Transcortical approach for the treatment of large intraventricular central neurocytoma

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Abstract

Background Central neurocytoma is a rare intracranial tumor. Due to the limited number of reported cases in the past, there is still controversy about the treatment strategy for central neurocytoma, especially large central neurocytomas occupying bilateral ventricles. This paper will discuss our clinical experience in the treatment of large central neurocytoma.

Methods A retrospective analysis of 29 patients with intraventricular central neurocytoma diagnosed and treated by the same surgeon between April 2012 and September 2019 at the Neurosurgery Departments of Beijing Tiantan Hospital and Hainan General Hospital was performed. The clinical characteristics, treatment plan and prognosis of these patients were discussed.

Results Among the 29 patients, the average age of onset was 31.93 (17-61) years, and the average maximum tumor diameter was 54.17 ± 15.62 mm. Among them, 23 patients (79.3%) had an average maximum diameter greater than 5 cm. Twenty-seven patients (93.1%) underwent transcortical tumor resection. Twenty-seven patients (93.1%) achieved gross total tumor resection. Five patients (17.2%) received radiotherapy after the first operation, and 3 patients (10.3%) had tumor recurrence. None of the patients died.

Conclusion Operation is the basis of the treatment of central neurocytoma. It is possible for patients to be cured by total resection of the tumor and protection of normal ventricular structure. Transcortical fistulotomy is a reliable approach for the removal of large central neurocytomas in the ventricle. Patients should be closely observed post-operation, and MRI of the head should be rechecked regularly. If tumor progression occurs, then radiotherapy should be considered.

Background

Central neurocytoma is a rare brain tumor mainly located in the lateral ventricle near the interventricular foramen [1]. It accounts for approximately 0.1–0.5% of primary central nervous system tumors. Hassoun proposed the concept of the pathological diagnosis of central neurocytoma for the first time in 1982 [2], which was classified as grade II by the World Health Organization in 2016 [3]. Large central neurocytomas occupying bilateral ventricles account for a certain proportion. Because of the large volume, deep location, high risk of operation and many postoperative complications, it is very difficult to achieve total tumor resection. The degree of difficulty is much more than that of small sized-tumors that are limited to the central neurocytoma of the unilateral ventricle. Surgery is the most fundamental treatment [4]. However, the choice of surgical approach, the degree of tumor resection, the prevention and treatment of postoperative brain edema and hydrocephalus, and whether postoperative radiotherapy should be applied are still controversial [5–8], especially for large tumors occupying bilateral ventricles. Therefore, it is necessary to summarize the clinical treatment experience of these patients.

In this study, we retrospectively analyzed patients with intraventricular central neurocytoma who underwent surgery by the same surgeon in 2012–2019 at the Neurosurgery Departments of Beijing

Tiantan Hospital and Hainan General Hospital. Their clinical characteristics, treatment and prognosis were analyzed to explore the treatment experience of these patients.

Methods

Patients

This study was approved by the Beijing Tiantan Hospital of the Capital Medical University of Medicine Institutional Review Board. Twenty-nine patients diagnosed with intraventricular central neurocytoma at the Neurosurgery Departments of Beijing Tiantan Hospital and Hainan General Hospital from 2012 to 2019 were included. The same surgeon performed the operations for all patients.

Data collection

We selected patients who conformed to the inclusion criteria according to the medical records system of Beijing Tiantan Hospital and Hainan General Hospital by viewing patient medical records, including resident admission notes, progress notes, operation records, discharge records and preoperative and postoperative imaging materials. Patient demographics, including age, sex, entering complaint, preoperative Karnofsky Performance Status (KPS) score, comorbidities, preoperative and postoperative neurological examinations, tumor volume, extent of resection, postoperative complications, pathology, and immunohistochemical outcomes, were recorded for these patients. The patients were followed up for adjuvant treatment, tumor progression and recovery status. The last follow-up time was March 2020.

Grouping method

The preoperative KPS score was used for the classification of functional status. A better functional status resulted in a more favorable KPS score. We identified the extent of resection by comparing the preoperative and postoperative imaging data. Gross total resection was defined as the complete resection of the main part of enhanced lesions observed in preoperative imaging. Others were categorized as subtotal resections. The largest diameter ≥ 5 cm was defined as a large central neurocytoma.

Statistical analysis

Continuous and categorical variables are expressed as medians and percentages, respectively. The Mann-Whitney U test or Kruskal-Wallis test was used for the comparison of continuous variables, and the chi-squared test was used for the comparison of categorical variables. All statistical analyses were performed using the statistical analysis software package SPSS (Windows version 22.0, IBM). Statistical significance was defined as a P value < 0.05.

Results

Twenty-nine patients met the enrollment criteria (Table 1). The average age of the patients was 31.93 years (range 17-61 years). There were 17 male patients (male: female = 1.4:1),

the average preoperative KPS score was 88.62 ± 6.39, and the average maximum diameter of the tumor was 54.17 ± 15.62 mm, of which 23 patients (79.3%) had an average maximum diameter ≥ 5 cm. Twenty-seven patients (93.1%) achieved gross total tumor resection by imaging (as shown in Figure 1).

Table 1. Clinical characteristics, treatment and prognosis of 29 patients with CN

	Total/average
	29
Age	31.93(17-61)
Male	17(58.6%)
KPS1	88.62±6.39
KPS2	77.59±7.40
KPS3	90.34±6.81
Large CN	23(79.3%)
Treatment	
Gross total resection	27(93.1%)
Radiotherapy*	5(17.2%)
Postoperative complications	
Hemiplegia	10(34.5%)
Aphasia	10(34.5%)
Epilepsy	4(13.8%)
Fever	12(41.4%)
Memory decline	15(51.7%)
V-P shunt	5(17.2%)
*Length of stay	28.28±17.41
Mean follow-up time	49.52±25.40

Tumor recurrence	3(10.3%)

One patient was hospitalized for 110 days, which was several times longer than that of the other patients. Radiotherapy: indicates patients who received radiotherapy after primary surgery. KPS1: Preoperative KPS; KPS2: Discharge KPS; KPS3: KPS at the last follow-up.

Operation

Twenty-seven patients (93.1%) were treated by gross total tumor resection, and no operative deaths occurred. Among them, 27 patients underwent transcortical approach, and surgical approach through the trigone of the lateral ventricle was performed in 2 cases. Of the 23 patients with large central neurocytoma, 21 (91.3%) underwent gross total resection. All 6 patients with non-large central neurocytoma underwent total resection. However, there was no significant correlation between the degree of resection and the recurrence rate.

Postoperative complications

Ten patients (34.5%) had hemiplegia, aphasia (34.5%), epilepsy (13.8%), memory decline (51.7%) and fever (41.4%). Five patients (17.2%) with hydrocephalus underwent ventriculoperitoneal shunting. Among 23 patients with large central neurocytoma (Table 2), 10 (43.5%) had hemiplegia, 8 (34.8%) had aphasia, 4 (17.3%) had epilepsy, 9 (39.1%) had fever, and 3 (13.0%) underwent ventriculoperitoneal shunting for hydrocephalus. Hemiplegia occurred more frequently in patients with large central neurocytoma than in patients with non-large central neurocytoma (P = 0.046). However, there was no significant difference in the incidence of aphasia, epilepsy, fever, severe hydrocephalus or memory decline between the two groups. Moreover, memory decline was significantly correlated with radiotherapy (Table 3) (P=0.017).

Table 2. Comparison of treatment and prognosis between large CN and non-large CN

	Large CN	Non-large CN	Chi square value	P value
Treatment				
Extent of resection			0.56	0.454
Gross total resection	21	6		
Subtotal resection	2	0		
V-P shunt			1.373	0.241
Yes	3	2		
No	20	4		
Radiotherapy			1.576	0.209
Yes	5	0		
No	18	6		
Postoperative complications				
Hemiplegia			3.982	**0.046**
Yes	10	0		
No	13	6		
Aphasia			0.004	0.950
Yes	8	2		
No	15	4		
Epilepsy			1.21	0.271
Yes	4	0		

No	19	6		
Fever			0.232	0.630
Yes	9	3		
No	14	3		
Memory decline			1.025	0.311
Yes	13	2		
No	10	4		
Recurrence			0.873	0.350
Yes	3	0		
No	20	6		

Table 3. Relationship between treatment and memory decline

	Memory decline	Without memory decline	Chi-square value	P value
Gross total resection			2.005	0.157
Yes	13	14		
No	2	0		
V-P shunt			0.166	0.684
Yes	3	2		
No	12	12		
*Radiotherapy			5.663	**0.017**
Yes	7	1		
No	8	13		

*Including direct postoperative radiotherapy and re radiotherapy after recurrence

Postoperative radiotherapy and recurrence

Five patients (17.2%) received radiotherapy after the first operation, and none of the patients who received postoperative radiotherapy had tumor progression. Among the 24 patients who did not receive radiotherapy, 3 large central neurocytoma patients had tumor recurrence in the first year, the third year and the second year. The first patient received radiotherapy after the second operation, and the other two patients received radiotherapy directly. As of the last follow-up, there was no sign of tumor progression, and no deaths occurred. However, there was no significant statistical correlation between radiotherapy and the tumor recurrence rate (Table 4).

Table 4. Correlation between tumor recurrence and treatment

	Recurrence	Non recurrence	Chi-square value	P value
Gross total resection			0.248	0.618
Yes	3	24		
No	0	2		
Radiotherapy			0.697	0.403
Yes	0	5		
No	3	21		

Average length of stay and KPS score

The average length of stay of the patients was 28.28 ± 17.41 days (12-110 days). The average KPS score of the patients at discharge was 77.59 ± 7.40. As of the last follow-up, the average KPS score was 90.34 ± 6.81. Except for one patient, who needs to be taken care of by his family, all the other patients can live and work independently and normally.

Discussion

Most central neurocytomas show benign biological behavior. If total tumor resection can be achieved, patients can obtain a good prognosis [9, 10]. However, because most of the central neurocytomas are located in the ventricles of the brain, and the tumors are deep and adjacent to many important brain structures, the operation risk is high. In particular, tumors with large volumes occupy bilateral ventricles. Therefore, the key to treatment is to choose the appropriate surgical approach to achieve the maximum range of safe tumor resection and the prevention and treatment of postoperative complications, such as brain edema and hydrocephalus. At the same time, due to the deep location of the tumor, it is difficult to achieve complete resection; therefore, it is still controversial whether radiotherapy can prevent tumor recurrence in such patients [11, 12]. Of the 29 patients in this group, 23 patients had an average maximum tumor diameter greater than 5 cm, 21 patients achieved total tumor resection, and 5 patients received radiotherapy after the first operation. We will discuss the experience of clinical treatment.

Surgical approach

Operation is the most basic treatment for central neurocytoma [4, 13]. The main purpose of the operation is to resect the tumor safely in the largest scope, open the circulation of cerebrospinal fluid to relieve hydrocephalus and clarify the pathological nature [14]. The common surgical approaches are transcortical and transcallosal approaches [15]. However, the best surgical approach is still controversial [16, 17]. Some studies have suggested that it is more appropriate to choose a transcortical approach when the tumor is located in the lateral ventricle, while the transcallosal approach for tumors located in the third ventricle can provide a shorter surgical path and reduce the destruction of the cortex [18]. Although some patients had hemiplegia, aphasia, fever, epilepsy and other complications, except for one patient, the other patients did not have permanent neurological deficits. The surgeon believed that although many of the tumors in this group occupied bilateral ventricles, most of the tumors originated from unilateral ventricles by squeezing the septum pellucidum to the contralateral ventricles. Therefore, large tumors can be completely removed through a unilateral transcortical approach. At the same time, transcortical access to the ventricles is more direct for the removal of tumors in the lateral ventricles and can also protect the corpus callosum. In addition, a transcortical approach can better protect the vein draining from the frontal cortex to the sinus to reduce postoperative complications such as brain edema. Therefore, we believe that the transcortical approach is an appropriate approach for the removal of large central neurocytomas occupying bilateral ventricles. Of course, in addition to the tumor volume, other major factors influencing the effect of surgery are also related to the degree of calcification of the tumor, the degree of adhesion between the tumor and the surroundings, the blood supply of the tumor, and the experience of the surgeon.

Prevention and treatment of postoperative brain edema

Brain edema is a serious postoperative complication of intraventricular central neurocytoma. First, we must protect the normal veins and tissue of the ventricle as much as possible and avoid over-stretching brain tissue during surgery [15]. Then, it is necessary to appropriately increase the dosage and frequency of dehydrating drugs to prevent and treat paraventricular edema. Additionally, the appropriate height of the drainage tube should be controlled after the operation to prevent the collapse of the ventricle caused by drainage that is too fast. Next, bleeding should be strictly controlled during the operation to prevent blood from flowing into the ventricle and inflammatory adhesion of the wall of the ventricle. Last, it is very important to recheck head computed tomography (CT) in a timely manner and to take corresponding treatment measures. In this group, 5 patients with hydrocephalus were treated with ventriculoperitoneal shunts after the failure of conservative treatment, but there was no statistical correlation between tumor volume and postoperative hydrocephalus.

Postoperative radiotherapy

It is still controversial whether radiotherapy should be used after central neurocytoma surgery. Some studies have suggested that central neurocytoma is highly sensitive to radiotherapy; thus, it is suggested that patients should be treated with postoperative radiotherapy to prevent and treat residual tumor recurrence [19–21]. In this group, 5 patients (23.8%) received radiotherapy after the first operation. None of the patients who received radiotherapy had tumor progression. Among the patients without

radiotherapy, three had tumor recurrence. One patient had tumor recurrence one year after the operation and then underwent reoperation and radiotherapy. The other two patients had tumor recurrence three years after the operation and two years after the operation. They received radiotherapy again. As of the last follow-up, these three patients had no sign of tumor recurrence. However, in recent years, it has been reported that postoperative radiotherapy has no effect on the overall survival rate of patients [12, 18] and will cause brain cognitive impairment and other adverse effects. There was no statistical correlation between radiotherapy and the tumor recurrence rate in this group of patients, and we found that there was a significant statistical correlation between memory decline and radiotherapy ($P = 0.017$). Considering that the pathological grade of central neurocytoma is WHO II, which belongs to benign tumors, the theoretical progress is slow. Therefore, after 2015, we no longer suggest that patients should receive radiotherapy directly after surgery, but we suggest that in these patients, MRI should be reviewed regularly after the operation, changes in condition should be monitored closely, and radiotherapy should be considered if there is progression.

Pathological diagnosis

Immunohistochemical results are mainly used for the diagnosis and prognosis of central neurocytoma. Syn [22] and neu-n are reliable diagnostic indexes of central neurocytoma. In most cases, syn staining was positive. Neu-n is mainly used to distinguish clear cell tumors of the central nervous system (central neurocytoma, oligodendrocytoma, clear cell ependymoma). According to previous literature, MIB-1 (Ki-67) may be a prognostic indicator [4, 23]. When MIB-1 (Ki-67) is more than 2%/3%, it may be harmful to the prognosis of patients [24]. In contrast to previous reports, we found that MIB-1 is not directly related to tumor recurrence in this group of patients, which may be related to our insufficient number of cases.

Limitation

Although we presented clinical data of 29 patients with large central neurocytoma, there are still some limitations to this study. First, due to the limited number of cases, there is a certain degree of statistical deviation. For example, we hold that extent of resection may be related to tumour recurrence, but our data analysis showed no statistical correlation. Therefore, a larger sample size will be needed in future studies.

Conclusions

Surgical resection of the tumor is the basis of the treatment of central neurocytoma. With total resection of the tumor and the protection of the normal ventricular structure and venous return, the patients may be cured. At the same time, the transcortical approach is a reliable approach for the removal of large tumors in the ventricle. This approach is not only conducive to the total removal of large central neurocytomas in the ventricle but also better to avoid injury to the corpus callosum and to protect normal venous return. Finally, the patients should be observed closely after surgery, and MRI of the head should be rechecked regularly. If the tumor has progressed, then radiotherapy should be considered.

Abbreviations

CN
Central Neurocytoma;
KPS
Karnofsky Performance Status

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committees of the two medical centers. The requirement for obtaining informed consent from patients was waived because the data sets were anonymous.

Consent for publication

Not applicable

Availability of data and materials

The datasets supporting the conclusions of this study are available from the corresponding author on reasonable request.

Conflicts of interest

The authors declare that they have no competing interests

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Authors' contributions

Conception and design: Zhixian Gao, Jiannong Zhao and Nan Ji. Acquisition of data: Lanbing Yu, Bo Cen, Yehong Fang, and Heyuan Jia. Analysis and interpretation of data: Chaocai Zhang, Xingchao Wang, and Junling Wang. Drafting the article: Chaocai Zhang. Critically revising the article: Zhixian Gao, Jiannong Zhao and Nan Ji. Reviewed the submitted version of the manuscript: Zhixian Gao, Jiannong

Zhao, Nan Ji, Lanbing Yu, and Shuyu Hao. Performed the statistical analysis: Chaocai Zhang. Study supervision: Zhixian Gao.

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Figures

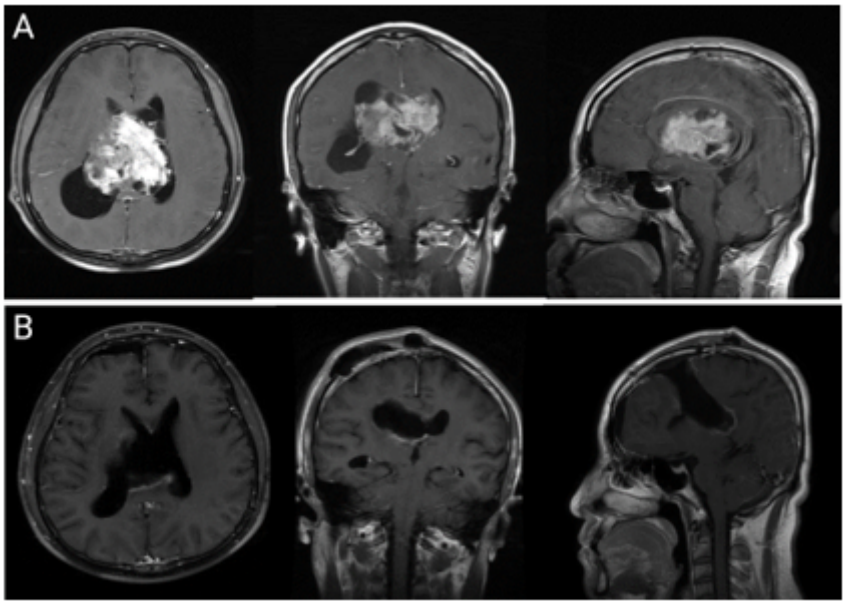

Figure 1

Head MRI of one central neurocytoma patient who underwent a transcortical approach tumor resection. A: Preoperative enhanced head MRI; B: Postoperative enhanced head MRI. The tumor was subjected to a gross total resection.