Folia Neuropathologica

Abstracts from XV Conference of Polish Association of Neuropathologists "Tumours of the nervous system"

May 29-30, 2009, Warsaw

[A1]

Fetus-in-fetu or teratoma? Considerations based on unusual case of tumor lesion localized partially intracranially

Adamek D[1,4], Drabik G[1], Kwiatkowski S[2], Lankosz-Lauterbach J[3], Mieżyński W[1], Radwańska E[4], Kobylarz K[5], Wyrobek Ł[6], Piniewska D[7]

[1]Department of Pathology, [2]Department of Pediatric Neurosurgery, [3]Department of Intensive Care, University Children's Hospital, [4]Department of Neuropathology, Chair of Pathology, [5]Department of Anaesthesiology, [6]Department of Radiology University Children's Hospital, [7]Chair of Forensic Medicine, Medical College, Jagiellonian University, Cracow

Introduction: Since the time of Johann Friedrich Meckel, who for the first time introduced the term "Fetus-in-fetu" (FIF) the relation between FIF and teratoma has not been solved. FIFs are very rare (less than 200 *bona fide* FIFs, mainly in retroperitoneal space, were reported up to date). Intracranial FIFs are extremely rarities (11 cases reported). The authors present the case of inborn, partially intracranial FIF.

Case description: A male newborn in a grave state presented with large partially intracranial tumor 9 cm of diameter distorting his head was admitted to University Children's Hospital in Cracow. The tumor was detected prenataly and the pregnancy was terminated in 33rd week of gestation by cesarean section (with prior induction of lung maturation by dexamethason). It has been decided that the tumor would be immediately removed surgically to give the child the chance of survival. However just at the moment of introduction to anesthesia the child abruptly deteriorated and eventually died the next day.

The general autopsy showed the features of fetal respiratory distress syndrome. The large tumor in the head was located in right anterior, medial, and pterygopalatinal cranial fossa partially displacing child's brain to the left. The tumor was entirely encapsulated and connected to the rest of the body by a distinct vascular stalk. After the incision of the capsule four relatively well developed limbs (with fingers) protruding from the rest of the tumor mass were seen.

Microscopically, apart from well formed and covered with skin limbs, there were haphazardly distributed different tissues or fragments of organs like intestine, glands, muscles and fat tissue. However different neuroectodermal derivatives, like structures resembling primitive neural tubes, ganglions, neuroglial and ependymal structures were dominant.

Discussion: According to some authors the presence of elements of axial skeleton (vertebrae) is necessary to diagnose FIF, however this postulate is questioned. Moreover many cases with FIF accompanied by teratoma were reported. This seems to be true also in the presented case. Such co-occurrence unnecessarily proves the common pathogenesis. One cannot exclude that e.g. FIF may play a role of merely predisposing factor for development of teratoma. Regardless this pathogenetical consideration considering the localization of FIF in the presented case it is hard to resist the general humanistic reflection that the mythical tale of the birth of Athena might have been based on a true event?

[A2]

Treatment of multifocal tumors of pilocytic astrocytoma during 10 years

Andrychowski J[1], Czernicki Z[1], Taraszewska A[2], Netczuk T[1], Dąbrowski P[1]

[1]Department of Neurosurgery, [2]Department of Clinical and Experimental Neuropathology, Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw; [3]Department of Neurosurgery, 2nd Faculty of Medicine, Medical University of Warsaw, Warsaw

The dissemination of low-grade gliomas is uncommon events. We report a unique case of dissemination of pilocytic astrocytoma (PA) in a young female patient, observed and treated at the Neurosurgical Department for the pe-

riod of 10 years, during which time she had frequent surgical procedures. The disease occurred at the age of 16years when the patient suffered from cerebral tumor in the right temporal lobe. The surgery of partial temporal lobe resection followed by re-operation and radiotherapy was performed. Five years later local recurrence of the tumor occurred and surgical treatment of total tumor removal was performed Histopathological diagnosis of ganglioglioma was initially suggested for primary tumour, but later the diagnosis of PA for both recurrent and primary tumour was established. During the next years of observation the neurological symptoms of motor deficit and disturbances of sense in lower extremity increased. Repeated MRI examination showed tumors of the spinal canal localized in thoracic region and subsequently in sacral region of the spine. The patient was operated for both tumors. Histopathological examinations of tumour specimens from both locations revealed neoplasm consistent with the feature of PA. The case illustrates a unique instance of multifocal spread of the benign WHO grade I astrocytoma in neuroaxis and possibilities of surgical therapy option in such unfavorable course of PA.

[A3]

Multiple intracranial tumours – analysis of archival material

Bierzyńska-Macyszyn G[1], Właszczuk P[1], Kwiek SJ[2], Stachura Z[2], Kowal E[1], Konicki P[1], Bażowski P[2]

[1]Department of Histopathology, [2]Department of Neurosurgery, Silesian Medical University, Katowice

Recently diagnosed tumour of double texture of glioma and meningioma, located in brain tissue in vault of right parietal lobe and within meninx of this region, induced us to re-analyse previously diagnosed and described multiple tumours. These cases involved 6 patients with multiple CNS tumours and 10 patients with multiple tumours located in CNS and internal organs.

Present case regards male patient (K.S.), 60 y., who developed acute symptoms of increased intracranial pressure. Imaging examinations showed hourglass–shaped tumour of diameter of 6 cm, located in the convexity of brain, partially united with the meninx, partially spreading in the cortex and white matter below the lesion. The material obtained for examination was macroscopically heterogenous. A membranous fragment of dura mater united with round, cohesive, partially calcified tumour of diameter of 1.5 cm was found. The tumour transsection showed fibromatous structure. Remaining material consisted of soft, fragile fragments of multicoloured heterogenous tumour with small areas of brain tissue, of total diameter of 4 cm. The fixed material was routinely processed in tissue processor and embedded in paraffin blocks. Slides were routinely stained (H+E), then differentiating immunohistochemical tests were performed (GFAP, VIM, S-100 protein, EMA, CD34, p-53 protein, Ki-67). These examinations enabled us to diagnose fibrous partly psammomatous meningioma WHO grade I (examination No 20350/M) in meningeal part and glioblastoma WHO grade IV (examination No 20348-349/M) in cerebral part of the material.

Literature data report that among CNS multiple tumours, co-existing gliomas are most common. They are followed by gliomas coupled with mesenchymal tumours (meningiomas and angiomas). In multiple intra- and extracranial tumours, different primary CNS neoplasms co-exist with tumours of other organs, such as breast, lung, large intestine, kidney and skin.

Our material (both intraoperative and post-mortem) encompassed 4 cases of gliomas (2 glioblastoma WHO grade IV, 1 anaplastic astrocytoma WHO grade III and 1 fibrillar astrocytoma WHO grade II) co-existing with meningiomas, 1 glioma (pilocytic astrocytoma WHO grade I) co-existing with arteriovenous angioma and 2 cases of multiple gliomas – anaplastic oligoastrocytoma WHO grade III with anaplastic ependymoma WHO grade III and glioblastoma WHO grade IV with fibrillar astrocytoma WHO grade II.

10 patients with multiple intra- and extracranial tumours were diagnosed as follows: 3 astrocytomas of different grades of histological malignancy co-existing with adenocarcinoma of large intestine, squamous cell carcinoma of the lung and renal cell carcinoma, 4 ependymomas WHO grade II and III co-existing with adenocarcinoma of the endometrium, squamous cell carcinoma of the lung and small cell carcinoma of the lung, and cavernous angioma of the liver, schwannoma of the VIII nerve with papillary carcinoma of the thyroid, angiomatous meningioma with follicular carcinoma of the thyroid; and in one case anaplastic meningioma co-existing with 2 carcinomas: squamous cell carcinoma of the lung and renal cell carcinoma.

In all these cases the diagnoses were confirmed with appropriate immunohistochemical tests.

Numerous hypotheses proposed to elucidate development of multiple tumours are in large measure mere speculations assuming, that an oncogene can trigger neoplasmatic transformation in adjacent cells of different histogenesis. According to Crohnheim theory, remnants of different cell elements from embryogenesis may undergo malignant transformations in different periods, giving rise to multiple tumours.

Mixed and combined tumours are usually classified into 3 basic types: collision, composite and dependent ones. Collision tumours are independent neoplasms of different structure, bordering each other. Composite tumours arise as a result of different tissue elements of parenchyma and stroma. In dependent tumours, malignant hyperplasia of one component trigger neoplasmatic transformation in the other, sometimes remote, component. It causes and effects relationship between two, so remote tumours. Often observed co-existing of gliomas and meningiomas may be accidental, but it may be an effect of mutual irritation and stimulation. About 45% of cases described in the literature are tumours arising close each other (excluding collision tumours). It suggest casual relationship between them.

[A4]

The role of epigenetic changes in DNA repair genes in high grade gliomas treated with radiation combined with temozolomide

Bujko M[1], Kober P[1], Nauman P[2], Matyja E[3], Rembiszewska A[4], Felisiak A[4], Dyttus-Cebulok K[5], Kupryjańczyk J[4], Bonicki W[2], Siedlecki JA[1]

[1]Department of Molecular Biology, [2]Department of Neurooncology, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw; [3]Department of Experimental and Clinical Neuropathology, M. Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw; [4]Department of Molecular Pathology, [5]Department of Radiotherapy, Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw

Introduce: Previous studies revealed important role of DNA repair mechanisms: direct repair by O6-methyltransferase (MGMT) and mismatch repair (MMR) in response to temozolomide treatment. Epigenetic silencing of *MGMT* gene was shown to have prognostic value in high grade gliomas treated with radiation combined with temozolomide. The role of MMR system in clinical response to treatment is not clear. In this study we determined promoter methylation status of three DNA repair genes: *MGMT* as well as *MLH1* and *MSH2* (encoding two MMR elements) and mutational analysis of the two latter genes. Molecular anlysis results were compared with expression status determined by immunohistochemical staining. The aim of the study was to determine the frequency of molecular changes and their correlation with protein expression and to examine the role of molecular changes for therapy response.

Patients and Methods: The study involved 100 patients with high grade gliomas including subgroup of 60 patients treated with radiation combined with concomitant and adjuvant temozolomide. DNA was extracted from either frozen or formalin-fixed, paraffin-embedded tissue samples. Promoter methylation status was determined by methylation specific PCR (MSP), mutational analysis of *MLH1* and *MSH2* was performed with the use of single strand conformation polymorphism analysis (PCR-SSCP). Expression status was determined by immunohistochemical staining.

Results: We observed methylation in 41%, 16% and 8% of patients in *MGMT*, *MLH1* and *MSH2* promoters respectively. We identified only three missense mutations in *MLH1* gene: I219V, E669S and V716M, two mutations in *MSH2*: S271C and G322D and several polymorphic variants in noncoding sequence. Only partial concordance of molecular changes and expression status was observed. Patients with *MGMT* promoter hypermethylation had significantly better outcome in terms of progression free survival (PFS) ($p < 0.01$) and overall survival (OS) ($p < 0.01$). Lack of MGMT expression was also associated with better prognosis (PFS, $p = 0.038$ and OS, $p = 0.019$). We observed tendency for poor prognosis in patients with promoter methylation of MMR genes but differences weren't statistically significant. We didn't observe any relationship between MLH1 or MSH2 expression status and OS or PFS in temozlomide treated patients.

[A5]

Multiple myeloma manifesting as a central nervous system tumour – dilemmas in diagnosis of two patients

Czapiewski P[1], Szmuda T[2], Dzierżanowski J[2], Słoniewski P[2], Sworczak K[3], Kaniuka S[3], Dubaniewicz-Wybieralska M[4], Hellman A[5], Biernat W[1]

[1]Department of Neuropathology and Molecular Pathology, [2]Department of Neurosurgery, [3]Department of Endocrinology and Internal Medicine, [4]Department of Radiology, [5]Department of Haematology and Transfusiology, Medical University of Gdansk, Gdansk

Multiple myeloma (MM) is a neoplasm of plasmacytes. It accounts for approx. 1% of all human malignancies that makes 15% of hematological neoplasms. Multiple myeloma usually involves the bone marrow, but extraosseus/extramedullary plasmacytomas also occur.

Central nervous system involvement in the course of multiple is rare and usually occurs after long standing disease. Initial presentation of MM as a CNS tumour is an exceptional finding and only a few cases have been reported so far.

We report two cases of MM manifesting as a CNS tumour. Case No 1 was a 64-years-old male with a tumor of the skull base causing complex cranial nerve disturbances. The operation by the pterional craniotomy was performed and the tumor was partially resected. The tumour was diagnosed as plasmablastic variant of multiple myeloma. Case No 2 was a 60-years-old female admitted with aphasia and limited logical contact. Gradual deterioration in speech, difficulties in construction of phrases and difficulties in speech understanding has been present for the last seven months. In addition, right upper extremity paresis appeared two days before. The tumour of the left occipital region of the skull was found. On CT, the tumour was based at the bone of the skull vault and infiltrated into the subcutaneous tissue.

The surgical biopsy enabled the diagnosis of plasmacytoma.

CNS involvement in the course of multiple myeloma, although rare, should be taken into account in the differential diagnosis of tumours involving the brain and the meninges.

[A6]

Role of modern techniques of magnetic resonance imaging in surgical treatment of central nervous system tumors in children

Daszkiewicz P, Roszkowski M

Department of Neurosurgery, Children's Memorial Heath Institute, Warsaw

The presentation was a review of modern techniques of magnetic resonance imaging (MRI) and their role in surgical treatment of central nervous system (CNS) tumors in children. MR imaging was presented in the context of general aspects of diagnosis and treatment of CNS tumors. Special emphasis was placed on "oncological vigilance" of first-line medical professionals (GPs and neurologists). Various neuroimaging modalities (e.g. X-ray, angiography, sonography, computed tomography and MRI) were briefly discussed, emphasizing the importance of adequate planning of diagnostic work-up. This should yield coherent information enabling optimal selection of therapeutic approach and adequate follow-up. Modern applications of MRI and interdisciplinary modalities (e.g. tractography, functional MR, MR spectroscopy, neuronavigation, neuroendoscopy and stereotactic biopsy) were discussed, as well as their role in planning and execution of surgical procedures. Examples of various types and locations of CNS tumors typical for the pediatric population were presented. Advantages of Image Guided Surgery (IGS) were summarized, i.e. more effective and less traumatic resections, better outcomes and reduced overall treatment costs. General trends in neurooncological surgery over the past century were presented, starting with blind or semiblind explorations, surgery guided by structural imaging and ending with structural-functional guidance. In the future, progress in interventional neuroradiology, radiosurgery and gene therapy may reduce the role of neurosurgery in the treatment of patients with CNS tumors.

[A7]

Expression of 8-oxoguanine DNA glycosylase 1 (OGG1) and level of 53 protein in peripheral lymphocytes in patients with Alzheimer's disease

Dezor M[1], Dorszewska J[1], Florczak J[2], Jaroszewska-Kolecka J[1], Kozubski W[2]

[1]Laboratory of Neurobiology, Department of Neurology, [2]Chair and Department of Neurology, University of Medical Sciences, Poznan

Reactive oxygen species (ROS) are highly reactive and may oxidize macromolecules in cells such as proteins, lipids and especially nucleic acids (DNA). ROS cause several base or sugar modifications in the structure of DNA, leading to strand breaks in DNA chain.

8-Oxo-2'-deoxyguanosine (8-oxo2dG) is one of the crucial lesions produced in DNA by oxygen radical-forming agents. OGG1 is a main DNA repair enzyme that excises 8-oxo2dG from DNA. It was postulated that decreased expression of OGG1 may lead to higher background mutation frequency and could increase the DNA damages risk. Damage of genomic DNA may lead to the cell death by apoptosis in result it causes degenerative disorders. P53 protein may induce apoptotic process in cells.

The aimed of the study was to determine the extent of oxidative DNA damage (levels of 8-oxo2dG) and expression of OGG1 and p53 proteins in leukocytes from Alzheimer's disease (AD) patients and in control group.

The studies were conducted on 41 patients with AD, including 25 women and 10 men aging 34-84 years. The control groups included 51 individuals, 20 women and 31 men aging 22-83 years.

The level of 8-oxo2dG was determined using HPLC/EC/UV (high-pressure liquid chromatography system with electrochemical and UV detection) technique and the level of OGG1 and p53 proteins was determined with Western Blot method.

We were observed increase of the level of 8-oxo2dG after 60 years of age (insignificant) and in AD patients (Mann-Whitney test, $p < 0.05$) as compared to the controls. Simultaneously, the level of OGG1 protein was decreased in individuals after 60 years of age (Mann-Whitney test, $p < 0.01$) and in AD patients (Mann-Whitney test, $p < 0.001$) as compared to the controls when the level of p53 protein was increased in individuals after 60 years as well as in AD patients (Mann-Whitney test, $p < 0.05$) as compared to the controls. However in patient with mild dementia (in MMSE scale) were observed the lowest level of 8-oxo2-dG and OGG1 and the highest level of p53 protein, when in the patients with moderate and severe dementia (in MMSE scale) higher level of 8-oxo2dG and OGG1 but lower level of p53 protein as compared to the patient with mild dementia.

It is possible that OGG1 and p53 proteins are involved in pathogenesis of AD by repair of oxidative DNA damage.

[A8]

Role of endocytosis in CADASIL pathogenesis

Dziewulska D[1,2], Rafałowska J[1], Lewandowska E[3], Wojda R[1], Chrzanowska H[1], Wąsowska L[1]

[1]Department of Experimental and Clinical Neuropathology, Mossakowski Medical Research Centre, Polish Academy of Sciences, [2]Department of Neurology, Medical University of Warsaw; [3]Department of Neuropathology, Institute of Psychiatry and Neurology, Warsaw

Introduce: Autosomal Dominant Arteriopathy with Ischemic Strokes and Leukoencephalopathy (CADASIL) is a generalized vasculopathy caused by mutations in notch 3 gene leading to degeneration of vascular smooth muscle cells (VSMC) and accumulation of the Notch 3 receptor extracellular domain (N3-ECD) and granular osmiophilic material (GOM) in the vessel wall. Since Notch3 signaling pathway requires receptor and ligand endocytosis for signal transduction, deposits of N3-ECD and GOMs may be a manifestation of the disturbed endocytosis in VSMC.

Material and Methods: In skin, muscle and brain vessels in biopsy and autopsy material from CADASIL patients and in control specimens we examined immunohistochemically expression of selected proteins (clathrin, caveolin-1, dynamin and ubiquitin) participating in two main types of endocytosis. Biopsy tissues were also assessed on electron microscopy.

Results: We did not find any difference in dynamin and clathrin immunoreactivity in CADASIL tissues in comparison to the control material. The immune reactions to caveolin-1 revealed diminished the protein

expression in vascular tunica media and lack of the immunoreactivity in a part of preserved VSMC. Ubiquitin expression was increased in CADASIL VSMC but absent in the control material. Ultrastructural assessment of CADASIL vessels showed that GOMs were often located inside VSMC membrane invaginations and surrounded by caveolae, a flash-shaped vesicles participating in endocytosis and cellular signaling.

Conclusions: In our opinion, increased ubiquitin expression and abnormal caveolin-1 immunoreactivity in CADASIL may be a manifestation of disturbed caveolin-dependent endocytosis in VSMC.

[A9]

Bilateral, intraventricular papillary glioneuronal tumour (PGNT). Case report.

Grajkowska W[1], Matyja E[2], Marchel A[3], Nowak A[3], Kunert P[3], Zielinska M[2]

[1]Department of Pathology, Children's Memorial Heath Institute, [2]Department of Neuropathology, Mossakowski Medical Research Centre, Polish Academy of Sciences, [3]Department of Neurosurgery, Warsaw Medical University, Warsaw

Papillary glioneuronal tumour (PGNT) is a rare, mixed, glioneuronal neoplasm included as a new clinicopathological entity in 2007 WHO classification of tumours of central nervous system. This tumour is composed of two components: pseudopapillae created by flat, GFAP-positive astrocytes covering hyalinized vascular core and interpapillary neurocytic elements. PGNT corresponds to WHO grade I.

We present a case of bilateral, intraventricular tumour in 27-years-old woman. MR imaging showed solid, partially cystic masses located inside of the left and right lateral ventricle. The tumour was partially resected. Microscopically, the neoplasm was composed of pseudopapillary structures and interpapillary sheets of neurocytes. The pseudopapillae were created by hyalinized vascular cores covered by cuboidal cells with vesicular nuclei. These cells revealed immunoexpression for GFAP. The interpapillary element showed strong reactivity for synaptophysin. MIB-1 labelling index was low. The diagnosis of papillary glioneuronal tumour was established.

This tumour was only partially resected. The patient received radiotherapy but the clinical outcome was unfovourable.

PGNT is a rare tumour that presents in children and adults, mainly in supratentorial location with a predilection for temporal lobe. The pathogenesis is unclear. The origin from mulitipotent precursors of the subependymal, germinal matrix is presumed.

[A10]

Greig cephalopolysyndactyly syndrome: a case report

Iwanowski P, Geppert A, Losy J, Kozubski W

Department of Neurology, University of Medical Sciences, Poznan

Aim: This paper presents thirty years old woman with a very rare cephalopolysyndactyly. Cephalopolysyndactyly known as the Greig syndrome is inherited in autosomal dominant manner and GLI 3 is the only one gene known to be associated with. The diagnosis is based on the clinical findings and family history.

Patient: 30 years old woman admitted to our department presented with polydactyly and corrected surgically cutaneus syndactyly, mental retardation (IQ 84), ocular hypertelorism, bossed forehead, epilepsy and delusions. Epilepsy with tonic-clonic seizures was diagnosed in age of 4 years. Hearing delusions occurred in age of 27 years.

Summary: We present a rare case with the late diagnosis of the Greig cephalopolysyndactyly syndrome.

[A11]

Malignant gliomas as the secondary neoplasms in the oncologically treated children.

Iżycka-Świeszewska E[1], Stefanowicz J[2], Grajkowska W[3], Drożyńska E[2], Niedźwiecki M[2], Maciejka-Kapuścińska L[2], Kobierska-Gulida G[1], Bien E[2], Stachowicz-Stencel T[2], Zaucha R[4], Szurowska E[5], Balcerska A[2]

[1]Department of Pathology, [2]Department of Pediatrics, Hematology, Oncology a& Endocrinology, Medical University of Gdansk, Gdansk; [3]Department of Pathology, Children's Memorial Health Institute, Warsaw; [4]Department of Oncology and Radiotherapy, [5]Department of Radiology, Medical University of Gdansk, Gdansk

Malignant gliomas are the most common secondary neoplasms in survivors of pediatric acute lymphoblastic leukemia (ALL). These neoplasms can develop also in the patients with other tumors, especially of the head and neck. The accepted predisposing factor in this group is performed radiotherapy and intensive chemotherapy.

We present the clinical, radiological and neuropathological picture of five patients aged 9-15 years, treated in our center (1992-2008) including four children with ALL and one with orbital RMS. The children revealed neurological symptoms (3), one had cerebral insult and the last was revealed at the control CT. The CNS tumors were diagnosed 3-6.5 years since the accomplishment of oncological treatment of the first cancer. Radiologically all tumors were supratentorial, contrast enhancing. Two were well demarcated, two widely infiltrating and one created hematoma. In three cases only stereotactic biopsy was performed. Two children after the biopsy were operated.

Presented group contained two anaplastic astrocytomas and three glioblastomas. Histologically all neoplasms were cellular-rich, made of small anaplastic cells. The differential diagnosis included leukemic infiltrates and others small- blue cell tumors. Immunophenotype of the tumors was: vimentin (5/5), GFAP (5/5, however faint and focal in two cases), nestin (3/5), neuronal markers (1 focally). Proliferative index (Ki-67) ranged 15-60%.

The patients were treated with chemo and radiotherapy. Three patients died 5-19 months since the diagnosis; two receive palliative treatment for glioma recurrence. Described secondary gliomas in the children create a diagnostic challenge for the clinicians and pathologist. Tumors morphology can suggests their origin from the glial stem cells transformed with aggressive therapy of the primary cancer.

[A12]

Activation of PI3K/AKT/mTOR signaling pathway in neuroblastic tumors – immunohistochemical study

Iżycka-Świeszewska E[1], Drożyńska E[2], Grajkowska W[3], Perek D[4], Klepacka T[5], Kobierska-Gulida G[1], Dembowska B[4], Kołtan S[6], Słociak M[7], Balcerska A[2], Jaśkiewicz K[1]

[1]Department of Pathology, [2]Department of Pediatrics, Hematology, Oncology and Endocrinology, Medical University of Gdansk, Gdansk; [3]Department of Pathology, [4]Department of Pediatric Oncology, Children's Memorial Health Institute, Warsaw; [5]Department. of Pathology, National Institute of Mother and Child, Warsaw; [6]Department of Pediatrics, Hematology and Oncology, University Hospital MCU Bydgoszcz, Bydgoszcz, [7]Department of Pediatric Oncology, Clinical Hospital, Medical University of Wroclaw, Wroclaw

Signaling pathway through PI3K is activated in many developmental, physiological and pathological processes including malignant tumor pathogenesis and progression. The role of PI3K/AKT/mTOR transduction stream is not well known in neuroblastic tumors.

The study is a preliminary immunohistochemical analysis of multiple components of PI3K signaling pathway in tissue arrays containing 90 neuroblastic tumors. The antibodies against PI3K 110, PI3K 85, pAKT, pmTOR, PTEN, p70S6K, 4EBP1 were used. The expression was assessed semiquantitatively as negative, weak, moderate or strong, depending of the number of positive cells and immunolabeling intensity.

PTEN expression was found in all tumors, however in 30% of cases the expression was weak. Cytoplasmic PI3K 100 was observed in 86%, PI3K 85- in 91% of tumors. pAKT (Ser-473) cytoplasmic staining was detected in 80% with variation of intensity. Expression of pmTOR (Ser-2481) characterized 76% of cases. Nuclear and cytoplasmic p70S6K labeling was found in 80% cases and cytoplasmic 4EBP1 in 82% neuroblastic tumors. The most intense expression of components of PI3K/AKT/mTOR pathway was observed in poorly differentiated and chemotherapy pretreated tumors.

Conclusion: Activation of PI3K signaling pathway is a common event in neuroblastic tumors, however in some tumors it involves all elements of transduction stream, since in the others – only few proteins are phosphorylated. The role of PI3K/AKT/mTOR pathway will be highlighted by correlations with tumors characteristics which are under the statistical elaboration.

Granted by Polish Government-project N40117631/3867.

[A13]

Paraneoplastic neurological syndromes in patients with ovarian tumors

Kossut A[1], Michalak S[2,3], Krygowska J[4], Szpurek D[4], Kozubski W[1], Sajdak S[4]

[1]Department of Neurology, [2]Department of Neurochemistry and Neuropathology, University of Medical Sciences, Poznan; [3]Neuroimunological Unit, Polish Academy of Sciences; [4]Division of Gynecological Surgery, University of Medical Sciences, Poznan

Introduce: The prevalence of paraneoplastic neurological syndromes (PNS) differs depending on population studied and diagnostic procedures used. In general population of patients with systemic malignancy the frequency of PNS is estimated as 1%, however ranges from 3% of Lambert-Eaton syndrome in small-cell lung cancer up to 50% of patients with demyelinating neuropathy and osteosclerotic myeloma. Certain studies revealed higher incidence of PNS in females. The aim of this study was to evaluate the clinical manifestation and onconeuronal antibodies in patients with ovarian tumors.

Material and Methods: We have included in the study 109 females (aged 43.9 ±16.1 yrs) with ovarian tumors hospitalized in Division of Gynecological Surgery, Poznan University of Medical Sciences and 10 consecutive patients (aged 57.5 ±9.0 yrs) with ovarian tumors selected from 522 subjects with suspicion of PNS hospitalized in Department of Neurology, Poznan University of Medical Sciences. All patients underwent neurological examination. Indirect immunofluorescence as screening and Western blotting as confirmation test for the presence of onconeuronal antibodies were performed.

Results: Patients with gynecological manifestation of ovarian tumor were significantly ($p = 0.0101$) younger than females with PNS preceding malignancy. Ovarian cancer was diagnosed in 38 (32%) patients and benign tumors in 81 patients (68%). Clinical PNS manifestation was found in 30 (25%) patients: 6 patients (5%) manifested isolated cerebellar syndrome, in 1 patient (0.8%) cerebellar syndrome was associated by pyramidal signs, in 2 (1.7%) by pyramidal signs and neuropathy, in 2 (1.7%) by neuropathy only. In 17 patients (14.3%) we have found signs of isolated neuropathy, in one (0.8%) – polymyositis and one patient (0.8%) had multiple sclerosis. In 89 patients (75%) there no clinical PNS symptoms. Anti-Hu antibodies were found in 8 (6.7%), anti-Yo in 7 (5.9%), anti-Ri in 10 (8.4%) patients, anti Ma/Ta in 2 (1.7%), anti-CV2 in 1 (0.8%), anti-amphiphysin in 4 patients (3.4%), as confirmed by WB. Moreover, on IF examination anti-neuroendothelium antibodies we have found in 18 (15%) and anti-myelin in further 18 patients (15%).

Conclusion: Cerebellar syndrome and neuropathy are dominant manifestations of PNS in the course of ovarian tumors. Clinical symptoms of PNS and onconeural antibodies develop both in malignant and benign ovarian tumors, however neurological symptoms precede the diagnosis in older population.

[A14]

Classical cancer markers in patients with ovarian tumors and onconeuronal antibodies

Krygowska J[1], Michalak S[2,3], Kossut A[4], Szpurek D[1], Kozubski W[4], Sajdak S[1]

[1]Department of Gynecological Oncology, [2]Department of Neurochemistry and Neuropathology, University of Medical Sciences, Poznan; [3]Neuroimmunological Unit, Polish Academy of Sciences; [4]Division of Gynecological Surgery, University of Medical Sciences, Poznan

Introduce: The analysis of onconeuronal antibodies is an important part among diagnostic procedures in patients suspected of paraneoplastic neurological syndromes (PNS). Remote effects of cancer on the nervous system precede the clinical diagnosis of systemic malignancy by 4 to 6 months. On the other hand, serological cancer markers do find application in diagnosis and tre-

atment monitoring of tumors. The aim of this study was to evaluate and correlate the levels of classical serum cancer markers in patients with ovarian tumors and the presence of onconeuronal antibodies.

Material and Methods: Females (n = 68) aged 42.8 ±14.3 hospitalized in Division of Gynecological Surgery, Poznan University of Medical Sciences Division of Gynecological Surgery, Poznan University of Medical Sciences were included in the study. The diagnosis of ovarian tumor was based on clinical and ultrasound examination and confirmed by microscopical examination performed after surgery. Classical cancer markers (Ca-125, CEA, AFP) were estimated in patients sera before surgical procedures. Onconeuronal antibodies were analyzed by means of indirect immunofluorescence (IF) as screening test and confirmed by Western blotting (WB). White blood cells count (WBC) was also taken into consideration.

Results: Positive reactions on IF were found in 61 patients (91%) and among WB performed as confirmation tests 50% of results were positive for well-defined onconeuronal antibodies. In 23.5% of patients anti-myelin antibodies were found on IF. Anti-amphiphysin antibodies were identified by WB in 18% of patients, anti-CV2 in 4%, anti-Ma/Ta in 4%. The remaining patients showed unidentified positive reactions. There were no significant differences ($p > 0.05$) between patients with positive and negative IF reactions. However, patients with onconeuronal antibodies detected in WB had higher ($p < 0.001$) levels of Ca-125 (1933.295 ±2816.084 IU/ml) than those with negative WB results (52.825 ±46.416 IU/ml). In the group of IF seronegative patients no ovarian cancer was present, and in WB seronegative 9% of patients had ovarian cancer. The serum CEA concentrations were higher ($p = 0.0360$) in WB negative patients (median 0.73; interquartile range 0.55 to 0.90 ng/ml) than in patients with onconeuronal antibodies (median 1.285; 0.968 to 1.970 ng/ml). In patients with ovarian cancer we have found higher Ca-125 levels both in cases with clinical PNS manifestation and without it, when compared to benign ovarian tumors (662.37 ±535.58 vs. 25.90 ±16.71 IU/ml, $p < 0.001$ and 605.55 – median; interquartile range: 210.25 to 1054.58 vs. 21.42 – median; interquartile range: 13.87 to 40.02 IU/ml, $p = 0.0037$, respectively). No significant differences were found in CEA and AFP levels and WBC. Non significant trend ($p = 0.0526$) for higher WBC in PNS patients was observed comparing to non-PNS patients with ovarian tumors.

Conclusion: Onconeuronal antibodies observed in patients with ovarian cancer are malignancy – specific. Classical serological cancer markers (Ca-125, CEA and AFP) are not affected by the clinical manifestation of PNS. Ca-125 remain useful for the diagnosis of ovarian cancer at the stage of malignancy associated with paraneoplastic neurological syndrome.

[A15]

Ultrastructural picture of granular cell astrocytoma

Lewandowska E[1], Wierzba-Bobrowicz T[1], Modzelewska J[1], Matyja E[4], Błażejewska-Hyżorek B[2], Pasennik E[1], Stępień T[1], Koszewski W[3]

[1]Department of Neuropathology, [2]Second Department of Neurology, [3]Department of Neurosurgery, Institute of Psychiatry and Neurology, Warsaw; [4]Department of Experimental and Clinical Neuropathology, Medical Research Centre, Polish Academy of Sciences, Warsaw

Granular cell astrocytoma (GCA) is a rare type of granular cell tumours in the central nervous system. It is important that granular cells in these tumours are of enigmatic origin. The aim of this study is to present the ultrastructural features of cerebral GCA in a 59-year-old man. The tumour was localized in the left parietal lobe.

At ultrastructural level, most tumour cells were round or oval with only a few or without filaments and filled electron-dense granular material limited by a single membrane. Some of the vacuoles containing cytoplasm with mitochondria resembled autophagosomes. A significantly lower number of tumour cells revealed abundant cytoplasm with numerous intermediate filaments, swollen rough endoplasmic reticulum, mitochondria with bizarre altered shape and a few granular material.

The data presented in our study indicate that the cells of GCA demonstrated two types ultrastructural morphology. Ultrastructural morphology and GFAP-positive reaction indicate astrocytic origin of tumour cells.

[A16]

Effect of opioid analogues on proliferative activity of human glioblastoma T98G cells in vitro

Łazarczyk M[1], Matyja E[1], Grzywaczewska E[1], Lipkowski AW[2]

[1]Department of Experimental and Clinical Neuropathology, [2]Department of Neuropeptides, M. Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw

Opioids are standard drugs delivered to patients in order to attenuate pain associated with advanced stage of cancer diseases. Besides the relief advantage, related with analgesic activity of opioid compounds, they are evidenced to have also an influence on tumour cell proliferation. Opioids might give distinct effects on cell growth. These substances reveal both stimulatory or inhibitory activity on cell cycle progression.

In our study we established distinct suppressive action of biphalin on human glioblastoma T98G cell growth. This novel opioid peptide exhibits much greater analgesic properties than those presented by morphine. On the contrary, the widely utilized in pain management compound - morphine, showed promoting effect on T98G cell proliferation in vitro. Biphalin-treated cells were less able to form colonies. They also exhibited lower Ki-67 expression level and impaired proliferation activity reflected by the decrease in cell number after incubation with tested compound. Morphine had a reverse effect on T98G cell growth than biphalin. Opioid receptors (mu, delta and kappa types), GFAP, nestin and vimentin immunoexpression patterns in T98G cells were not altered after tested substances treatment and similar to control level.

Development of effective strategy for simultaneous anticancer and pain therapy has become a great challenge in contemporary medicine. Our experiments have proved that biphalin might constitute a significant and alternative solution for morphine application.

Acknowledgements: This work has been partially supported by grant No. NN 401228334.

[A17]

Spindle cell oncocytoma of adenohypophysis – immunohistochemical and electron-microscopy study of two cases

Maksymowicz M[1], Matyja E[2], Grajkowska W[3], Olszewski WT[1], Zieliński G[4], Bonicki W[5]

[1]Department of Pathology, M. Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, [2]Department of Experimental and Clinical Neuropathology, M. Mossakowski Medical Research Centre, Polish Academy of Sciences, [3]Department of Pathology, Children's Memorial Health Institute, [4]Department of Neurosurgery, Medical Military Institute, [5]Department of Neurosurgery, M. Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw

Spindle cell oncocytoma (SCO) of the pituitary gland is a newly established distinct clinic-pathologic entity that was introduced in the fourth edition of WHO classification of central nervous tumours (2007).

We report two cases of SOC occurring in females aged 64 years (Case. 1) and 65 years (Case. 2) who presented with pan-hypopituitarism, headache and visual field defect. In both cases the MRI showed solid sellar mass of moderate size with suprasellar extension. Clinically and radiologically the tumours suggested pituitary macroadenomas without evidence of invasive growth. The tumours were removed by transsphenoidal surgery. One patient undergone initial surgery with tumour resection by frontal craniotomy followed by tumour recurrence after 3 years.

Histologically, both tumours were similar and composed of fascicles formed by spindle cells with eosinophilic, more or less oncocytic cytoplasm. Mitoses were rare and necroses were absent. In Case 1 the advanced lymphocytic inflammations within neoplastic tissue were observed. Tumour cells exhibited immunoreactivity for S-100 protein, galectin-3, vimentin and epithelial membrane antigen but they were negative for GFAP, anterior pituitary hormones, chromogranin, synaptophysin, cytokeratin CK (AE1/AE3), smooth muscle actin, desmin, CD34 and CD68. MIB1 labeling index did not exceed 10%. Ultrastructurally, the neoplastic cells contained numerous mitochondria with lamellar cristae. In Case 2, some tumour cells revealed a few giant mitochondria with severely destructed internal matrix.

Spindle cell oncocytoma of the anterior hypophysis is a rare and often misdiagnosed entity that corresponds to WHO grade I. The differential diagnosis should include

nonfunctioning oncocytic pituitary adenoma, intrasellar schwannoma, pituicytoma, granular cell tumour and other lesions of sellar region.

[A18]

Catecholamines and their metabolites in patients with trigeminal neuralgia

Marcinkowski M[1], Osmola K[1], Dorszewska J[2], Krahel A[1], Lewandowski L[1]

[1]Department and Clinic of Maxillo-Facial Surgery, [2]Laboratory of Neurobiology, Department of Neurology, University of Medical Sciences, Poznan

The pathogenesis of trigeminal neuralgia remains largely unknown. Neurochemical studies point to a local inflammation of the trigeminovascular system in which the release of excitatory neuropeptides such as substance P and somatostatin, plays an important role. Simultaneously it is known that serotonergic and adrenergic system modulate nociceptive transmission through the trigeminal system. To investigate the role of noradrenergic system is use to determine the concentration of plasma norepinephrine, NE; epinephrine, E and their metabolites in urine, normetanephrine, NMeta; metanephrine, Meta.

The aim of study was to estimate of plasma levels: NE and E, and their metabolites in urine: NMeta and Meta in patients with trigeminal neuralgia and in controls.

Studies were conducted on the levels of NE, E, NMeta and Meta estimated by HPLC with electrochemical detection on 12 patients with trigeminal neuralgia in age 54-80 years, and matches controls. The study disclosed that in 90% of patients with trigeminal neuralgia concentration of NMETA was higher than references limits and only in 10% of patients with trigeminal neuralgia concentration of META was higher than references limits. Simultaneously only in 10% of patients with trigeminal neuralgia concentration of NMETA as well as META was higher than references limits and only in 10% of patients with trigeminal neuralgia concentration of NMETA as well as META was in references limits.

Seem to be possible that changes in metabolism of NE and E to NMeta and Meta may plays a role in the pathogenesis of trigeminal neuralgia.

[A19]

Papillary tumour of the pineal region – histopathology and immunomorphology of two cases

Matyja E[1], Grajkowska W[2], Nauman P[3], Bonicki W[4], Baraniecka J[1]

[1]Department of Experimental and Clinical Neuropathology, M. Mossakowski Medical Research Centre, Polish Academy of Sciences, [2]Department of Pathology, Children's Memorial Health Institute, [3]Department of Neurosurgery, M. Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw

Neoplasm of the pineal region are uncommon and account for only 1% of all intracranial tumors. They might represent various histological subtypes, including papillary tumours. The critical diagnosis is often difficult because the histology is similar to other tumours with papillary features including papillary ependymoma, papillary meningioma, choroid plexus papilloma or metastatic papillary carcinoma.

Papillary tumor of the pineal region (PTPR) is extremely rare, recently described distinct pathological entity included in the 2007 World Health Organization Classification. PTPR is rare, with only about 40 reported cases, and the natural history and standardized treatment strategy remain controversial.

We describe two case of PTPR.

Histological examination of both tumors revealed characteristic papillary structure. The tumor exhibited epithelial-like growth pattern and consisted of columnar and cuboidal cells with eosinophilic cytolasm. In one case the cells lining papillary structures exhibited polymorphic, atypical, often plump nuclei. Some areas were hypocellular with perivascular pseudorosettes formations.

Immunohistochemical staining showed diffuse positive reaction for neuron-specific enolase (NSE), S-100 protein and vimentin. Moreover, focal reaction for synaptophysin and chromogranin A, cytokeratin and epithelial membrane antigen (EMA) were observed. The Ki-67 labeling index was relatively low. The final diagnosis was PTPR based on morphological and immunohistochemical

[A20]

Rosette-forming glioneuronal tumour of the fourth ventricle – case report

Matyja E[1], Grajkowska W[2], Nauman P[3], Bonicki W[3], Oziębło A[3]

[1]Department of Experimental and Clinical Neuropathology, M. Mossakowski Medical Research Centre, Polish Academy of Sciences, [2]Department of Pathology, Children's Memorial Health Institute, [3]Department of Neurosurgery, M. Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw

Rosette-forming glioneuronal tumour (RGNT) of the fourth ventricle is a recently described new type of primary brain tumour that was included into the latest edition of WHO classification of tumors of central nervous system. It is a very rare, slowly growing, mixed glioneuronal neoplasm originally described in cerebellar localization. This tumour represents a separate clinic-pathological entity with unique histopathological features.

We present a case of 20-year-old female patient with RGNT at typical localization in the fourth ventricle. MRI revealed the tumor mass that filled the fourth ventricle and largely involved the cerebellar vermis. Histopathologically, two distinct components were easily identified. The main component consisted of prominent neurocytic rosettes formed by round, isomorphic nuclei arranged around eosinophylic neuropil cores with strong synaptophysin expression. Additionally, a few pseudopapillary arrangements of neurocytes around small vessels could be noticed. The second component was not so abundant and consisted of astroglial cells exhibiting piloid features. There were some areas similar to pilocytic astrocytoma exhibiting spindle or stellate astroglial cells, Rosenthal fibers and eosinophilic granular bodies. Focally, the pattern strongly resembled dysembryoplastic neuroepithelial tumor with characteristic glio-neuronal elements. The tumour was partly cystic and at its periphery the marked microvascular proliferation was present. Ki67 labeling index generally was low; however in areas exhibiting distinct microvascular proliferation its expression was higher.

The differential diagnosis of RGNT ought to consider other glioneuronal tumors including dysembryoplastic neuroepithelial tumor (DNT) and papillary glioneuronal tumor (PGNT).

[A21]

Analysis mutations of *IDH1* gene in glial tumors

Piaskowski S[1], Rieske P[1], Woźniak K[1], Stawski R[1], Jaskólski DJ[2], Zakrzewski K[3], Papierz W[4], Liberski PP[1]

[1]Department of Molecular Pathology and Neuropathology, Chair of Oncology, [2]Department of Neurosurgery, [3]Department of Pediatric Neurosurgery, Chair of Pediatric Neurosurgery and Neurology, [4]Department of Pathomorphology, Medical University of Łódź, Łódź

Missense mutations of the isocitrate dehydrogenase-1 (*IDH1*) gene are frequent in astrocytomas (88%), secondary gliomas (82%), oligodendrogliomas (79%), oligoastrocytomas (94%) but rare primary glioblastomas (5%). Interestingly the mutations occur in tumors that were known to be evolved from lower-grade gliomas (secondary glioblastomas). The selective occurrence of the *IDH1* mutations in codon 132 may suggest that this mutation play important role in the pathogenesis of glial tumors, but their role in tumor development is unknown. Here we attempt to confirm the occurrence of the *IDH1* mutations in glial tumors of Polish patients. Our investigation confirms earlier analysis.

This study was sponsored by the Polish State Research Committee, grant No. NN401 1558 331558.

[A22]

CNS toxoplasmosis and blood vessels in AIDS

Rafałowska J[1], Dziewulska D[1,2], Żuławnik T[1], Ogonowska W[1], Modrzewska-Lewczuk M[3]

[1]Department of Experimental and Clinical Neuropathology, Mossakowski Medical Research Centre, Polish Academy of Sciences, [2]Department of Neurology, Warsaw Medical University, [3]Laboratory of Photographic Documentation, Mossakowski Medical Research Centre, Polish Academy of Sciences. Warsaw

Department of Neuropathology of the Institute of Experimental and Clinical Medicine collected 218 brains of patients deceased from AIDS. In this material, CNS toxoplasmosis was diagnosed in 32 cases and in 15 of them toxoplasmosis was the only opportunistic infection. Four-

teen of these patients were at the age of 30-40 years and one was 52 years old.

In all of the examined cases encysted *Toxoplasma gondii* organisms and bradyzoities were observed. *Toxoplasma* abscesses were manifested as various sizes coagulative necrotic lesions. Within the necrotic centre, blood vessel thrombotic occlusions of variable severity were observed. *Toxoplasma* abscesses were surrounded by inflammatory ridge containing lymphocytes, histiocytes, macrophages and, infrequently, plasmatic cells.

In granulomatous tissue, very numerous blood vessels surrounded by inflammatory infiltrates were visible. In majority of these arteries, veins and arterioles inflammatory cells were also present within vessel wall. Although both in granulomatous tissues and vessel walls lymphocytes T predominated in inflammatory infiltrates, lymphocytes B were also found in single vessels. Apart from the mentioned above inflammatory changes, in five toxoplasmosis cases fibrinoid eosinophilic necrosis of the medial arterial lamina was found.

In some of the blood vessels immunopositive reactions to IgM and IgG were seen. This finding as well as panarteritis nodosa – like changes in vessels and a presence of lymphocytes B in vascular infiltrates suggest that humoral type of the immunological reaction may also participate in toxoplasmosis vasculitis in AIDS and triggers autoimmunological vasculitis.

[A23]

Comparative expression study of genes from short arm of chromosome first in meningiomas

Stawski R[1], Piaskowski S[1], Woźniak K[1], Bieńkowski M[1], Zakrzewska M[1], Och W[3], Jaskólski DJ[2], Rieske P[1], Liberski PP[1]

[1]Department of Molecular Pathology and Neuropathology, [2]Department of Neurosurgery, Medical University of Lodz, Lodz, [3]Department of Neurosurgery, WSS Olsztyn, Olsztyn

Introduce: Region 1p is frequently lost in variety of tumors, this alternation affects meningiomas as well. Our (LOH) loss of heterozygosity results have shown discrepancies in frequency of such loss in tumor tissue according the patient gender. Additionally high number of publication indicates presence of tumor suppressor gene (TSG) in this region. This facts inspire us to make complex expression analysis. We selected 12 genes suggested as tumor suppressor and/or showing association with gender.

Material and Methods: We analyzed 32 tumors using real-time PCR based on TaqMan Gene Expression Assay (Applied Biosystems). We examined association between genes expression and patient age, gender, histological type, grade and presence of LOH. Normalization was done according to the 3 different endogenous controls: *s18*, *GAPDH* and *PGK1*.

Results: We find that expression level normalized according to s18 showed, gene dosage effect, where samples with present LOH revealed decreased expression. However results normalized according to *GAPDH* and *PGK1* didn't confirmed this fact. No correlation with patient age, tumor type or grade was noted. To this end, normalization according *GAPDH* and *PGK1* suggest imbalances in mRNA level of analyzed genes in association with gender, however statistical significance was confirmed only for *ELAVL4* (almost absent in male). Moreover, most of these genes except *TP73* showed expression relationship.

Conclusion: The results showed correlation between most of the genes from 1p might indicate unknown epigenetic mechanism affecting transcription regulation of this region. Additionally the fact that selection of reference gene had such strong impact on received results, require additional consideration.

This study was sponsored by the Polish State Research Committee, grant No. NN401 0585 33

[A24]

Diagnostic difficulties in a case of clear-cell meningioma with epithelial and rhabdoid features

Taraszewska A[1], Matyja E[1], Białowąs W[2], Baranowski P[2], Bardadin K[3], Gębarowska J[1]

[1]Department of Experimental and Clinical Neuropathology, Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw; [2]Prof. M. Weiss Rehabilitation Center „STOCER", Konstancin; [3]Department of Pathomorphology, Medical Centre for Postgraduate Education, Bielanski District Hospital, Warsaw

Clear cell meningioma (CCM) is an uncommon variant of meningioma showing high rates of local recur-

rences and progression. We report a case of recurrent clear cell meningioma of cervical spine, presenting unusual histopathological feature with epithelial and rhabdoid transformation of tumor cells.

The patient, a 26-year-old woman presented with tetraplegia that appeared first time in 1995 during pregnancy. Neuroradiological examination revealed tumor of the spinal canal at C3-C4 level, compressing spinal cord and extending extraspinally. A partial resection of tumor, followed by postoperative radiotherapy, was performed. Second surgery with total tumor removal and stabilization of cervical spine was done in 1996. The patient recovered good clinical status, without neurological deficits in follow-up over next 10 years. In 2006 the patient complained of pain of the left arm. MRI examination showed signs of tumor recurrence at the primary location in cervical region of spine. The patient was operated in 2007, however, due to massive hemorrhage the tumor was only partial removed. Since 2008 increasing pain and paresis of the left arm manifested. The last operation of subtotal tumor resection was performed in March 2009, getting slight clinical improvement.

Histological examination of surgical specimens from primary and recurring tumors revealed similar sheeting pattern of clear and epithelioid tumor cells, stained with PAS and prominent intercellular network of reticulin. In specimens of recurrent tumor obtained in 2009, the frequent necroses, mitoses and significantly higher MIB-1 labelling index than in primary tumor were observed. Primary and recurrent tumor were strongly immunopositive for EMA, vimentin, CK and focally for synaptophysin. Occasional cells were positive for CD34 and SMA. Immunostains for HMB-45, GFAP, NFP and desmin were negative. Histological diagnoses of metastatic carcinoma, angioblastic meningioma and papillary meningioma were considered for primary operated tumor. The final histological diagnosis was clear cell meningioma with rhabdoid transformation. To our knowledge, such feature of CCM undergoing partial epithelial and rhabdoid transformation has not been previously reported.

[A25]

Bilateral giant cell glioblastoma of cerebellopontine angles in 24-old women

Taraszewska A[1], Powała A[2], Matyja E[1], Bogucki J[3,4], Raczkowska B[1], Szopiński R[5]

[1]Department of Experimental and Clinical Neuropathology, Mossakowski Medical Research Centre, Polish Academy of Sciences, [2]Department of Pathomorphology, [3]Department of Neurosurgery, Bielanski District Hospital, [4]Department of Neurosurgery, 5Laboratory of Photographic Documentation, Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw

The majority of cerebellopontine angle (CPA) tumors are either primary extraaxial masses (schwannoma, meningioma) or secondary exophytic extensions of primary brain stem and cerebellar tumors. Extraparenchymal CPA gliomas are extremely rare tumors.

Here, we present an unusual fatal case of extraperenchymal giant cell glioblastoma in a 29-year-old woman with familial and clinical history of NF1. The patient dead shortly after diagnosis of bilateral CPA tumor. Postmortem neuropathological study of the brain revealed large tumor masses located in both cerebellopontine angles, demarcated from brainstem and cerebellum, however, surrounding the brainstem, infiltrating cranial nerves and subpial part of the left medial cerebellar peduncle. Additionally, teleangiectasis angioma was found in middle part of the pons. Any definite intraparenchymatous tumor was observed in a several coronal sections of the complete brain.

Histologically the tumor showed highly pleomorphic, multinucleated giant cells, with bizarre nuclei and abundant eosinophilic cytoplasm, admixed with prominent mononuclear cell infiltration as well as densely cellular areas of small or fusiform cells with frequent mitoses and focal necroses. Immunohistochemically tumor cells were positive for GFAP, S-100 protein, vimentin and negative for neuronal antigens. Mononuclear infiltrative cells were positive for CD-68. MIB-1 proliferative index was very high in densely cellular areas and significantly lower in predominated giant tumor cells. Multiple capillary teleangiectases in the pons and severe odematous and ischemic tissue changes were microscopically disclosed.

The presented case revealed an extremely rare coexistence of extraparenchymal malignant glioma and

intraparenchymal vascular malformation in the brainstem region in the patient with NF1.

[A26]

Combined ganglioglioma and pleomorphic xanthoastrocytoma

Wierzba-Bobrowicz T[1], Schmidt-Sidor B[1], Stępień T[1], Nauman P[2], Poniatowska R[3]

[1]Department of Neuropathology, [2]Department of Neurosurgery, [3]Department of Neuroradiology, Institute of Psychiatry and Neurology, Warsaw

We described the case of a 64-year-old male with right temporal lobe tumour composed of a ganglioglioma (GG) and pleomorphic xanthoastrocytoma (PXA).

He presented with a short history of headache and of generalized seizure. MRI showed a 8.0 x 10.0 sized indistinct demarcation lesion in the gyrus of right temporal lobe with marked surrounding oedema.

Microscopically, the lesion had two different components. The lager component showed an aggregation of oligodendroglial stroma with neuronal cells with prominent nucleoli . The smaller part was composed of pleomorphic cells with many multinuclear giant cells and single foamy cells. Immunohistochemical reaction with antibody to synaptophysin and neurophilaments demonstrated neoplastic neurons in the ganglioglioma, while expression of GFAP was found mostly in a subset of PXA tumour cells showing giant, multinuclear cells or spindle cells sometimes with intranuclear inclusions. Vacuoles in this neoplastic cells of PXA component, were positive with sudan black histological staining. The mitotic figures were sporadically noticeable.

We concluded that the composite GG-PXA is a rare neoplasm consisting of characteristic componets of both of these types of tumours.

[A27]

Sudden elimination of glioblastoma cells presenting *EGFR* amplification in standard cell culture conditions

Witusik-Perkowska M[1], Zakrzewska M[1], Bigoszewska K[1], Stawski R[1], Kluczycka-Wojdala D[1], Jaskólski DJ[2], Gresner S[1], Bieńkowski M[1], Piaskowski S[1], Liberski PP[1], Rieske P[1]

[1]Department of Molecular Pathology and Neuropathology, Chair of Oncology, [2]Department of Neurosurgery, Medical University of Łódź, Łódź

Rapid loss of *EGFR* amplification was observed after growing glioblastomas cells in standard, cell culture conditions (monolayer, 10% FBS). Probably elimination of glioblastoma cells presenting *EGFR* amplification was responsible for this phenomenon, since glioblastoma cells presenting *EGFR* amplification, cultured in standard conditions, showed features of apoptosis more frequently than glioblastoma cells without *EGFR* amplification. Factors responsible for this apoptosis should be defined. To this end, we have detected that glioblastoma cells showing *EGFR* amplification cultured as aggregates survive for months. These results suggest that glioblastoma cells presenting amplification of *EGFR* become quickly apoptotic, if cultured as monolayer, and survive longer aggregated.

Our cell culture protocols allow to investigate *in vitro* glioblastoma cells presenting *EGFR* amplification. Many applications such as testing new therapeutics directed against glioblastoma cells can be proposed based on this protocols.

In addition our analysis showed that: DNA multiplex PCR, and DNA Real time PCR, should be used only as FISH supporting techniques, to detect *EGFR* amplification in glioblastomas.

[A28]

Catecholamines in patients with Parkinson's disease and multiple system atrophy

Wolny Ł[1], Dorszewska J[1], Florczak J[2], Owecki M[2], Kozubski W[2]

[1]Laboratory of Neurobiology, Department of Neurology, [2]Chair and Department of Neurology, University of Medical Sciences, Poznan

Catecholamines, norepinephrine, NE; epinephrine, E and dopamine play important roles in higher animals as brain and peripheral sympathoadrenal medullary neurotransmitters. Measurement of catecholamines provides important information regarding sympathoadrenal activity. Simultaneously measurement concentration of plasma catecholamines (NE, E) and their metabolites in urine (normetanephrine, NMeta; metanephrine, Meta) as one of the tests for diagnosis of the neuroendocrine tumors. Catecholamines are important factor for regulation of blood pressure in autonomic system. Many patients with Parkinson's disease (PD) and with multiple system atrophy (MSA) showed symptoms autonomic dysfunction. The aim of study was to estimate of plasma levels: NE and E, and their metabolites in urine: NMeta and Meta in patients with PD and MSA and in controls.

Studies were conducted on the levels of NE, E, NMeta and Meta estimated by HPLC with electrochemical detection on patients with PD in age 35-81 years, and MSA in age 51-60 years, and matches controls. The study disclosed that in patients with MSA the concentration of plasma NE increased above reference limits but concentrations of NMeta and Meta are in references limits. However, in all PD patients concentration of plasma NE was in references limits, but concentrations of metabolite NE (NMeta) was markedly higher than reference limits. Simultaneously, in the same patients concentration of E metabolite (Meta) was higher than reference limits only in the patients treated L-dopa more than 5 years.

Monitoring of NE, E, NMeta and Meta levels in patients with PD and MSA may be a new diagnostic factor.

[A29]

The *Polycomb* genes expression analysis in medulloblastoma

Zakrzewska M[1], Grešner SM[1], Piaskowski S[1], Zalewska-Szewczyk B[2], Zakrzewski K[3], Liberski PP[1]

[1]Department of Molecular Pathology and Neuropathology, Chair of Oncology, [2]Department of Pediatrics Oncology, Hematology and Diabetology, 1st Chair of Pediatrics, Medical University of Łódź, [3]Department of Neurosurgery Polish Mother Memorial Hospital Research Institute, Łódź

Medulloblastoma (MB) is the most frequent type of embryonal tumors in pediatric population accounting for 20-25% of all brain tumors in children. Recently, a suspected contribution of the *Polycomb* group (PcG) genes in medulloblastoma growth was described. PcG genes play an important role in development processes, but they are also involved in self-renewal of neural stem cells and malignant transformation in adults.

In this study, we analyzed the activity of *BMI-1* and *MEL-18* genes, members of the PcG family and their potential target, *c-MYC* gene. Expression of *c-MYC* is considered as a strong prognostic marker connected with poor outcome in children with medulloblastoma, but up to now such analyses for *BMI-1* and *MEL-18* were not conducted. For that purpose we studied associations between expression level of above mentioned genes with demographic data (age and gender) and clinical data (clinical risk and patients survival).

Thirty one children with medulloblastoma undergoing surgery at the Department of Neurosurgery, Polish Mother Memorial Hospital Research Institute, were included in this study. Among them, there were 18 males and 13 females, aged from 5 months to 17 years. The expression levels of genes were measured by quantitative real-time PCR performed by 2-color multiplexing technique.

Statistical analysis revealed no significant differences in expression level of any of the three genes studied between two age groups (under 3 years vs. over 3 years) or between two groups obtained based on the clinical risk stratification (high risk vs. standard risk). Significant differences between gender were found only in case of MEL-18 gene with higher expression level observed among females ($p = 0.03$). The survival analysis was performed following the group stratification based on the median expression level of each gene. We found that higher expression levels of *BMI-1* and *MEL-18* were

associated with significantly decreased patients' survival (p = 0.02 and p = 0.012, respectively).

This work was supported by Minister of Science and Higher Education Grant No. N401 180 32/3580.

[A30]

Ependymoma WHO grade II and anaplastic ependymoma: Validation of morphological and immunohistochemical differentiation criteria

Żawrocki A[1], Iżycka-Świeszewska E[2], Papierz W[3], Liberski PP[4], Zakrzewski K[5], Biernat W[1]

[1]Department of Neuropathology and Molecular Pathology, [2]Department of Pathomorphology, Medical University of Gdańsk, [3]Department of Pathomorphology, [4]Department of Molecular Pathology and Neuropathology, Medical University of Łódź, [5]Department of Neurosurgery, Polish Mother Memorial Hospital Research Institute, Łódź

Ependymomas are neoplasms that arise from the ependyma of the cerebral ventricles and the central canal of the spinal cord. They constitute 3-9% of all primary tumors of the central nervous system (CNS), and are most commonly found in children.

According to the most recent WHO classification of the tumors of the CNS (2007), ependymomas are divided into the three classes, based on the morphological criteria. Whereas in the case of ependymomas grade I, the diagnosis is unambiguous and prognosis is usually good, no clear-cut criteria exist to differentiate between the classical (WHO grade II) and anaplastic (WHO grade III) ependymoma.

We conducted a survey of 39 patients – adults and children – diagnosed with ependymoma of either grade II (30) or grade III (9).

The relation between the histopathological and immunohistochemical features of neoplasms and mortality rates was evaluated. The survival time of the patients to a large extent depended on the cellularity, the number of mitotic figures, Ki67 labeling index, and cyclin D1 expression.

[A31]

Expression of elements of WNT/Wingless signaling pathway in ependymomas.

Żawrocki A[1], Iżycka-Świeszewska E[2], Papierz W[3], Liberski PP[4], Zakrzewski K[5], Biernat W[1]

[1]Department of Neuropathology and Molecular Pathology, [2]Department of Pathology Medical University of Gdańsk, [3]Chair and Department of Pathomorphology, [4]Department of Molecular Pathology and Neuropathology, Medical University of Łódź, [5]Department of Neurosurgery, Polish Mother Memorial Hospital Research Institute, Łódź

Wnt/Wingless signaling pathway plays a significant role in the embryogenesis and in pathogenesis of various diseases, including neoplasms. Beta-catenin is a submembranous protein which is one of the major components of this functional pathway. WNT particle activates the pathway, inhibits ubiquitination of beta-catenin and initiates the transcription process. *APC* protein is a vital element of the destruction complex.

A few cases of ependymoma developing in Turcot syndrome have been described in the literature. Mutations of the APC gene are the basis of the Turcot syndrome. This may suggest the activation of the WNT pathway in ependymomas. The nuclear expression of beta-catenin, a marker of WNT pathway activation, in the colorectal cancer constitutes a negative prognostic factor.

Beta-catenin and APC protein expression was examined in 39 ependymomas WHO grade II and grade III.

Expression of beta-catenin was found in 92% of those neoplasms, irrespective of grade, localization of tumor or patients age.

No significant correlations were identified between the expression of beta-catenin and the survival rate of ependymoma patients. None of the cases showed APC protein expression. These results suggest lack of role of Wnt/Wingless pathway in ependymomas.

Index of authors