The clinical features and surgical outcomes of patients with intramedullary spinal cord cavernous malformations

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The clinical features and surgical outcomes of patients with intramedullary spinal cord cavernous malformations

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<TABLE OF CONTENTS>

ABSTRACT ····· 1

I. INTRODUCTION ····· 3

II. MATERIALS AND METHODS ····· 5

1. Patient Population ····· 5

2. Radiologic Study ····· 6

3. Surgery ····· 7

4. Follow-up ····· 7

5. Statistical Analysis ····· 7

III. RESULTS ····· 8

1. Clinical presentation and radiologic findings ····· 8

2. Surgical procedures and findings ····· 12

3. Surgical outcomes and prognostic factors ····· 12

4. Illustrative Cases ····· 15

IV. DISCUSSION ····· 21

V. CONCLUSION ····· 24

REFERENCES ····· 25

ABSTRACT(IN KOREAN) ····· 29

LIST OF FIGURES

Figure 1. Case 11. CM located at T2 level. ····· 15

Figure 2. Case 12. CM located at cervicomedullary junction. ····· 17

Figure 3. Case 16. CM located at C5 level. ····· 19

LIST OF TABLES

Table 1. Modified McCormick scale for functional classification of patients with CMs ····· 6

Table 2. The clinical characteristics of patients with CMs ····· 9

Table 3. The Summary of characteristics of patients with intramedullary CMs ····· 11

Table 4. The Preoperative neurological status and postoperative outcome (MMCS) ····· 13

Table 5. Type of symptom presentation and postoperative outcome (MMCS) ····· 14

ABSTRACT

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CMs are not uncommon, but most of them are found in intracranial location. Intramedullary CMs are rare, accounting for only 3–5% of the total central nervous system lesions identified. The natural history of intramedullary CMs and their clinical features including the risk of hemorrhages from a large series still remains unclear and need to be elucidated.

Between March 2004 and March 2010, a total of 21 patients with intramedullary spinal cord CMs were surgically treated in a single institution. Data from 21 patients were analyzed retrospectively.

There were thirteen females and eight males who ranged in age from 10 to 70

years (mean age 39.3 years). All patients harbored single symptomatic CM of the nervous system, and multiple lesions were not found. The annual retrospective hemorrhage rate was 2.2% per patient/year. All except one CM were completely resected and the average follow-up period was 22.1 months (1–73 months). Ten of the 21 patients experienced an improvement of the neurological state, nine patients remained unchanged, and two patients worsened.

Symptomatic intramedullary CMs should be surgically removed to avoid further neurological deterioration. The prognosis was related to the preoperative neurologic state and the type of symptom presentation.

Key words : Cavernous malformations, Spinal cord, Intramedullary

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I. INTRODUCTION

Cavernous malformations (CMs) are angiographically occult vascular malformations that can arise in any part of the central nervous system. Two large retrospective reviews found an overall incidence rate of 0.4-0.5% in general populations[1,2]. They are not uncommon, but most of them are found in intracranial locations, especially in supratentorial compartments[3]. Intramedullary CMs are rare, accounting for only 3–5% of the total CNS lesions identified[4-9].

There are many reports regarding the natural history and surgical outcomes of the intramedullary CMs. In contrast, most of them are case series with a small number of patients and few authors presented a series of more than ten cases[10,11]. The natural history of intramedullary CMs and their potential risk of hemorrhage from a large series still remains unclear and need to be elucidated. In this study, we retrospectively reviewed a series of 21 patients with surgically treated intramedullary CMs in a single institution and discuss the clinical features, potential risk of hemorrhage, surgical outcomes and prognostic factors

II. MATERIALS AND METHODS

1. Patient Population

Between March 2004 and March 2010, a total of 618 patients with spinal cord tumors were surgically treated in our institution. Among them, 21 patients harbored histologically proven intramedullary spinal cord CMs and their charts were reviewed retrospectively. All patients had single symptomatic CM of the nervous system, and multiple lesions were not found. There were 13 female and 8 male patients ranging in age from 10 to 70 years (mean age 39.3 years. Our criteria for a hemorrhage were sudden the onset of neurologic symptoms and corresponding manifestation of neurologic deficits. The annual retrospective hemorrhage rate was calculated by the following formula.

Hemorrhage rate = the number of the hemorrhagic events/ summation of patient age in years

The patient's pre- and postoperative neurological states were classified according to the modified McCormick scale (MMCS)[12](Table 1).

Table 1.

Grade	Definition
1	neurologically intact, ambulates normally, may have minimal dysesthesia
2	mild motor or sensory deficit, maintains functional independence
3	moderate deficit, limitation of function, independent with external aid
4	severe motor or sensory deficit, dependent with external aid
5	paraplegia or quadriplegia

We identified some common features of symptom presentation among patients with CMs and classified the patients into the following 3 groups:

1) A: acute onset of symptoms
2) C: chronic progressive myelopathy
3) M: acute neurologic decline from various sequelae by previous attack

2. Radiologic Study

The preoperative radiological investigation included the plain films and magnetic resonance imaging (MRI) in all cases. The postoperative MRI was performed in selected cases under the agreement of the patients during the follow-up period.

3. Surgery

Patients were placed prone and additional 3-point skull fixation was used for lesions above the upper thoracic level. An operative approach was made through conventional laminectomy in the early days of surgery and through laminoplastic laminotomy. The surgery was performed under the standard microsurgical conditions with intraoperative monitoring of somatosensory evoked potentials (SSEP) to minimize the risk of neurologic injury. After the opening of the dura over the location of the lesion as defined by MRI, the myelotomy was performed and the lesion was removed along the gliotic plane surrounding the malformation.

4. Follow-up

The follow-up of patients were performed via an outpatient department clinic or by telephone interviews. The average follow-up period was 22.1 months (1–73 months).

5. Statistical Analysis

Statistical analysis was carried out using Kruskal-Wallis test and Mann-Whitney test with SPSS (Statistical Package for Social Science) for Windows Release 14.0 to analyze the differences in outcomes. A p value less than 0.05 was considered statistically significant.

III. RESULTS

1. Clinical presentation and radiologic findings

The clinical data of the patients with cavernous malformations are listed in Table 2.

Table 2.

Case No.	Age (yrs)	Sex	Symptoms & signs	Duration (mos)	Symptom type	Radiologic findings			Extent of resection	MMCS			F/u (mos)
						Level	Size(mm)	Location		Preop	Postop	Last	
1	35	M	Lt hemiparesis, sensory change	2	A	C2	9.6	Lt	Total	3	2	2	73
2	32	F	Paraparesis, voiding & defecation difficulty	1	A	T7	9.2	C	Total	4	4	2	61
3	10	F	back pain, gait disturbance, Lt hand pain	0.1	A	C6/7	19.5	C	Total	2	2	1	60.5
4	70	F	Both leg pain, paraparesis	24	M	T6/7	9.9	Rt	Total	3	3	3	60
5	69	M	Paraparesis, both leg pain, hypoesthesia below T4	36	M	T5	12.0	C	Total	2	3	2	55
6	17	F	Lt leg pain, paraparesis, voiding & defecation difficulty	0.5	M	L1	15.8	C	Total	3	3	2	54
7	29	M	Rt arm pain, Lt arm & leg numbness	96	C	C3-4	26.7	C	Subtotal	1	1	1	52
8	37	F	Paraparesis, Lt leg sensory change	14	C	T3	6.4	Rt	Total	3	2	2	50
9	33	F	Lt arm tingling, sensory change, gait disturbance	60	C	C5/6	11.4	Lt	Total	2	2	2	43
10	27	F	Paraplegia, leg pain, sole tingling sense	24	M	T11	11.6	C	Total	5	3	2	40
11	45	F	Lt leg numbness, tingling sense	2	C	T2	9.0	C	Total	1	1	1	26
12	43	M	Hand paresthesia and pain	6	C	C-M junction	15.5	C	Total	2	2	2	25
13	33	M	Lt hand and hemibody tingling sense, Lt arm pain	4	C	C4/5	7.2	C	Total	1	2	2	20
14	26	F	Paraparesis, Rt foot tingling sense	19	A	T12/L1	7.0	C	Total	1	1	1	13
15	49	M	Lt hand weakness, Rt hand numbness	1	A	C5	7.7	Lt	Total	3	1	1	12
16	24	F	Quadriparesis	0.1	A	C5	14.6	Rt	Total	4	2	2	17
17	59	F	Quadriparesis	312	A	C2	16.6	Rt	Total	2	1	1	12
18	57	F	Sensory change below T6, subjective paraparesis	24	C	T2/3	11.6	Rt	Total	2	1	1	12
19	40	M	Paraparesis, unrinary urgency	46	M	T9	12.4	Rt	Total	2	3	3	6
20	56	F	Lt arm pain	36	C	C4	4.9	Lt	Total	1	1	1	5
21	35	M	Lt butock, inguinal area pain, voiding difficulty	2	A	T11	10.9	C	Total	1	1	1	1

* No=number; yrs=years; mos=months; C-M=cervicomedullary; Lt=left; Rt=right;Op=operation; F/u=follow up; C=Central; A=acute onset of symptoms; C=chronic progressive myelopathy; M=acute neurologic decline from various sequelae by previous attack

We observed total 18 hemorrhagic episodes in 826 patient-years of life. Namely, there were 8 patients with 1 hemorrhagic episode and 5 patients with 2 hemorrhagic episodes. Assuming that patients were harboring cavernous malformation already at birth, the retrospective hemorrhage rate would be 2.2 % per lesion and year. The most common presenting symptom was a motor deficit. According to the above mentioned classification of symptom presentation, 8 patients were included in type A, 8 patients in type B, and 5 patients in type M, respectively. The level of the lesion was cervical in 9 patients, thoracic in 9 patients, lumbar in 1 patient, cervicomedullary junction in 1 patient, and thoracolumbar junction in 1 patient. The mean size of the lesion was 11.7 mm (4.9~26.7 mm). The location of the lesion within the spinal cord was central in 11 patients and lateral in 10 patients (Table 3).

Table 3.

Variables	
Mean age	38.4 (10-70) years
M : F	8 : 13
Mean symptom duration	37.0 (0.1-312) months
Symptom type	
A	8
C	8
M	5
Number of hemorrhages	
1	8
2	5
Mean size of lesion	11.7 (4.9-26.7) mm
Level	
Cervical	9
Thoracic	9
Lumbar	1
Cervicomedullary junction	1
Thoracolumbar junction	1
Location	
Central	11
Lateral	10
Extent of resection	
Total	20
Subtotal	1
Long term outcome	
Improved	10(48%)
Unchanged	9(43%)
Worsen	2(10%)

* No=number; A=acute onset of symptoms; C=chronic progressive myelopathy; M=acute neurologic decline from various sequelae by previous attack

2. Surgical procedures and findings

For the surgical approach, 10 patients underwent conventional laminectomy and 1 patient underwent additional suboccipital craniectomy. Nine patients underwent laminoplastic laminotomy and the remaining patient (Case 17) was reoperated case whose first operation was 13 years ago through laminectomy at the another hospital. After bony removal and the opening of the dura, the lesion itself or bluish discoloration of the pial surface was easily found in most of the patients. The myelotomy was performed over this area using the operating microscope. Cavernous angiomas generally have a gliotic plane separating the lesion from normal spinal cord and the complete resection from the center to periphery was possible in all except 1 patient. Intraoperative SSEP monitoring showed no significant change during the operation in all patients. We observed no major complications related to the surgical procedures.

3. Surgical outcomes and prognostic factors

Postoperatively, there were 8 patients with MMCS 1, 7 patients with MMCS 2, 5 patients with MMCS 3, and 1 patient with MMCS 4, respectively (Table 4).

Table 4.

Preop grade	Long term outcome					Total
	1	2	3	4	5	
1	5	1	0	0	0	6
2	3	3	1	0	0	7
3	1	3	1	0	0	5
4	0	2	0	0	0	2
5	0	1	0	0	0	1
Total	9	10	2	0	0	21

$P = 0.034$

Compared to preoperative status, 7 patients experienced improvement of the neurological state on the MMCS and 11 patients remained unchanged. There were 3 patients who experienced postoperative worsening of the neurological state (Case 5, 13, 19). One of them (Case 5) recovered preoperative motor strength at the last follow-up evaluation, but remaining 2 patients showed persistent neurologic worsening.

Case 7, the only patient whose lesion was subtotally resected re-experienced arm pain and additional subjective weakness 5 months after the operation. We thought the extent of previous surgical resection was complete, but re-bleeding of the lesion at the same level was observed on the follow-up MRI taken at the another hospital. The reoperation was not performed due to his concerns related

to the surgical morbidity of revision surgery.

At the long term follow-up evaluation, the satisfying (improved and unchanged) results were seen in 19 of 21 patients (91%)(Table 3). The preoperative neurologic state and the type of symptom presentation were significant prognostic factors related to the long term surgical outcome. That is, patients with a good preoperative neurological state (p = 0.034) and presenting type A or C symptoms rather than M revealed good postoperative neurological outcome (p = 0.024)(Table 4, 5).

Table 5.

Type of symptom	Long term outcome					Total
	1	2	3	4	5	
A	5	3	0	0	0	8
C	4	4	0	0	0	8
M	0	3	2	0	0	5
Total	9	10	2	0	0	21

P = 0.024

Any other factors including age, sex, level of lesion, size of lesion, duration of symptoms, and number of hemorrhagic episodes did not correlate with the postoperative neurological outcome with statistical significance.

4. Illustrative Cases

Case 11 (Fig. 1)

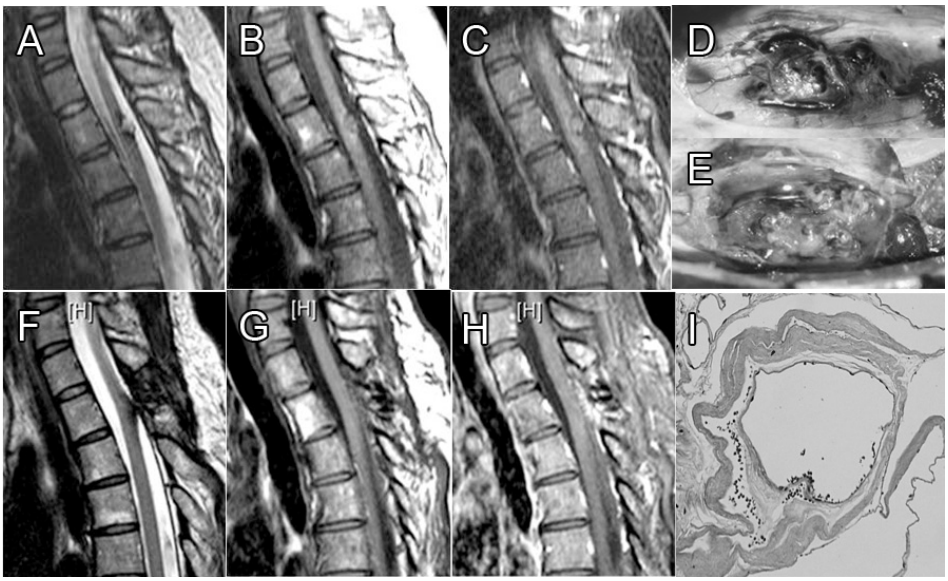

Fig. 1.Case 11. CM located at T2 level. A-C.Preoperative MRI.D, E.Intraoperative photographs. F-H.Postoperative MRI.I. Pathologic image. A. Sagittal T2-weighted image showing the intramedullary lesion with hemosiderin ring. B. Sagittal T1-weighted image demonstrating mixed signal intensity inside the lesion. C. Sagittal contrast enhanced T1-weighted image revealing poor enhancement of lesion. D, E. Operative photographs showing complete removal of lesion. F, G, H. Postoperative MRI showed no remnant. I. Pathologic image showing large, dilated, blood-filled vessels lined by a single layer of flattened endothelial cells without intervening parenchyma. Hematoxylin and eosin, ×100.

This 45-year-old female presented with a tingling sensation and numbness of the left lower extremity for 2 months. The neurologic examination revealed no deficit except numbness of the left lower extremity. The MR images of her thoracic spine demonstrated a 9mm-sized intramedullary lesion with mixed signal intensity on T1- and T2-weighted sequences. The dark signal intensity rim on T2-weighted images to suggest a hemosiderin ring was also observed. The preoperative diagnosis was intramedullary CM and she underwent an operation through T2 laminoplastic laminotomy. After the opening of the dura, the lesion was identified directly on the surface of the spinal cord and was completely excised along the gliotic plane. The histopathological findings were consistent with CM. She complained of brief aggravation of the tingling sensation of the left lower extremity postoperatively, but there was mild numbness only at her last follow-up 26 months postoperatively. The postoperative MR images showed complete resection of the lesion.

Case 12 (Fig. 2)

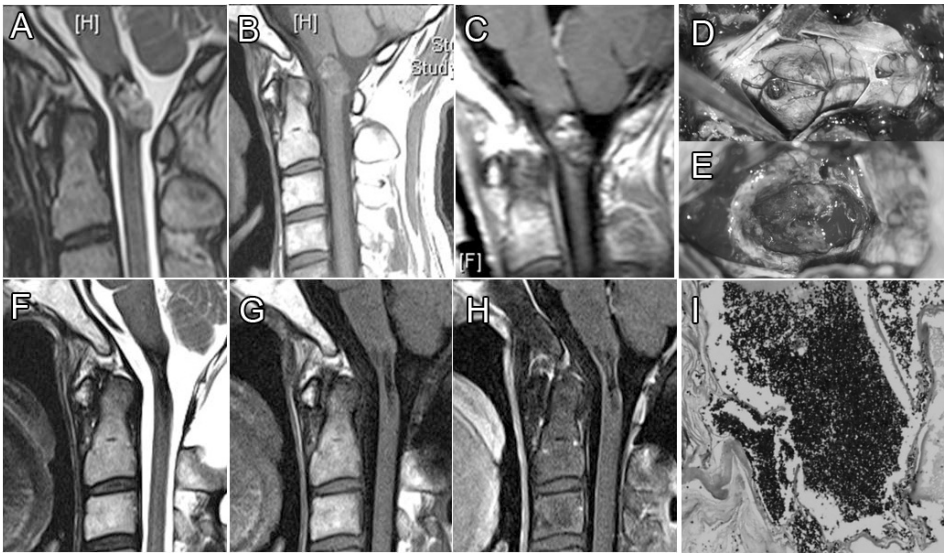

Fig. 2.Case 12. CM located at cervicomedullary junction. A-C.Preoperative MRI. D, E.Intraoperative photographs. F-H.Postoperative MRI. I. Pathologic image. A, B, C. Preoperative MRI showing the irregular shaped, sharply defined and poorly enhancing intramedullary lesion with hemosiderin ring. D, E. Operative photographs showing abnormal dilated vessel and grayish discoloration of the pial surface.F, G, H Postoperative MRI showed no remnant. I. Pathologic image compatable with the diagnosis of CM. Hematoxylin and eosin, ×40.

This 43-year-old male presented with pain and paresthesia in both hands for 6 months. On the neurologic examination, he was quadriparetic and the motor strength was grade 4 on all extremities. The MR images showed a 15mm-sized mixed signal intensity lesion at the cervicomedullary junction on T1- and T2-weighted images. Mild to moderate and heterogenous enhancement was observed after administration of gadolinium. Total laminectomy of C1, C2, and additional suboccipital craniectomy was performed and the lesion was completely excised. The histopathological examination revealed a diagnosis of CM. No remnant of the tumor was identified on postoperative MR images performed 9 months after the operation. At the last follow-up, the objective muscle strength was the same with preoperative state, but he appealed the worsening of subjective weakness.

Case 16 (Fig. 3)

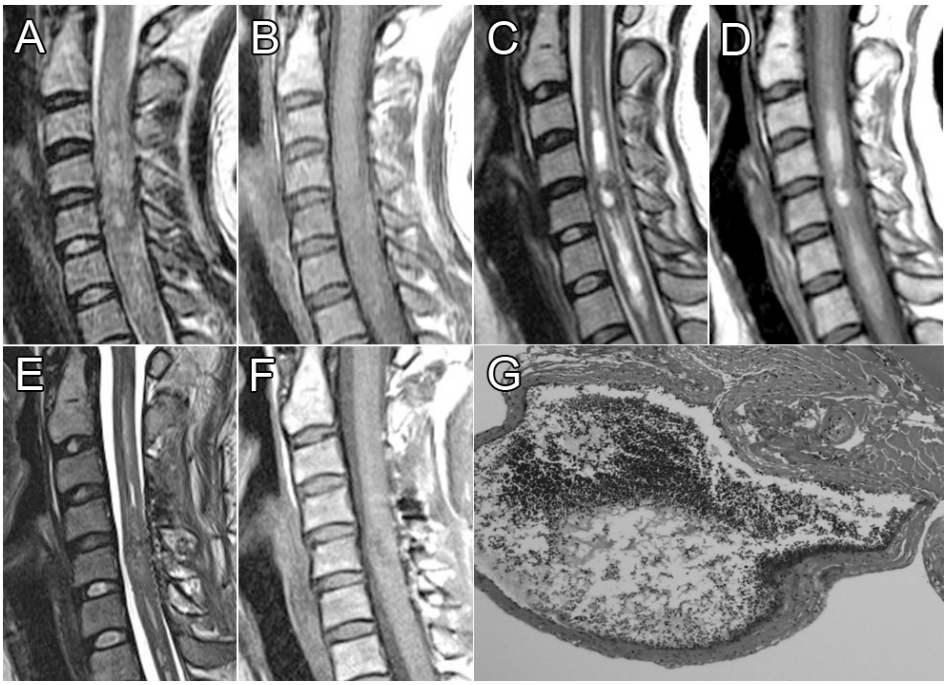

Fig. 3.Case 16. CM located at C5 level. A, B.Initial MRI. C, D. MRI 3 weeks after admission.E, F. Postoperative MRI.G. Pathologic image. H, I. Postoperative plain X ray.A, B. Initial MRI showing hematomyelia accompanied by severe cord swelling. C, D. MRI 3 weeks after the initial MRI demonstrating resolved cord swelling and the dark intensity rim on T2- weighted images at the center of hematoma. E, F. Postoperative MRI showing complete removal of lesion and some residual hematoma inside the spinal cord.G. Pathologic image compatible with the diagnosis of CM. Hematoxylin and eosin, ×40.

This 24-year-old female presented with sudden onset tingling sensation of her right hand and progressive quadriparesis for 4 days. She had no significant past medical history or trauma history. The neurologic examination revealed grade 2 to 3 quadriparesis. The initial MR images of her cervical spine showed hematomyelia accompanied by severe cord swelling. After the conservative care of 3 weeks, repeated MR images were obtained and revealed resolved cord swelling and a dark intensity rim on T2- weighted images at the center of the hematoma. She underwent an operation through C4, C5, C6 laminoplastic laminotomy. The postoperative diagnosis of CM was confirmed histopathologically. Her neurological state remained immediately unchanged postoperatively, but it improved to grade 4 to 5 of muscle strength at 13 months postoperatively.

IV. DISCUSSION

Although CMs can be found in all locations within the central nervous system, most of them are found in the intracranial region and intramedullary spinal location is relatively rare, accounting for only 3–5% of the total CNS lesions identified[4-9]. They are a type of vascular malformations composed of abnormal, dilated, thin-walled vascular sinusoidalchannels[13]. Typically, no brain parenchyma intervenes between these vascular channels[14,15]. There is often gliotic and hemosiderin-stained neural tissue parenchyma around the lesion, and small low-flow feeding arteries and draining veins also can be found[8,14].

Because of the paucity of a large case series with this lesion, it is hard to establish the epidemiological features of cavernous malformations. These lesions have a slightly higher predominance of incidence in women and a peak age presentation in the fourth decade[16-18]. The findings of our case series were concordant with these observations. But, the site of development showed equal distribution of cervical and thoracic location unlike previous reports documenting thoracic predilection[17,18].

Assuming the lesion was already present at birth, the calculated retrospective annual hemorrhage rate was 2.18% per person and year, similar to the previous reports (1.4–4.5%)[6,18,19]. But it would be the rate for symptomatic cases and the hemorrhage rate of patients including asymptomatic patients was hard to

estimate with this case series.

Magnetic resonance imaging is the imaging modality of choice for the diagnosis of cavernous malformations. Actually, most of the cases with cavernous malformations were reported after the introduction of MRI because these lesions are angiographically occult and difficult to diagnose with conventional tomography and myelography. A typical finding includes a peripheral hypointense ring of hemosiderin on T2-weighted images. The central core of the lesion shows mixed heterogenous signal intensity on both T1- and T2-weighted images with little contrast enhancement[17,18,20,21]

The symptom presentation of patients with CMs may be acute or slowly progressive. The acute neurologic deterioration occurs in cases with significant bleeding within the spinal cord and the slow progressive deterioration is related to multiple repeated microhemorrhages, subsequent thrombosis, hyalinization, and possible enlargement of the malformations[22].

Ogilvy et al.[17] reported 4 types of clinical presentation previously in patients with CMs.

1) Discrete episodes of neurological decline with varying degrees of recovery between episodes
2) Slow progressive myelopathy
3) Rapid decline after acute onset of symptoms
4) Gradual decline after acute onset of symptoms

In our case series, we observed 3 common patterns of symptom presentation and this pattern was closely related to the prognosis of the patients. In symptomatic patients with cavernous malformations, the complete surgical removal of the lesion is the only method to stop progression of the lesion and reduce further neurological deterioration. The rate of re-bleeding is unknown, but given the significant risk related to further neurological deterioration and low surgical morbidity, the surgery should be the mainstay treatment, especially in symptomatic patients. Our results that patients with type M symptom presentation (acute neurologic decline from pre-existing sequelae) show poor surgical outcome support this also. Furthermore, spinal CMs can cause more aggressive clinical symptoms and signs compared to their brain counterpart due to a lower degree of tolerance of the spinal cord for mass lesions[23,24]. But, there are some controversies regarding the treatment of asymptomatic patients. In such cases, we generally recommend a close follow-up of patients performing serial MRI rather than immediate surgery.

Perilesional edema or significant mass effect is not a common finding in patients with intramedullary CMs. 1 of our cases (case no. 16) showed severe cord swelling accompanied by hematomyelia in the initial MRI. In such cases, the timing of surgery is something to think. Immediate operation of these lesions could be harmful for an already stressed spinal cord. Several weeks of postponed surgery will be helpful for the resolution of the hematoma,

diminished cord swelling and resultant creation of discrete border of the lesion itself.

V. CONCLUSION

Symptomatic intramedullary CMs should be surgically removed to avoid further neurological deterioration. The prognosis was related to the preoperative neurologic state and the type of symptom presentation

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ABSTRACT(IN KOREAN)

수질 내 척수 해면상 혈관종 환자의 임상양상과 수술적 치료 성적

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해면상 혈관종은 드물지 않은 질환이나, 대부분 두개강 내에서 발생한다. 수질 내 척수 해면상 혈관종은 중추 신경계 종양의 3-5% 정도로 매우 드물게 보고 된다. 많은 환자군을 대상으로 수질 내 해면상 혈관종의 자연 경과나 출혈 위험을 비롯한 임상양상을 분석한 연구는 아직까지 부족하여 이를 분석하였다.

2004년 3월부터 2010년 3월 까지 수질 내 척수 해면상 혈관종으로 수술적 치료를 받은 총 21명의 환자를 대상으로 하여 자료를 후향적으로 분석하였다.

여자가 13명, 남자가 8명 이었으며, 평균나이는 39.3 세였다. 모든 환자에서 한 개의 혈관종이 발견되었고, 2개의 이상의 혈관종을 가진 환자는 없었다. 연간 출혈률은 2.2%로 분석되었다. 한 명을 제외한 20명의 환자에서 병소의 완전 절제가 이루어 졌고, 평균 추적 관찰 기간은 22.1 개월 이었다. 21명 중 10명의 환자에서 신경학적 호전이 관찰되었고, 9명에서는 변화가 없었으며, 2명의 환자에서 신경학적 악화가 발생했다.

증상이 있는 수질 내 척수 혈관종은 반드시 수술적으로 제거를 하여 더 이상의 신경학적 악화를 막아야 한다. 환자의 예후에는 수술 전 신경학적 상태와 증상의 발현 양상 2가지가 영향을 끼친다.

핵심되는 말 : 해면상 혈관종, 척수, 수질 내