BACKGROUND: Pilocytic astrocytoma is one of the common tumors found during childhood. However, the clinical course of disseminated pilocytic astrocytoma is not clearly known. Here, we present two cases with disseminated pilocytic astrocytoma and discuss the treatment strategy. Patients We treated a 7-year-old female (case 1) and 9-year-old male (case 2) with hypothalamic pilocytic astrocytomas. The results of magnetic resonance imaging showed diffuse spinal dissemination at diagnosis. Chemotherapy with vincristine and carboplatin was administered as the firstline therapy. The tumors showed some shrinkage, and symptoms improved. During chemotherapy, the patients developed allergies to carboplatin. Therefore, we changed the chemotherapy treatment to vincristine. Other adverse events were not observed. In Case 1, we observed an intratumoral hemorrhage and hydrocephalus due to occlusion of the foramen Monro. Endoscopic surgery was performed, and no clinical deficit was observed. Case 2 underwent ventricular peritoneal shunt procedure for communicating hydrocephalus and a reoperation for shunt malfunction because of dense cerebrospinal fluid with elevated protein levels. The patients have not undergone radiotherapy until now. They had no severe clinical symptoms and went to school for 5 and 10 years, respectively, after the diagnoses. CONCLUSION: Chemotherapy for disseminated pilocytic astrocytoma is effective and may help in avoiding radiotherapy. Chemotherapy should be administered before radiotherapy, considering long-term complications.

PEDT-07

RECURRENT MEDULLOBLASTOMA 9 YEARS AFTER THE PRIMARY TUMOR

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Medulloblastoma is one of the most common malignant brain tumors in children. Despite multi-disciplinary treatment for medulloblastoma, including surgery, chemotherapy, and radiation, which have resulted in significant improvement of the prognosis, about 30% of patients still experience recurrence. Most recurrences occur within the first 15 months from diagnosis and late relapse of the tumor is quite rare. We report a case of a 15-year-old female patient with recurrent medulloblastoma 9 years after the primary tumor. At the age of 6, this patient developed a posterior fossa tumor without metastasis and underwent near-total resection. The pathological diagnosis was medulloblastoma with focal desmoplasia. After the surgery, she received multi-agent chemotherapy and radiation therapy consisting of 18 Gy craniospinal irradiation and 51.2 Gy local irradiation. She was in complete remission for 9 years after the treatment. However, gait disturbance began to gradually appear, and magnetic resonance imaging (MRI) showed an intradural lesion in her thoracic spine. The lesion was biopsied, and the pathological findings confirmed the recurrence of medulloblastoma. Currently, we plan to administer local radiation therapy concomitantly with temozolomide to the patient. The case reminds us of the importance of long-term careful follow-up of patients with medulloblastoma. Further studies are warranted for the treatment of relapsed medulloblastomas due to the limited information available at present.

IMMUNOLOGIC THERAPY (IMT)

IMT-01

THERAPEUTIC EFFECT AGAINST LOWER GRADE GLIOMA INDUCED BY DENDRITIC CELL BASED IMMUNOTHERAPY

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BACKGROUND: This trial was designed to evaluate the safety and clinical responses to an immunotherapy with fusions of dendritic and glioma cells in patients with lower grade glioma (LGG; WHO grade II-III glioma). METHOD: Autologous cultured glioma cells obtained from surgical specimens were fused with autologous dendritic cells (DC) using polyethylene glycol. The fusion cells (FC) were inoculated intradermally in the cervical region of subjects. Toxicity, progression-free survival (PFS), overall survival (OS), and MRI findings were evaluated. DNA for whole exome and RNA for whole transcriptome extracted from HLA-A*24:02 positive glioma cells were analyzed by next generation sequencer. Variant peptides showing strong binding affinity to HLA-A*24:02 but not the corresponding wild type peptides were selected as candidate of neo-antigens. RESULTS: The number of subjects of this trial were 24 (initially diagnosed cases: 20, recurrence cases: 4). WHO grade III cases were 20, and grade II cases were 4. Male were 15, and female were 9. Mean of follow up periods were 53.0 months (the longest follow up period: 1322 months). The number of events on PFS and OS were 8 and 6, respectively. Mean of candidate of neo-antigen peptides in HLA-A*24:02 positive patients (n=8) was 34. Among these candidates, twelve types of common neo-antigen peptide were identified. Neo-antigen peptides specifically expressed in the glioma cells from the effective group were not identified. CONCLUSIONS: These results indicate that the efficacy of FC-immunotherapy may not always depend on the number of gene mutations or the expression of the specific neo-antigens. FC-immunotherapy, as a means of producing specific immunity against neo-antigens may safely induce anti-tumor effects in patients with LGG. Analysis of prognostic factor in glioma immunotherapy may be the next area of major interest.

IMT-02

VEGF RECEPTORS EXPRESSION AND REPORT OF CLINICAL TRIAL OF PEPTIDE VACCINE IN SKULL BASE CHORDOMA

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Chordoma is a rare refractory neoplasm that arises from the embryological remnants of the notochord. Vascular endothelial growth factor (VEGF) is a potent activator of angiogenesis that is associated with the tumor-immune microenvironment. To evaluate the characteristics of vascular and tumor cells in chordoma, we first analyzed the expression of VEGF receptor (VEGFR) 1, VEGFR2, CD34, and Brachyury in a cell line and 54 tumor tissues. Patients with primary skull base chordomas were divided into the two groups as per the tumor growth rate. The expressions of VEGF-A, VEGFR1, and VEGFR2 on tumor cells; tumor infiltrative immune cells, including regulatory T cells (Tregs) and tumor-associated macrophages (TAMs); and immune-checkpoint molecules (PD-1/PD-L1) were analyzed with the clinical courses. Both VEGFR1 and VEGFR2 were strongly expressed not only on vascular endothelial cells, but also on tumor cells. The recurrent cases showed significantly higher VEGFR1 expressions on tumor cells than the primary cases. The expression of VEGF-A, and the numbers of CD163+ TAMs and Foxp3+ Tregs were significantly higher in the patients with rapid progressive course than the patients with slow progressive course. Based on the present results, VEGFRs-targeted therapy may show efficacy in regulating growth of chordomas.

IMT-03

CLINICAL TRIAL FOR NEWLY DIAGNOSED MALIGNANT GLIOMA WITH WT1-W10 VACCINATION

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OBJECT: Wilms' tumor 1 (WT1) peptide vaccination is considered a potentially effective therapy against malignant glioma. We conducted a Phase I/II study to investigate the safety and feasibility of novel WT1 peptide (W10) vaccination therapy for patients with newly diagnosed malignant glioma. METHODS: WT1 vaccination therapy was performed for patients with malignant glioma who have undergone concurrent radiotherapy and temozolomide therapy. A mixture of WT1 peptide with inactivated pertussis whole cell vaccine was injected intradermally once a week for at least 12 weeks. RESULTS: Twenty-seven patients (12 men, 15 women; median 65 years) with the following tumors were enrolled: WHO grade IV (15), WHO grade III (12). PFS and OS of glioblastoma cases were 12.7 months 21.9 months, respectively. PFS of the MGMT unmethylated group was shorter than the methylated group. Interestingly enough, overall survival in the MGMT unmethylated group was not significantly different from the methylated group. Analysis of recurrent cases after immunotherapy showed decreased expression of WT1 antigen and increased Treg. They were suggested as a cause of treatment resistance. No serious adverse events were observed except for Grade 1 erythema at the injection sites. CONCLUSIONS: This study of a novel WT1 vaccination therapy demonstrated safety and feasibility in the management of newly diagnosed malignant gliomas.

IMT-05

PHASE III RANDOMIZED CLINICAL TRIAL OF AFTV FOR NEWLY DIAGNOSED GLIOBLASTOMA

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BACKGROUND: The highly fatal glioblastoma has an extremely poor prognosis and development of a new treatment is desired. Local treatment