

Intracranial germ cell tumor case series

2021

Total 189 patients with [intracranial germ cell tumors](#) were treated with RT alone (n=50) and RT with upfront chemotherapy (CRT) (n=139). All cases were confirmed histologically. RT fields comprised the extended-field and involved-field only for primary site. The extended-field, including craniospinal, whole-brain (WB), and whole-ventricle (WV) for cranial field, is followed by involved-field boost. The median follow-up duration was 115 months.

The relapses developed in 13 patients (6.9%). For the extended-field, cranial RT dose down to 18 Gy exhibited no cranial recurrence in 34 patients. In CRT, 74 patients (56.5%) showed complete response to chemotherapy and no involved-field recurrence with low-dose RT of 30 Gy. WV RT with chemotherapy for the basal ganglia or thalamus germinoma showed no recurrence. Secondary malignancy developed in ten patients (5.3 %) with a latency of 20 years (range, 4-26) and caused mortalities in six. WB or craniospinal field rather than WV or involved-field significantly increased the rate of hormone deficiencies and secondary malignancy. RT dose for extended-field correlated significantly with the rate of hormone deficiencies, secondary malignancy, and neurocognitive dysfunction.

Reduced dose and volume of extended-field rather than total dose or involved-field will be critical to decrease the late toxicities. Upfront [chemotherapy](#) could be beneficial for the patients with complete response to minimize the RT dose down to 30 Gy. [Prospective trials](#) focused on de-intensification of the extended-field RT are warranted. ¹⁾

Patients with bifocal germinoma who received radiotherapy (RT) from March 1990 to August 2017 were included for analysis. A total of 21 patients were included. The median follow-up period was 76.2 months (range, 6.2-305.4 months). There were 17 patients who received cranio-spinal irradiation (CSI) with local RT; 3, whole ventricular RT (WVRT) with local RT; and 1, local RT only. Three recurrences occurred (1 patient each among those who underwent CSI, WVRT, and local RT). Recurrence in the patient who received CSI and who received WVRT occurred in the right thalamus and right frontal convexity, respectively. Meanwhile, the patient who received local RT showed not only a recurred lesion in the hypothalamus, but also cerebrospinal fluid seeding. For this patient, salvage CSI was performed and complete response was achieved after treatment. However, after 9 years and 6 months, he was diagnosed with glioblastoma and expired. As for toxicity, although 17 patients showed decrease in complete blood count levels during treatment, all patients recovered soon after treatment completion. Our findings suggest that bifocal germinoma may be considered as a disseminated disease when considering the patterns of failure according to RT fields. In addition, patients who received CSI showed low acute toxicity rates. However, further studies are necessary to confirm these findings ²⁾

Ninety-one patients from five institutions were registered in the KSPNO G051/G081 Protocol. Germinomas were classified as solitary or multiple/disseminated diseases, and upfront chemotherapy was administered. For all patients with multiple or disseminated disease, and patients with partial

response after chemotherapy, 19.5-24 Gy of craniospinal irradiation plus 10.8-19.8 Gy of tumor bed boost were planned. For patients with complete response (CR), reduced-dose RT (30.6 Gy) was planned, along with a reduced field for solitary lesions.

The median patient age was 14 (range, 3-30) years. Sixty-five patients (71.4%) had a solitary lesion. The median follow-up duration was 67.9 (range, 6.6-119.3) months. Recurrence was not observed in 32 patients in the protocol compliant group. Four patients (4.4%) in the protocol non-compliant group experienced relapse after CR and one patient died of the disease. The 5-year and 7-year overall survival rates were 98.8% and 98.8%, while the corresponding event-free survival rates were 96.6% and 93.8%, respectively. All three patients with basal ganglia germinomas who were treated with local RT experienced recurrence outside the RT field. Among the 23 patients with pineal or suprasellar lesions who received whole-ventricle RT, there was no recurrence.

Currently used upfront chemotherapy followed by reduced-dose, reduced-volume RT appears acceptable, when whole-ventricle RT for pineal or suprasellar tumors and, at minimum, whole-brain RT for basal ganglia/thalamus lesions are applied ³⁾.

Children with intracranial GCTs treated at a single institution between January 2000 and October 2016 were retrospectively reviewed under an Institutional Review Board-approved protocol. Imaging variables identified on pretreatment imaging were [calcifications](#), cysts, heterogeneity of enhancement, blood products, hydrocephalus, gradient echo susceptibility, restricted diffusion, invasiveness, and extent of edema. Tumor recurrence was used as the primary outcome variable.

Fifty-two patients (39 males, mean age at diagnosis: 13 ± 5 years, 34 germinoma, 18 nongerminomatous GCT [NGGCT]) were reviewed. Thirty-three percent of the patients reviewed had recurrence (7 germinoma, 11 NGGCT). Recurrence was associated with invasiveness as seen on preoperative imaging ($p = 0.0385$) and cystic tumor ($p = 0.048$) ⁴⁾.

2018

Forty-five [children](#) treated at Gustave Roussy between 1991 and 2010 were assessed with [neuropsychological tests](#) to measure IQ, memory, visuospatial, motor, and executive skills at a mean delay of 4.2 years after diagnosis. All patients have received chemotherapy associated with surgery in 17 cases. Thirty-nine patients received, radiotherapy (focal 27, focal plus ventricles 8, craniospinal 4). Twenty-three patients had 2 IQ assessments with a mean delay of 4.1 years between the first and second.

Full scale IQ was preserved, with higher verbal IQ than other IQ indexes. Visuospatial, fine-motor, and executive difficulties were present in a significant proportion of patients. Visuospatial and fine-motor deficits were significantly associated with oculomotor difficulties, more present in the pineal than in the suprasellar group. No cognitive decline was observed between the first and the second IQ assessment.

Overall cognitive abilities were preserved in children treated for central nervous system germ cell tumor ⁵⁾.

2015

38 patients who received definitive treatment and were followed-up >5 years between 1980 and 2009.

The median age at diagnosis and follow-up period were 16.5 years and 128.3 months, respectively. Treatment was irradiation alone or adjuvant platinum-based chemotherapy followed by reduced-dose local irradiation. Seven patients progressed at 12.9-133.9 months and 1 died of disease 89.3 months after therapy initiation.

The treatment strategies were divided into 3 groups: group A (1980-1988, n = 5), whole brain with local irradiation; group B (1989-2002, n = 16), chemotherapy with or without reduced irradiation dose; and group C (2003-2009, n = 17): neoadjuvant chemotherapy (3 courses) followed by 30.6 Gy of whole ventricle irradiation for patients with localized complete response, and additional local boost of 19.8 Gy for others. There were 7 recurrent cases, all in group B. The progression-free survival was significantly longer in groups A and C versus group B ($P < 0.001$). Decreased Karnofsky performance status was observed in 2 (40%), 6 (37.5%), and 0 cases in groups A-C, respectively. The main reasons for the good results in group C might be the neoadjuvant chemotherapy with whole ventricle radiotherapy and introduction of neuroendoscopy, especially for pineal lesions, resulting in a substantial reduction of time from the diagnosis to first treatment.

Chemotherapy followed by whole ventricle radiotherapy, with or without local boost, and with use of neuroendoscopy results in good disease control without late complications in patients with germinomas ⁶.

All patients with confirmed intracranial [germ cell tumors](#) treated at the Hospital of Sick Children during the period January, 1952, to December, 1989, were reviewed. Of the 51 tumors reviewed, 16 were located in the suprasellar region, 32 in the pineal region, and three in both the pineal and the suprasellar regions. Forty-nine patients underwent surgical resection which was total in seven and partial in 20, and consisted of a biopsy in 22. Two patients were managed on the basis of serum and cerebrospinal fluid markers. Surgical tools such as the operating microscope, the ultrasonic surgical aspirator, and the laser beam allowed safe debulking and removal of the deep-seated tumors in the pineal region. There were no operative deaths in the 36 patients treated since 1972, who included 23 with pineal tumors. Twenty-five patients with germinomas received radiotherapy and had a 5-year survival rate of 85.1%. Thirteen patients with non-germinoma germ-cell tumors received radiotherapy and had a 5-year survival rate of 45.5%. On the basis of this review, the authors recommend resection of pineal and suprasellar germ-cell tumors in order to firmly establish an accurate histological diagnosis to guide the extent of adjuvant therapy. In the case of a pure germinoma without evidence of dissemination, adjuvant therapy consists only of local radiotherapy. On the other hand, for malignant non-germinoma germ-cell tumors, adjuvant therapy must include chemotherapy as well as craniospinal axis radiotherapy ⁷.

Case reports

A 19-year-old Caucasian male presented with complaints of headaches and syncope. Suspicion of hydrocephalus prompted computed tomography (CT) and magnetic resonance imaging (MRI), which revealed pineal and suprasellar prominences with diffuse, thick, nodular subependymal enhancement

of the lateral and third ventricles. Based on imaging, the differential diagnosis consisted primarily of malignancy, such as lymphoma, with inflammatory and infectious etiologies not excluded. Cerebrospinal fluid (CSF) samples were non-specific, and neuroendoscopic tissue biopsy histologically confirmed the diagnosis of pure germinoma. The patient was treated with radiation, and follow-up MRIs at one, three, six, and 12 months demonstrated progressive resolution of tumor burden with marked clinical improvement. Germinomas are rare germ cell tumors that are more frequently diagnosed in Asian countries. They uncommonly seed into the lateral ventricles, and only two other cases have been described with diffuse subependymal involvement. Unlike other malignant germ cell tumors, germinomas have marker negative CSF samples that are important in the normal diagnostic workup of diffuse subependymal lesions. Histopathologic correlation is required for definitive diagnosis in the United States and can be achieved with endoscopic tissue sampling. Germinomas are highly radio- and chemotherapy sensitive and have a fair prognosis with modern therapeutic techniques. Germinoma should be considered with simultaneous midline and diffuse ventricular lesions ⁸⁾.

2017

Two cases of germ cell tumors in which a positive 5-aminolevulinic acid fluorescent signal was visualized with a neuroendoscope. Both cases had a tumor in the pineal region that was associated with hydrocephalus. The patients underwent surgery after administration of 5-ALA. After ventricular puncture of the anterior horn, we could observe the ventricular wall and tumor using the Karl Storz Photodynamic diagnosis system endoscope. Then, biopsy of the pineal tumor and endoscopic third ventriculostomy were performed in both cases. In case 1, a 22-year-old man, part of the ventricular wall and tumor tissue showed red fluorescence. In case 2, a 16-year-old man, part of the fornix and infundibular recess showed red fluorescence, and the tumor showed relatively weak red fluorescence. The histopathological diagnosis of both cases was pure germinoma. This is the first report of direct visualization of mixed germinomas with 5-ALA fluorescence-guided endoscopic surgery. This method not only allows visualization of the tumor mass, but may also be useful for detailed observation in the ventricular wall ⁹⁾.

2015

A 19-year-old woman with a highly malignant intracranial germ cell tumor (GCT) that developed 14 years after treatment for neurohypophyseal germinoma. Magnetic resonance imaging (MRI) showed a large neurohypophyseal mass and a synchronous lesion in the pineal region. Plasma alpha fetoprotein was elevated to 3038 ng/mL. Although the tumor shrank and tumor marker levels normalized after chemotherapy and craniospinal irradiation, treatment was switched to oral etoposide for the residual tumor because of adverse events. MRI after oral etoposide introduction showed additional tumor shrinkage for 27 months after the onset of the second tumor. To the best of the author knowledge, this is the longest interval between germinoma onset and the development of highly malignant recurrent GCT to be reported in the English-language literature. Oral etoposide prevented regrowth of the GCT, which has a poor prognosis, and decreased the size of the residual tumor ¹⁰⁾.

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