suboccipital craniotomy was performed in the sitting position, a head-up surgery was performed using a 4K / 3D video microscope system (ORBEYE exoscope, Olympus) by the infratentorial supracerebellar approach (ITSCA). The bridging veins and precentral cerebellar vein were dissected to expose the posterior surface of the tumor, and internal decompression was performed. For the complication of air embolism, artificial cerebrospinal fluid was sprayed, and the bilateral internal jugular veins were compressed to confirm the inflow point. There was strong adhesion to the Rt vein of Rosenthal, and the site was removed intracapsularly. Finally, subtotal resection was performed with remaining the upper part of the tumor, a blind lesion behind the Vein of Galen. Vertical gaze palsy occurred after this operation, but it gradually improved over time. Tumor showed pathologically remarkable polymorphism, poor microvascular proliferation and necrosis, but mitotic figures 4–5 / 10HPF, MIB-1 index 10%, GFAP positive, no BRAF V600E mutation. There are few reports of PXA occurring in the pineal gland, and this case is the sixth case. It is also the first report for pineal tumors using ORBEYE through ITSCA in the sitting position.

Key words: PXA | pineal region | sitting position

CS-6

A CASE OF POORLY DIFFERENTIATED CHORDOMA WITH SYSTEMIC METASTASIS

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A case report: The patient was a 32-year-old man with diplopia. He was diagnosed as sphenoid sinusitis on MRI by a local doctor and visited an otolaryngologist. MRI showed extensive extension of neoplastic lesions from the clivus to the sphenoid sinus to the anterior ethmoid sinuses, bilateral cavernous sinuses, and the right medial and lateral pterygoid muscles. The right Lebiere's lymph node was enlarged and thought to be a metastatic site. Based on the rapid growth and extension of the tumor, the patient was referred to the Department of Otolaryngology at our hospital on suspicion of sinonasal carcinoma. The possibility of chordoma could not be denied, so the patient was referred to our department. The patient underwent a joint endoscopic extended transsphenoidal tumor resection. The pathological diagnosis showed mitotic and necrotic features, and the majority of the cells showed highly atypical components without mucous substrate. However, brachyury, a marker for chordoma, was diffusely positive, and there was loss of INI1 (SMARCB1) expression. The final diagnosis was poorly differentiated chordoma. Postoperatively, the tumor in the right cavernous sinus grew rapidly, and the right eye became blind due to obstruction of the superior ophthalmic vein. The patient was treated with Gamma Knife as soon as possible in the hope of local control by high-dose irradiation, and after a total of three irradiations, the residual tumor shrank markedly and symptoms improved, but systemic metastasis occurred in a short period of time and the patient died. The number of cases of poorly differentiated chordoma has been reported rarely (more than 50), and it is more common in children and even rarer in adults. We report this case with a review of the literature.

Key words: poorly differentiated chordoma | systemic metastasis | poor prognosis

CS-7

A CASE OF LYMPHOMATOID GRANULOMATOSIS WITH SKIN, LUNG, AND INTRACRANIAL LESIONS DUE TO MULTICENTRIC DEVELOPMENT

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Introduction: LYG is very rare tumor and composed of large EB-positive B cells and reactive T cells. In this study, we experienced a case of LYG with multiple intracranial, cutaneous, and pulmonary masses. We report the pathogenesis and pathophysiology of LYG, including a discussion of the literature. case: A 69-year-old female presented with a growing lump in her lower back that had been present for several years. Six months later, she was found to have multiple masses in her lungs and intracranial region and underwent surgical removal for diagnostic purposes. Intraoperative findings: The tumor was substantial, reddish to grayish-white in color, and the margins of the tumor were whitish and hard, with some areas that could not be detached. Pathological findings: There were no atypical lymphocytes, and a small number of EBER-positive cells were observed. IgVH PCR: IgVH PCR was performed on the skin lesions and intracranial lesions, and bands of different sizes were detected, suggesting that the IgVH clone was present in the polyclonal region. Finally, we diagnosed LYG grade 1. discussion: EB-associated lymphoproliferative disease can lead to polyclonal reactive growth or monoclonal neoplastic growth depending on the balance between morphology and host immunity. The results of IgVH PCR suggest that the skin lesions did not cause multiple metastases, but rather that the enlargement of the skin lesions triggered intracranial and pulmonary lesions in an allo-centric manner. The results of IgVH PCR suggested that the skin lesions did not cause multiple metastases, but rather that the skin lesions grew to cause intracranial and pulmonary involvement in an other-centric manner.

Key words: Lymphmatoid granulomatosis | EBER | IgVH clonality

CLINICAL OTHERS (COT)

COT-1

CLINICAL QUESTIONS AND ANSWERS ABOUT GLIOMA-RELATED EPILEPSY (GRE): REAL-WORLD DATA IN WAKAYAMA MEDICAL UNIVERSITY HOSPITAL

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Introduction: In glioma patients, epilepsy not infrequently occurred and anti-epileptic drugs (AEDs) are commonly used. In this study, we revealed the real-world data on clinical practice of glioma-related epilepsy in Wakayama Medical University Hospital (WMUH). Methods. We collected clinical and molecular data of glioma patients operated at WMUH from January 1996 to December 2020 and analyzed the data to answer clinical questions as follows: 1) location/histology related GRE, 2) molecular features related GRE, 3) prophylactic AEDs and postoperative seizure, 4) tumor progression and convulsion, 5) GRE and survival. Results. Fifty-five of 113 glioma patients (49%) presented with seizure. CQ1. In tumors located at frontal, temporal and parietal lobe, the occurrence rate of GRE was 27/39 (69%), 13/19 (69%) and 9/14 (64%), respectively. Patients with glioblastoma, astrocytic tumors and oligodendroglial tumors presented with GRE at the rate of 26/54 (48%), 14/30 (47%) and 12/13 (92%), respectively. CQ2. GRE occurred in tumors with IDH mutated (16 cases, 29%), TERT mutated (32 cases, 58%) and MGMT methylated (32 cases, 58%). CQ3. Seizure in peri- or postoperative period occurred in 14 cases (12%); 4 cases in AED(+) group (4/29, 14%) and 10 cases in AED(-) group (10/84, 12%). CQ4. Tumor progression became apparent at the time of seizure in 12 cases (12/55, 22%). CQ5. According to the prognostic IDH/TERT classification of diffuse glioma cases (n = 94), overall survival (OS) times of GRE(+) cases tended to be longer than that of GRE(-) ones, especially in IDH wildtype/TERT mutated group (22.7 months vs. 8.3 months, p = 0.0397). Conclusion. GRE is likely associated with specific clinical and molecular features. Seizure in glioma patients can occur in specific situation regardless of the use of AEDs. Possible better prognosis of GRE(+) cases requires further investigation.

Key words: Epilepsy | Glioma | Clinical questions

COT-3

EXOSOMAL MICRORNA EXPRESSION SIGNATURE IN BLOOD AND CEREBROSPINAL FLUID OF GLIOBLASTOMA PATIENTS

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Analysis of exosomes derived from plasma or cerebrospinal fluid (CSF) has emerged as a promising biomarker platform for therapeutic monitoring in glioblastoma patients. However, the contents of the various subpopulations of exosomes in these clinical specimens remain poorly defined. Here we characterize the relative abundance of miRNA species in exosomes derived from the plasma and CSF of glioblastoma patients. To this end, we first employed

miRNA arrays to measure the expression of exosomal miRNAs in the plasma from glioblastoma patients (n = 24) and healthy volunteers (n = 7) as control. In addition, we performed global miRNA profiling of exosomal miRNAs in the CSF from glioblastoma patients (n = 5) and non-tumoral patients (n = 3; hydrocephalus patients) as control. In plasma derived exosomes, 80 miRNAs were altered by >2-fold in glioblastoma patients compared to controls. In CSF, 92 miRNAs were altered by >2-fold in glioblastoma patients compared to controls. Combined analysis of plasma and CSF revealed a similar fold difference in eight miRNAs. Next, we measured these eight miRNAs expression in in the plasma from pre- and post-operative glioblastoma patients (n = 9). Among these eight miRNAs, we identified only one miRNA (miR-34b-3p) that was upregulated in exosomes from pre-operative glioblastoma patients. Our results suggest that miR-34b-3p might have a potential as a novel diagnostic marker or a therapeutic tool for glioblastoma patients.

Key words: glioblastoma | icroRNA | exosome

COT-6

BODY MASS INDEX AND HEIGHT IN RELATION TO BRAIN TUMOR RISK IN A JAPANESE POPULATION

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Purpose: Because the prognosis of the malignant brain tumor including glioblastoma is extremely worse than other cancer, it is important to clarify the preventive factors of the brain tumor in the prospective cohort study. In the Japanese epidemiologic study of the brain tumor, the report of the prospective cohort study has not been accomplished. Therefore, we have reported the study in recent years from a multipurpose cohort study (Japan Public Health Center-based Prospective Study: JPHC study) that the national cancer center was mainly conducted. This prospective study investigated the association between height and BMI (Body mass index) and brain tumor risk in an Asian population, whose distribution of anthropometric data differs from Westerners. Methods: A total of 106,324 subjects (50,438 men and 55,886 women) enrolled in JPHC Study, was followed from 1990. We divided participants into 5 categories based on the distribution of BMI as <18.5, 18.5- <23, 23- <25, 25- <27.5, and >-27.5 Kg/m2. We used the Cox proportional hazards regression model and estimated brain tumor incidence by gender and tumor subtype, with adjustment for potential confounding variables; age, sex, pack-years of cigarette smoking, alcohol intake, coffee intake, green tea intake, past history of allergy and past history of diabetes mellitus.Results: During an average follow-up of 18.1 years, 157 incident cases of brain tumor were newly identified, included glioma (n=60), meningioma (n =51), lymphoma(n=9), schwannoma(n=3), pituitary adenoma(n=2), and others(n=32). Higher BMI was significantly positively associated with the risk of brain tumor. This positive association of BMI was stronger in men and for meningioma in subgroup analyses. In contrast, height showed no clear association with brain tumor risk. Conclusion: Higher BMI was associated with an increased risk of brain tumor, in particular of meningioma, and among men.Full article has been published annals of epidemiology.

Key words: JPHC study | Body mass index | Prospective study

COT-7

ONLINE SUPPORTS FOR OPENING OF THE TUMOR TREATING FIELD

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Background: EF-14 trial showed the efficacy of tumor treating fields (TTF), and TTF was approved as a standard therapy for glioblastoma in Japan. In TTF opening, Device Support Specialist (DSS) explains how to use it for the patient and the family. Because there is no DSS in Yamaguchi prefecture, DSS has to come to our hospital across other prefectures. On the other hand, COVID-19 is still spreading and it is sometimes tough to move from a big city to countryside. Here, we would present the experiences of TTF opening with online DSS support. Method: From June 2020, Zoom was used for 4 patients, and from June 2021, iPad/Face-Time was used for one patient. TTF was introduced via online DSS support with direct support from our nurse in our out clinic. After that, initial times of TTF change were performed via online DSS support in patient's home. Two patients who used Zoom had trouble to connect to internet, however finally completed with relative helps.Conclusion: Online medicine should be absolutely spreading in country sides. Now, we change from Zoom to iPad, because the old patients in country sides were hard to use internet utility. We should make efforts to provide patients more brief methods of online support.

Key words: glioblastoma | TT field | online support

COT-9

PROGNOSTIC IMPACT OF HYPERCOAGULATION IN GLIOBLASTOMA AND MOLECULAR MECHANISM THEREOF

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Introduction: Pathological features of glioblastoma include intravascular thrombosis, suggesting that the thrombus formation in tumor microenvironment contributes to progression of gliomas. Meanwhile, glioblastoma has been known to be high risk malignant tumor for venous thromboembolism, however, it remains unclear how the coagulation-fibrinolysis system is disrupted, which essentially grow within the cranium in a localized manner, and how the disruption contributes to the malignant transformation. Methods: Total 64 patients with glioblastoma between January 2014 and April 2021 who underwent a D-dimer test before the therapeutic intervention were divided into two groups: the high D-dimer group (D-dimer level >3.0μg/ml) and the low D-dimer group (D-dimer level <3.0μg/ml). We compared the two groups in the maximum gadolinium-enhanced MRI lesions, MIB-1 index, and gene abnormalities (IDH mutation, TERT promoter mutation, and MGMT promotor methylation). The progression-free survival (PFS) and overall survival were analyzed using the Kaplan-Meier method. Furthermore, in 23 patients who underwent a D-dimer test at recurrence, the time to death after recurrence was analyzed. Results: The PFS in high D-dimer group was significantly shorter than that in the low D-dimer group (log-rank p = 0.0075). The D-dimer increase at the time of recurrence significantly correlated with the decrease in post-recurrence survival duration (log-rank p = 0.0226). Moreover, the gadolinium-enhanced lesions in the high D-dimer group were significantly larger. Conclusion: The Pre-intervention D-dimer levels and PFS suggest that glioblastoma-induced systemic enhancement of the coagulation-fibrinolysis system plays a role in the malignant transformation. The D-dimer increase during the treatment was found to be a predictor of poor prognosis after recurrence. Furthermore, the MRI findings revealed a correlation between the D-dimer increase and the size of intratumoral necrosis. Meanwhile, no correlation with the MIB-1 index was found, suggesting that the mechanism of malignant transformation by hypercoagulation differ from enhanced cell proliferation.

Key words: glioblastoma | coagulation | D-dimer

COT-11

RELATIONSHIP BETWEEN PREOPERATIVE LIQUID BIOPSY AND PROGNOSIS OF GLIOBLASTOMA -NEXT GENERATION SEQUENCING OF SMALL NONCODING RNA-

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Background: Non-invasive biomarkers are required in clinical practice of glioblastoma (GBM). We have previously reported the liquid biopsy for differentiating glioblastoma, central nervous system primary lymphoma and healthy control. In this study, we analyzed the relationship between the preoperative serum expression of circulating small non-coding RNAs and the prognosis of GBM patients. **Methods**: Preoperative blood samples of GBM, IDH-wildtype patients (N=26) were centrifuged and collected all small RNAs in serum. The expression of small non-coding RNAs were analyzed using a next-generation sequencing system. The small non-coding RNAs that could predict short-term survivals in GBM patients were selected by the stepwise analysis. A diagnostic model was created using the combination of these RNAs and evaluated with ROC curve. **Results**: GBM patients treated with adjuvant therapy of temozolomide and radiotherapy were divided into two groups: (1) a short-term survival group (N=11) with a survival time less than 15 months and (2) a long-term survival group (N=15) with a survival time more than 15 months. In the short-term survival group, the preoperative serum expression levels of small RNA-X and small RNA-Y were high, and the expression levels of small RNA-Z and small RNA-W were low. Using these four small non-coding RNAs, a prognostic model was created. The model was able to predict the short-term survival group of GBM patients with a sensitivity of 90.9% and specificity of 93.3% (AUC: 0.969). **Conclusion**: The prognostic model developed with preoperative small non-coding RNA in GBM patients may be useful for estimating the survival of GBM patients treated with adjuvant therapy of temozolomide and radiotherapy.

Key words: Glioblastoma | liquid biopsy | small noncoding RNA