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Original Investigation

Operative Management of Intraventricular Central Neurocytomas: An Analysis of a Surgical Experience with 32 Cases

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ABSTRACT

AIM: To better understand the clinical characteristics of central neurocytoma (CN), as well as to assess the optimum therapeutic schedule.

MATERIAL and METHODS: This was a retrospective study of 32 patients with CN who visited our department between January 2008 and January 2013. We analyzed the clinical and radiological presentations, tumor characteristics, surgical strategies, and the prognosis.

RESULTS: We performed operation guided by combined intraoperative magnetic resonance imaging (iMRI) and neuronavigation in 25 patients. The iMRI detected residual tumor in 9 cases, and further resection was performed in 5 cases. Total and nearly total tumor resection was achieved in 29 cases (91%). There was no significant difference between transcortical and transcallosal approaches in complications. Two cases (6%) with recurrence received respectively repeat salvage surgery and radiosurgery at 46 and 50 months after surgery. Thirty patients (94%) had excellent functional outcome (Karnofsky Performance Score ≥80) and 28 patients (88%) resumed their occupations.

CONCLUSION: Our study demonstrates radical surgery with excellent neurological outcomes is the primary treatment of CN. The techniques of resection guided by combined iMRI and neuronavigation seems to enable a higher complete resection rate and reduce the morbidity rate during surgery. We suggest careful clinical observation after initial surgery, and repeat salvage surgery or radiosurgery for recurrent CN.

KEYWORDS: Central neurocytoma, Neuronavigation, Surgery, Transventricular approach, Radiosurgery

INTRODUCTION

Central neurocytomas (CNs) are rare brain tumors of young adults, typically located in deep midline structures near the foramen of Monro (28). The tumors were first described as a distinct clinicopathologic entity by Hassoun et al. in 1982 (9, 11). These well-differentiated tumors with neuronal differentiation have an indolent clinical course. Gross total resection (GTR) is the first optimal treatment option for most patients with central neurocytoma (CN) (11). However, the proximity to the deep critical neural and vascular structures and rich blood supply increase the risk of surgical treatment. Resection of CN is still a challenging procedure for most neurosurgeons. The best selection of the common surgical approaches including transcortical transventricular approach and interhemispheric-transcallosal transventricular approach is still controversial, and the optimal selection and timing of adjuvant radiotherapy and chemotherapy also remain unclear.

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As CN is rare, it is very difficult to collect many cases in a short period in one institution, and histological diagnosis and treatment strategies may evolve during the period of the study. Between January 2008 and January 2013, we performed microsurgery in 32 patients with CN. We reviewed our therapeutic strategies and postoperative follow-ups by retrospective analysis in the present study. The aim was to better understand the clinical and radiological presentation, tumor characteristics, surgical strategies, adjuvant therapy and the prognosis, as well as to assess the optimum therapeutic schedule.

MATERIAL and METHODS

Patients

During a 5-year period between January 2008 and January 2013, 32 consecutive patients with histologically verified CN were treated in the Department of Neurosurgery of our hospital by the senior neurosurgeons. All of the 32 patients provided informed consent. Seven cases were operated from January 2008 to January 2009, and five of the 7 cases were operated with a neuronavigation (BrainLab, Germany) system. A dual-room intraoperative magnetic resonance imaging (iMRI) suite with a scanner with a movable 1.5-T magnet (Siemens Espree, Erlangen, Germany) was installed at our center in February 2009 (5). We performed the operation guided by combined iMRI (Siemens Espree, Erlangen, Germany) and neuronavigation (BrainLab, Germany) in the other 25 patients from February 2009 to January 2013. The clinical information was obtained from hospital charts, clinic notes, and operative reports.

Patient Evaluation

The patients underwent radiological assessment of their lesions by computed tomography (CT) and magnetic resonance imaging (MRI). Tumor size was defined as the greatest contrast-enhancing tumor diameter on MRI. All patients received postoperative follow-up by neuroimaging and neurological examinations. The neurological function and neuroimaging evaluations of the patients were recorded preoperatively, at 3 months postoperatively, and at 1 year to 5 years intervals after surgery. Gross total resection (GTR) was defined as 100% macroscopic resection of the tumor; nearly total resection (NTR) was close to total resection, but an intended incomplete resection; Subtotal resection (STR) was defined as removal of <100% but >90%. A Karnofsky performance status score (KPS) was also determined for each patient based on clinical evaluations.

Surgical Approaches and Surgical Techniques

The surgery was performed with general anaesthesia. The details of the iMRI scans were the same as reported in our previous reports (5, 22). The surgical approaches include the interhemispheric transcallosal approach and the transcortical approach. A conventional right frontal craniotomy was performed with the patient in the supine position (Figure 1A). After the dural opening, we used the operating microscope. The frontal lobe and falx cerebri were slightly retracted laterally via the interhemispheric transcallosal approach (Figure 1B). The middle frontal gyrus was penetrated via the transcortical approach and the corpus callosum was dissected via the interhemispheric transcallosal approach guided by neuronavigation. Most tumors arose from the septum pellucidum and extended into the lateral ventricles, and generally had a good interface of cleavage from the ependyma of the ventricular walls, but were seen to merge with the septum pellucidum (21). We precisely differentiated and dissected the interface between the tumor surface and the normal tissue of the ventricular wall guided by neuronavigation. Piecemeal tumor resection with the cavitron aspirator was recommended. Most tumors were high vascular, friable in consistency, and associated with quite profuse bleeding. It was necessary to differentiate and protect the main draining vein early (Figures 1C, D). Keeping the operative field clear with gradually debulking the tumor was also very important. When the surgeon believed that the tumor was completely resected, iMRI was performed. If residual tumor was detected, the surgeon would continue resection until subsequent iMRI confirmed complete resection. We retained a ventricular drain in all patients of CN, which was usually removed 48 hours after surgery once the draining cerebrospinal fluid (CSF) became clear and we then clipped the ventricular drain for 24 hours.

Comparisons and Statistical Method

Seven patients with CN treated without the iMRI system from January 2008 to January 2009 were reviewed as the control group. Comparisons between the iMRI-assisted group and the control group were focused on age, tumor size, surgical approach, the extent of resection, operation time, operation-related dysfunction, and tumor recurrence. Comparisons between the two surgical approaches were focused on the extent of resection and postoperative complication. Fisher's exact test (two-tailed) or Student's test (t test) was used. $P<0.05$ was considered significant. Statistical analysis was performed with the SPSS software version 19 (SPSS version 19, SPSS Inc.).

RESULTS

Preoperative Characteristics

The patient demographics and the presenting symptoms are shown in Table I.

There were 25 CT scans and 32 MRI scans available in this study. On the CT scans, the tumors were either isodense or mild hyperdense (Figure 2A, Figure 3A). All the tumors showed moderate or strong enhancement on contrast-enhanced MRI in this series (Figures 2B,C, Figures 3B,C). Three patients (9%) had tumors smaller than 3 cm, 18 patients (56%) had tumors between 3 and 5 cm, and the other 11 patients (34%) had tumors larger than 5 cm. Other radiological features are described in Table I.

Surgical Characteristics and Pathology

All the patients initially underwent surgery, and the postoperative improvements of the symptoms are listed in Table I. The first iMRI scan detected residual tumor in 9

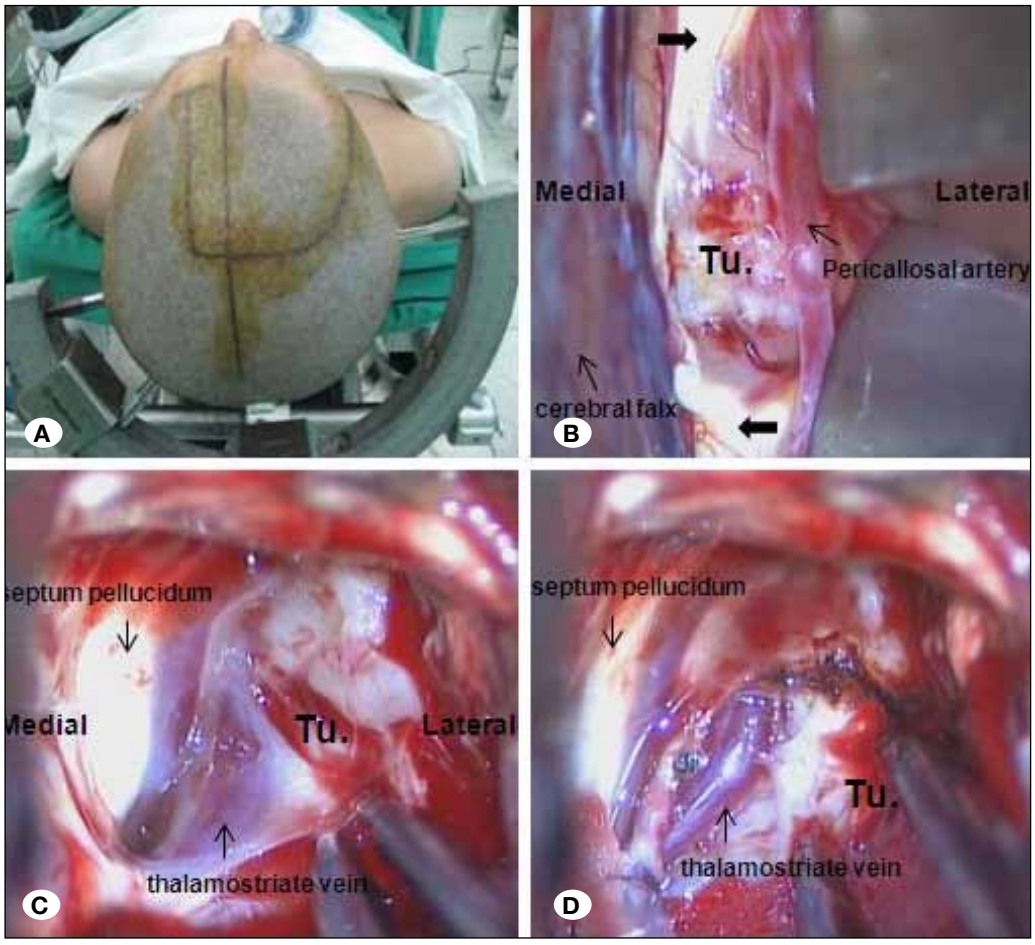

Figure 1: Intraoperative photographs of the central neurocytoma removal showing:
A) A conventional right frontal craniotomy was performed with the patient in the supine position; **B)** The right frontal lobe and falx cerebri were slightly retracted laterally via the interhemispheric transcallosal approach. The falx cerebri, right pericallosal artery, corpus callosum (think arrow), and tumor (Tu.) were visible; **C)** The tumor (Tu.) was adhesive with the thalamostriate vein; **D)** The complete tumor resection was achieved, and the thalamostriate vein was intact.

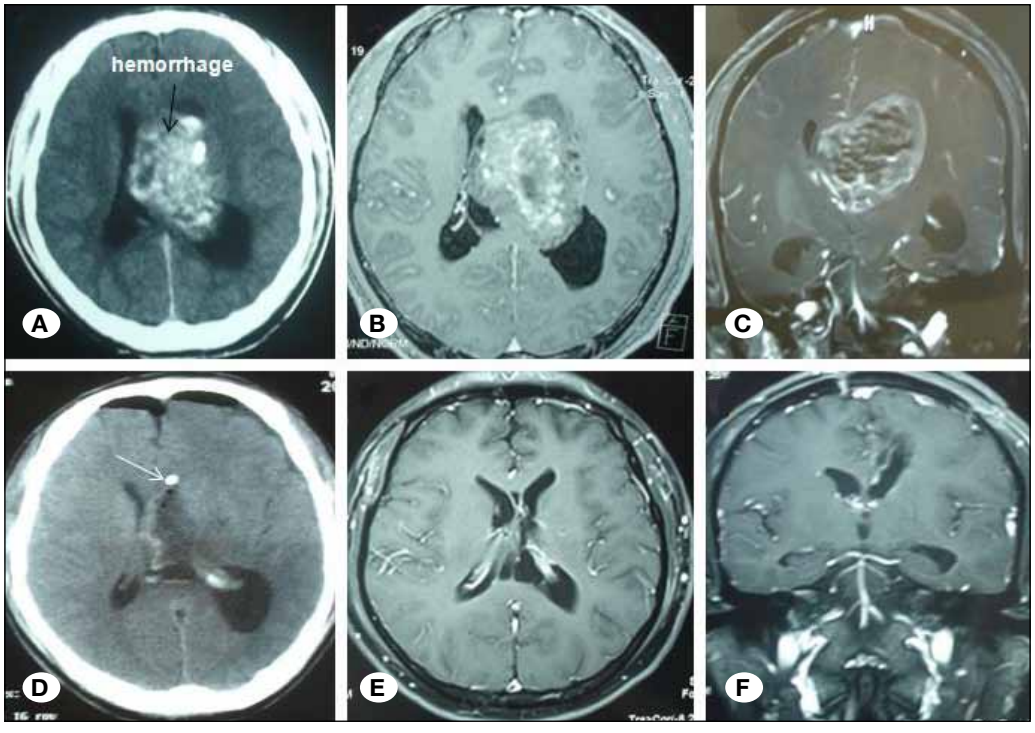

Figure 2: Preoperative **A)** CT, **B)** axial and **C)** coronal T1-weighted contrast-enhanced MRI showed a large central neurocytoma, which extended into both lateral ventricles, and the intratumoral hemorrhage could be observed. The patient was operated via the transcortical approach without any complication. **D)** CT at 1 day after surgery displayed complete tumor removal and the external ventricular drainage tube (write arrow). **E)** Axial and **F)** coronal T1-weighted contrast-enhanced MRI at 36 months after surgery showed complete tumor removal.

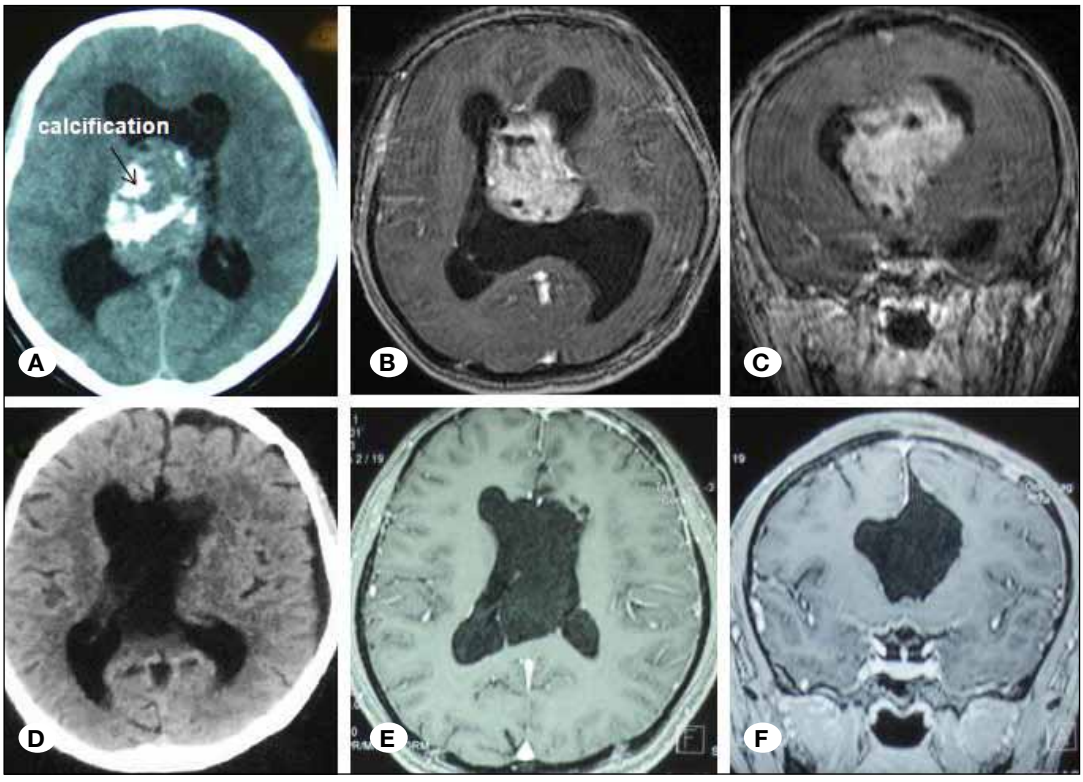

Figure 3: Preoperative **A)** CT, **B)** axial and **C)** coronal T1-weighted contrast-enhanced MRI showed a central neurocytoma, which extended into both lateral ventricles and the third ventricle. The intratumoral calcification could be observed. The patient was operated via the interhemispheric transcallosal approach without any complication. **D)** CT, **E)** axial and **F)** coronal T1-weighted contrast-enhanced MRI at 48 months after surgery showed complete tumor removal.

of the 25 cases, and the surgeons continued resection in 5 cases with residual tumor until subsequent confirmation of complete resection by repeat iMRI. The major impediment to GTR was the difficulty in dissection from adjacent critical structures, such as the thalamus or thalamostriate vein. The iMRI-assisted group showed a higher rate of total resection of tumor and a lower rate of operation-related dysfunction and tumor recurrence (Table II). The initial extent of tumor removed did not differ significantly according to the two surgical approaches selected (Table III, Figures 2D-F, Figures 3D-F). The details are shown in Tables II and III. The senior neuropathologist verified the histological examinations of all the tumors that were grade II tumors in the WHO classification of tumors.

Postoperative Course

There was no perioperative mortality. Postoperative symptomatic improvement is shown in Table I, and the operative outcome by two different approaches within 1 month and 6 months after surgery is summarized in Table III. Two patients with CSF infection were successfully treated with lumbar drainage for 5-7 days and intravenous antibiotic administration. There was no difference in surgical complications between the two surgical approaches at the final follow-up. A total of 30 patients (94%) became independent at 6 months after surgery, and 28 patients (88%) resumed their occupations. The KPS scores of the 30 patients ranged from 80 to 100, and the KPS scores of another two patients were 70 and 60, respectively. One patient received a permanent shunt because of hydrocephalus.

No patient received adjuvant radiotherapy and chemotherapy after the initial resection. Re-growth was clinically and radiologically observed in 2 patients at 46 and 50 months after the initial resection. Among them, 1 patient who was operated with STR via the transcortical approach underwent repeat surgery, whereas the other one who was operated with STR via the transcallosal approach received adjuvant radiosurgery (Leksell Gamma Knife). The two patients had no recurrence during the additional follow-up period (12 months and 6 months, respectively).

■ DISCUSSION

Epidemiology

The incidence of CN is estimated to be only 0.1-0.5% of all primary brain tumors (9, 16, 19, 26). The tumors typically affect adolescents and young adults with the highest incidence occurring in the third decade. It occurs rarely in people younger than 20 years or older than 40 years of age. Most studies have reported that the patients seem to be equally prevalent in either sex (9, 16, 19, 26). In our series, there was no significant sex variation with the male/female ratio being 1:1.1, and the patients ranged from 14 to 59 years of age (mean, 26.3 years). We had 7 patients younger than 20 years and 3 patients older than 40 years.

Clinical Presentation

CNs usually have a long and benign clinical course. A common presentation of most CNs is hydrocephalus, caused by obstruction of the foramen of Monro by the tumor. The

Table I: Characteristics in 32 Patients with Central Neurocytomas

Characteristics/ Number of Cases	n = 32	Postoperative improvement (%)	
		Immediate [a]	Medium term [b]
Demographics			
Mean age, (years) (range)	26.3 (14-59)	-	-
Sex (male/female)	15:17	-	-
Tumor features			
Mean size, (cm) (range)	4.8 (2.5-5.7)	-	-
Tumor location			
Unilateral ventricles	5 (16%)	-	-
Both lateral ventricles	27 (84%)	-	-
Third ventricle	14 (44%)	-	-
Intratumoral texture			
Calcification	19 (59%)	-	-
Cystic	22 (69%)	-	-
Hemorrhage	2 (6%)	-	-
Flow void	17 (53%)		
Major symptoms and signs			
Headache and dizziness	24 (75%)	22 (92%)	24 (100%)
Nausea and vomiting	21 (66%)	21 (100%)	21 (100%)
Ataxia	12 (38%)	10 (83%)	12 (100%)
Visual disturbance	7 (22%)	5 (71%)	6 (86%)
Seizure	3 (9%)	1 (33%)	1 (33%)
Coma	1 (3%)	1 (100%)	1 (100%)
Weakness	1 (3%)	0 (0%)	1 (100%)
Hydrocephalus	26 (81%)	22 (85%)	25 (96%)
Mean symptoms duration, (months)	5.5	-	-
Range	2 days-2 years	-	-
Median preoperative KPS [c]	80	-	-
Mean follow-up duration, (months) (range)	38 (12-60)	-	-

[a]1 months after operation in the series; [b]6 months after operation in the series; [c] ***KPS,*** *Karnofsky Performance Scale.*

Table II: Comparisons Between the iMRI-Assisted Group and no iMRI-Assisted Group

Parameters/ Group	iMRI-assisted Group (n = 25)	No iMRI-assisted group (n = 7)	p
Age (years)	25.3±14.7	30.4±6.8	0.192
Mean size (cm)	4.8±0.7	4.6±1.0	0.581
Surgical approach(TCO/TCA) [a]	12/13	3/4	0.576 [b]
Operation time (hours)	6.3±0.7	6.0±0.7	0.882
Blood loss (cm^3)	495±134.9	489±123.4	0.148
Total resection	84% (21/25)	42.9% (3/7)	0.047 [b]
Nearly total	16% (4/25)	14.3% (1/7)	-
Subtotal	0 (0/25)	42.9% (3/7)	-
Operation-related dysfunction [c]	8% (2/25)	28.6% (2/7)	0.201 [b]
Recurrence	0 (0/25)	28.6% (2/7)	0.042 [b]

[a] ***TCO,*** *transcortical;* ***TCA,*** *transcallosal; [b] Fisher's exact test (two-tailed) was used. Student's test (t test) was used for others. P<0.05 was considered significant; [c] new neurological deficits or worsening of pre-existing deficits at 6 months after operation in the series.*

symptoms include headaches, nausea-vomiting, seizures, visual impairment, and memory disturbance. The duration of symptoms is usually less than 6 months (4). Intratumoral and/or intraventricular hemorrhage are also rarely reported (21). In our series, preoperative symptom duration ranged from 2 days to 2 years (mean, 5.5 months). The common symptom was headache, and only two patients (6%) had intratumoral hemorrhage.

Radiology

A typical CN is usually located in the supratentorial ventricular system, and the anterior half of the lateral ventricle is the most frequent location (1, 7). 26% of CNs can extend into the third ventricle, and isolated third or fourth ventricular occurrence, extraventricular sites and craniospinal dissemination are rare (2, 4, 17, 27). The tumor is usually isointense in T1-weighted and T2-weighted images, with a "soap-bubble" appearance in T2-weighted images and there is usually moderate to strong enhancement with contrast (21), and approximately 51% demonstrate calcification (9). Our series confirmed to the general observation reported above. CT scan revealed calcification in 59%. MRI showed that 69% of the tumors contained multiple small cysts, 17 tumors (53%) exhibited evidence of flow voids from tumor vessels on MRI and 44% of the tumors extended into the third ventricle.

Surgical Approach

The goals of surgery for CN are to maximize a safe resection, provide tissue for histological diagnosis and re-establish CSF pathways (24). The selection of the optimal surgical approach should consider the tumor's location, size, expansion, and the degree of hydrocephalus (16, 25). Kim et al. (10) reported the initial extent of tumor removed did not differ significantly according to the surgical approach used. The interhemispheric transcallosal approach had a better seizure outcome than did the transcortical approach (15), and there were no differences in other functional outcomes. We selected the surgical approach according to the location and size of the tumor, the degree of hydrocephalus, and the surgeon's preference. Operations of 25 cases were guided by the combined iMRI and neuronavigation in the present study. The neuronavigation helped us to determine the best location for incision of the brain cortex or corpus callosum and minimized surgical injury to the brain. In our series, there were no significant differences in functional outcomes including memory deficit, and motor weakness according to the surgical approach selected. As the interhemispheric transcallosal approach is a natural approach with less damage to the cortical area, we have a slight preference for it.

Surgical Strategy

As CNs have a deep-seated intraventricular location, an abundant blood supply, and proximity to critical structures such as the fornix and thalamus, the surgical morbidity and mortality rates were relative high (6,8,10-14,19,23). Some reported rates of GTR ranged from 31% to 88%, mortality rates varied between 0% and 19%, and morbidity rates varied between 16% and 52% (Table IV). GTR was usually associated with high morbidity and mortality rates. Some authors (10,11,19) advocated that GTR should not be pursued at all costs, and that the patient's quality of life and tumor control should be the ultimate strategies of treatment. We agreed with them, and we incurred a 91% radical removal rate with a permanent postoperative morbidity rate of 13%. The better outcome (Table IV) in our series seemed to be attributed to the combined iMRI and neuronavigation system. When the ventricle was opened and CSF flowed out, brain shifts were usually detected during the operation of the intraventricular tumor. This can be resolved by the combined iMRI and neuronavigation. After the main part of the tumor was removed, iMRI was used to update the neuronavigation after the brain shift and enabled the more accurate recognition

Table III: Operative Outcome of 32 Patients with Central Neurocytomas[a]

Parameters/ Approach	TCO (n = 15)	TCA (n= 17)	P [b]
Extent of resection			
Total	11	13	0.579
Nearly total	3	2	-
Subtotal	1	2	-
Hydrocephalus			
Immediate [c]	2	1	0.452
Medium term [d]	1	0	0.469
Memory deficit			
Immediate [c]	1	3	0.452
Medium term [d]	1	1	0.726
Seizure			
Preoperative	2	1	-
Medium term [d]	1	1	0.726
Weakness			
Immediate [c]	1	1	0.726
Medium term [d]	1	1	0.726
Infection			
Immediate [c]	1	1	0.726
Medium term [d]	0	0	-
Median postoperative KPS			
Immediate [c]	80	80	-
Medium term [d]	90	90	-
Postoperative death	0	0	0 (0%)

*[a]**TCO,** transcortical; **TCA,**transcallosal; **KPS,** Karnofsky Performance Scale; [b] Fisher's exact test (two-tailed) was used. P<0.05 was considered significant; [c]1 month after operation in the series; [d] 6 months after operation in the series.*

Table IV: Some of the Major Retrospective Series on Central Neurocytomas (n>15)

Author & Year	Cases (n)	Radical removal (%)	Mortality (%)	Morbidity (%)[a]	Follow-up (months) Mean(range)	Recurrence rate (%)	Survival rate (%)
Figarella-Branger et al. 1992, (6)	20	9 (45%)	10%	ND	36 (6-108)	ND	70%
Schild et al. 1997, (23)	32	10 (31%)	9%	ND	56 (28-184)	ND	91%
Mackenzie 1999, (13)	15	8 (53%)	0%	ND	68 (13-255)	20%	93%
Mena et al. 2001, (14)	32	12 (38%)	19%	ND	93 (11-204)	4%	65%
Lenzi et al. 2006, (12)	20	10 (50%)	10%	20%	84 (9-136)	35%	90%
Leenstra et al. 2007, (11)	45	21 (47%)	7%	ND	120 (19-280)	33%	80%
Hallock et al. 2011, (8)	19	10 (53%)	5%	16%	105 (1-262)	32%	89%
Qian et al. 2012, (19)	92	65 (71%)	3%	40%	43 (6-84)	4%	97%
Kim et al. 2013, (10)	48	42 (88%)	2%	52%	119 (18-304)	13%	90%
Chen 2014 (present series)	32	29 (91%)	0%	13%	38 (12-60)	6%	100%

[a] 6 months after operation in the series. ***ND:*** *not described.*

of tumor borders and avoidance of important structures. The rate of operation-related dysfunction was 8% in the iMRI-assisted group, and 28.6% in the no iMRI-assisted group. Though the statistical result was not significant, it may still imply an advantage.

IMRI also helped to detect residual tumor and achieve radical removal. IMRI was used to detect the residual tumor in 9 of the 25 patients and the surgeon continued resection in 5 cases with residual tumor until subsequent confirmation of complete resection by repeat iMRI in the present study. We achieved 84% of GTR and 16% of NTR in the iMRI-assisted group, higher than that of the iMRI-unassisted group. In contrast to Qian et al.'s report (19), calcifications seemed not to act against GTR, and the major impediment to GTR was adherence to the critical structures including thalamus or thalamostriate vein in our series. If there were difficulties in dissection from the critical structures, STR should be recommended.

Complications

The main reported complications included hydrocephalus, memory deficit, paresis, epidural hematoma, seizure, and intracranial infection (6, 8, 10-14, 19, 23). Among them, hydrocephalus is the most common complication. In our series, only one postoperative patient with the non-obstructive hydrocephalus received a ventriculoperitoneal shunt. Decreased memory is most probably caused by injury to the corpus callosum and fornix or hydrocephalus. We emphasize that the length of dissected corpus callosum should be less than 3 cm. In our series, 2 patients had permanent memory deficits, and 88% of the patients returned to work during follow-up.

Treatment Options

Because of the rarity of CN, no randomized clinical trials and few prospective studies have been done, and the optimal management strategies are still evolving. The question of further treatment for residual and recurrent tumors remains controversial (3). Conventional radiotherapy is not theoretically necessary for most of the tumors because of their benign indolent clinical course. Moreover, the experiences in radiotherapy are still limited, and the long-term effect that induces cognitive dysfunction and other potential radiation toxicity cannot be ignored (18). Rades and Fehlauer (20) reported significant improvement in the 5-year local control rate with adjuvant radiosurgery after STR (83%) compared with STR alone in a meta-analysis of data from 310 patients. They suggested that postoperative radiosurgery should be administered after STR in all patients to avoid the risks associated with a second resection and concerns regarding craniospinal dissemination. We recommend a "wait-and-see" strategy for asymptomatic residual CNs. We advocate re-operation or radiosurgery for recurrent CNs. In our series, 2 patients who were operated with STR had recurrence. Among them, one patient received adjuvant radiosurgery, and another one received reoperation. The two patients had no recurrence during the additional follow-up period. There is no study performed to prove the effect of adjuvant chemotherapy. We do not recommend adjuvant chemotherapy for the patients.

■ CONCLUSION

Our study demonstrates that radical surgery is the primary treatment of CN with its excellent neurological outcomes. The techniques of resection guided by combined iMRI and neuronavigation seems to enable a higher complete resection rate and reduce the morbidity rate during surgery. We suggest careful clinical observation after initial surgery, and repeat salvage surgery or radiosurgery for recurrent CN.

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