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ORIGINAL ARTICLE

Variety of preoperative MRI changes in spinal cord ependymoma of WHO grade II: a case series

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Abstract

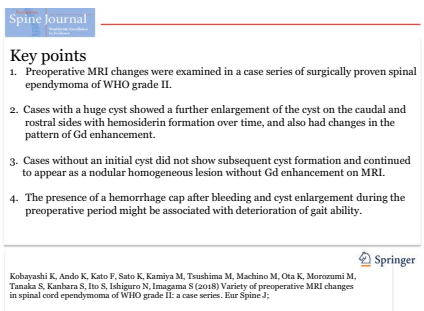
Purpose To report a case series of surgically proven spinal ependymomas of WHO grade II in which there were changes in the preoperative MRI characteristics over time.

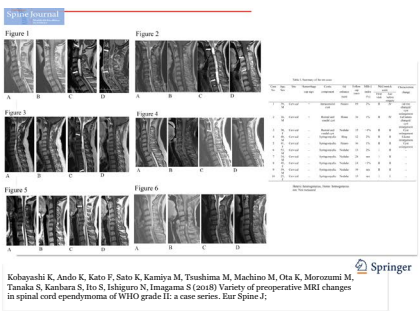
Methods A total of 71 patients with spinal cord ependymoma of WHO grade II underwent surgery. There were ten cases in which surgery was performed at an average of 2.2 years after the tumor was found. Cystic components, syringomyelia, hemorrhage "cap sign," Gd enhancement pattern, characteristic changes in MRI, MIB-1 index, and neurological assessment during the preoperative period were examined.

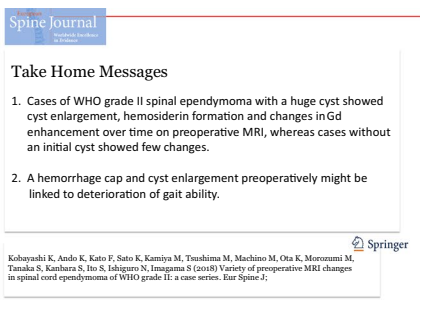
Results Cases with a huge cyst showed further enlargement of the cyst on the caudal and rostral sides with hemosiderin formation over time and changes in the pattern of Gd enhancement. In contrast, cases without initial cyst did not show cyst formation, and nodular homogeneous lesion remained without changes in Gd enhancement. Regarding neurological status, two cases with cyst enlargement and hemosiderin formation had worsened non-independent gait preoperatively.

Conclusions MRI in cases of spinal ependymomas of WHO grade II showed characteristics such as hemorrhage and cyst formation that varied over time. In particular, cases with cyst and hemosiderin showed tumor enlargement, including enlargement of lesions on the caudal and rostral sides and enlargement of Gd-enhanced lesions. These characteristics might influence gait ability during preoperative period. We emphasize that early surgery is still the standard of care for cervical intramedullary ependymoma, and our findings in this study should not be interpreted to indicate that such early surgery is not necessary in symptomatic cases.

Graphical abstract These slides can be retrieved under electronic supplementary material.







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Extended author information available on the last page of the article

Keywords Ependymoma · MRI · WHO classification · Cyst formation · Gd enhancement

Introduction

Ependymomas are the most common intramedullary spinal cord tumors in adults and are glial tumors that arise from ependymal cells in the central nervous system [1–6]. Most ependymomas have benign pathological behavior and slow growth and tend to compress, rather than infiltrate, adjacent cord parenchyma, although the tumor is primarily unencapsulated [7–9]. Preoperative prediction of the pathological diagnosis could enhance surgical planning and the ability of the surgeon to describe the procedure to patients. However, spinal ependymomas exhibit a variety of MRI findings [10–14], and understanding MRI changes in the natural history of the tumor is difficult.

Many cases have spinal cord symptoms that worsen over time, and preoperative motor status is related to postoperative performance, which suggests that surgery should be performed before neurological deficit worsens to promote recovery of the spinal cord [15–17]. Early surgery including biopsy for pathological examination is the appropriate approach for symptomatic improvement and confirmation of diagnosis.

Various features of spinal ependymoma on MRI have been described, including cyst formation, hemorrhage cap sign, Gd enhancement, and syringomyelia [1–12, 14]. However, there have been no reports on preoperative changes in MRI for spinal ependymomas. Here, we report ten cases of surgically proven spinal ependymoma of WHO grade II with preoperative MRI findings over the natural course and neurological assessment during the preoperative period, as the first such longitudinal study of MRI features of this tumor.

Materials and methods

Between June 2000 and December 2016, 71 surgeries (39 males and 32 females) were performed for spinal cord ependymoma of WHO grade II at five institutions in the Nagoya Spine Group (NSG). The average age was 51 (range 19–77) years. Data were obtained retrospectively from medical records. The pathological diagnosis in all 71 cases was confirmed to be cellular ependymoma by surgical biopsy by two pathologists. Based on histology of microsections stained with hematoxylin and eosin, all tumors were grade II in the WHO classification for tumors derived from ependymal cells, and grades I and III were excluded [18]. Grade II includes four histological variants: cellular ependymoma, which has hypercellularity and an increased mitotic rate, papillary ependymoma, clear cell ependymoma, and tanycytic ependymoma [19]. MIB-1 was determined as an index of cell proliferative activity. Of the 71 surgeries, 61 were performed within 1 year after the tumor was found, but in ten cases surgery was performed after more than 1 year.

MRI was performed with a field strength of 1.5 T. All patients underwent serial MRI using T1-weighted (TR 400–700 ms; TE, 9–25 ms), fast spin-echo T2-weighted (TR 3000–5000 ms; TE 96–150 ms), and gadolinium Gd-enhanced contrast (0.1 mmol/kg Gd-DTPA) T1-weighted sequences. The presence and type of cystic components or syringomyelia, evidence of hemorrhage, extent of involvement, gadolinium enhancement pattern, surrounding cord edema, and hemorrhage "cap sign" were examined. A tumor was considered to have a cystic component if a cyst associated with the tumor contained an enhanced nodule or had an enhanced wall. This type of tumor is in contrast to the non-enhanced, non-neoplastic rostral and caudal reactive cysts that are often associated with spinal cord tumors. Reactive dilatation of the central canal was defined as syringomyelia. A cap sign was considered to be secondary to hemorrhage, with a rim of extreme hypointensity due to hemosiderin at the poles of the tumor on T2-weighted images. Changes in these characteristics were examined over time.

For neurological assessment, patients were assigned a preoperative neurological clinical grade using the modified McCormick scale (grade I = normal gait, II = mild gait disturbance not requiring support, III = gait with support, IV = assistance required, and V = wheelchair needed) [20]. McCormick grades I and II were defined as stable gait with no support required for walking, which indicate independent gait ability. Functional examinations were conducted at the first visit and just before surgery during the preoperative period.

Approval for the study was obtained from our institutional review board.

Results

The ten cases in which surgery was delayed after tumor identification are given in Table 1. All tumors were located in the cervical spine. In these cases, surgery was performed at an average of 2.2 years (range 1–7 years) after the tumor was found, and this allowed an analysis of MRI changes over the natural course of the tumor.

In all ten cases, images showed tumor enhancement after intravenous Gd administration: Six had nodular enhancement, two had heterogeneous enhancement, one had homogeneous enhancement, and one had ring enhancement. Two cases (cases 1 and 2) with a cap sign and cyst had marked

Table 1 Summary of the ten cases

Case no.	Age, Sex	Site	Hemorrhage cap sign	Cystic component	Gd enhancement	Follow-up (mo)	MIB-1 index (%)	McCormick scale		Characteristic change
								First visit	Just before surgery	
1	39, M	Cervical	+	Intratumoral cyst	Hetero	89	2%	II	IV	Gd rim changed/cyst enlargement
2	16, M	Cervical	+	Rostral and caudal cyst	Homo	36	1%	II	IV	Gd hetero changed/cyst enlargement
3	38, F	Cervical	–	Rostral and caudal cyst	Nodular	15	< 1%	II	II	Cyst enlargement
4	40, M	Cervical	–	Syringomyelia	Ring	12	2%	II	II	Edema enlargement
5	41, F	Cervical	–	Syringomyelia	Hetero	16	1%	II	II	Cyst enlargement
6	53, M	Cervical	–	Syringomyelia	Nodular	13	2%	I	II	-
7	54, M	Cervical	–	Syringomyelia	Nodular	28	nm	I	II	-
8	45, F	Cervical	–	Syringomyelia	Nodular	24	< 1%	II	II	-
9	59, M	Cervical	–	Syringomyelia	Nodular	19	nm	II	II	-
10	25, F	Cervical	–	Syringomyelia	Nodular	13	nm	I	I	-

Hetero heterogeneous, *Homo* homogeneous, *nm* not measured

changes in Gd enhancement over time, whereas there were no obvious changes in any of the other eight cases. Three tumors were cystic and seven tumors were not cystic. Two cases (cases 2 and 3) had both rostral and caudal cysts, and one case (case 1) had an intratumoral cyst. All of the cysts increased in size over the course (Figs. 1, 2, 3, 4, 5, 6). The two cases (cases 1 and 2) with a cap sign showed marked cyst enlargement over time, but there was no obvious enlargement in any of the other eight cases. Syringomyelia was seen in seven cases, but only one case (case 4) showed enlargement over 16 months and this case did not develop a cyst.

The MIB-1 index of cell proliferative activity was determined in seven cases (Table 1). All indexes were generally low: 1% or less or 1–2%. In neurological assessment, at the first visit the McCormick grade was I or II. In cases 1 and 2, which had cyst enlargement and a hemorrhage cap, McCormick grades worsened to IV just before the surgery, indicating the reduced independent gait ability. In contrast, the other six cases maintained a stable gait with no support required for walking during the preoperative period.

In patients with (+) and without (−) characteristic MRI changes in cyst/edema enlargement, the rates were 60% versus 0% for a cystic component, 40% versus 0% for non-nodular Gd enhancement, 40% versus 0% for a ≥ 2 grade deterioration on the McCormick scale, and 40% versus 0% for McCormick grades III, IV, and V just before the surgery (Table 2).

Discussion

Previous reports on the characteristics of MRI in intramedullary ependymoma have identified variations such as cord enlargement, cystic components, reactive dilatation of the central canal, hemorrhage, surrounding cord edema, Gd enhancement pattern, and a hemorrhage cap sign [7, 9–12]. Honda et al. [13] examined multiple intradural extramedullary spinal ependymomas that were histologically confirmed to be composed of two subtypes of ependymomas. Kobayashi et al. [14] described the characteristic imaging features of 59 spinal ependymomas of WHO grade II, of which 50 (85%) had surrounding cord edema, 52 (88%) had associated cysts, including 36 (61%) rostral or caudal cysts, 10 (17%) intratumoral cysts, and 6 (10%) with syringomyelia; 17 (29%) had a cap sign, a rim of extreme hypointensity due to hemosiderin at the poles of the tumor on T2-weighted images; and 4 (7%) had formed a fluid–fluid level inside the cyst. On gadolinium-enhanced T1-weighted images, all cases were enhanced, and 27 (46%), 16 (27%), 11 (19%), and 5 (8%) tumors had homogeneous, heterogeneous, rim, and nodular enhancement, respectively [14]. However, there

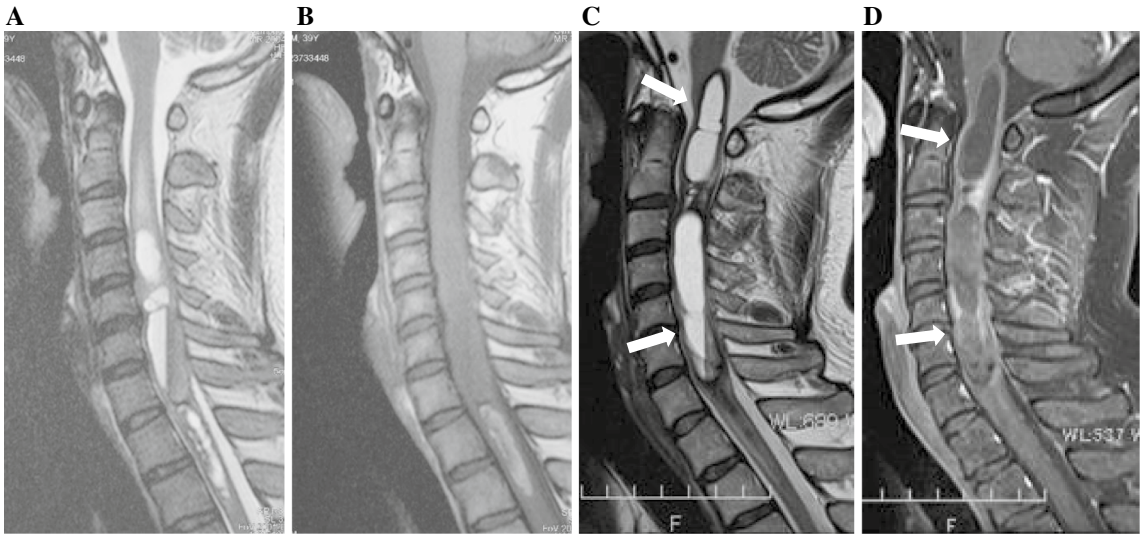

Fig. 1 Case 1: Sequential changes in T2-weighted (**a**, **c**) and gadolinium-enhanced T1-weighted (**b**, **d**) MRI showed cervical cystic components with fluid–fluid level formation (**a**) and Gd enhancement (**b**). Eighty-nine months later, MRI showed enlarged cystic components with a hemorrhage "cap sign" on the rostral and caudal sides (arrows) (**c**) and a cystic component with Gd enhancement (arrows) (**d**)

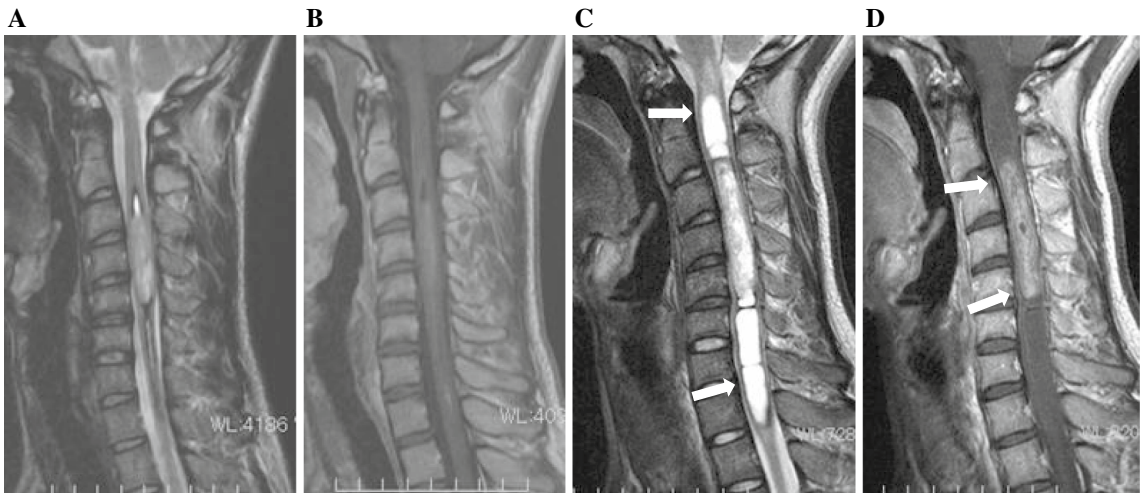

Fig. 2 Case 2: Sequential changes in T2-weighted (**a**, **c**) and gadolinium-enhanced T1-weighted (**b**, **d**) MRI showed a cervical cystic component with cord edema (**a**) and Gd enhancement (**b**). Thirty-six months later, MRI showed enlarged cystic components with a hemorrhage "cap sign" on the rostral and caudal sides (arrows) (**c**) and a heterogeneous pattern of Gd enhancement (arrows) (**d**)

have been no previous studies focused on long-term preoperative changes in MRI features of ependymomas of WHO grade II.

In our series of ten cases (Table 1), two initially had a huge cyst with hemosiderin formation (cases 1 and 2), and subsequently, the cyst enlarged on the caudal and rostral sides with fluid–fluid level formation in both cases. In another case (case 3), a rostral and caudal cyst enlarged over time. In contrast, in the other seven cases (cases 4–10), a nodular homogeneous or heterogeneous lesion was enhanced, but with no cyst formation, and there were no remarkable changes in Gd enhancement over time. These results suggest that only cases of intramedullary ependymoma with hemorrhage or a cyst component are likely to undergo major changes in MRI over time, including marked enlargement of Gd-enhanced lesions.

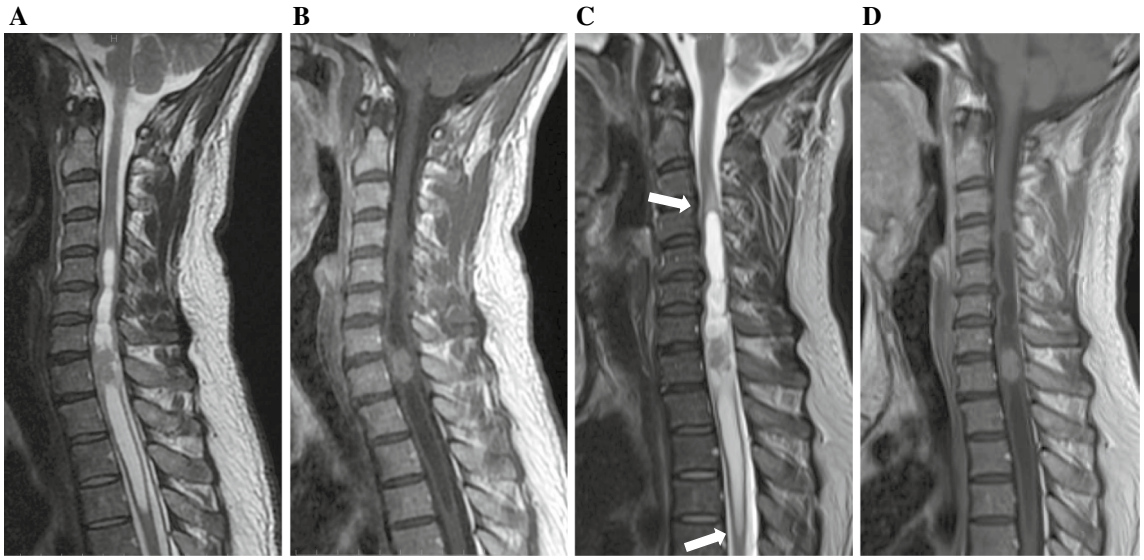

Fig. 3 Case 3: Sequential changes in T2-weighted (**a**, **c**) and gadolinium-enhanced T1-weighted (**b**, **d**) MRI showed cystic components in rostral and caudal regions around the tumor (**a**) and nodular homogeneous with Gd enhancement. Fifteen months later, the cervical lesion with cystic component (arrows) was enlarged (**c**), but Gd enhancement was unchanged (**d**)

Ependymoma of WHO grade II should undergo total resection and careful follow-up after complete resection is confirmed by imaging [14, 17]. In our series, five cases were followed without surgery due to transient improvement in symptoms, three cases were interrupted in follow-up due to the patient's choice, and two cases received medical treatment under a different diagnosis of multiple sclerosis. Therefore, surgery was significantly delayed in all cases. However, we performed gross resection after intraoperative pathological examination confirmed the tumor to be WHO grade II, and the preoperative symptoms were improved.

Enlargement of cysts and edema was detected as MRI changes during the time course. As given in Table 2, cases with these changes on MRI were frequently characterized by the presence of a cystic component at the first visit and non-nodular Gd enhancement, such as hetero, hem, and ring types. The number of cases is too small to give a statistically significant difference, but these results suggest that a tumor with a cystic component may undergo enlargement over time, whereas a lesion with nodular Gd enhancement is more likely to have lower tumor growth. In Gd enhancement, a contrast intense signal may reflect proliferation and

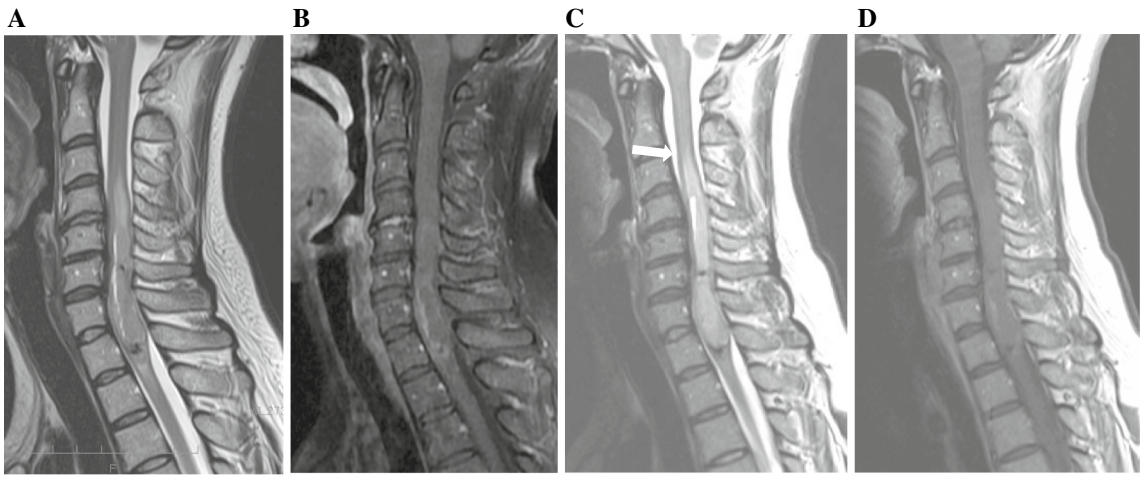

Fig. 4 Case 4: Sequential changes in T2-weighted (**a**, **c**) and gadolinium-enhanced T1-weighted (**b**, **d**) MRI showed syringomyelia around the tumor with edema (**a**) and a ring with Gd enhancement. Twelve months later, the cervical lesion with edema was enlarged (arrows) (**c**), but Gd enhancement was unchanged (**d**)

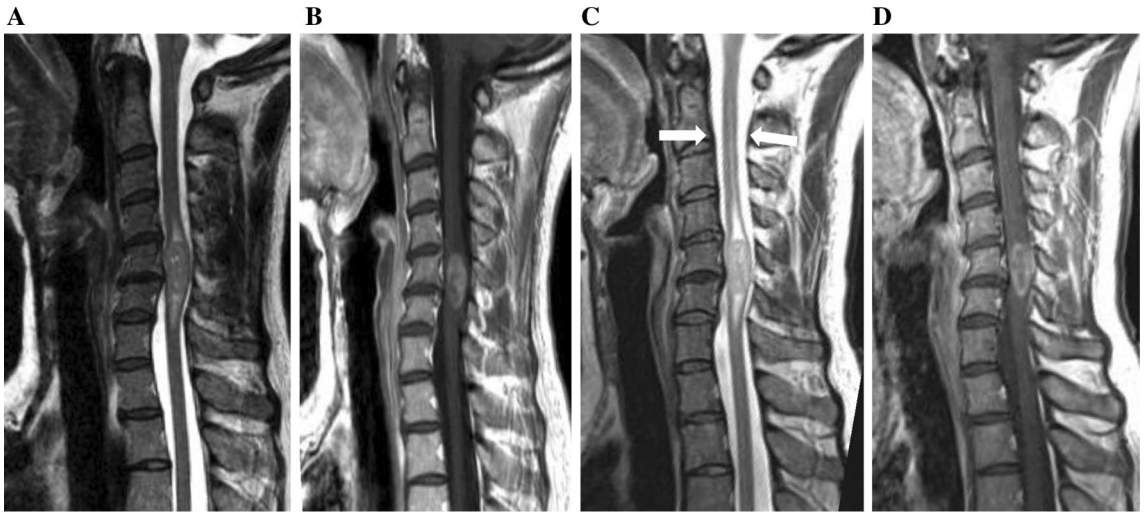

Fig. 5 Case 5: Sequential changes in T2-weighted (**a**, **c**) and gadolinium-enhanced T1-weighted (**b**, **d**) MRI showed syringomyelia in rostral and caudal regions around the tumor (**a**) and a heterogeneous lesion with Gd enhancement. Sixteen months later, the cervical lesion with rostral syringomyelia (arrows) was enlarged (**c**), but Gd enhancement was unchanged (**d**)

differentiation [14], which might lead to an increased tumor and cystic component size. From the viewpoint of the clinical course, no symptomatic improvement occurred in any cases. However, in our series, cyst/edema enlargement was frequently associated with deterioration of neurological status, which might be caused by increased vulnerability due to continuous compression of the spinal cord.

The MIB-1 index was uniformly low in most cases. Two cases had worsened non-independent gait preoperatively, and these cases also had a hemorrhage cap after bleeding and cyst enlargement during the preoperative period, which suggests that these characteristics might be associated with deterioration of gait ability. A hemorrhage cap sign indicates that hemorrhage had previously occurred, and bleeding is also a concern for vulnerability of the spinal cord, which may be followed by attachment of the spinal cord and reflux disorder, with possible subsequent cyst enlargement.

This study is limited by the small number of cases, limited MRI methods, and relatively short average course of 2.2 years. In particular, the two cases with marked cyst enlargement (cases 1 and 2) had progressed for a relatively long time, which prevented a conclusion on the relationship between follow-up period and MRI changes. However, changes in MRI features over the natural course of surgically proven spinal ependymoma of WHO grade II have not previously been described in a longitudinal study. These

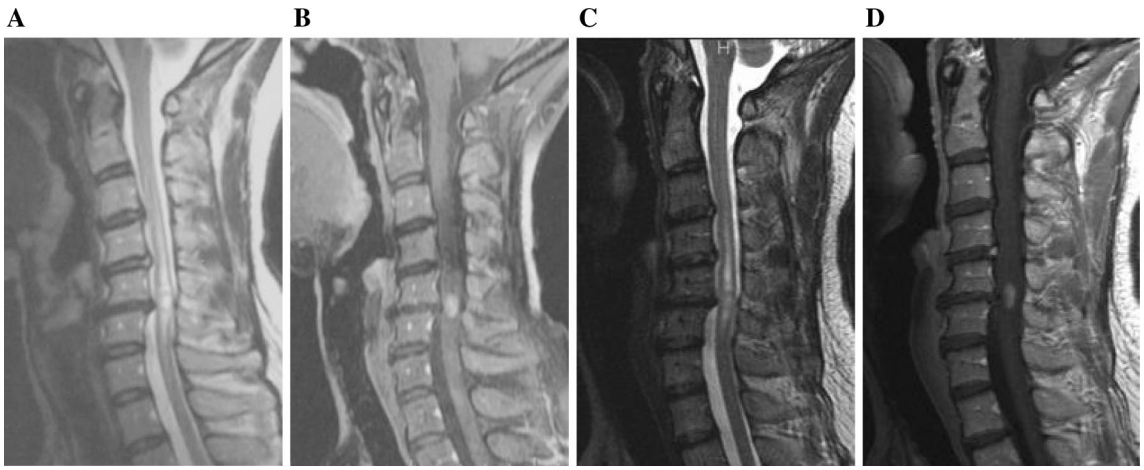

Fig. 6 Case 6: Sequential changes in T2-weighted (**a**, **c**) and gadolinium-enhanced T1-weighted (**b**, **d**) MRI showed a cervical lesion with syringomyelia (**a**) and homogeneous nodular Gd enhancement (**b**). Thirteen months later, syringomyelia (**c**) and the Gd-enhanced nodular lesion (**d**) were unchanged

Table 2 Characteristics of cases with (+) and without (−) cyst or edema enlargement on MRI

Items	Cyst/edema enlargement on MRI	
	(+) ($n=5$)	(−) ($n=5$)
Age (years)	34.8 ± 10.5	47.2 ± 13.4
Follow-up period (months)	33.6	19.4
MRI features		
Presence of cystic component	60% (3)	0% (0)
Non-nodular Gd enhancement	80% (4)	0% (0)
Clinical features (McCormick scale)		
≥ 2 grades of deterioration	40% (2)	0% (0)
III/IV/V just before surgery	40% (2)	0% (0)

preoperative MRI characteristics over time may be useful for evaluation of future cases. Key variations in this tumor include hemorrhage and cyst formation, and cases with cyst and hemosiderin showed enlarged lesions on the caudal and rostral side and enlarged Gd-enhanced lesions over time. The presence of a hemorrhage cap and cyst enlargement preoperatively might be linked to worsened non-independent gait ability, and these characteristic changes might be useful for determining the best timing for surgical intervention. However, we would like to emphasize that early surgery is still the standard of care for cervical intramedullary ependymoma, and our findings in this study should not be interpreted to indicate that such early surgery is not necessary in symptomatic cases.

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Compliance with ethical standards

Conflict of interest None of the authors have a conflict of interest.

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