

Neurosurgery Division

Introduction

Patients with primary and metastatic brain tumors are treated by four neurosurgeons and one resident in the Neurosurgery Division. Three hundred and twenty-three patients were admitted and 87 craniotomies were carried out in 2003 including 27 gliomas, 27 metastatic brain tumors, and 12 meningiomas. Forty-one minor surgeries such as placement of Ommaya's reservoir (15 patients) and ventriculoperitoneal shunt (10 patients) were performed and most of them were emergency operations. Every craniotomy was assisted by the surgical navigation system (Stealth station) which had been introduced in 2001. The site of craniotomy and the extent of tumor removal were pointed out on the CRT of this system in real time. It contributed to safer and more precise surgery. Postoperative radiotherapy and chemotherapy were carried out for malignant tumors, but it is still hard to obtain complete response. In order to design a more effective chemotherapy regimen, molecular biological studies for drug resistance, growth factors and cell kinetic studies on individual tumors are ongoing.

Routine Activities

A weekly conference is held with doctors of Radiation Oncology Division on diagnosis and treatment of the patients with brain tumors. Usually 14 patients are hospitalized and two or three of them undergo surgical treatment every week. Stealth navigation system is used for surgical planning during every craniotomy. The patients with malignant brain tumors receive postoperative radiotherapy and chemotherapy. Statistical analysis revealed that surgical removal of as much of the tumor as possible yielded better survival even for the most malignant glioblastomas. However, they usually recur soon after the surgery without radiotherapy. Concomitant use

of chemotherapy is considered to enhance the anti-tumor effect of radiotherapy. ACNU (nimustin hydrochloride) and the other chemotherapeutic agents are administered intravenously during radiotherapy. One-year and 2-year survival rates of the patients with anaplastic astrocytomas were 79.8% and 55.5%, which were better than those of Brain Tumor Registry of Japan. (Table) Recurrent malignant gliomas are treated with alternative chemotherapy such as carboplatin and etoposide and some of them respond to it. But the five-year survival rate of patients with glioblastomas is still less than 10%. Decision on the indication for surgery of metastatic brain tumors is not simple. Multiplicity of brain metastasis, stage of primary malignancy and performance status of patients should be taken into careful consideration.

Research Activities

Patients with brain tumors have been registered in Brain Tumor Registry of Japan (BTRJ) since 1969. More than 100,000 patients were registered and followed up. Neurosurgery Division of National Cancer Center Hospital contributes as a managing office of BTRJ.

Somatostatin receptors exist in various neuroendocrine tumors such as carcinoid and islet cell tumors, and they are also detected in some of brain tumors. Radioisotope-labeled somatostatin analogues combine these receptors and are expected to be visualized by the single photon emission tomography (SPECT). Clinical research targeting on somatostatin receptors started. The receptor positive tumors detected by SPECT are treated by the somatostatin analogues with more active radioisotopes.

Clinical Trials

A multiinstitutional phase II study is ongoing in order to establish a postsurgical combined chemo-

therapy and radiation therapy for patients with primary germ cell tumors of the brain. After surgical debulking of the tumor, patients received chemotherapy such as carboplatin-etoposide or ifosfamide-cisplatin-etoposide prior to radiotherapy. This treatment protocol was considered to be effective to germ cell tumors and the better quality of life of the patients could be expected by reduction of total dose of irradiation. On the other hand, long-term follow up study is carried out to investigate the intellectual activities of patients with brain tumor who received radiotherapy in childhood.

Japan Clinical Oncology Group (JCOG)-Brain Tumor Study Group was organized in 2002 and it is

now preparing a multi-institutional randomized controlled trial entitled "A randomized controlled phase II/III study of chemoradiotherapy using ACNU versus procarbazine and ACNU for astrocytoma grade 3 and 4". The overall survival and response rates will be compared between the patients treated with ACNU and those treated with ACNU plus procarbazine. This study, under the surveillance of JCOG, aims to set a standard protocol for treating malignant glioma patients. Moreover, a proper methodology for performing randomized studies will be established in the field of neuro-oncology.

● S. Shibui ●

Number of operation (2001-2003)

	2001	2002	2003
Craniotomy	65	66	87
Glioma	22	27	27
Metastasis	16	18	27
Meningioma	11	11	12
Malignant lymphoma	1	1	3
Others	15	9	18
Minor surgery	13	20	36
Total	78	86	123

Survival rate of patients with malignant glioma (1980-2003)

	no.of pts	1yr	2yr	3yr	4yr	5yr
Glioblastoma						
NCCH	99	59.7	21	13.5	10.1	3.4
BTRJ	2,125	55.2	19.6	11.4	8.8	7
Anaplastic astrocytoma						
NCCH	67	79.8	55.5	45.9	37	34.6
BTRJ	1,066	67.6	43	32.2	26.4	23.4

NCCH, patients who were admitted to National Cancer Center Hospital between 1980 and 2003.; BTRJ, patients registered in the Brain Tumor Registry of Japan, 1991-1996.