Anaplastic Oligodendroglioma with Ganglioglioma-like Maturation

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Neuronal differentiation of anaplastic oligodendroglioma has been demonstrated by immunohistochemical and ultrastructural examinations in recent studies. A 58-year-old male patient was admitted with a tension headache with dull and tightening in left occipital area. Computed tomography findings reveal a low density mass in right frontal lobe. Magnetic resonance imaging of his brain demonstrated a 2.4 × 1.8 cm-sized solid mass in right frontoparietal opercular cortex. The tumor was composed of anaplastic oligodendroglioma cells and ganglioglioma-like cells in mixing growth pattern.

Key Words: Anaplastic; Oligodendroglioma; Ganglioglioma; Neuronal; Differentiation

Prognostic Value of Immunophenotypical Subclassification in Primary Central Nervous System Lymphoma

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Background: The primary central nervous system lymphoma (PCNSL) is an aggressive form of non-Hodgkin’s lymphoma which is mostly diffuse large B-cell lymphomas (DLBCL). In nodal DLBCL, germinal center B-cell (GCB) type is associated with better prognosis compared to activated B cell (ABC) type. Methods: Total thirty-four cases of PCNSL, DLBCL, from 2000 to 2012 were selected in Seoul St. Mary’s Hospital in Seoul, Korea. Immunohistochemistry for CD10, BCL-6, MUM-1, and Ki-67 and Epstein-Barr virus (EBV) in-situ hybridization were performed. All the cases were subclassified into GCB and ABC based on immunoprofile. We analyzed whether subclassification of PCNSL, DLBCL have prognostic impact. Results: The median age was 57 years old ranging from 38 to 86. The median overall survival time (OS) and progression free survival time (PFS) were each 38.9 and 19.6 months. Younger patients under 70 and patients with methotrexate chemotherapy had better prognosis (p = 0.037 and p = 0.031, respectively). Four (11.8%) cases were positive for EBV infection. Other clinical features and immunologic markers, including EBV, had no prognostic impact. Thirty two (94.1%) cases were categorized as ABC type and only 2 (5.9%) were GCB type. Two-year overall survival rates were 58% and 100%, respectively. But there was no statistically significant difference for OS and PFS. Conclusions: We observed that most of the PCNSL, DLBCL were ABC type (94.1%) in our institute. Compared with published studies, ABC type comprised higher percentage in our study. However, the subclassification of primary central nervous system DLBCL into GBC and ABC type did not seem to have association with patients’ prognosis.

Key Words: Primary central nervous system lymphoma; Lymphoma, large B-cell, diffuse; Prognosis

Historical Perspective, Diagnostic Criteria’s and Challenging Surgical Management in a Case of Neurofibromatosis Type 1

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Neurofibromatosis type 1 (NF1), also known as von Recklinghausen’s disease, is a human genetic disorder. It is probably the most commonly inherited disorder caused by a single gene. This is a report of 5 cases of neurofibromatosis type 1. Case 1 to 4 presented with diagnostic difficulties and a 57-year-old man (case 5) affected by NF1 who has severe atrophy of the jaws and extremely unsatisfactory anatomical conditions for conventional dental restoration. Radiographic and clinical evaluations showed inadequate quantity of bone for immediate implant rehabilitation. Delayed implant protocol was performed to obtain the correct bone volume and implants were inserted in the anterior parts of both jaws to support a prosthetic restoration.

Key Words: Neurofibromatosis 1; Dental prosthesis, implant-supported; Diagnostic criteria
There were 39 patients (28%) of recurrent disease. Mean and median time to recurrence were 59.6 and 47 months with 1-year, 5-year, and 10-year recurrence free survival rates of 98%, 72%, and 45%. Thirteen patients (9%) developed extracranial metastases. Adjuvant radiation therapy, histologic grades, feasibility of gross-total resection and tumor size (≥ 6 cm) were associated with disease free survival (stratified log rank test, \( p = 0.0023 \), \( p = 0.0022 \), \( p = 0.0140 \), and \( p = 0.0469 \)). **Conclusions**: The survival rate in patients with hemangiopericytoma of the CNS is comparable to that of previously reported series. Recurrence remains a critical clinical issue of the disease. Identification of NAB2-STAT6 fusion with surrogate immunohistochemical marker is a valuable diagnostic tool in the differential diagnosis of the disease.

**Key Words**: Hemangiopericytoma; Meninges; NAB2; STAT6 transcription factor

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**Clinicopathological Characteristics of Primary Central Nervous System Lymphoma**

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**Background**: Primary central nervous system lymphoma (PCNSL) is a rare craniospinal, extranodal non-Hodgkin lymphoma that may present as an intracerebral, orbital, leptomeningeal or spinal-cord mass. Its peak incidence in immunocompetent subjects is in the 6th-7th decades but it occurs earlier in immunocompromised patient. PCNSL usually manifests as focal B-cell origin lesions. **Methods**: The histopathologically proven PCNSL lesions in immunocompetent patients (age, 17 to 70 years; mean, 51.9 years; male:female = 6:4) received during last four years at tertiary care center in north India were retrospectively analyzed. **Results**: Their main presentations included raised intracranial pressure, visual or sensorium alteration, hyponatremia or seizures. They occurred in frontal cortex (n = 4), orbit (n = 1), cerebellum (n = 1), and cervical spinal-cord (n = 1). Surgical decompression and establishment of histopathological diagnosis was done in all cases. Histopathology revealed: diffuse large B-cell lymphoma (n = 7), marginal zone B-cell lymphoma (n = 2), and lymphoblastic lymphoma (n = 1). Diffuse large-cell lymphoma showed prominent atypical, perivascular lymphoid cells. Immunohistochemistry revealed leukocyte common antigen and CD20 in all patients. Following surgical decompression and histological confirmation, a radio-chemotherapy schedule was effective in bring out remission. The major causes of perioperative mortality (n = 3) were medical such as pneumonitis and renal failure. **Conclusions**: This study focuses on the histopathological characteristics and management options in PCNSL in immunocompetent individuals.

**Key Words**: Central nervous system; Lymphoma; Clinicopathological; Characteristics

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**The Characteristics of 155 Primary Central Nervous System Germ Cell Tumors in Korea**

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**Background**: Central nervous system germ cell tumors (CNSGCT) accounted for 2-3% of primary intracranial neoplasm. They are prevalent in far-east Asian countries and the incidence thought to be higher than western countries. A few data existed in regard to clinicopathological features of Korean germ cell tumors (GCTs). **Methods**: We analyzed histologically verified 155 GCTs. **Results**: The most common histological subtypes were germinoma (68%), followed by teratoma (17.4%), and mixed GCT (13.5%). The patients’ age ranged from 0 to 38 years (mean, 14.6 years). The incidence peaked in 11-20 years olds (52.9%), followed by in 0-10 years olds (29.0%), and in 21-30 years olds (14.8%). The highest mean ages was found in germinoma (16.2 years), followed by mixed GCT (14 years), and teratoma (10 years). The mean age was not statistically different in GCT. The most prevalent ages in male and female patients was not different. The male to female ratio were in 4:1. Mean age was not statistically different in male and female patients (15.2 years and 12 years). Pineal gland (n = 61) was the most common site, followed by the suprasellar compartment (n = 30) and basal ganglia (n = 21). The most common site of germinoma was different according to the gender, which was pineal gland (29.8%) in male and suprasella (45.1%) in female. **Conclusions**: The age, gender, order frequency and the common location of our series of CNSGCT are similar to those of Western cases. This study could be a stepping stone to understand prevalence and clinical manifestations of CNSGCT of Korean.

**Key Words**: Central nervous system; Neoplasms, germ cell and embryonal; Clinicopathological features

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**Glioblastoma with Oligodendroglioma Component Represents a Subgroup of Glioblastoma with High Prevalence of IDH1 Mutation and Association with Younger Age**

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**Background**: Glioblastoma with an oligodendroglioma component (GBMO) is recognized as a subgroup of glioblastoma (GBM); however, the molecular and clinicopathological characteristics of GBMO are obscure. **Methods**: We evaluated the methylation status of MGMT, IDH1/2 mutation, deletions of 1p and 19q and expression of IDH1, p53, p16, CD151, and galectin3 proteins in 42 GBMOS (32 primary and 10 secondary tumors). We correlated our molecular findings with clinicopathologic features, and to compare molecular-to-clinical correlations in the 42 GBMOS with the corresponding correlations in 45 GBMs. **Results**: GBMO was subdivided into two subgroups according to the predominant cell component comprising 50% of tumors: the astrocytic predominant type (GBMO-A) and oligodendroglioma pre-
dominant type (GBMO-O). Methylation of MGMT, IDH1/2 mutation, and co-deletion of 1p and 19q were found in 31.0, 26.2, and 17.9% of patients with GBMO, respectively. Clinicopathological and molecular characteristics did not differ significantly between GBMO-A and GBMO-O. However, patients with GBMO-O experienced better outcomes than patients with GBMO-A (p=0.007). On multivariate analysis the predominant cell type was an independent prognostic factor in overall survival (hazard ratio, 4.2; p=0.011). When compared to patients with classic GBM, those with GBMO were younger (49.21 vs 57.47, p=0.003) and more frequently had tumors with IDH1 mutation (23.8% vs 4.4%, p=0.009). Survival was similar in patients with GBMO and with classic GBM. Conclusions: GBMO may represent a subgroup of GBM that is associated with IDH1 mutation and younger age, although similar to classic GBM in prognosis.

**Key Words:** Glioblastoma; Oligodendroglioma; MGMT; IDH1; 1p 19q

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**Does CD24 and OCT 3/4 Gene Expression in Human Glioblastoma Predict Survival?**

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**Background:** CD24 stimulates migration of gliomas in vivo and Oct 3/4 is a key regulator of stemness-related genes and is expressed in cancer stem cells. The current study quantified gene expression of CD24 and Oct 3/4 in cases of glioblastoma multiforme (GBM) and correlated with survival. Methods: cDNA was synthesized from RNA isolated from snap-frozen tissues of GBM. Relative quantification of CD24 and Oct 3/4 transcripts was performed in real time polymerase chain reaction (PCR). Immunohistochemistry was done in paraffin embedded tissues using anti CD24 (Thermoscientific, USA) and anti Oct 3/4 (Novocastra, UK) with polymer based secondary detection kit (Dakopatts, Denmark). Results: Gene expression profiling by real time PCR demonstrated that the mRNA for CD24 and Oct 3/4 was overexpressed in 10/35 and 3/35 cases. Patients with upregulated CD24 showed poor prognosis with mean survival ± standard error of 396 ± 60.53 days as compared to cases with down-regulated CD24 with a mean survival of 426.54 ± 43.09 (p<0.001). Oct 3/4 up-regulated cases had a mean survival of 309.33 ± 45.61 while down-regulated cases had a mean survival of 427.03 ± 37.36 (p=0.21). Immunohistochemistry results correlated with gene profiling. Conclusions: Uregulation of CD24 appears to be a useful predictor of survival in GBM. Poor survival may be attributed to the invasiveness and renewal properties linked to these markers. Targeting therapy against stem cells in glioblastoma with increased cancer stem cells may improve survival.

**Key Words:** Glioblastoma; Antigens, CD24; OCT 3/4; Survival

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**Expression of KITENIN and Its Association with Tumor Progression in Human Glioma**

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**Background:** KITENIN contributes to tumor invasion and metastasis in various cancers, but the implication of KITENIN in glioma progression remains unclear. The aim of this study was to investigate the effect of KITENIN on biological behaviors of human gliomas and its expression in glioma samples in association with patients’ survival data. Methods: KITENIN expression was examined using western blot and immunohistochemistry on human samples. The 90 cases for immunohistochemistry and survival analysis included 6 Worlds Health Organization (WHO) grade I gliomas, 28 grade II gliomas, 12 grade III anaplastic gliomas, and 44 grade IV glioblastomas. KITENIN expression rate was compared in each histological grade, and survival rates were analyzed. Invasion assays were performed after overexpression by gene transfection and suppression by siRNA treatment on human glioma cell lines. Results: Stronger expression of KITENIN was more likely to be observed in high-grade gliomas compared to low-grade gliomas by western blot on frozen human tumor samples and by immunohistochemistry on paraffin-embedded tissues as well. Proportions of strong KITENIN expression were 16.7%, 21.4%, 33.3%, and 56.8%, respectively, from grade I through IV (p=0.001). In addition, KITENIN overexpression promoted invasion of U118 cells and KITENIN suppression decreased invasion of U343 cells. However, survival analysis using the Kaplan-Meier method did not reveal statistical significant difference between the high KITENIN expression group and low KITENIN group in terms of overall survival and progression free survival (p=0.55 and p=0.807, respectively). Conclusions: KITENIN expressed more strongly in high-grade gliomas and KITENIN was strongly associated migration and invasion in glioma cell lines.

**Key Words:** Glioma; V ANGL1 protein, human; Gene expression; Survival
mass with high choline/creatine ratio (3:1) at left periventricular region, involving left lentiform nucleus, left thalamus and extending to left side of midbrain. Lymphoma or high grade glioma were suspected. Brain biopsies showed diffuse infiltration by foamy macrophages with some perivascular neutrophil and lymphocyte infiltration, area of necrosis and hemorrhage. Reactive gliosis was also noted. No microorganism is seen in special stains. Bielschowsky, Luxol fast blue periodic acid-Schiff stains and electron microscopic study revealed demyelination with axon preservation, which were compatible with TMS. Her conditions were improved after pulse methylprednisolone treatment.

Key Words: Multiple sclerosis; Stroke; High grade glioma; Demyelinating diseases

Prognostic Significance of Ror2 and Wnt5a Expression in Medulloblastoma

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Background: Medulloblastoma (MB) is a clinically and biologically heterogeneous group of tumors, and currently classified into four molecular subgroups (Wnt, Shh, group 3, and group 4). Intracellular signaling of the Wnt pathway has been divided into two classes: the ‘canonical’ and the ‘non-canonical’ signaling pathway. The canonical signaling pathway is a well-established, β-catenin-dependent signaling pathway in MB. In contrast, very little research about the non-canonical WNT signaling pathway in MB exists. Methods: In order to identify the roles of Wnt5a and Ror2, two non-canonical WNT pathway-related genes, we studied 76 cases of MB with immunohistochemistry and quantitative real-time polymerase chain reaction and correlated the results with clinicopathological and other molecular parameters and prognosis. Results: Wnt5a and Ror2 were immunopositive in 20 (29.4%) and 35 (51.5%) of 68 cases, respectively. There were positive associations among protein expression of Wnt5a, Ror2, and β-catenin. Ror2 mRNA levels were well-correlated with immunoexpression. Ror2 mRNA expression was significantly associated with CTNNB1 mutation. High Ror2 mRNA expression was an independent favorable prognostic factor. Conclusions: In conclusion, our study demonstrates the first attempt to identify Wnt5a and Ror2 as additional mechanisms contributing to dysregulation of the non-canonical WNT signaling pathway in MB. Ror2 may play a role as an oncosuppressor in MB.

Key Words: Medulloblastoma; Receptor tyrosine kinase-like orphan receptors; WNT5A protein, human; Wnt signaling pathway; Prognostic factor