas composed of pseudostratified columnar cells, most often arranged in perivascular pseudorosette formations. Mitotic figures were rare and areas of necrosis were observed in one case. Immunohistochemical staining displayed diffuse immunoreactivity of neuron-specific enolase, S-100 protein, vimentin and focal reaction for synaptophysin, chromogranin A, cytokeratin and epithelial membrane antigen (EMA). The Ki-67 labelling index was relatively low, but its focal increase was observed. The critical diagnosis of PTPRs was based on predominant papillary morphology and supported by immunohistochemical study.

PTPRs should be considered in diagnosis of pineal tumours but sometimes their morphology might be controversial.

## [A16]

### Cancer cell lines – what do we test, what should we test?

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It has been reported recently by several sources that cell phenotypes or genotypes cannot be maintained *in vitro*. For example, heterozygous mutations of *TP53* have frequently been described *in vivo*, but we met strong obstacles trying to find any cell lines showing stably and/or in reality, single heterozygous mutation of *TP53*. More importantly, elimination of *EGFR* amplification during glioblastoma cell cultures is a well known phenomenon, the causes of which however remain enigmatic. It should also be considered that similar problems were observed by us in standard cell culture conditions referring to *IDH1* mutated cells. *IDH1* mutations seem to play a significant role in glial tumours. However, the specific role of the *IDH1* mutation in glial tumours such as astrocytic tumours and secondary glioblastomas is unknown. Surprisingly, none of 20 commercially available astrocytoma cell lines present *IDH1* mutations, whereas, according to the literature, up to 80% of astrocytomas should present *IDH1* mutations. The cell culture conditions currently used are artificial and thus unsuitable for the growth and analysis of all types of cancer cells since they cause too many artefacts. Nonetheless, factors responsible for eliminating these cells from cultures should be identified for possible pharmacological use. In the case of glioblastoma cells we have developed an *in vitro* 3D model to analyse the original genotype, especially *EGFR* amplification.

*This study was supported by the Ministry of Science and Higher Education projects no. N N 401 1558 33.*

## [A17]

### Analysis of *PARK2* gene mutation in sporadic Parkinson's disease

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Parkinson's disease (PD) is one of the most common neurodegenerative disorders, not only in Poland. However, early diagnosis of PD is often difficult. Although the genetic basis of familial PD is now fairly well established, the majority of PD is sporadic. The aetiology of sporadic PD is not clear, but it is currently assumed that genetic susceptibilities may be involved.

Increasing evidence supporting a direct role mainly for *PARK2* in sporadic both early- and late-onset disease make this gene a particularly compelling candidate for intensified investigation.

The aim of the study was to perform analysis and identification of *PARK2* mutation in Polish patients with sporadic PD, those with other degenerative and non-degenerative neurological diseases, as well as in a control group.

Peripheral blood was collected from 32 patients with sporadic late-onset PD clinical diagnosis (average age 59 years), 11 patients with other extrapyramidal disorders (multiple system atrophy, Parkinsonism) (average age 59 years) and 12 patients with other neurological diseases without characteristics of dementia (average age 62 years) as well as from 25 healthy donors (average age 60 years).

Genomic DNA was isolated using standard protocols. PCR amplification of parkin exons 2 and 4 was performed to detect exon deletion. Moreover, exons 4, 7 and 11 of the *PARK2* gene were screened using real-time PCR/HRM and exon sequencing.

None of the patients or control subjects tested had exon 2 or 4 deletion. Mutations in tested exons of the *PARK2* gene were identified in 7 (22%) patients with sporadic late-onset PD, no patients with other extrapyramidal disorders, 1 (8%) patient with other neurological disorders, and 1 (4%) control subject. All detected mutations were heterozygous. One of the PD patients had two mutations in the *PARK2* gene (G1281A, G601A).

It can be concluded that deletion of exons 2 and 4 of the parkin gene are rare causes of PD in Poland. Moreover, point mutation in *PARK2* seems to be associated with sporadic late-onset PD in the Polish population. Thus, the results of this study suggest that screening for *PARK2* mutations may be a component of genetic testing for sporadic PD.

## [A18]

### Meningiomas of the middle ear. Report of 3 cases

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Extracranial middle ear meningiomas are rare tumours that are mostly unrecognized or misdiagnosed preoperatively. They represent up to 2% of all primary tumours involving the ear and temporal bone. We report 3 cases of meningiomas of the middle ear that were surgically removed and histopathologically diagnosed after long-term conventional pharmacological management for assumed chronic otitis media. All cases were women, aged 47, 57 and 59 years. The clinical symptoms included progressive unilateral hearing loss, otalgia, and in one case headache with vertigo. Duration of symptoms before surgery ranged from 3 to 15 years. Preoperative CT examination in 2 cases revealed tumour-like masses suspected as chemodectoma. Histopathological examination of the surgical specimens demonstrated meningothelial meningioma in all cases. Immunohistochemically the tumour cells stained positive for epithelial membrane antigen and negative for chromogranin or synaptophysin and cytokeratins. The presented cases indicate that meningiomas of the middle ear are slow growing tumours with non-specific clinical symptoms. Their correct diagnosis requires histopathological evaluation and differentiation with

more common tumours in this region such as paraganglioma, schwannoma, adenoma and adenocarcinoma.

including determination of 1p/19q deletion in the diagnostic and treatment algorithm in low-grade gliomas.

## [A19]

### Prognostic value of 1p and 19q chromosomal arms deletion in supratentorial low-grade gliomas

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Diffuse gliomas can constitute up to one third of all gliomas diagnosed in neurosurgical centres. Their invasive growth, progression to more malignant lesions, and the lack of standardized management guidelines constitute a significant clinical problem. The discovery of 1p and 19q chromosomal arms deletion in neoplastic cells will probably influence both more objective diagnosis and more accurate prediction of chemotherapeutic response. Defining the above-mentioned deletion is becoming a standard procedure in Western European countries and in the USA when low-grade glioma is diagnosed. As a result an attempt has been made to detect the deletion using fluorescence in situ hybridization and to determine its prognostic value.

Genetic material from 34 grade 2 gliomas was examined. Separate 1p and 19q deletions were discovered in 16 cases and simultaneous occurrence of both in 12. The frequency of occurrence of simultaneous 1p and 19q deletions varied based on histopathological diagnosis. This disorder was not observed in astrocytomas, while in oligoastrocytomas it appeared in 50% of cases. The highest incidence of deletion was noted in oligodendrogliomas and was 66.7%, $p < 0.005$. Median survival in patients with diagnosed 1p and 19q deletion in their neoplastic cells is twice as long as in patients in whom no such deletion was observed (80 months vs. 41 months, $p < 0.05$). Frontal location of a tumour was found to be a statistically significant factor unfavourable for prognosis, $p < 0.05$.

In the presented work, fluorescence in situ hybridization was successfully applied to identify 1p/19q deletion. Its incidence depends on the type of diagnosed glioma. Deletions also have prognostic significance in the test group, which provides a basis for

## [A20]

### Brain lobar haemorrhage; cerebral amyloid angiopathy in a hypertensive person and PAN-like changes – an overlapping syndrome?

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After advanced age, cerebral amyloid angiopathy (CAA) and hypertension (HTN) are the two most important risk factors for hemorrhagic stroke. Inflammatory changes of amyloid-laden vessels have been reported only in rare sporadic CAA cases.

We present the case of a 78-year-old woman with a history of hypertension, dementia and haemorrhagic stroke of the right frontal lobe 2 years before admission. She was admitted with symptoms of transient aphasia and central, right-side facial paresis that occurred an hour before arrival at the hospital. In the admission unit, she was only slightly confused, with no other neurological deficits. An urgent CT scan revealed a recent haemorrhagic stroke in the left frontal lobe. In an hour her condition suddenly deteriorated; after generalized seizure she presented with right-side hemiparesis with signs of uncal herniation and remained unconscious. A control CT scan showed a large haemorrhagic expansion that comprised the whole left brain hemisphere with 2 cm midline shift. She died about 10 hours after the onset of symptoms. At autopsy chronic inflammation of the thyroid gland, bronchopneumonia, fibrous and fatty heart degeneration and kidney haemorrhagic infarcts were documented. Amyloid deposition and systemic immune disorders in the inner organs were not demonstrated. Neither fibrinoid necrosis of glomerular capillaries, nor endarteritis of arterioles and small arteries, regarded as characteristic changes in malignant hypertension, was found. On neuropathological examination the coexistence of a few vascular changes of different

types in the wall of cerebral small vessels, including capillaries, was revealed. In numerous small leptomeningeal and cortical arteries and arterioles, Congo red and β-amyloid positive depositions and loss of SMA-positive vascular smooth muscular cells (VSMC) were found. A number of both HTN- and CAA-related angiodestructive changes (vessels with double barrel appearance, fibrinoid necrosis, lipohyalinosis and miliary aneurysm formation) were observed. Leptomeningeal and cortical medium and small arteries and arterioles were surrounded by panarteritis (PAN)-like inflammatory infiltrates of different size composed mainly of T lymphocytes. Transmural infiltration and obliterative changes without multinucleated cells were seen in some vessels. In addition, lymphocytic inflammation of the subarachnoid space was found. Perivascular infiltration was also noted around unruptured miliary aneurysms, whereas petechiae surrounded ruptured aneurysmatic changes.

In summary, the conjunction of different types of cerebral small vessel diseases, present in our patient, poses a few questions:

- Overlapping HTN and CAA was presented.

HTN- and CAA-related vascular changes, sometimes termed "mixed microangiopathy", was microscopically confirmed. In numerous vessels superimposed fibrinoid necrosis and amyloid deposition were developed. Advanced and mixed vascular changes caused rapid progress of brain haemorrhage. High blood pressure may exacerbate the tendency to CAA-related haemorrhage and vice versa.

- Overlapping of PACNS (primary angiitis of the central nervous system) and CAA?

PACNS and sporadic CAA are generally considered as two distinct devastating diseases of cerebral vessels. Their overlapping cannot be ruled out. However, in our patient apart from HT-related features other systemic immune disorders were not found.

- PACNS associated with CAA, also termed amyloid-β-related angiitis?

To date only a few case reports on probable amyloid-associated inflammation have been presented. Granulomatous subtype of PACNS has frequently been revealed. In our CAA patient, PAN-like changes were consistent with necrotizing and lymphocytic PAN-like subtype of PACNS. The presence of morphological changes similar to those observed in panarteritis may indicate a possible immunological origin of PACNS in our CAA patient. The Mayo Clinic study has recently suggested that PACNS-associated CAA can be triggered by vascular Aβ-deposition. Thus the proposed acronym "ABRA" for PACNS-associated CAA is formed from the initial letters of amyloid-β-related angiitis.

- Time will show whether the cited authors are right.

## [A21]

### Disseminated tumour emboli and cerebral infarcts in a case of lung carcinoma with metastasis to the left ventricle of the heart

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Ischaemic cerebrovascular complications in cancer patients are commonly associated with hypercoagulability, resulting in thrombosis or thromboembolism in advanced malignancy. Tumour embolism with secondary infarcts of the brain has been rarely reported, in most cases as a postmortem finding.

This report presents a case of a 58-year-old man with widespread tumour emboli that were also diagnosed *post mortem*. The patient was admitted to the hospital with symptoms of dyspnoea, fever, dementia and consciousness disturbances. X-ray and CT scan of the chest suggested tumour of the right lung. MRI examination of the brain revealed multiple ischaemic foci, presumably of vascular origin, in the cortico-subcortical regions of both hemispheres. The patient died suddenly. Autopsy pathological study revealed squamous cell carcinoma of the right lung with metastases to regional lymph nodes, spleen, and, unexpectedly, to the left ventricle of the heart. Histologically, a left intraventricular mass was consistent with metastatic squamous cell carcinoma of the lung. Moreover, intravascular emboli of the tumour were seen in coronary, pulmonary, renal and cerebral arteries. Neuropathological examination of the brain revealed disseminated tumour emboli occluding the meningeal arteries and intracerebral arterioles. Multiple small cortical infarcts, developed secondary to embolization, were seen in cerebral and cerebellar hemispheres. The source of arterial tumour emboli in this case was metastasis to the left ventricle of the

heart, which is an extremely rare event associated with primary lung carcinoma.

## [A22]

### Bone tuberculosis suggesting neoplastic metastatic process: a case report

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Extra-pulmonary tuberculosis (TB) may involve any organic system and clinical symptoms are non-specific. Bone tuberculosis may mimic primary or metastatic neoplastic disease. Lumbar and thoracic regions are often involved, whereas TB occurrence in the cervical spine is uncommon.

We describe the case of a 48-year-old Vietnamese woman, who was admitted to the Department of Surgery because of a cervical spine (C7) compression fracture. Several months earlier, the patient complained of neck pain and numbness of the hand. Ten years ago she had a total hysterectomy. On physical examination, the patient was subfebrile and complained of pain over the cervical spinal area.

Neurological examination revealed no focal motor weakness. Laboratory results were near or within normal limits; only the tumour marker cancer antigen (CA) 19-9 was slightly increased. Abdominal ultrasonography was normal.

The roentgenograms of the chest, pelvis and cranium were also normal. Radioisotope bone scanning showed abnormal accumulation of isotope in the lower cervical region, thoracic vertebra (Th7), as well as the articulation of knees and shoulders and in the left tibial bone. An MRI scan revealed compression fracture of the C7 vertebral body with infiltration of paraspinal tissues at the vertebral column with indentation of osseous masses into the spinal canal. The lesion resembled neoplasm metastasis.

The neoplasm infiltrating vertebral body C7, two discs, C6-7 and C7-Th1, and ligament were removed surgically. The masses of soft tissue looked like metastasis.

Neuropathological examination of the removed material showed typical granulomatous inflammation with characteristic infiltrate of lymphocytes, epithelioid macrophages and Langhans-type multinucleated giant cells.

The spoligotyping method confirmed the presence of *Mycobacterium tuberculosis* complex in the specimens.

## [A23]

### High number of the plaque-like VV sCJD subtype among the Polish sCJD – is there a connection with BASE?

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Amyloidotic spongiform encephalopathy (BASE) or L type BSE is overrepresented in Poland (15% of all cases of BSE). Moreover, the number of BASE cases in Poland per million bovines is the highest in Europe. A potential human risk from BASE is evident from experimental transmission to "humanized" transgenic animals and primates. Taking into consideration that non-human primate inoculated with BASE had a shorter incubation period than monkeys infected with classical BSE, and that humanized Tg mice have been found to be highly susceptible to infection with atypical form of BSE, it seems probable that BASE may be more pathogenic for humans than BSE, but the transmitted disease may differ from BSE-derived vCJD. Among 47 cases which have been diagnosed as definite in our laboratory, in 19 cases complete histopathological examination and codon 129 status were available. On the basis of the histological pattern and codon 129 status the cases of sCJD were divided into subtypes according to the Parchi&Gambetti classification. The results are as follows: type 1 (MMorMV) – 44%, type 2 (VV) – 32%, type 3 (MV) – 8% , type 4c (MM) – 12% and type 5 (VV) – 4%. Although the number of cases is too low to conclude a significantly different distribution of sCJD subtypes in Polish population those data show surprisingly high number of the plaque-like VV sCJD subtype. Interestingly, it was shown before that Tg mice inoculated with BASE showed granular and plaque-like aggregates or PrPSc in brains resembling VV2 subtype of sCJD.