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Treatment Outcomes of Intraventricular Meningiomas

뇌실내 수막종에 대한 치료결과

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ABSTRACT

Introduction: Intraventricular meningioma is a rare disease among all meningiomas. Although microsurgery for intraventricular meningiomas remains a standard treatment, it is challenging procedure because of relatively high incidence of post-operative neurologic deficit. As result, stereotactic radiosurgery has been introduced as alternative. We summarized treatment outcomes of two modalities.

Methods: A total 55 patients were enrolled; 36 and 19 patients underwent microsurgery and stereotactic radiosurgery for primary treatment, respectively. Under approval of review board, demographic and clinical data was obtained using electronic medical records. Radiologic studies were reviewed for measuring volumes of tumors as well as identifying recurrence. Risk factor analysis for tumor recurrence and post-operative neurologic deficit was performed.

Results: The mean age of patients was 46.0±14.8. There were 40 (72.7%) female patients. The most common symptom was headache. The mean tumor diameter was measured as 4.2cm. In microsurgery group, gross total resection was achieved in 32 (88.9%) cases. Benign pathology was confirmed in 29 (80.6%) cases. In 4 cases with remained choroid plexus during microsurgery, 2 experienced tumor recurrence. Remained choroid plexus was a single risk factor related with tumor recurrence. Nineteen (52.8%) experienced newly developed neurologic deficit and it was remained permanently in 14 (38.9%) patients. Left-sided tumor was identified as risk factor. In stereotactic radiosurgery group, there was no progression case during 43 months follow-up. However temporary tumor expansion was observed in 6 (31.6%) cases. There was no patient presenting neurological change.

Conclusions: For preventing tumor recurrence, resection of choroid plexus seems to be important during microsurgery. The incidence of post-operative neurologic deficit is relatively high, especially in the case of left-sided tumors. In limited cases, stereotactic radiosurgery seems to be effective and safe.

Keywords: Intraventricular meningioma; Microsurgery; Stereotactic Radiosurgery

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Contents

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LIST OF ABBREVIATIONS

C.I., confidential interval

GTR, gross total resection

IVMNG, intraventricular meningioma

KPS, Karnofsky performance status

MRI, magnetic resonance image

PFS, progression-free survival

SRS, stereotactic radiosurgery

STR, subtotal resection

WHO, World Health Organization

Introduction

Meningiomas are one of the most common intracranial tumors. The incidence of meningioma was revealed as 3.5 per 100,000 person-years and it occupied 30.6% of all primary tumors of central nervous system by nationwide epidemiologic study in Korea.[1]

Among all meningiomas, intraventricular meningiomas (IVMNGs) represented rare portion. The incidence of IVMNGs had been reported as rare as 0.5-5% of all meningiomas.[2-6] Several studies about clinical outcomes after microsurgery had been reported.[3-9] However, microsurgery for IVMNGs remains a challenging procedure because of deep location of tumor, surrounding vascular structures, eloquent cortical area, and the course of subcortical tracts.[6] As results, several authors reported relatively high incidence of post-operative permanent neurologic deficit.[3,5,6] Due to these high surgical morbidities, stereotactic radiosurgery (SRS) for small IVMNGs has been introduced as alternative.[10-12] But, as far as we known, treatment outcomes after SRS for IVMNGs had been reported only as small series of cases.

In this study, we investigated clinical data about treatment outcomes of microsurgery for IVMNGs including possible factors related with tumor recurrence and post-operative neurologic deficits. And we summarized treatment outcomes of SRS with measurement of serial volume changes as well as clinical features.

Materials and Methods

Patients

Between 1991 and 2011, a total 3856 patients were treated meningiomas in our two institutions (Seoul National University Hospital and Seoul National University Bundang Hospital). In the period, 61 patients (1.6%) received primary treatment for IVMNGs. Microsurgery was performed as primary treatment for 38 patients (62.3%) and SRS was done for 23 patients (37.7%). Among them, follow up medical record was not available for 1 patient and pathologic report was not for 1 patient underwent microsurgery. And follow up magnetic resonance image (MRI) was not available in 4 patients underwent SRS. After exclusion of these 6 patients, 55 patients (36 microsurgery, 19 SRS) were enrolled finally.

All patient data were collected under approval of institutional review board. Ages, sex, neurological status with Karnofsky performance status (KPS) scale at the time of treatment, follow-up and tumor recurrence were reviewed with medical records. Tumor location, size, and volume were measured with MRI taken at pre- and post-treatment. Pathologic reports of patients underwent microsurgery were reviewed also.

Treatment modalities

Among 36 patients underwent microsurgery, transcortical approach was used for 35 patients (97.2%); temporal transcortical approach was most commonly used (21 patients, 60.0%), followed by parietal transcortical (12 patients, 34.3%), occipital transcortical (2 patients, 5.7%). Interhemispheric approach was used in a single case (3.8%).

The extent of surgical removal was classified using post-operative MRI. And descriptions of medical record were used for 2 patients underwent MRI at other hospital. The classifications were as in the following, gross total resection (GTR, no residual enhancement), subtotal resection (STR, any residual enhancement related with tumor). Pathologic report was reviewed and classified in benign (WHO grade I) and high-grade (WHO grade II or III).

After installation of Gammaknife (Elekta Instrument, Stockholm, Sweden) in 1997, SRS has been applied for IVMNG, which was smaller than 3cm in diameter without severe neurologic symptoms thought to be caused by mass effect. The patients underwent SRS were diagnosed radiologically using MRI features following; an isolated mass in lateral ventricle with homogeneous enhancement after gadolinium enhancement, and isointense or hyperintense signal on T2-weighted images.[10]

For SRS, Leksell Model G frame was installed to the patients' head under local anesthesia. Thin-sliced multi-planar MR images were obtained with and without contrast for treatment planning with Leksell Gamma Plan. The mean marginal dose of 14.5±1.70 was eradiated for IVMNGs (mean volume, 6.64cc). Isodose line was targeted at 50% in 18 patients, 49% in 1 patient. All of patients were given 10mg of dexamethasone intravenously followed by tapering with oral prednisolone over 1 week.

Follow-up and Data Analysis

Follow-up MRI was taken at 12 months for most of patients. Especially, for patients underwent SRS, 3 months and 6 months follow-up MRI was performed routinely. The volume and diameter of tumors were measured with our picture archiving and communication systems; INFINITT (Infinitt healthcare, Seoul, Korea) and Maroview (Marotech, Seoul, Korea).

The radiologic volume status was defined as either tumor shrinkage (the sum of products of diameters decreased by ≥20%) or tumor expansion (the sum of products of diameters increased by ≥20%) according to the previous measurement classification used in the field of SRS for vestibular schwannomas.[13] Tumor recurrence was defined as following; any progression from residual tumor after operation, or newly detected tumor after gross total removal.

Statistical analysis was made by computing package, SPSS 19 (IBM, Chicago, Illinois, USA). The categorical data were analyzed by Pearson chi-square test and Fisher’s exact test. The continuous variables were presented as mean±standard deviation and analyzed by Mann-Whitney U test because of modest size of patients. Kaplan-Meier survival analysis was performed to calculate 5-year tumor recurrence rate. Factors affecting progression and post-operative neurologic deficit were analyzed with Cox regression test and Binominal regression test, respectively.

Study Approval

This study was approved by institutional review board of Seoul National University Hospital (J-1309-011-518) and Seoul National University Bundang Hospital (B-1309/220-401).

Results

The mean age of patients was 46.0±14.8. The patients underwent microsurgery was younger than SRS group (42.6±14.9 vs. 52.3±12.8). Female predominance was observed in both groups (66.7% in microsurgery, 84.2% in SRS). The mean follow-up duration was 65.3±63.0 months.

The most common initial symptom was headache (n=26, 47.3%), followed by hemiparesis (n=8, 14.5%), dizziness (n=7, 12.7%), nausea/vomiting (n=6, 10.9%), seizure (n=2, 3.6%) and others (n=2, 3.6%). Four patients were incidentally diagnosed (7.3%).

Table 1. The characteristics of patients.

		Microsurgery n=36	SRS n=19	Total n=55	p-value
Age		42.6±14.9	52.3±12.8	46.0±14.8	0.026*†
Sex	Male	12(33.3)	3(15.8)	15(27.3)	0.165‡
	Female	24(66.7)	16(84.2)	40(72.7)	
KPS scale	Pre-treatment	90.8±12.0	95.8±9.0	92.6±11.3	0.041*†
	Post-treatment	79.2±24.9	96.3±9.0	85.1±22.3	<0.001*†
Follow up duration		77.2±71.1	42.7±35.3	65.3±63.0	0.184†
Initial symptoms	Headache	21(58.3)	5(26.3)	26(47.3)	
	Weakness	6(16.7)	2(10.5)	8(14.5)	
	Dizziness	1(2.8)	6(31.6)	7(12.7)	
	Vomiting	4(11.1)	2(10.5)	6(10.9)	
	Seizure	2(5.6)	0(0)	2(3.6)	
	Incidental	1(2.8)	3(15.8)	4(7.3)	
	Etc.	1(2.8)	1(5.3)	2(3.6)	

Continuous variables are presented as mean±standard deviation. Categorical variables are presented as number (percentage).

*, statistical significance; †, Mann-Whitney U test; ‡, Pearson chi-square test

SRS, stereotactic radiosurgery; KPS, Karnofsky Performance Status

Patients in the microsurgery group showed poorer performance at the time of treatment compared with the SRS group (90.8 vs. 95.8, KPS scale, p=0.041). The clinical data of all enrolled patients were summarized in Table. 1

Twenty-eight tumors are found in right side and 27 tumors in left side. The distribution of tumor were trigone (n=46, 83.6%), temporal horn (n=5, 9.1%), occipital horn (n=3, 5.5%) and frontal horn (n=1, 1.8%). The mean of maximal diameter of tumors was 4.20±1.76cm (range, 1.41-9.00cm). It was significantly larger in the microsurgery group (5.19cm vs. 2.44cm, p<0.001). However, tumor locations including left/right distribution were similar between two groups. IVMNGS were found most commonly in trigone in both groups. The characteristics of tumors were summarized in Table. 2

Table 2. The characteristics of tumors.

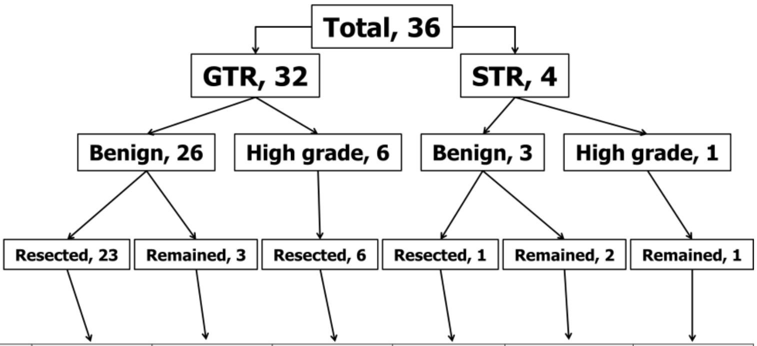
	Microsurgery n=36	SRS n=19	Total n=55	p-value
Diameter	5.19±1.38	2.44±0.56	4.20±1.76	<0.001*†
Left	17(47.2)	10(52.6)	27(49.1)	0.703‡
Right	19(52.8)	9(47.4)	28(50.9)	
Trigone	28(77.8)	18(94.7)	46(83.6)	
Temporal horn	4(11.1)	1(5.3)	5(9.1)	
Occipital horn	3(8.3)	0(0)	3(5.5)	
Frontal horn	1(2.8)	0(0)	1(1.8)	

Continuous variables are presented as mean±standard deviation. Categorical variables are presented as number (percentage).
*, statistical significance; †, Mann-Whitney U test; ‡, Pearson chi-square test
SRS, stereotactic radiosurgery

Subgroup analysis: Microsurgery

GTR was achieved in 32 (88.9%) cases, and STR in 4 cases (11.1%). The reason of STR cases were as followed; due to poor visualization of tumor combined with the result of frozen biopsy (high grade ependymoma), massive brain swelling during operation, strong adhesion to ependyma, small residual enhanced tumor despite of surgeon's judgment of GTR. But in the first case, pathologic report revealed that it was meningioma.

In 36 operation records, we could found mention about handling of choroid plexus during microsurgery. Among them, removal of choroid plexus after cauterization was identified in 28 cases. In four cases, choroid plexus was visible in the ventricle after resection of IVMNGs according operation note. In remaining two of four cases, choroid plexus was not observed in post-operative T1 enhanced MRI. (Figure 1)



No recurrence	22	1	5	1	1	1
Recurrence	1 (4.3%)	2 (66.7%)	1 (16.7%)	0 (0.0%)	1(50.0%)	0(0.0%)
Interval (months)	48	12, 99	37		18	

Figure 1. Schematic diagram of treatment course of 36 patients. Resected, Remained, refer to handling of choroid plexus during microsurgery.
GTR, gross total resection; STR, subtotal resection

Two patient underwent GTR was treated with whole brain radiotherapy considering pathologic diagnosis (high-grade). Also, for 2 patients who underwent STR, SRS was performed as adjuvant treatment.

Histopathologic examination revealed that 29 (80.6%) tumors were benign; 18 (50.0%) transitional, 7 (19.4%) meningothelial, 3 (8.3%) fibrous and 1 (2.8%) sclerosing meningiomas. On the other hand, 7 (19.4%) were high-grade meningiomas; 6 (16.7%) WHO grade II and 1 (2.8%) anaplastic.

Recurrence was observed in 5 of 36 (13.9%) microsurgery group patients during mean follow-up duration of 77 months. The mean time interval of recurrence was 42.8±34.5 months. Among 26 patients underwent GTR for benign IVMNGs, 3 (11.5%) experienced recurrence within 53 months of mean interval. Among 3 patients, choroid plexus was remained and resected in each single case.

One (16.7%) of 6 high grade IVMNGs of GTR group recurred at 37 months follow-up, whereas there was no recurrence among two of six got radiotherapy as adjuvant treatment. One (25.0%) of 4 patients underwent STR, 1 patients experienced recurrence after adjuvant SRS for benign IVMNG at 18 months follow-up. In this patient, choroid plexus was remained with residual tumor. (Table 3)

Table 3. Five patients experienced tumor recurrence after microsurgery.

Sex/Age	Location	Diameter (cm)	Resection	Choroid Plexus	Adjuvant	Pathology	Interval (months)
M/20	Frontal horn	4.4	GTR	Remained	No	Meningothelial	12
F/58	Occipital horn	6.5	STR	Remained	SRS	Transitional	18
M/51	Trigone	7.0	GTR	Resected	No	Atypical	37
F/27	Trigone	5.2	GTR	Resected	No	Transitional	48
M/29	Temporal horn	5.0	GTR	Unknown	No	Meningothelial	99

GTR, gross total resection; SRT, subtotal resection; SRS, stereotactic radiosurgery

The overall 5-year tumor recurrence rate was 16.8%. Within the GTR group, it was 14.5%, whereas it was measured as high as 33.3% in STR group. In the aspect of pathology, 5-year tumor recurrence rate was 14.6% in benign group and 25.0% in high-grade group. Among patients underwent resection of choroid plexus, 5-year tumor recurrence rate was 13.3%. It was 66.7% in remained choroid plexus group.

Remained choroid plexus was revealed as a single significant risk factor by Cox regression, univariate analysis for tumor recurrence. Multivariate analysis was not performed.

Table 4. Risk factor analysis related with tumor recurrence.

	Hazard ratio	*p*-value	95% Confidence interval
Age	0.978	0.511	
Sex (Male)	3.555	0.169	
Side (Left)	0.296	0.277	
Diameter	1.342	0.393	
Pathology(High grade)	1.250	0.843	
Extent of resection (STR)	3.885	0.246	
Choroid plexus resection	0.095	0.010*	0.016 – 0.573
Adjuvant treatment	0.430	0.465	

Hazard ratio was measured with Cox regression test
*, statistical significance; STR, subtotal resection

Newly developed or aggravated neurologic deficits after operation were occurred in 19 (52.8%) patients. Most common immediate post-operative neurologic deficit was hemiparesis (n=8, 22.2%), and in 5 of those cases experienced gradual recovery enough to walk without assistance. The following deficit was visual disturbance (e.g., field defect) (n=6, 16.7%). Five (13.9%) patients suffered from language problem such as motor or sensory aphasia. However, no one experienced improvement of visual or aphasia symptoms during follow-up period. Permanent neurologic deficit was remained as sequalae in 14 (38.9%) cases. The most common permanent neurologic deficit was visual field defect. (Table 5) One patient became bed-ridden status after cardio-pulmonary resuscitation caused by massive bleeding followed by hypovolemic shock during operation.

Table 5. Summary of neurologic deficit related with microsurgery

	Weakness	Visual disturbance	Language disturbance	Total
Temporary	5(13.9)	-	-	5(13.9)
Permanent	3(8.3)	6(16.7)	5(13.9)	14(38.9)
Total	8(22.2)	6(16.7)	5(13.9)	19(52.8)

Categorical variables are presented as number (percentage).

We could not identify risk factors showed statistical correlation with all post-operative neurologic deficits. But as to permanent neurologic deficit, left sided tumor was revealed as a single risk factor. (Table 6)

One patient died of post-operative hemorrhagic complication. Immediate post-operative mortality and morbidity rate were 2.8% and 58.3%, respectively.

Table 6. Risk factor analysis related with permanent neurologic deficit.

	Hazard ratio	*p*-value	95% Confidence interval
Age	1.030	0.233	
Sex (Male)	2.538	0.234	
Side (Left)	5.357	0.025*	1.2 – 23.2
Diameter	0.884	0.640	
Pathology(High grade)	1.765	0.536	
Extent of resection (STR)	0.175	0.150	
Choroid plexus (Remained)	0.515	0.586*	

Hazard ratio was measured with Binominal logistic regression
*, statistical significance; STR, subtotal resection

Subgroup analysis: SRS

The mean follow-up duration of 19 patients underwent primary SRS for IVMNGs was 42.7±35.3 months after SRS. The tumor size ratio was measured by the sum of products of diameters comparing to initial MRI. In 6, 12, 24 and 60 months follow-up MRI, the mean tumor size ratios were 1.06±0.07, 1.08±0.08, 1.10±0.05 and 1.02±0.04, respectively. Gradual changes of tumor size ratio were diagrammatized in Figure 2.

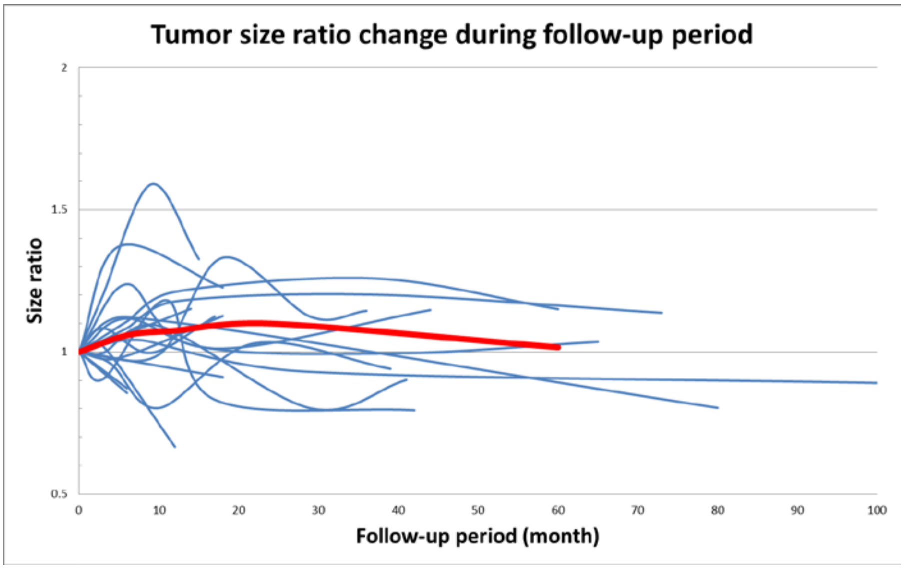


Figure 2. Each line represents the change of tumor size ratio during follow-up of single case underwent SRS. Thick red line means mean value of tumor size ratio.

Transient tumor expansion was observed in 6 (31.6%) patients. The mean time interval was 13.5 months from SRS. However, further treatment for radiologic progression was not considered because no patients presented related symptoms. After careful observation, the tumor size ratios were decreased after peak in all patients. The mean regression period was 16.2 months from detection. The parameters of SRS (e.g. volume, dose) did not influence tumor expansion.

There were 2 (10.5%) cases presenting tumor shrinkage. Tumor size ratio was measured as 0.67 and 0.80 in follow up MRI taken 12 and 42 months from SRS, respectively.

Tumor size ratio of other 11 (57.9%) patients presented stable during follow up. One of these patients presented aggravated left side weakness after 3 months from SRS. Follow-up MRI revealed enlarged peri-tumoral edema with stable tumor size. This symptom was transient and recovered by temporary prescribed steroid. There were no patients presenting newly developed post treatment neurologic change.

In spite of several cases of transient tumor expansion, overall clinical tumor control rate was 100% because no patient needed additional treatment for IVMNGs after SRS.

Discussion

In this study, 5 (13.9%) patients experienced tumor recurrence and overall 5–year tumor recurrence rate was measured as 16.8% after microsurgical resection. Previous studies had reported various rate of recurrence (4.5-16.7%) during various follow up duration.[3-5,7,8] Despite the authors of previous works did not provide either time courses of recurrences or mean follow-up duration, simple proportion of tumor recurrence was similar with literatures. However, these results should be interpreted carefully, because the proportions of GTR/STR and benign/high-grade were different among literatures.

In recent investigation for meningioma recurrence after resection, The 5-year recurrence after Simpson Grades I, II, III, and IV resections was 5, 15, 12, and 19%, respectively for benign meningiomas.[14] In subgroup analysis of benign IVMNGs in this study, 5-year recurrence rate was 14.6%. Among patients underwent resection of choroid plexus, it was lowered as 8.3% which was comparable to the result of Simpson Grade I resection. While it was uncertain, the histologic origin of IVMNGs was thought to be derived from arachnoid of choroid plexus.[15] In this regard, identifying and resecting the choroid plexus is thought to be crucial for preventing recurrence of tumor after resection, which is similar with removing originated dura of other meningiomas.

In this study, 8 (22.2%) patients experienced new onset or worsened hemiparesis after microsurgery. Though hemiparesis was the most common immediate post-operative neurologic deficit, 5 patients recovered and could walk without assistance. Only 3 (8.3%) patients remained dependent. In the aspect of post-operative hemiparesis, gradual improvement was reported by other investigators.[3,9]

On the other hand, most common new onset permanent neurologic deficit was visual disturbance which was occurred in 6 (16.7%) patients. This neurologic change was known to be due to injury of the optic radiation during transcortical approach. Previous reports showed various rate of post-operative visual disturbance (7.8-22.7%).[3,5-7,9] The following permanent neurologic disturbance was language disturbance (n=5, 13.9%). Wang et al. reported 3.9% incidence of post-operative sensory aphasia and Lyngdoh et al. did 11.1% of transient expressive aphasia. Comparing with visual disturbance, there had been few reports regarding post-operative aphasias.

We could identify left-sided tumor as a risk factor of post-operative neurologic deficit. This finding was thought to be reasonable because the majority of permanent post-operative neurologic deficit was consisted with visual and language disturbance.

Because of these high incidences of morbidity, SRS for IVMNGs had been introduced as alternative. SRS for primary treatment of other meningiomas had shown acceptable outcomes and complication profiles.[16-18] However, there had been few reports about SRS for IVMNGs. In the largest series before this study, 5 patients underwent SRS for IVMNGs as a primary treatment.[10] During long-term follow up, 1 patient experienced tumor progression after 61 months from SRS. Authors reported that there was no SRS related complication. In this study, we reviewed 19 cases of small IVMNGs (<3cm in diameter) treated with SRS. In this study, there was no clinical progression after SRS during 42.7±35.3 months follow up period. And treatment related complication was observed in only 1 (5.3%) patient transiently. However, it was hard to expect reduction of the tumor size. Furthermore, transient volume expansion was observed in 6 (31.6%) cases. Therefore, for patients suffered from severe neurologic symptoms thought to be caused by mass effect, microsurgery should be performed for prompt decompression.

The comparison between treatment modalities for IVMNGs could not be conducted. First of all, critical selection bias existed necessarily due to the difference of indications. Moreover, initial patients' conditions including age and KPS were significantly different. Nevertheless, long term series published before as well as this study could provide valuable information for consideration of treatment for IVMNGs.

Conclusion

The incidence of permanent post-operative neurologic deficit is relatively high, especially in the case of left-sided IVMNGs. However, surgical resection should be performed in cases of larger IVMNG causing neurologic deterioration. During microsurgery, resection of choroid plexus as origin of IVMNGs seems to be important for preventing tumor recurrence.

For small sized IVMNGs, SRS for IVMNGs seems to be effective and safe modality as primary treatment.

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국문초록

배경: 뇌실내 수막종은 전체 수막종 중 드문 비율을 보이는 질환이다. 이데 해나 표준치료는 수술적 제거이지만, 수술 후 신경학적 장애를 보이는 비율이 높은 편이다. 이러한 위험 때문에 최근 정위적 방사선수술이 뇌실내 수막종의 치료에 도입되었다. 본 연구에서는 뇌실내 수막종에 대한 미세수술 및 방사선수술의 결과를 고찰하였다.

방법: 뇌실내 수막종에 대한 일차치료로 미세수술을 받은 36례와 방사선수술을 받은 19례의 의무기록 및 영상학적 검사 소견을 후향적으로 정리하였다. 종양의 재발 및 크기 변화를 측정하였고, 미세수술 및 방사선수술 이후 신경학적인 변화를 조사하였다. 총 55례에 대하여 윤리위원회의 승인을 획득하였다.

결과: 환자군의 평균 연령은 46.0±14.8세 였다. 40명의 환자(72.7%)는 여성이었다. 진단당시 증상은 두통이 가장 흔하였다. 수막종의 평균 지름은 4.2cm였다. 미세수술군에서 32명의 환자가 종양 전적출을 시행받았다. 36례 중 29례에서 WHO grade I 수막종으로 진단되었다. 수술기록과 수술 후 영상을 분석한 결과 맥락총의 제거 여부가 종양 재발에 대한 위험인자로 확인되었다. 수술 후 신경학적 결손은 19례 (52.8%) 에서 보였고, 이 중 14례 (38.9%)는 영구적 신경학적 장애가 남았다. 수술 후 신경학적 장애에 대해서는 좌반구에 위치한 종양이 위험인자로 확인되었다. 방사선수술군에서는 일시적인 종양용적의 증가가 6례 (21.6%)에서 관찰되었으나, 임상적으로 재치료가 필요한 경우는 추적관찰 기간 중 없었다.

결론: 뇌실내 수막종을 미세수술로 제거할 시에는 맥락총을 제거하는 것이 재발방지를 위해 중요하다. 수술 후 신경학적 결손은 특히 좌반구에 위치한 종양을 수술할 때 높은 빈도로 발생하였다. 크기가 작고 증상이 심하지 않은 경우에 방사선수술은 뇌실내 수막종에 대한 치료로 안전하며 유용하다.

주요어: 뇌실내 수막종; 미세수술; 방사선수술

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