

COT-14

CLINICAL FEATURES OF PEDIATRIC CENTRAL NERVOUS SYSTEM TUMORS

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INTRODUCTION: Here, we discuss the presentation, histology, therapy, and outcome of central nervous system tumors in children. **METHODS:** Treatment outcome and management was assessed for children diagnosed with central nervous tumors from 2007 to 2017 at Kagoshima University. **RESULTS:** Eight-eight patients (56 boys, 32 girls) with a mean age of 10.3 years were included in this study. Patient tumor types included: germ cell tumor (n = 26); medulloblastoma (n = 16); pilocytic astrocytoma (n = 8); glioblastoma (n = 8); ependymoma (n = 6, 1 with grade 2, 5 with grade 3); hemangioblastoma, schwannoma, and ganglioglioma (n = 3 each); SEGA, pilomyxoid astrocytoma, and diffuse astrocytoma (n = 2 each), and anaplastic astrocytoma, PPTID, PNET, PXA, DIA, central neurocytoma, astroblastoma, meningioma, and choroid plexus papilloma (n = 1 each). The most common patient clinical features were headache and vomiting associated with hydrocephalus. The median follow-up period was 61 months. All patients with germ cell tumors underwent adjuvant chemotherapy and radiation therapy (RT); patients with germinoma or immature teratoma were still alive, while patients with embryonal carcinoma, yolk sac tumor, or choriocarcinoma had poor prognosis with a median survival of 16 months. For cases of ependymoma, three patients received ICE chemotherapy and RT, and two patients received RT alone; median survival time was 31 months. For high grade glioma, seven patients received temozolomide and RT, and two patients received temozolomide alone; median survival time was 13 months. **CONCLUSIONS:** Patients with germ cell tumors had a relatively good prognosis, while patients with ependymoma or high grade glioma had a poor prognosis. As treatment strategies for ependymoma and high grade glioma are currently limited, it is necessary to evaluate treatment options in consideration of clinical course and quality of life, in addition to histologic and genetic findings.

COT-15

LITERATURE REVIEW ON THE DECISION MAKING OF THE BRAIN TUMOR PATIENT

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BACKGROUND: Patients with primary brain tumors find it difficult to make decisions during the advanced disease stage and experience decreased consciousness. It is important for patients to receive supported decision-making early. Medical staff should know what to do and when to do it, but there are no clear guidelines. Therefore, we reviewed the literature for supported decision-making for primary brain tumor patients, particularly to provide information for understanding trends reported in previous research. **METHOD:** On January 1, 2019, we conducted a search using keywords, such as "brain tumor" and "decision-making," via PubMed and "Igakuchuo-zashi" in Japan. We extracted literature about treatment decision support and end-of-life care for patients with primary brain tumors. Furthermore, we studied and chose the documents for information provision. **RESULT:** Upon observing 7 studies, we found: 1) about 50% of the patients want more prognostic information; 2) patients with brain tumor tend to be anxious, but they want more information to develop a good understanding of the disease and to lower their anxiety; 3) about half of the brain tumor patients in end-of-life care are unable to make decisions sooner owing to impaired consciousness, and hence are unable to share treatment preferences with their doctors; 4) when medical professionals provide information, such as adding video tools about end-of-life care to oral explanations, it facilitates supported decision-making; and 5) when the caregiver intends to notify patients, the family feels conflicted. **DISCUSSION:** The results suggested that if the timing of the end-of-life conversation is late, it becomes difficult for the patient to make decisions and the burden of decision-making falls on the family. It is necessary to examine effective supported decision-making tools for patients by assessing and comprehending information needs and anxiety levels of primary brain tumor patients.

COT-16

INDICATION OF SYSTEMIC THERAPY FOR ELDER PATIENTS WITH BRAIN TUMORS: A SYSTEMATIC REVIEW AND PERSPECTIVE

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BACKGROUND: Little is known about indications and outcome prediction of systemic therapy for elderly patients with brain tumours. Clin-

ical conditions of individuals are heterogeneous from healthy to frail or diseased, moreover, are often reversible. **METHOD:** We retrieved the literature of brain tumour, systemic therapy, chemotherapy, immunotherapy, in randomized controlled trials (RCTs) and reviews on PubMed database from 2008 to 2018. **RESULTS:** 1) Definition of elderly by age in years: Depending on each protocol, the definition is arbitrary. Patients older than 60 or 70 years are usually in the elderly group. 2) Systemic evaluation: Performance status (PS) and visceral function are not sufficient to assess elderly patients. Assessment tools specifically developed for the geriatric population are recommended to evaluate individual patients. 3) Effects and toxicity of systemic therapy: Only a few RCT showed no inferiority of outcome in patients older than 60 or 65 years. There are only few evidences about the senile fragility of blood-brain barrier or distribution of drugs in the elderly brain. Molecular subtyping of brain tumours might predict the effects and toxicities of therapies for elderly patients. **CONCLUSION:** Feasibility of modern systemic therapies are not well studied for elderly patients with brain tumours. Clinical condition varies in individual elderly patients. We need prospective studies of systemic therapy in elderly patients based on an eligibility with not only chronologic age but comprehensive geriatric assessments.

COT-17

EFFECT OF BEVACIZUMAB AGAINST CYSTIC COMPONENT OF PRIMARY/METASTATIC BRAIN TUMORS

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BACKGROUND: Bevacizumab (BEV) improves the symptom via reducing the peritumoral edema and sometimes via reducing the size of brain tumor. However, the effect of BEV against cystic part of brain tumor has not been documented yet. In this report, we investigated the effect of BEV on cystic component of brain tumors. **MATERIALS AND METHODS:** Our institutional review board approved this retrospective study. Between 2008 and 2018, 139 patients with primary or metastatic brain tumor were treated with BEV in our Hospital. We defined cystic lesions as high intense lesion of size 1 cm or bigger on T2WI, and excluded necrotizing cysts and cystic changes in surgical resection cavity. The symptoms and images before and after administration of bevacizumab were evaluated. Changes in cyst size of brain tumor was evaluated as follows: CR (complete response=disappearance), PR (reduction by 50% or more), MR (reduction by 25–50%), SD (size change less than 25%), PD (increase by 25% or more). The effect of bevacizumab on tumor itself was determined according to RANO criteria. **RESULTS:** Of the 139 patients, 21 (15.1%) brain tumors had cystic component. The best response of cyst to BEV were as follows: CR 6, PR 7, MR 4, SD 4. The group of patients with progressively increasing cysts prior to BEV administration had significant cyst size reduction compared to stable cyst size groups at best response timing (mean 76.3% vs. 32.8%, $P < 0.01$). Patients with cyst showed significant improvement of symptoms after the treatment with BEV compared to patients without cyst ($P < 0.01$). However, response rate against tumor itself was not different between patients with or without cyst. Overall survival of glioblastoma patients after starting BEV was not different between tumor with cyst and without cyst. **CONCLUSION:** BEV may be effective for patients who are symptomatic due to cystic enlargement.

COT-18

TWO CASES OF GLIOBLASTOMA WITH ASYMPTOMATIC PULMONARY ARTERY EMBOLISM AND DEEP VEIN THROMBOSIS FROM ADMISSION TO HOSPITAL

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Patients with malignant tumors are susceptible to concurrent venous thromboembolism. We report two cases of glioblastomas that showed asymptomatic pulmonary embolism and deep vein thrombosis on admission. The first case was a 77-year-old male. He was referred to our clinic for a tumor found in the left temporal lobe on computed tomography scan performed when he suffered pneumonia. On admission, he had a Karnofsky performance status (KPS) score of 50 and an elevated D-dimer level (16.46 µg/ml). Pulmonary embolism and deep vein thrombosis were noted on detailed examination. Direct oral anticoagulant (DOAC) therapy resulted in the disappearance of pulmonary embolism. On biopsy, the tumor was diagnosed as glioblastoma. The patient underwent radiation therapy in combination with chemotherapy. The second case was a 71-year-old female. She developed a disorder of consciousness and was admitted to a clinic. Brain magnetic resonance imaging (MRI) revealed a high T2 signal area in the left temporal lobe. The patient was initially diagnosed with encephalitis. Though the consciousness disorder improved quickly, she was referred to our clinic after a hyperintense area was observed on MRI. On admission, she

had a KPS score of 100, and an elevated D-dimer level (7.59 µg/ml), revealing pulmonary embolism and deep vein thrombosis. She was started on a DOAC and underwent surgical removal of the tumor via craniotomy. She was diagnosed with glioblastoma and underwent radiation therapy in combination with chemotherapy. Approximately 20% of the patients with glioblastomas suffer concurrent symptomatic venous thromboembolism. The incidence of venous thromboembolism is further elevated in patients with a poor KPS score or elderly people. Many patients with glioblastomas suffer asymptomatic venous thromboembolism. In this report, asymptomatic venous thromboembolism was noted in patients with a good KPS score. In glioblastoma patients, it is necessary to test for venous thromboembolism by measuring D-dimer levels before surgery.

COT-19

TREATMENT EXPERIENCE OF AND TIPS FOR ADMINISTERING NOVO TTF

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BACKGROUNDS: Current standard of care for glioblastoma, consists of postoperative temozolomide (TMZ) concomitant with radiotherapy, followed by adjuvant TMZ monotherapy. Recently, an international phase 3 trial (EF-14) demonstrated that addition of tumor-treating fields (TTF) to adjuvant TMZ after completion of chemoradiotherapy extended median progression-free survival and overall survival by 2.7 months and 4.8 months, respectively, compared with TMZ alone in patients with newly diagnosed glioblastoma. TTF is now considered as a part of its initial treatment in the guideline in Japan (recommendation grade B). However, distinct from anticancer drugs, little is known or experienced using TTF as a therapeutic device so far, especially in management and handling. **METHODS:** First six patients with newly diagnosed glioblastoma who underwent TTF were analyzed with special interest in medical and social supports to execute TTF at home. **RESULTS:** TTF was first introduced in our institution in May 2016, but no patients were treated because of no coverage by medical insurance until December 2017. We further needed to wait to initiate TTF treatment until January 2019 when the contract to use TTF systems was finally made between the company and institution. Since then six patients were registered in five months. For its introduction to clinical practice, it is essential to establish new in-house environment with medical professions division in the facility including documentations of calculating instruction fees and usage guidance for home care application of TTF. It is also important to initiate providing information of TTF such as timing of visit by specific practitioners and potential medical and psychologic burdens to patients and their families during and after chemoradiotherapy to better understand this new modality leading to the consent acquisition. **CONCLUSIONS:** Introducing TTF into clinical practice should accompany improvement of management in not only medical equipment and documentations but also patient care in hospital and home.

COT-20

PERIOPERATIVE STATUS OF SERUM D-DIMER LEVEL AND VENOUS THROMBOSIS IN PATIENTS WITH MALIGNANT BRAIN TUMOR

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BACKGROUNDS: The patients with malignant brain tumors frequently show the hypercoagulability state and a decrease in fibrinolysis ability with an elevation in D-dimer. This is partially due to tumor-related hemiparesis or surgical stress including long-term bed-ridden positioning during and after operation, which could lead to development and extension of deep venous thrombosis (DVT) in lower extremities and eventually fatal pulmonary embolism. **METHODS:** We retrospectively examined the pre- and postoperative serum D-dimer levels and DVT state in 75 consecutive patients with malignant brain tumors (i.e. glioma, malignant lymphoma; mean age 64 yo, 28 females) operated at our hospital from January 2015 to April 2017. Serial D-dimer levels were measured with the latex agglutination method (Roche) at 2 days before and right after operation, postoperative day (POD) 1, 3, and 7. Lower limb venous ultrasound (LVUS) or contrast CT was performed if preoperative D-dimer was 0.5 µg/ml or higher.

RESULTS: Average BMI was 21.3, nine patients with diabetes mellitus, 10 had recurrent diseases after chemotherapy, and 10 presented paresis in the lower extremities preoperatively while two developed transient paresis postoperatively. While two patients had prior DVT history, central and calf DVTs were identified preoperatively in one and 12 (15%) patients, respectively. Among four patients with re-elevation of D-dimer after POD 7, infection (2 patients), new DVT (2), and hemorrhagic events (gastrointestinal 2, including 1 death; epistaxis 2) developed, where a cut-off value D-dimer > 1.69 yielded sensitivity 100% and specificity 80%. Intraoperative intermittent calf compression prevented perioperative pulmonary embolism in those with calf DVT. **CONCLUSIONS:** Appropriate perioperative DVT managements could pre-

vent development of pulmonary embolisms in all patients with "high-risk" malignant brain tumors. Not only D-dimer > 1.5, but age of 80 or older, high preoperative D-dimer levels with calf DVT and taking DOAC may be risk factors for postoperative venous thromboembolism.

COT-21

EFFECT OF BEVACIZUMAB FOR PEDIATRIC HIGH GRADE GLIOMA

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INTRODUCTION: Bevacizumab (BEV) therapy has been used for pediatric high grade glioma, however the evidence and effectiveness are not understood yet. **METHODS:** We report 7 cases (age 2 to 10 years old) of pediatric high grade glioma treated with BEV. One case is thalamic diffuse midline glioma H3K27 mutant (DMGH3K27M), one case is brain stem DMGH3K27M, one case is cerebellar high grade glioma, and 4 cases are diffuse intrinsic pontine glioma (DIPG) diagnosed clinically without biopsy. 5 cases were treated with BEV when diagnosed as recurrence after chemoradiotherapy. One case was treated for rapid tumor progression during radiotherapy. One case was started on BEV therapy with radiation and concomitant temozolomide therapy. **RESULT:** The number of times of BEV was 2 to 13 times (median 7 times). The period of BEV was 1 to 9 months (median 4 months). One case which was treated with BEV at rapid progression during radiation showed good response on imaging and improvement of symptoms. 4 of 5 cases who were treated at recurrence clinically showed mild symptomatic improvement. One case treated with BEV and radiotherapy initially was not evaluated. The adverse effects of BEV included wound complication of tracheostomy and rash. **CONCLUSION:** BEV showed good response for rapid progression during radiotherapy, and mild response for recurrence cases. BEV is thought to be an effective therapeutic agent for pediatric HGG at recurrence and rapid tumor progression during radiotherapy.

COT-22

TIMING OF SURGERY AND BEVACIZUMAB THERAPY FOR MALIGNANT GLIOMAS

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BACKGROUND: The drug manufacturer recommends postponing initiation of bevacizumab for malignant gliomas at least 4 weeks later postoperatively. Malignant glioma patients with significant neurological deficits due to postoperative residual tumors are preferably needed earlier bevacizumab therapy that expecting improvement of neurological state and brain edema. There is a literature review indicating that the timing for administration of postoperative bevacizumab was at least 2 weeks. The authors assessed the safety, tolerability, efficacy for bevacizumab therapy less than 4 weeks later postoperatively. **METHODS:** Six patients of malignant gliomas with residual tumors and neurological deficits were treated by bevacizumab (10mg/kg every 2 weeks) therapy 2–3 weeks later postoperatively with chemoradiotherapy. Patients included 31-year-old female with thalamic-midbrain glioblastoma (initial), 11-year-old female with anaplastic ependymoma (recurrent), 71-year-old female with initial cervical cord anaplastic astrocytoma (initial), 88-year-old female bilateral frontal glioblastoma (initial), 27-year-old female with thalamic midbrain glioblastoma (initial) and 3-year-old female with brain stem glioblastoma (initial). **RESULTS:** All the patients did not experienced hemorrhage and impair wound healing. Every patient neurological state and perifocal brain edema following bevacizumab therapy demonstrated early improvement. Earlier bevacizumab therapy did not delay and cease postoperative chemoradiotherapy. **CONCLUSIONS:** Initiation of bevacizumab therapy 2–3 weeks later postoperatively seems to be safe and effective for malignant glioma patients with worse neurological state due to residual tumor and perifocal edema. The optimal interval which balances the risk of complications and the risk of tumor progression should be considered.

COT-23

INITIAL EXPERIENCE OF TREATMENT FOR GLIOBLASTOMA BY NOVO-TTF

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PURPOSE: In 2018, Optune (TTF) became available covered by public insurance for patients with glioblastoma, based on the effectiveness of the US