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ABSTRACT

教育講演Ⅱ

Tips to survive in international academic activities
国際的学術活動の中で生き抜くための秘訣

Takaomi Taira, MD, PhD

Department of Neurosurgery Tokyo Women's Medical University Tokyo, Japan

As a matured neurosurgeon, the past ten years was very exciting and fruitful for me. I was invited from abroad many times to give lectures, to teach operative techniques, to perform difficult operations, and to talk and drink with many friends. I wrote chapters of famous international textbooks, published many papers in high impact journals, and hosted international meetings. I introduced new operations, new indications, and new devices which cured many previously untreatable patients. I still do about 200 functional surgeries per year. I was lucky to teach many young fellows both in Japan and from abroad. Many of them are brilliant and now they are taking over my work as members of Taira's international Mafia. I think my dream came true, and I am very sure that this was not possible without experience in JNEF and SIGNS.

In this education lecture, I would like to suggest tips on how to survive in international academic activities especially for young doctors who wish to be international. The tips are based on my personal international experience. Of course, writing scientific papers and talking at international meetings are important. However, this is not enough at all.

English is very important in every aspect. However, I must say, we, Japanese, need to give up perfect English. What is more important is to express what you consider and to be able to explain why, even if your English is not good enough. Many foreigners ask us, for example, why the Japanese like United States despite the disastrous experience of Hiroshima and Nagasaki. They may also ask why there are so many neurosurgeons in Japan and why many of them work as emergency doctors, which is deviated from the world standard. You must be able to answer such questions. We must understand that the common sense in Japan is not always international, and United State is not a global standard. You must show your face. What is important is not where you are from or which University you belong. You yourself is more important. You must make others understood what kind of person you are and what you are considering. In this sense, you must have strong opinions and be able to assert even in front of millions of opponents. Very strong will supported by scientific and unbiased academic work is necessary. Being a nice person is also important.; friendly talk, humor, mild jokes, nice smiles, frank attitude, and so on. Expensive dinner with vintage wine is not necessary at all. The following is some of the tips I suggest for young doctors.

Change your computer and mobile phone in English mode.
Watch Japanese movies with English subtitles.
Do not spend time with Japanese colleagues when in abroad.
Always attend banquet, drink and talk with others, and make many friends.
Remember that everything is decided at night.
Try to ask questions just before your presentation

a-1 Intraoperative 5-ALA-induced fluorescence intensity as an indicator for 11C-Methionine Positron Emission Tomography uptake in astrocytomas

Kazuhide Shimizu, Kaoru Tamura, Takashi Sugawara, Motoki Inaji, Yoji Tanaka, Tadashi Nariai, Taketoshi Maehara

Department of Neurosurgery, Tokyo Medical and Dental University

Background: 5-aminolevulinic acid (5-ALA) induces red fluorescence in malignant brain tumors that has been used for intraoperative guidance for tumor removal. Positron emission tomography with 11C-Methionine (Met-PET) is a promising imaging modality to depict actively proliferating site of infiltrating glioma. We studied the correlation between preoperative Met-PET uptake and intraoperative 5-ALA fluorescence to investigate the correlation between these pre- and intraoperative modalities.

Method: Patients who underwent preoperative Met-PET study and tumor removal using 5-ALA over a period of two years were analyzed. The regional uptake of Met-PET was expressed as the ratio of the maximum of standardized uptake value (SUV-max) to the contralateral normal brain. 5-ALA fluorescence from tumor sample was immediately measured during surgery using blue laser and spectrometer. Fluorescence intensity was categorized into four groups (None, Weak, Moderate, Strong) with ten-hold differences.

Results: 16 cases with pathological diagnosis of astrocytic tumors were analyzed. Met-PET uptake was markedly high in "Strong" fluorescence group (3.81 ± 0.77). Particularly, among 11 newly-diagnosed cases, the difference was statistically significant ($p=0.017$). "Strong" fluorescence group still showed significant difference when compared with other groups together, in all cases and newly-diagnosed cases ($p=0.01$ and $p=0.004$, respectively).

Discussion/Conclusion: There are limited number of reports regarding 5-ALA and Met-PET, stating that Met-PET and 5-ALA fluorescence should be considered separately. However, the fluorescence was grossly distinguished whether positive or negative. Our study utilized objective spectroscopic measurement of fluorescence intensity. The results suggested that strong fluorescence intensity induced by 5-ALA reflects high Met-PET uptake. Hence, this may help neurosurgeons estimate high Met-PET uptake by bright fluorescence from 5-ALA, and assist decision making during glioma surgery.

Key words: Brain Tumor, Astrocytoma, 5-Aminolevuinic Acid, 5-ALA, 11C-Methionine, Positron Emission Tomography, PET, Fluorescence-Guided Surgery, Photodynamic Diagnosis, PDD, Spectroscopy

a-2 The drainage tube tip location is the key for adequate volume reduction of cystic metastatic brain tumors preceding Gamma Knife radiosurgery

Akito Oshima[1,2], Atsuya Akabane[2], Jun Suenaga[1], Tetsuya Yamamoto[1]

Department of Neurosurgery, Yokohama City University Hospital, Kanagawa, Japan[1]
Department of Neurosurgery, NTT Medical Center Tokyo, Tokyo, Japan[2]

Introduction: Although Ommaya reservoir implantation is effective in reducing the target volume of cystic brain metastases preceding stereotactic radiosurgery, adequate volume reduction cannot be achieved in some cases, and the factors leading to failure in volume reduction have not been clearly identified. In this study, we investigated the factors leading to failure in volume reduction after use of the Ommaya reservoir.

Materials and methods: Between December 2007 and February 2015, 38 consecutive patients with 40 cystic metastases underwent Ommaya reservoir implantation at our institution. The patient characteristics, treatment parameters, and all available clinical and neuroimaging follow-ups were analyzed retrospectively.

Results: The rate of volume reduction was significantly related to the location of the tube tip inside the cyst. By placing the tip at or near the center, 58.7% reduction was achieved, whereas reduction of 42.6% and 7.7% occurred with deep and shallow tip placement, respectively ($p = 0.011$). Although there was no additional surgery in the center placement group, additional surgeries were performed in 5 out of the 23 deep and shallow cases due to inadequate volume reduction. No other factors were correlated with successful volume reduction.

Conclusion: For adequate volume reduction using the Ommaya reservoir in the treatment of cystic brain metastases prior to stereotactic radiosurgery, the tip of the reservoir tube should be placed at the center of the cyst.

Key words: Ommaya reservoir　オンマヤリザーバ、drainage tube　ドレナージ管、
Stereotactic radiosurgery　定位放射線治療、Cystic brain metastasis　嚢胞性の転移性脳腫瘍、
tumor volume reduction　腫瘍体積の減少

a-3 Introduction of tumor-treating fields (TTF) for the treatment of glioblastoma

Yasue Tanaka[1,2], Yoshiharu Oki[1], Daisuke Sakamoto[2], Shinichi Yoshimura[2]

Department of Neurosurgery, Goshi Hospital[1]
Hyogo College of Medicine[2]

Background: Gliomas should be diagnosed by WHO2016 integrated diagnosis. It consists of histopathology, WHO grading, and molecular information. Therefore, it is important to analyze tumor specimen carefully, and perform following multimodality treatment.

Case presentation: A 61-year-old, left-handed man with right-sided weakness and partial seizures. Contrast-enhanced T1-weighted MR image showed ring-enhancing lesion in left frontal lobe. He was scheduled to be transferred to a medical college hospital because we suspected high-grade glioma. However, the patient's wife insisted on transferring other hospital with many surgical numbers. He was transferred to the hospital, performed craniotomy, and enhanced lesion was totally removed. The histopathological diagnosis was glioblastoma, IDH1 wild-type. The mitotic index was 23%. There was no other molecular information of tumor tissue because of the cost. After surgical treatment, he was transferred to the other hospital for radiation therapy, chemotherapy using temozolomide and bevacizumab. However, the hospital was very far from his home, so he finally decided to come back to our hospital after radiation therapy. His Karnofsky Performance Status (KPS) was almost 80, so we preferably applied tumor-treating fields (TTF) therapy. At present, his condition is stable, we continue chemotherapy and TTF.

Discussion: The patient is finally treated by multimodality therapy, but there's no enough information of tumor tissue essential for WHO2016 classification. There is a period for introducing TTF, we should never miss the opportunity for following multimodality treatment of glioblastoma.

Conclusion: We would like to stress that patients of glioblastoma should be performed multimodality treatment by detailed histopathological diagnosis, and seamless collaboration with neuro-oncologists is also important.

Key words: glioblastoma, WHO2016 classification, integrated diagnosis, molecular information, multimodality therapy, tumor-treating fields (TTF) therapy, neuro-oncology, neuro-oncologist, seamless collaboration

a-4 Role of photodynamic therapy using talaporfin sodium and a semiconductor laser in patients with newly diagnosed glioblastoma

Atsushi Fukui[1], Masayuki Nitta[1,2], Yoshihiro Muragaki[1,2], Takashi Maruyama[1,2], Hiroshi Iseki[2], Takashi Komori[3], Soko Ikuta[2], Taiichi Saito[1], Takayuki Yasuda[1], Junji Hosono[1], Saori Okamoto[1], Shunichi Koriyama[1], Takakazu Kawamata[1]

Department of Neurosurgery, Tokyo Women's Medical University[1]
Faculty of Advanced Techno-Surgery, Institute of Biomedical Engineering and Science, Tokyo Women's Medical University[2]
Department of Laboratory Medicine and Pathology (Neuropathology), Tokyo Metropolitan Neurological Hospital, Tokyo, Japan[3]

Objective: In this study on the effectiveness and safety of photodynamic therapy (PDT) using talaporfin sodium, the long-term follow-up results of 30 patients with newly diagnosed glioblastoma enrolled from 2009 to 2016 were analyzed and compared with those of 164 patients treated without PDT during the same period.

Methods: The main outcome measures were the median overall survival (OS) and progression-free survival (PFS) times. Moreover, the adverse events and radiological changes after PDT, as well as the patterns of recurrence, were compared between the groups. Univariate and multivariate analyses were performed to identify the prognostic factors, including PDT, among patients with newly diagnosed glioblastoma.

Results: The median PFS times of the PDT and control groups were 19.6 and 9.0 months respectively ($p = 0.016$). The median OS times were 27.4 and 22.1 months respectively ($p = 0.0327$). Multivariate analyses found PDT, preoperative Karnofsky Performance Scale score, and IDH mutation to be significant independent prognostic factors for both OS and PFS. Eighteen of 30 patients in the PDT group experienced tumor recurrence, including local recurrence, distant recurrence, and dissemination in 10, 3, and 4 patients, respectively. Conversely, 141 of 164 patients in the control group experienced tumor recurrence, including 101 cases of local recurrence. The rate of local recurrence tended to be lower in the PDT group ($p = 0.06$).

Conclusions: The results of the present study suggest that PDT with talaporfin sodium provides excellent local control, with few adverse effects even in cases of multiple laser irradiations, as well as potential survival benefits for patients with newly diagnosed glioblastoma.

Key words: photodynamic therapy; talaporfin sodium; semiconductor laser; glioblastoma; newly diagnosed; oncology

a-5 Titanium might be suitable for adult epilepsy surgery following subdural placement to avoid surgical site infection

Yuki Amano[1], Ayataka Fujimoto[2], Naoki Ichikawa[2], Keishiro Sato[2], Shimpei Baba[2], Shinji Itamura[2], Mitsuyo Nishimura[2], Hideo Enoki[2], Tohru Okanishi[2]

Department of Neurosurgery, Seirei Mikatahara General Hospital[1]
Department of Neurosurgery, Seirei Hamamatsu General Hospital[2]

Background: The purpose of this study was to compare surgical site infection (SSI) rate between resorbable plates and titanium plates which were used for adult patients with intractable epilepsy who underwent epilepsy surgery following subdural electrodes placement.

Methods: We performed subdural electrode surgery followed by epilepsy surgery for 87 patients with intractable epilepsy. The epilepsy surgery included 75 focus resection, 12 corpus callosotomy surgeries. We had introduced this bioresorbable polyester implants in January 2015. Therefore, before December 2014 we used titanium plates and after January 2015, we used resorbable plates.

Results: Among the 87 patients, 43 patients underwent cranioplasty with resorbable plates (group A) and 44 patients underwent cranioplasty with titanium plate (group B). There were seven patients (16.3 %) developed SSI in group A. Of the 44 patients who received titanium plates, 1 (2.3 %) developed SSI. The group A had statistically higher infection rate than group B ($p = 0.03$) with Fisher exact test. Uni-variate logistic analysis also showed statistically higher infection rate in resorbable plate ($p = 0.024$).

Conclusion: In epilepsy surgery following subdural electrode placement surgery, adult patients who underwent cranioplasty with resorbable plates had higher surgical site infection rate than titanium plate.

Key words: resorbable plate　吸収性プレート、focus resection　焦点切除術、
corpus callosotomy　脳梁離断術、cranioplasty　頭蓋形成術

b-1 Cavernous malformation arising from cerebellopontine angle presenting subarachnoid hemorrhage

Iori Kojima, Yoshinori Higuchi, Masaki Izumi, Shiro Ikegami, Kentaro Horiguchi, Yasuo Iwadate

Department of Neurological Surgery, Chiba University Graduate School of Medicine, Chiba, Japan

Introduction: Extra-axial cavernous malformation of cerebellopontine angle (CPA) is rare and usually involves the cranial nerves. Cavernous malformation presenting with subarachnoid hemorrhage is extremely rare, and a limited number of the reports has been published. We report a case of cavernous malformation of the CPA cavernous malformation presenting with subarachnoid hemorrhage.

Case report: A 46-year-old woman presented with a sudden headache. Neurological examination revealed mild abducens nerve palsy. CT scans of the brain revealed a left CPA hematoma with diffuse subarachnoid hemorrhage. Cerebral angiograms showed no evidence of aneurysm or arterial dissection of the posterior circulation. We initially applied conservative management to get an appropriate diagnosis. T1-weighted images demonstrated the CPA lesion with high intensity in the center part. Serial magnetic resonance images demonstrated the volume decrease of CPA lesion in one month. Gadolinium-enhanced T1-weighted images showed a right enhanced mass adjacent to the jugular foramen.

Two months later, the CPA lesion was enlarged without subarachnoid hemorrhage. She underwent a left transcondylar fossa approach for resection of the lesion under continuous intraoperative electrophysiologic monitoring. Intraoperatively, the lesion was located ventrally to the lower cranial nerves and was removed completely. Histology confirmed the diagnosis of cavernous malformation. MRI confirmed no evidence of residual lesion. No neurological sequelae except mild hoarseness sustained one year after surgery.

Conclusion: Our report presents a unique combination of location and presentation in the intracranial cavernous malformation. Cavernous malformation in CPA is rare; however, cavernous malformation should be considered in the differential diagnosis for subarachnoid hemorrhage.

Key words: cavernous malformation 海綿状血管腫、cerebellopontine angle 小脳橋角部、
posterior fossa 後頭蓋窩、subarachnoid hemorrhage くも膜下出、
transcondylar fossa approach 経後頭顆窩到達法、thrombosed aneurysm 血栓化動脈瘤

b-2 A case of acute development of left an internal carotid artery anterior wall aneurysm immediately after the rupture of left middle cerebral artery aneurysm

Masamichi Endo, Soichi Oya, Toru Matui

Department of Neurosurgery, Saitama Medical Center, Saitama Medical University, Saitama, Japan

Background: Angiography plays some critical roles in the treatment of aneurysmal subarachnoid hemorrhage (SAH). In general, however, attentions tend to be paid only to the structure adjacent to the aneurysm.

Case presentation: A 66-year-old woman was emergently transported to our hospital because of consciousness disorder. On arrival, her Japan Coma Scale (JCS) was Ⅲ-200. CT scan showed an intracerebral hemorrhage in the left temporal lobe with intraventricular hematoma, and a small amount of SAH in the left sylvian fissure. CT angiography demonstrated an aneurysm at the left M1-M2 bifurcation. We performed an operation of clipping the aneurysm and evacuating the hematoma. According to our routine radiological examination schedule for SAH, we conducted angiography on day 8, which revealed the complete clipping and mild vasospasm. On day 13, however, she gradually developed right hemiparalysis. We performed the second angiography and treated left MCA vasospasm causing the hemiparesis with intraarterial injection of fasudil hydrochloride. On this angiography, we noticed a bulging at the anterior wall of the left internal carotid artery (ICA). We then performed the third angiography and found the acute development of a left ICA anterior wall aneurysm. This was the portion where the cisternal drain was inserted. She underwent the trapping of the ICA with high flow bypass. She was transferred to a rehabilitation center with moderate aphasia.

Conclusions: We are liable to focus on the aneurysms and their neighboring structure in treating patients with aneurysmal SAH. However, a valuable lesson should be learnt from this unusual but didactic case. We should pay attention to all the regions we manipulated during surgery because some acute and unexpected changes may occur during the life-threatening stroke such as SAH.

b-3 Does vertebral artery dissection have favourable outcome?

Hidehiro Okura[1,2], Ryogo Ikemura[1], Senshu Nonaka[1], Satoshi Tsutsumi[1], Takamoto Suzuki[1], Hisato Ishii[1], Yukimasa Yasumoto[1], Akira Fukamachi[2]

Department of Neurosurgery, Juntendo Urayasu Hospital, Chiba[1]
Division of Neurosurgery, Nasu Neurosurgery Hospital, Tochigi[2]

Background and Purpose: With the development of the radiological diagnostic modalities, intracranial vertebral artery dissection (VAD) has been increasingly recognized. VAD can cause both subarachnoid hemorrhage (SAH) and cerebral infarction. However, most of patients with VAD presented with only headache and/or minor symptoms. The natural history of VAD still remain poorly elucidated. The aim of this study is to reveal the long-term natural history of VAD.

Materials and Methods: A retrospective chat review was performed for diagnoses of VAD at Nasu Neurosurgery Hospital. Patient age, sex, symptoms, outcome were reviewed. Imaging findings were also studied. A mean follow-up period was 65.2 months (1-270 months).

Results: 79 patients (87 vertebral arteries) diagnosed with VAD were identified; they included 49 male and 30 female patients, with an age range of 29 to 78 years. Vertebral arteries affected were 40 right, 32 left and 7 both. 68 (78.1%) presented with ipsilateral occipitalgia, 11 (13%) with occipitalgia, one (1.1%) with contralateral occipitalgia. Others; two with dysarthria and dysphagia, three with vomit, four with numbness of extremities, three with vertigo, three with periauricular pain, one with asymptomatic. 82 (94.2%) did not develop ischemic or hemorrhagic stroke. Two and Three presented with SAH and cerebral infarction (Wallenberg syndrome), respectively. One with SAH presented with headache. The follow-up radiological assessment demonstrated a complete cure. However, VAD recurred causing SAH (Grade IV) 15 years after. None of the patients with SAH had smoking history. All patients with cerebral infarction presented with either vertigo, dysarthria, numbness and ataxia. All of them were diagnosed with Wallenberg syndrome at the time of presentation and had smoking history.

Conclusion: Most of the cases of VAD have favorable outcome. However, one patient presented with serious SAH 15 years after the initial diagnosis of VAD. Long-term follow-up of VAD would be recommended.

Key Words: Vertebral artery dissection, SAH, Wallenberg syndrome, smoking history, dyslipidemia

b-4 Coexistence of ischemic and hemorrhagic lesions in a pediatric patient with moyamoya disease: A case report

Hiroki Sugiyama, Joji Tokugawa, Ryo Miyahara, Kentaro Kudo, Takashi Mitsuhashi, Makoto Hishii

Department of Neurosurgery, Juntendo University Nerima Hospital, Tokyo, Japan

Introduction: Hemorrhagic moyamoya disease in pediatric patients is rare. We describe a pediatric patient with moyamoya disease with a coexistence of cerebral infarction and intracerebral hemorrhage at the first presentation.

Case Presentation: A 5-year-old girl presented to the emergency department complaining of sudden onset of headache. Computed tomography showed cerebral infarction in the left temporo-occipital region and hemorrhage in the right caudate nucleus with intraventricular hemorrhage. She had no history of a recent head injury, fever, or convulsions. She had felt mild “sensational discomfort” on both sides of her extremities for several minutes, which were thought to be transient ischemic attacks (TIAs). On neurological examination, no obvious deficit was recognized. Magnetic resonance (MR) angiography showed narrowing at the terminal of both internal carotid arteries. We diagnosed an acute cerebral infarction and intracerebral hemorrhage due to moyamoya disease. Digital subtraction angiography revealed Suzuki stage 1 on the right and stage 2-3 on the left. She underwent a direct bypass combined with indirect bypass surgery on the left side. Her postoperative course was uneventful. The number of TIAs drastically decreased after surgery. She is currently under close observation for further surgical intervention for the contralateral lesion.

Discussion: The coexistence of ischemic and hemorrhagic lesions in pediatric patients with moyamoya disease is extremely rare. There is no standard treatment for such patients. It is important for surgeons to carefully examine the literature and customize treatment for each patient in such cases.

Key words: Coexsistence 共存、同時に存在する、Pediatric 小児、Sensational discomfort 不快な感覚、Transient ischemic attack 一過性脳虚血発作、Direct bypass 直接バイパス、Indirect bypass 間接バイパス、Drastically 劇的に

b-5 Carotid endarterectomy increases the chorioretinal blood flow and improves the visual dysfunction due to chronic ocular ischemia

Shinsuke Yoshida, Soichi Oya, Naoaki Fujisawa, Tsukasa Tsuchiya, Toru Matsui

Department of Neurosurgery, Saitama Medical Center, Saitama, Japan

Introduction: The incidence of stroke due to cervical internal carotid artery (cICA) stenosis can be successfully lowered by carotid endarterectomy (CEA). However, whether the visual impairment from chronic ocular ischemia can be treated by CEA remains to be elucidated.

Methods: We prospectively enrolled 41 patients who underwent CEA from 2015 to 2018 at our institution. We measured the chorioretinal blood flow (CRBF) by laser speckled flowgraphy before and after CEA, and analyzed the association between the CRBF change and postoperative visual recovery. Visual recovery was assessed by subjective improvement reported by patients and objective quantification using CSV1000 (Vector Vision). To eliminate the effect of blood pressure, we adjusted CRBF for values on the non-operative side. Variables such as age, side, degree of stenosis, symptoms, diabetes mellitus, and hypertension were assessed along with CRBF changes.

Results: Subjective visual improvement after CEA was observed in 23 patients (56%). CRBFs increased only on the operative side (vascular area: 33.5 vs 38.5, p=0.0005, tissue area: 10.3 vs 11.5, p=0.002). Univariate analysis revealed only increase of CRBF was associated with the subjective visual improvement. The objective score of CSV-1000 also significantly improved following CEA on the operative side (p=0.007). CRBF increased more in the patients with visual improvement than in those without visual improvement (vascular area: p=0.03, tissue area: p=0.02).

Conclusions: CRBF increased after CEA. Postoperative subjective and objective visual improvement was significantly associated with the increase of CRBF. CEA might contribute to restoring the chronic visual deficit in patients with cICA stenosis that cannot otherwise be explained by ophthalmological diseases.

Key words: carotid endarterectomy 内頚動脈内膜剥離術、chorioretinal blood flow 網脈絡膜血流、ocular ischemia 虚血性眼症、visual dysfunction 視力障害

c-1 Ventralis intermedius thalamotomy with focused ultrasound for patients with low skull density ratio

Kazuaki Yamamoto[1,2], Hisashi Ito[3], Shigeru Fukutake[3], Tetsumasa Kamei[3], Toshio Yamaguch[4], Takaomi Taira[1]

Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan[1]
Department of Neurosurgery, Shonan Kamakura General Hospital, Kamakura, Japan[2]
Department of Neurology, Shonan Fujisawa Tokushukai Hospital, Fujisawa, Japan[3]
Research Institute of Diagnostic Imaging, Shin-Yurigaoka General Hospital, Kawasaki, Japan[4]

Background: Transcranial magnetic resonance-guided focused ultrasound (MRgFUS) therapy is a novel and promising treatment in the field of stereotactic neurosurgery. While patients with high skull density ratio (SDR) tend to be treated successfully, the safety and efficacy of MRgFUS for low-SDR patients are still unknown.

Objective: To investigate the safety and efficacy of MRgFUS for low-SDR patients.

Methods: We retrospectively reviewed data from a clinical trial that involved MRgFUS ventralis intermedius nucleus thalamotomy. Low SDR was defined as 0.40 or less.

Results: A total of 13 patients were included, 6 with essential tremor and 7 with tremor-dominant Parkinson's disease. The mean maximum temperature (± standard deviation) in the targeted spot was 58.9 ± 3.7 ℃. The mean number of sonications was 9.4 ± 1.4. The mean contralateral hand tremor score on the Clinical Rating Scale for Tremor significantly improved from a baseline score of 17.5 ± 6.3 to a score of 9.5 ± 8.1 at 12 months in patients with essential tremor, and from a baseline score of 10.0 ± 7.5 to a score of 2.1 ± 2.2 at 3 months in patients with tremor-dominant Parkinson's disease.

Conclusions: MRgFUS for low-SDR patients is safe and effective. Patients with SDR of 0.40 or less can be treated successfully by careful and ingenious application.

Key words: Essential tremor 本態性振戦、skull density ratio 頭蓋骨密度比、thalamotomy 視床凝固術、tremor-dominant Parkinson's disease 振戦優位型パーキンソン病、
transcranial magnetic resonance-guided focused ultrasound therapy 経頭蓋集束超音波治療、
ventralis intermedius nucleus 視床中間腹側核

c-2 Whether preoperative evaluation of neuropsychological tests could predict the cognitive change following DBS in Parkinson's disease?

Maidinamu Yakufujiang[1], Yoshinori Higuchi[1], Yoji Okahara[2], Kyoko Aoyagi[2], Masaki Izumi[1], Tatsuya Yamamoto[3], Midori Abe[4], Atsushi Murata[4] and Yasuo Iwadate[1]

Department of Neurological Surgery, Chiba University Graduate School of Medicine[1]
Department of Neurosurgery, Chiba Cerebral and Cardiovascular Center[2]
Department of Neurology, Chiba University Graduate School of Medicine[3]
Department of Rehabilitation, Chiba University Hospital[4]

Background: The effects of DBS on non-motor symptoms, such as cognitive function, have been documented. We aimed to investigate whether the preoperative evaluation of neuropsychological function can predict the change in visuospatial function after DBS in patients with Parkinson's disease.

Methods: We included 35 patients with a median age of 60 years (Interquartile range (IQR), 60–68 years) and median disease duration of 11.9 years (IQR, 10.4–15.1) who underwent bilateral subthalamic nucleus-DBS (STN-DBS). The mean UPDRS-III score was 43.0 ± 13.8 / 16.4 ± 8.6 (on/off), the mean L-dopa equivalent dose (LED) was 1187 ± 326.1 (mean ± standard deviation). Cognitive function was evaluated with the Wechsler Adult Intelligence Scale -Third Edition (WAIS-III) and Rey-Osterrieth Complex Figure Test (ROCFT) preoperatively and one year after the surgery. Block design and matrix reasoning subtests of WAIS-III and ROCFT were categorized as visuospatial function domain. A correlation analysis was performed to investigate the relationship between visuospatial function and preoperative neuropsychological factors.

Results: STN-DBS significantly improved motor scores, LED significantly reduced one year after the surgery. The patients' performance on the ROCFT-copy test significantly changed after DBS. Factors, such as age, gender or preoperative motor score were not related to the postoperative change in the ROCFT-copy test scores. Decrease in the postoperative ROCFT-copy test scores correlates with the preoperative low score in the block design subtest.

Conclusion: The preoperative evaluation of block design subtests might be useful to identify the patients who are susceptible to developing a decline in visuospatial functioning after DBS.

Key words: deep brain stimulation (DBS) 脳深部刺激療法、Parkinson's disease パーキンソン病、subthalamic nucleus 視床下核、cognitive function 認知機能

c-3 Botulinum toxin (BTX) was effective for the chronic refractory pain caused by spasticity with a 10-year history of post-stroke: a case report

Kyoko Tatebayashi[1], Kenichi Amagasaki[1], Kazuaki Fukasaku[2], Kengo Takahashi[2], Hiroki Yoshioka[2], Fumio Saito[2]

Mitsui Memorial Hospital[1], Niiza Shiki Central General Hospital[2]

Background: Some chronic pains are observed after stroke. They include central post-stroke pain, peripheral neuropathic pain, pain from spasticity and pain from shoulder subluxation. Because pain affects the daily life of the patients, it is important to control pain depending on the pathology

We present a case in which BTX freed a patient from refractory pain caused by spasticity that lasted for 10 years after stroke.

Case presentation: A 48-year-old man has been treated at our hospital for 11 years. First, he was hospitalized when he was diagnosed of fresh cerebral infarction of right putamen. He was discharged and continued an antiplatelet agent. During outpatient care, he felt forearm pain caused by his spastic muscle. His wrist and some fingers were always overextended. For about 10 years he had been treated with oral medication of muscle relaxants and various analgesics, however, with no effect.

He underwent botulinum toxin (BTX) injection to extensor digitorum muscles, and the same time, he was educated home-based stretching after injection. These therapies resulted in relaxation of the muscle and sustained about 8 months. He was relieved from pain and no longer needed the oral medicines for pain.

Spasticity is recognized as involuntary muscle hyperactivity after central nerve damage. Its treatment is a physical and pharmacological management. It is clear that direct injection of BTX into the muscle gives much stronger effect on muscle relaxation than oral medication. Furthermore, it can be effective even after 10 years onset of stroke. This case suggests effectiveness of BTX for chronic pain.

Conclusion: BTX was effective for chronic refractory pain due to spasticity.

Key words: Botulinum toxin (BTX) ボツリヌス毒素、Chronic refractory pain 慢性難治性疼痛、Cerebral infarction 脳梗塞、Putamen 被殻、Spasticity 痙縮、Muscle hyperactivity 筋肉の過活動、Extensor digitorum muscle 総指伸筋、Stretching ストレッチ、Relaxant 筋弛緩薬、Analgesic 鎮痛薬

c-4 取り下げ

c-5 Amyloid-β oligomers in cerebrospinal fluid distinguish idiopathic normal pressure hydrocephalus from other neurodegenerative diseases

Kaito Kawamura[1], Masakazu Miyajima[1,2], Madoka Nakajima[1], Ikuko Ogino[1], Chihiro Akiba[1,2], Jyo Kanpyo[1], Chihiro Kamohara[1], Wei Meng[1], Hajime Arai[1]

Department of Neurosurgery, Graduate School of Medicine, Juntendo University, Tokyo[1]
Department of Neurosurgery, Juntendo Tokyo Koto Geriatric Medical Center[2]

Introduction: Idiopathic normal pressure hydrocephalus (iNPH) is known as treatable dementia and characterized by its clinical triad: gait disturbance, cognitive impairment, and urinary incontinence. However it sometimes mimics the clinical symptoms of other neurodegenerative diseases. Various biomarkers have been used to distinguish iNPH, but none have been entirely successful. We hypothesized that, in iNPH, stagnation of cerebrospinal fluid (CSF) turnover may cause amyloid-β peptide (Aβ) accumulation. Therefore, measuring high molecular weight Aβ42 oligomer (HMAβ) with at least nine subunits (≥30 kDa), could support differentiation of iNPH from Alzheimer's disease (AD), Parkinson's disease (PD), and progressive supranuclear palsy (PSP).

Materials and Methods: Fifty-three patients with NPH, 30 healthy controls, 16 patients with AD, 14 patients with PD, and 14 patients with PSP were included. All patients with NPH had lumbo-peritoneal shunt (LPS); CSF samples were taken before surgery to measure phosphorylated tau (p-Tau), Aβ1-42, Aβ1-38, and HMAβ via sandwich ELISA. NPH patients were divided into four subgroups: iNPH (18), NPH with AD pathology (17), NPH with Parkinson's spectrum (PS) (14), and NPH with AD pathology and PS (5), according to the p-Tau level and ^{123}I-ioflupane SPECT.

Results: NPH had significantly higher levels of HMAβ (6.56 ± 1.64 pM) than HC (3.38 ± 1.45 pM), PD (3.33 ± 0.90 pM), and PSP (4.46 ± 0.98 pM), but there was no significance with AD (6.01 ± 1.18 pM); area under curve (AUC) was 0.850. On the other hand, iNPH had significantly higher levels of HMAβ (7.26 ± 0.88 pM) than HC, AD, PD, and PSP; AUC was 0.949.

Conclusions: CSF HMAβ level of iNPH showed higher level compared with other neurodegenerative diseases, and it supported differential diagnosis of iNPH.

Key words: idiopathic normal pressure hydrocephalus 特発性正常圧水頭症、
amyloid beta peptide アミロイドβ蛋白、high molecular weight Aβ42 oligomer 高分子アミロイドβ42凝集体、
neurodegenerative diseases 神経変性疾患、CSF biomarker 髄液バイオマーカー

d-1 Preoperative embolization via non internal carotid artery for intracranial meningioma or solitary fibrous tumor is a safe and useful method

Jun Suenaga, Nobuyuki Shimizu, Jun Isozaki, Tadashi Ogura, Shutaro Matsumoto, Keita Fujii, Akito Ohshima, Taishi Nakamura, Naoki Ikegaya, Mitsuru Sato, Kensuke Tateishi, Hidetoshi Murata, Tetsuya Yamamoto

Department of Neurosurgery, Yokohama City University, Kanagawa, Japan

Objective: Surgery is the best way for meningioma. But we sometimes encounter the hyper vascular tumor and suffer from the maneuver of dural attachment, and tumor bleeds much in such cases. We perform preoperative embolization, if proper feeder is obvious, within 7 days before surgery. Purpose of this study is to evaluate the safety and efficacy of embolization by single expert surgeon in single institute retrospectively.

Materials and Methods: There were 41 patients, 45 embolization maneuver (4 are staged embolization). M:F=1:2, mean 55 years old (median 57). Meningioma 38 (grade 2 was 1), solitary fibrous tumor 3 (grade 2 was 1, grade 3 was 2). Location was 24 skull base (5 sphenoid ridge, 4 petroclival, 3 sphenoorbital, and so on), and 17 non skull base (7 convexity, 7 parasagittal, 2 posterior convexity, 1 trigone). Tumor size was 20-120 mm (mean 43 mm). The most frequent feeder was middle meningeal artery (MMA). Embolization via ICA wasn't performed. As for embolization material, combination of 100-500 μm particle plus coil was 16, 10-20% NBCA was 15, and other combination was utilized.

Results: Targeted artery embolization was achieved in all cases. The reduction rate of vascularity was average 70% (30-95%). Provocation test was negative in 16, but positive in 8 cases, that is 2 oculomotor palsy via petrosal branch of MMA, 5 facial numbness via AMA, that had all recovered. There was no simultaneous complication concerning the maneuver.

Conclusion: Embolization via non ICA by expert surgeon was effective and safe method reducing the intraoperative hemorrhage and facilitating the extent of resection.

Key words: embolization 塞栓術、meningioma 髄膜腫、solitary fibrous tumor 孤発線維性腫瘍、complication 合併症

d-2 Transvenous embolization for craniocervical junction epidural arteriovenous fistula with a pial feeder aneurysm: A Case Report

Keisuke Yoshida

Department of Neurosurgery, Keio University School of Medicine

Background: Arteriovenous fistulas (AVFs) at the craniocervical junction (CCJ) are rare vascular malformations with frequent hemorrhagic presentations sometimes accompanied by a pial feeder aneurysm. Among them, high-flow epidural AVFs are difficult to approach with open surgery due to a risk of massive bleeding from shunted epidural venous system. Transarterial embolization is also quite challenging especially when pial feeders are involved because of a risk of cord infarction. Transvenous approach is a safe and effective method, although it can't provide access to a feeder aneurysm.

Theoretically, flow-related aneurysms associated with arteriovenous shunt will regress by complete obliteration of the shunt. In contrast, partial obliteration of the shunt leaves a risk of recanalization of aneurysms secondary to recruitment of new shunt flow. We experienced a case of CCJ epidural AVF with a pial feeder aneurysm, which clearly substantiate such a theory, indicating the importance of complete obliteration in AVF treatment.

Case description: A 65-year-old man presented with subarachnoid hemorrhage and angiography showed an epidural arteriovenous fistula at the C-2 vertebral level with a pial feeder aneurysm without perimedullary venous drainage. We first performed transarterial coil embolization of the ruptured aneurysm and partial Onyx embolization of the shunt in the acute phase and thrombotic obliteration of the aneurysm was achieved. However, three years later angiography showed an increased shunt flow and recurrence of the aneurysm. Transvenous embolization of the shunt using coils and Onyx yielded complete obliteration of the shunt. Angiography three months after the treatment showed complete disappearance of the aneurysm with no recurrence of the shunt.

Conclusions: Partial transarterial embolization of AVF at CCJ leaves a risk of rebleeding due to recurrence of a feeder aneurysm with an increased shunt flow. Complete obliteration of the shunt with a transvenous approach can lead to disappearance of the flow-related aneurysm without embolization of the aneurysm itself, thus preventing rehemorrhage.

Key words: spinal epidural arteriovenous fistula, craniocervical junction, transvenous embolization, pial feeder aneurysm, anterior spinal artery, Onyx, coil

d-3 Increased Oxygen Extraction Fraction during Balloon-protected Carotid Artery Stenting Can Predict New Microembolic Infarctions

Hidemichi Ito, Masashi Uchida, Hiroshi Takasuna, Ichiro Takumi, Kotaro Oshio, Yuichiro Tanaka

Department of Neurosurgery, St. Marianna University School of Medicine, Kawasaki, Kanagawa, Japan

Background: Atherosclerotic carotid stenosis with impaired cerebral perfusion could inhibit the washout of debris from the plaque during intracranial circulation. In major carotid steno-occlusive diseases, increased oxygen extraction fraction (OEF) is strongly associated with ischemic stroke. Balloon-protected carotid artery stenting (CAS) is valuable for high-grade carotid stenosis. However, while balloon-protected CAS could effectively reduce the occurrence of ischemic complications by blocking anterograde carotid flow, cerebral hypoperfusion results in possible simultaneous cerebral ischemia.

Objective: To determine whether increased OEF during balloon-protected CAS can predict postprocedural microembolic infarction (MI).

Methods: Sixty-four patients who underwent balloon-protected CAS were enrolled. Initial and intraprocedural OEF was respectively calculated from the cerebral arteriovenous oxygen difference using blood sampled just before the temporary occlusion and reperfusion of the internal carotid artery. MIs were evaluated by diffusion-weighted imaging (DWI). Patients were classified into two groups based on the presence or absence of new MIs, and the relationship between the OEF and postprocedural MIs was analyzed.

Results: New ipsilateral DWI-positive lesions were found in 29 cases (45.3%). Age and the difference between initial and intraprocedural OEF (ΔOEF) were significantly higher in the DWI-positive group. Increased ΔOEF was the independent risk factor in multivariate logistic regression analysis. MIs significantly correlated with the ΔOEF.

Conclusion: Increased ΔOEF obtained by blood sampling during balloon-protected CAS can predict the incidence of new postprocedural MIs. In carotid stenosis, there could be patients hemodynamically compromised by carotid flow blockage during balloon-protected CAS.

Key words: balloon protection, carotid artery stenting, carotid stenosis, diffusion, oxygen extraction fraction

d-4 Asymptomatic spinal dural arteriovenous fistula: case series and systematic review

Kiyoharu Shimizu[1], Masaaki Takeda[1], Takafumi Mitsuhara[1], Kaoru Kurisu[1], Satoshi Yamaguchi[2]

Hiroshima University[1], University of Iowa Hospitals and Clinic[2]

Purpose: Asymptomatic spinal dural arteriovenous fistulas (SDAVFs) are rarely encountered. To elucidate the clinical characteristics of asymptomatic SDAVFs, the authors presented five 5 new cases of asymptomatic SDAVF and report the results of their systematically review of the associated literature.

Materials & Methods: Five databases were systematically searched for all relevant English-language articles on SDAVFs published from 1990 to 2018. The clinical features and imaging findings of asymptomatic SDAVFs were collected and compared with those of symptomatic SDAVFs.

Results: Twenty cases, including the 5 cases from the authors' experience, were found. Asymptomatic SDAVFs were more prevalent in the cervical region (35.0%); only 2% of cases in this region were symptomatic (2%). The affected perimedullary veins tended to drain more cranially (50.0%) than caudally (10.0%). Four cases of asymptomatic SDAVF became symptomatic form, 1 case spontaneously disappeared, and the remaining 15 cases were unchanged or surgically treated.

Conclusions: The higher prevalence of asymptomatic SDAVFs in the cervical spine might be a distinct feature of asymptomatic SDAVFs. Abundant collateral venous pathways and unique flow dynamics of the CSF in the cervical spine might prevent asymptomatic cervical SDAVFs from becoming symptomatic. Not all asymptomatic SDAVFs will become symptomatic.

Key words: spinal arteriovenous fistulas, asymptomatic, symptomatic, systemic review

e-1 Endoscopic observation successfully identified bleeding source in the ventral dura of the cervical spine in a case of superficial siderosis

Yoshimichi Sato[1], Toshiki Endo[1,2], Tomoo Inoue[2], Miki Fujimura[1], Teiji Tominaga[3]

Department of Neurosurgery, Kohnan Hospital, Miyagi, Japan[1]
Department of Neurosurgery, Sendai Medical Center[2]
Department of Neurosurgery, Tohoku University Graduate School of Medicine[3]

Introduction: Repeated hemorrhage into the subarachnoid space can cause superficial siderosis (SS). In half of the SS patients, the bleeding source has remained unknown. In the presented case of SS, use of an endoscope helped to identify the bleeding source in fluid-filled intraspinal cavity in the ventral cervical spine. Here we present the case to indicated rupture of fragile bridging veins as a new etiology of SS.

Case presentation: A 65-year-old man complaining gait disturbance and hearing impairment was referred to our hospital. Brain T2*-weighted magnetic resonance imaging (MRI) established diagnosis of SS. Spinal T2-weighted MRI revealed a fluid-filled intraspinal cavity extending from C2 to T8 with a dural defect in the ventral C7. Surgery was offered to explore and close the dural defect intending to stop the bleeding and expect recovery from SS. Following C7 and T1 laminectomy and durotomy, the dural defect was identified. The dural defect was connected to fluid filled cavity where xanthochromic CSF pooled. Importantly, an endoscopic observation confirmed that rupture of fragile bridging veins running through the cavity as the bleeding source. Postoperative MRI confirmed disappearance of the intraspinal cavity. Patients symptoms gradually improved after the operation.

Conclusions: In this case report, fragile bridging veins in the fluid-filled intraspinal cavity was newly identified to cause SS. Assisted use of endoscopy contributed to establish this pathology as a new etiology of SS.

Key words: Superficial siderosis　脳表ヘモジデリン沈着症、bleeding source　出血源、
fluid-filled cavity　硬膜外腔、dural defect　硬膜欠損

e-2 Cervical radicular arteriovenous fistula can cause intramedullary hemorrhage

Atsuhiko Ninomiya[1], Toshiki Endo[2], Naoto Kimura[1], Keisuke Sasaki[1], Michiko Yokosawa[1], Takayuki Sugawara[1]

Department of Neurosurgery, Iwate Prefectural Central Hospital[1]
Department of Neurosurgery, Sendai Medical Center[2]

Background: Radicular arteriovenous fistula (AVF) is a rare type of spinal arteriovenous malformation (AVM), which has AVF on spinal nerve roots. It has been reported to cause congestive myelopathy or subarachnoid hemorrhage. However, no case of radicular AVF presenting with intramedullary hemorrhage was reported. Here, we present a new case of radicular AVF in which rupture of a varix caused intramedullary hemorrhage.

Case presentation: A 74-year-old woman complaint of sudden onset of neck pain and quadriplegia. Magnetic resonance imaging showed intramedullary hemorrhage at C2-C3 without subarachnoid hemorrhage. Spinal angiography showed spinal AVM fed by a C3 segmental artery. Varix was formed along the anterior spinal vein which was considered to cause the hemorrhage. Open surgery was performed to prevent rebleeding. An endoscope was also used to visualize the ventral spinal cord. AVF was successfully located on the C3 posterior nerve roots, which established the diagnosis. Following obliteration of the AVF, intradural arterialized veins including the varix shrank. An endoscope helped to visualize the ventral spinal cord and confirm obliteration of AVF. After the surgery, the patient experienced partial neurological recovery. Postoperative angiograms confirmed complete obliteration of the AVF.

Conclusion: This is a first case report of intramedullary hemorrhage caused by radicular AVF. When patients suffer intramedullary hemorrhage due to spinal AVM, intramedullary AVM or perimedullary AVF can be listed as differential diagnosis. Recognition of this phenomenon is important since it may help to establish precise diagnosis and proper management of radicular AVF.

Key words: radicular arteriovenous fistula 神経根動静脈瘻、
intramedullary spinal hemorrhage 脊髄髄内出血、spinal angiography 脊髄血管撮影

e-3 Principal component analysis predicts neurological improvements in patients with cervical spinal cord injury

Tomoo Inoue[1], Shinsuke Suzuki[1], Toshiki Endo[1], Hiroshi Uenohara[1] and Teiji Tominaga[2]

Department of Neurosurgery, Sendai Medical Center[1]
Department of Neurosurgery, Tohoku University Graduate School of Medicine[2]

Object: Patients with cervical spinal cord injury (SCI) show different clinical outcomes. There is a significant association between the magnetic resonance (MR) imaging of cervical SCI and neurological recovery of cervical SCI. We speculated that principal component analysis (PCA), a dimension reduction procedure, would detect clinically predictive patterns in complex MR imaging and predict neurological improvements assessed by the American Spinal Injury Association Impairment Scale (AIS).

Methods: We performed a retrospective analysis of 50 patients with cervical SCI who underwent surgical decompression less than 48 hours after the trauma. We analyzed seven types of MR imaging assessments: axial grade assessed by the Brain and Spinal Injury Center score, longitudinal intramedurallry lesion length, spinal cord signal intensity on T1 and T2 weighted image, maximum canal compromise, maximum spinal cord compression, Subaxial Cervical Spine Injury Classification System. PCA was applied on these multivariate data to identify factors that contribute to recovery after cervical SCI.

Results: Nonlinear principal component evaluation detected 2 features of MR imaging. PCA revealed principal component (PC) 1 (40.6 %) explaining the intramedullary signal abnormalities that were negatively associated with postoperative AIS conversion. PC2 (18.5 %) suggested extrinsic morphological variables, but did not predict outcomes. This result suggested that the intramedullary signal abnormalities reflect delayed neurological improvements in patients with cervical SCI.

Conclusions: PCA could be a useful data-mining tool to show the complex relationships between acute MR imaging findings in cervical SCI. This study emphasized the importance of multivariable intramedullary MR imaging as clinical outcome predictors.

Key words: American Spinal Injury Association Impairment Scale, cervical spinal cord injury, magnetic resonance imaging, principal component analysis

e-4 取り下げ

e-5 Two cases of acute epidural hematoma and chronic subdural hematoma with good outcome after emergency operation using idarucizumab for neutralizing dabigatran

Jun Isozaki[1, 2, 3, 4], Takafumi Kawasaki[2], Shigeo Matsunaga[4], Jun Suenaga[3], Nobuyuki Shimizu[3], Junya Tatezuki[4], Naoki Ikegaya[3], Natsuki Kobayashi[4], Takahiro Hayashi[4], Takashi Shuto[4] and Tetsuya Yamamoto[3]

Department of Neurosurgery, Nishiarai Hospital, Tokyo, Japan[1]
Department of Critical Care Center, Yokohama City University Medical Center, Kanagawa, Japan[2]
Department of Neurosurgery, Yokohama City University, Kanagawa, Japan[3]
Department of Neurosurgery, Yokohama Rousai Hospital, Kanagawa, Japan[4]

Direct oral anticoagulants (DOACs) is equal to or more effective than warfarin in preventing embolic stroke due to non-valvular atrial fibrillation (Af), and are generally used nowadays. On the other hand, hemorrhagic complications are serious problems. In recent years, idarucizumab, a neutralizing agent for dabigatran, has been introduced. We report 2 cases of acute epidural hematoma (AEDH) and chronic subdural hematoma (CSDH) which had good outcome after emergency surgery after neutralizing dabigatran with idarucizumab.

Case1; A 75-year-old woman presented consciousness disorder after head injury. Computed tomography (CT) images showed AEDH, which increased and worsened consciousness over time. It turned out taking dabigatran for chronic Af after worsening. Therefore, we administered idarucizumab and then performed emergency craniotomy. There was no obvious bleeding and no difficulty in hemostasis. After the operation her consciousness improved and she was discharged home with Glasgow Outcome Scale (GOS) 5.

Case 2; A 83-year-old man taking dabigatran for chronic Af got head injury 1 month ago, then presented progressive consciousness disorder. CT images showed CSDH. We administered idarucizumab and then performed emergency burr hole irrigation surgery. It's not difficult for hemostasis and drainage was not different from usual. After the operation his consciousness improved immediately and he was discharged home with GOS 5.

For traumatic cases taking dabigatran, we performed emergency surgery after administrating idarucizumab and got good outcome without hemorrhagic and thrombotic complications. Hemostasis was not difficult and we thought the neutralization effect was effective. With the accumulation of experience of using idarucizumab, the report on efficacy and safety is awaited.

Key words: idarucizumab イダルシズマブ、dabigatran ダビガトラン、neutralization 中和、hemostasis 止血、consciousness disorder 意識障害

f-1 New irradiation method for multiple metastatic brain tumors: split-time method

Yusuke Kinoshita, Masami Takanashi, Kenichi Sato, Yoshimaru Ozaki, Taku Asanome, Hirohiko Nakamura

Nakamura Memorial Hospital Gamma Knife Center

Objective: Stereotactic radiosurgery (SRS) has been one of treatments for the metastatic brain tumor. Greater number of tumors to irradiate tends to cause total irradiation time longer. Leksell Gamma Knife Icon was introduced to our hospital in August, 2018. Mask fixation enabled to do irradiation for consecutive days without any pain by pin fixation. We report a new irradiation method (split-time method) that long time of irradiation is divided into short time per one time and irradiation is given for consecutive days.

Materials and Methods: Planning of irradiation to lesions is set using Gamma Plan as usual way. Fraction is set to one. A protocol is sent to an operator console. Irradiation can stop anytime according to a patient condition and treatment progress. It can restart at the same point from the next time.

Results: Twelve Patients were treated (breast cancer 4, lung cancer 6, renal cancer 1, unknown 1). Mean age was 58.3 years old. Median of KPS was 90%. Mean irradiation time was 277.4 minutes. Mean number of lesions was 10.0. Isodose was selected at 18-20Gy/50%. All irradiated lesions were controlled during follow-up.

Conclusion: Split-time method is the useful way to irradiate more lesions with less burden for patients with the multiple metastatic brain tumors.

Key words: metastatic brain tumor 転移性脳腫瘍、Gamma Knife ガンマナイフ、
stereotactic radiosurgery 定位放射線手術、multiple 多発性、irradiation 照射、split-time 時間分割

f-2 Surgical biopsy and cyberknife radiotherapy in an adult patient with a rapidly growing ring-enhanced lesion located from the lower midbrain to the upper pons

Mayuko Imamura[1], Tadahiro Ishiwada[1], Daisu Abe[2], Masaru Aoyagi[1]

Department of Neurosurgery, Shioda Memorial Hospital[1]
Department of Neurosurgery, Tokyo Medical and Dental University[2]

Background: Although histopathological diagnosis is important for the management of ring-enhanced lesions in the brain, it is sometimes difficult in cases of brain stem lesions because of their critical locations. We encountered an adult patient with a rapidly growing ring-enhanced lesion located from the lower midbrain to the upper pons.

Case presentation: The patient was a 67-year-old man with complaints of diplopia, left side sensory disturbance, and severe ataxic gait lasting one month. Brain MRI revealed a ring-enhanced lesion located from the lower midbrain to the upper pons. PET CT showed an uptake of methionine coincident with the enhanced area. Differential diagnosis included high-grade gliomas, brain abscess, and others. The lesion rapidly enlarged from 22 to 30 mm during 18 days interval. Because of the superficial dorsolateral location of the brain stem, we selected surgical biopsy via supra and trans-cerebellar approach. Histological diagnosis was high-grade glioma and he underwent cyberknife with 12 fractions at a total dose of 44Gy. Bevacizumab was used every 2 weeks thereafter. The tumor shrank in size 1 month after the radiotherapy. His neurological symptoms improved, though he underwent tracheostomy due to dysphagia.

Conclusion: Histological diagnosis is important for adult patients with suspected high-grade gliomas in the brain stem because treatment response and the prognosis is quite different from pediatric diffuse pontine gliomas. Surgical biopsy and subsequent radiochemotheray could control the tumor growth potentially with long-term survival.

Key words: brain stem 脳幹、high-grade glioma 高悪性度神経膠腫、adult 成人、
surgery 摘出術、histological diagnosis 組織診断、radiotherapy 放射線治療

f-3 Detection of *MYD88* mutations in circulating tumor DNA is helpful for the diagnosis of central nervous system lymphomas

Manabu Natsumeda, Jun Watanabe, Yu Kanemaru, Yoshihiro Tsukamoto, Yukihiko Fujii

Department of Neurosurgery, Brain Research Institute, Niigata University

Background: Biopsy is the golden standard for diagnosis of central nervous system (CNS) lymphomas. Diagnosis can be challenging, as lesions tend to be located in deep structures. We have shown that the detection of *MYD88* mutation in circulating tumor DNA (ctDNA) taken from cerebrospinal fluid (CSF) is reliable. We report three cases in which detection of *MYD88* mutation aided in the diagnosis.

Case 1: A 67-year-old man with a history of systemic B-cell lymphoma, experienced right hemiparesis. Magnetic resonance (MR) images showed a small, non-enhancing lesion located in the midbrain. A point mutation was found in the *MYD88* gene upon digital droplet PCR analysis of ctDNA extracted from CSF. The patient underwent a needle biopsy, and was diagnosed as having "diffuse large B-cell lymphoma".

Case 2: A 32-year-old man was diagnosed as having a demyelinating lesion after experiencing severe headaches. A slightly enhancing lesion was found in the right frontal lobe, and the patient was treated with steroids. The lesions repeatedly disappeared and reappeared and finally, stopped responding to steroids. *MYD88* mutation was detected. A biopsy was performed, and the diagnosis was PCNSL.

Case 3: A 49-year-old man underwent a biopsy for a right frontal lesion after experiencing memory loss; the pathology showed massive T-cell infiltration but only some perivascular B-cells with little atypia. The patient was tapered off steroids, and the lesion spread rapidly. An open biopsy was performed, but the pathology was not typical for B-cell lymphoma. The patient's symptoms rapidly worsened, and whole brain irradiation was performed. At recurrence, *MYD88* mutation was detected.

Conclusion: Detection of *MYD88* mutation from ctDNA extracted from CSF can aid in the diagnosis of B-cell lymphoma of the CNS.

Key words: Primary central nervous system lymphoma 髄液、Circulating tumor DNA 診断、
Digital droplet PCR 検出、Point mutation 造影 MRI

f-4 Unilateral occipital transtentorial approach with multimodal assistance for resection of large supracerebellar hemangioblastomas: Preliminary experience of two cases

Daisuke Kawauchi, Yoshinori Higuchi, Shiro Ikegami, Akihiko Adachi, Ko Ozaki, Izumi Suda, Eiichi Kobayashi, Yasuo Iwadate

Department of Neurological Surgery, Chiba University Graduate School of Medicine, Chiba, Japan

Background: The surgical resection of large supracerebellar hemangioblastomas (SHBs) is exceptionally challenging due to their vascularity and deep anatomical location and is associated with a high risk of postoperative complications and mortality. Access to the posterior incisural space can be achieved by either an infratentorial supracerebellar approach or an occipital transtentorial approach (OTA). However, the optimal surgical strategy has not yet been established. Here, we report two cases of large SHBs that were successfully and safely resected via a unilateral OTA with multimodal assistance.

Case Description: Two patients presented to our hospital with ataxia due to large, solid SHBs. Following preoperative embolization, gross total resection of the SHBs was achieved via an OTA. Furthermore, endoscopic assistance was used to resect the remnant portion of the tumor in the second patient. Both patients experienced transient ataxia but were discharged from the hospital without serious complications.

Conclusions: The combination of an OTA with preoperative embolization and endoscopic assistance may reduce the intraoperative risk and contribute to improved outcome in patients with such clinically challenging tumors.

Key words: Supracerebellar hemangioblastomas, Occipital transtentorial approach, Supracerebellar infratentorial approach