Primary Malignant Lymphoma of the Brain in Childhood

—Case Report—

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Abstract

A 5-year-old boy presented with a 1-year history of frontal headache and nausea. Neurological examination showed left abducens nerve palsy, left facial nerve palsy, Bruns' nystagmus, and wide-based gait. Neuroimaging demonstrated a lesion with moderate linear enhancement in the left cerebellar hemisphere. He underwent stereotactic needle biopsy. The histological diagnosis was well-differentiated small lymphocytic type of malignant lymphoma. Following the biopsy, the patient underwent radiotherapy (whole brain 30 Gy, local 20 Gy). He has been in good condition for more than 5 years. The long-term survival is attributable to the absence of aggressiveness and the good response to radiation of this subtype of malignant lymphoma.

Key words: brain, childhood, malignant lymphoma

Introduction

Primary malignant lymphoma of the brain is responsible for 0.8% to 2% of all primary intracranial tumors.^{12,18)} The incidence of malignant lymphoma of the brain has apparently increased in immunocompromised and non-immunocompromised patients.^{17,20)} The majority of patients with primary malignant lymphoma of the brain are adults. The incidence of malignant lymphoma of the brain peaks in patients aged 50–60 years.^{11,12,16)} Primary malignant lymphoma of the brain in children is rare, accounting for 1.2% and 1.5% in large series of pediatric tumors.^{8,11)} The prognosis of malignant lymphoma of the brain in children is very poor.¹³⁾

We treated a 15-year-old boy with primary malignant lymphoma of the brain who continued to be in good condition more than 5 years after diagnosis and treatment, and discuss the characteristics of primary malignant lymphoma of the brain in childhood.

Case Report

A 5-year-old boy with a 1-year history of frontal headache and nausea was admitted to our hospital in March 1991. Physical examination revealed no ab-

normalities, including the lymph nodes. Neurological examination showed left abducens nerve palsy, left facial nerve palsy, Bruns' nystagmus, and wide-based gait. Computed tomography (CT) revealed a low density area in the left cerebellar hemisphere which was moderately linearly enhanced after intravenous administration of the contrast medium (Fig. 1). Magnetic resonance imaging demonstrated

Fig. 1 Computed tomography scans showing a low density area in the left cerebellar hemisphere (left) with moderate linear enhancement after administration of contrast medium (right).

Fig. 2 Axial T₁-weighted magnetic resonance image with gadolinium showing the lesion is linearly enhanced.

Fig. 4 Axial T₁-weighted magnetic resonance image with gadolinium 5 years after treatment showing no recurrence of the tumor.

Fig. 3 Photomicrograph showing a malignant lymphoma of the small lymphocytic subtype. The neoplastic cells are small with round nuclei and ill-defined cytoplasm. HE stain, $\times 400$.

the lesion as low intensity on T₁-weighted images and high intensity on T₂-weighted images, with linear enhancement after the administration of gadolinium-diethylenetriaminepenta-acetic acid (Fig. 2). He underwent stereotactic needle biopsy of the lesion.

Histological examination showed the tumor was composed of atypical small lymphoid cells. The histological diagnosis was malignant lymphoma of

the small lymphocytic subtype (Fig. 3). Immunohistological staining showed the tumor cells were positive for anti-immunoglobulin G antibody, suggesting the B cell type.

Blood tests showed his immunological state was normal. Bone marrow analysis was normal. CT and gallium scintigraphy detected no abnormality outside the cerebellum. Following the biopsy, the patient underwent radiotherapy (whole brain 30 Gy, local 20 Gy). Two months after the radiotherapy, the tumor had completely disappeared and neurological examination found only mild nystagmus. Five years after diagnosis and treatment, he continued to be in good condition without tumor recurrence (Fig. 4). No mental or somatopsychic deterioration was evident. He is now enjoying school uneventfully with a Karnofsky performance status score of 100.

Discussion

Primary malignant lymphoma of the brain in children is rare. The Brain Tumor Registry of Japan (1969–1990) contains only nine pediatric cases (1.5%) among 596 cases of primary malignant lymphoma of the brain.⁶⁾ We have treated 36 patients with primary malignant lymphoma of the brain, but only one (the present patient) in a child.¹⁶⁾ Only 32 pediatric cases (18 males, 13 females, and 1 unknown) of malignant lymphoma in the brain have been reported (including the present

Table 1 Summary of pediatric cases of primary malignant lymphoma of the brain

Author (Year)	Age/ Sex	Location	Operation	Radiation (dose)	Chemotherapy	Histological type	Meningeal dissemina- tion	Leukemic trans- formation	Outcome (mos)
Kumanishi et al. (1975) ³³⁾	10/M	frontal lobe	partial	—	—	—	no	no	dead (1)
Littman and Wang (1975) ³⁸⁾	7/M	cerebellum	none	none	none	—	no	no	dead (2)
	7/F	cerebellum	subtotal	+ (?)	none	—	no	no	dead (7)
	9/F	parietal lobe	biopsy	+ (?)	none	—	no	no	dead (36)
	3/M	cerebellum	none	none	none	—	no	no	dead (1.2)
	6/F	frontal lobe	subtotal	+ (?)	none	—	no	no	dead (12)
	0.2/F	cerebellum	subtotal	+ (?)	none	—	no	no	dead (10)
Jellinger et al. (1975) ¹²⁾	0.1/—	—	—	—	—	—	no	no	—
Yenrudi and Shuangshoti (1978) ³⁴⁾	1.5/F	cerebellum	none	none	none	—	yes	no	dead (0.8)
Tooyama et al. (1980) ²⁹⁾	10/F	temporal lobe	total	+ (40 Gy)	VCR, 6-MP, Ara-C, Pre, CPM	—	yes	yes	dead (20)
	2/F	third ventricle	subtotal	+ (32 Gy)	none	lymphocytic	no	yes	dead (9)
	8/M	temporal lobe	total	+ (45 Gy)	none	—	no	yes	dead (15)
	4/M	cerebellum	biopsy	+ (36 Gy)	VCR, VLB, Pre	lymphoblastic	yes	no	dead (7)
Takahashi et al. (1982) ²⁷⁾	1/M	parieto- occipital lobe	partial	+ (30 Gy)	MTX, Pre	—	yes	no	dead (3)
Matsutani et al. (1982) ²¹⁾	0.6/M	parietal lobe	partial	none	none	large	no	no	dead (0.3)
Kobayashi et al. (1983) ¹⁴⁾	7/M	parietal lobe	partial	+ (30-40 Gy)	none	large	no	yes	dead (3)
	11/M	parietal lobe	partial	+ (30-40 Gy)	none	lymphoblastic	no	no	dead (18)
	14/M	multiple	biopsy	+ (40 Gy)	none	small non- cleaved	yes	no	alive (58)
	2/M	multiple	biopsy	none	none	diffuse	no	no	dead (5)
Berry et al. (1985) ¹³⁾	1.2/F	multiple	partial	+ (25 Gy)	VCR, Pre, L-Asp, VLB, MTX, 6- thioguanine, hydroxyurea, BCNU, Ara-C, DNR	mixed immuno- blastic	yes	no	dead (23)

Contd.

Table 1, contd.

Author (Year)	Age/ Sex	Location	Operation	Radiation (dose)	Chemotherapy	Histological type	Meningeal dissemina- tion	Leukemic trans- forma- tion	Outcome (mos)
Jones et al. (1985) ^[3]	4/M	multiple	none	+ (24 Gy)	VLB, Dex	—	yes	no	alive (15)
Takahashi et al. (1985) ^[20]	6/F	cerebellum	partial	+ (40 Gy)	MTX, Dex, ACNU, DNR, Pre	—	yes	no	dead (10)
Bogdahn et al. (1986) ^[4]	2/F	cerebellum	partial	+ (24 Gy)	—	lympho- blastic	no	no	alive (24)
Choen et al. (1986) ^[5]	3.5/M	temporo- occipital lobe	partial	none	DEMBO	—	no	no	alive (36)
Vakili et al. (1986) ^[31]	5/F	bifrontal lobe	partial	none	none	histiocytic	no	no	dead (3)
	8/F	fronto- temporal lobe	partial	none	none	histiocytic	no	no	alive (7)
	15/M	fronto- parietal lobe	biopsy	+ (50 Gy)	none	lymphocytic	no	no	alive (36)
Yasunaga et al. (1986) ^[32]	0.2/M	basal ganglia	biopsy	+ (40 Gy)	VCR, VLB, DXR	—	no	no	dead (6.5)
Aozasa et al. (1990) ^[2]	1/F	occipital lobe	—	none	VCR, VLB	—	no	no	alive (6)
Hayashi et al. (1990) ^[8]	6/M	frontal lobe	total	+ (36 Gy)	VCR, CPM, DNR, Pre, MTX, Ara-C	—	no	no	dead (78)
Schulman et al. (1991) ^[25]	3/M	temporo- parietal lobe	partial	—	—	lymphocytic	no	no	—
Present case	5/M	cerebellum	biopsy	+ (50 Gy)	none	lymphocytic	no	no	alive (60)

ACNU: nimustine hydrochloride, Ara-C: cytosine arabinoside, BCNU: carmustine hydrochloride, CPM: cyclophosphamide, DEMBO: methotrexate (MTX)/vincristine (VCR)/BCNU, Dex: dexamethasone, DNR: daunorubicin hydrochloride, DXR: doxorubicin hydrochloride, L-Asp: L-asparaginase, 6-MP: mercaptopurine, Pre: predonine, VLB: vinblastine sulfate, — : not reported.

case).^{2-5,9,10,12-15,18,21,25,27-29,31,33,34)} The mean age was 5.1 years, ranging from 0.1 to 15 years (Table 1).

Primary malignant lymphoma of the brain in children differs significantly from that in adults. The posterior fossa seems to be the predominant location in children (11/31 patients, 35.5%), whereas only 9% to 11% are located in the posterior fossa in adults, and the supratentorial region is the predominant site.⁸⁾

Pediatric cases occasionally have an unusual radiological pattern of irregular enhanced mass with severe edema, or no evidence of an intracranial mass. Meningeal dissemination occurs frequently in pediatric cases (8/32, 25.0%) compared to 6% in adult cases.⁸⁾ The characteristic CT features of malignant lymphoma in children are a non-homogeneous pattern, marked edema and prominent mass effect, and especially the "ring-like" peripheral pattern of enhancement.²⁵⁾ One child with primary malignant lymphoma of the brain had no radiological evidence of nodular involvement.¹³⁾ The CT findings in our patient were hypodensity and linear irregular enhancement after contrast medium administration in contrast to findings in adults.

The histological classification of the present case was the small lymphocytic type of B cell type tumor. The histological pattern of malignant lymphoma of the brain seems to depend on the age of the patient. The lymphoblastic type occurs most frequently in children, followed by the null-cell type. The diffuse, large cell type occurs most frequently in adults, and all are B cell type.^{8,10,17)}

The prognosis for primary malignant lymphoma of the brain is very poor. Most patients die within a year of diagnosis and the mean survival is about 9–44.5 months.^{11,18,33)} The prognosis in children seems to be poorer than in adults. The survival for all reported pediatric cases was 0.3–78 months, and the mean survival time was 17.1 months (Table 1). The prognosis for patients with primary malignant lymphoma of the brain may depend on the histological subtype.^{10,22)} However, there may be no correlation between histological findings and prognosis.^{7,24)} Patients with the lymphoblastic type, which seems to predominate in pediatric cases, have a much poorer prognosis because of a high recurrence rate and a tendency to leukemic transformation.¹²⁾ Leukemic transformation was observed in four of the previously reported pediatric cases.^{14,29)} Our patient had the small lymphocytic type, which has a low recurrence rate and a high sensitivity for radiotherapy. Radiotherapy without subsequent chemotherapy is effective for the treatment of small lymphocytic lymphoma.

Our patient was doing well more than 5 years after

the biopsy and radiotherapy. Thirty patients with primary malignant lymphoma of the brain have survived more than 5 years,^{1,5,18-20,23,30,32)} but only one was a child.⁹⁾ Chemotherapy and/or radiotherapy have yielded good results in two children with primary malignant lymphoma of the brain.^{5,9)} These two patients were alive at 36 and 78 months, respectively. Our patient did not receive chemotherapy. His long-term survival is probably attributable to the absence of aggressiveness and the good response to radiation of the well-differentiated small lymphocytic type of malignant lymphoma.

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