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H.S. Seo, J.-h. Kim, D.H. Lee, Y.H. Lee, S.-i. Suh, S.Y. Kim and D.G. Na

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ORIGINAL
RESEARCH

H.S. Seo
J.-h. Kim
D.H. Lee
Y.H. Lee
S.-i. Suh
S.Y. Kim
D.G. Na



Nonenhancing Intramedullary Astrocytomas and Other MR Imaging Features: A Retrospective Study and Systematic Review

BACKGROUND AND PURPOSE: Most intramedullary astrocytomas have been known to exhibit at least some enhancement on MR imaging regardless of cell type or tumor grade. The purpose of this study was to evaluate the incidence of nonenhancing intramedullary astrocytomas through a retrospective study within our institutions and a systematic review of the medical literature.

MATERIALS AND METHODS: A total of 19 consecutive patients (male to female ratio, 11:8; mean age, 27.84 ± 19.0 years) with primary intramedullary astrocytomas (3 WHO grade I, 13 WHO grade II, 3 WHO grade III) who underwent preoperative MR imaging with contrast enhancement were included in this retrospective study from 4 institutions. The tumor-enhancement patterns were classified into the following categories: 1) no enhancement, 2) focal nodular enhancement, 3) patchy enhancement, 4) inhomogeneous diffuse enhancement, and 5) homogeneous diffuse enhancement. Seven articles including MR imaging enhancement studies of intramedullary astrocytomas were eligible for literature review.

RESULTS: In the retrospective study, 6 astrocytomas (32%), including 2 anaplastic astrocytomas, did not enhance at all. Focal nodular enhancement was identified in 5 astrocytomas (26%); patchy enhancement, in 3 (16%); inhomogeneous diffuse enhancement, in 5 (26%); and homogeneous diffuse enhancement, in none. In the literature review, the frequency of nonenhancing intramedullary astrocytomas was 14 of 76 (18%), including 2 anaplastic astrocytomas.

CONCLUSIONS: Nonenhancing intramedullary astrocytomas are not uncommon and comprise between 20% and 30% of intramedullary astrocytomas. Therefore, astrocytoma must remain in the differential diagnosis of nonenhancing intramedullary lesions, particularly if the lesion demonstrates a prominent mass effect or cord expansion.

ABBREVIATIONS: Gd-DTPA = gadopentate dimeglumine; WHO = World Health Organization

Astrocytomas account for approximately 30% of spinal cord tumors. They are the most common childhood intramedullary neoplasms of the spinal cord and are second only to ependymomas in adults.^{1,2} Clinical presentation varies from nonspecific back pain to sensory and motor deficits, according to the size and location. Their infiltrative nature leads to a worse prognosis than that in ependymoma.³

The classic MR imaging appearance of intramedullary astrocytoma is a cord-enlarging tumor with poorly defined margins. It is typically iso- to hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging.³ Peritumoral and tumoral cysts are frequently associated with astrocytomas.⁴ In contrast to intracerebral astrocytomas, most intramedullary astrocytomas exhibit at least some enhancement with administration of intravenous contrast material, regardless of cell type or tumor grade.^{5,6}

However, reports of nonenhancing intramedullary astrocytomas exist in our institutions, as well as in the literature.⁷⁻¹⁰ The purpose of this study was to evaluate the incidence of

nonenhancing intramedullary astrocytoma through a retrospective study within our institutions and a systematic review of the medical literature. A detailed analysis of other MR imaging features is also presented.

Materials and Methods

Subjects of the Retrospective Study

Pathologically proved primary intramedullary astrocytoma was diagnosed in 21 patients at our 4 institutions from 1998 through 2008. Preoperative MR imaging studies were unavailable in 2 patients; therefore, a total of 19 consecutive patients with intramedullary astrocytomas were included in the present study. Tumors in 3 patients were WHO grade I (pilocytic astrocytoma), 13 were WHO grade II (fibrillary astrocytoma), and 3 were WHO grade III (anaplastic astrocytoma). All patients underwent preoperative MR imaging with contrast enhancement by using Gd-DTPA. The patient population included 11 males and 8 females, 2–63 years of age (mean age, 27.84 ± 19.0 years).

There was no history of steroid therapy before MR imaging in any patient. One patient diagnosed as having anaplastic astrocytoma underwent Korean traditional medical treatment before MR imaging. The institutional review board of my institution approved this study, and the requirement for informed consent was waived.

MR Imaging and Image Analysis of the Retrospective Study

MR imaging was performed with surface coils on 6 MR imaging systems, ranging from 1T to 3T (Magnetom Expert 1T, Magnetom Vi-

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From the Department of Radiology (H.S.S., Y.H.L.), Korea University Ansan Hospital, Kyunggi-do, Korea; Department of Radiology and Institute of Radiation Medicine (J.-h.K., S.Y.K., D.G.N.), Seoul National University College of Medicine, Seoul, Korea; Department of Radiology (S.-i.S.), Korea University Guro Hospital, Seoul, Korea; Department of Radiology (D.H.L.), Seoul Medical Center, Seoul, Korea; and Human Medical Imaging and Intervention Center (D.G.N.), Seoul, Korea.

Please address correspondence to Dong Gyu Na, MD, Director of Neuroradiology, Thyroid Clinic, Human Medical Imaging and Intervention Center, 12–25, Jamwon-dong, Seocho-gu, Seoul, 137–902, Korea; e-mail: nndgna@gmail.com

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Table 1: Contrast-enhancement patterns of intramedullary astrocytomas

Enhancement Pattern	WHO Grade			Total (n = 19) (%)
	I (n = 3) (%)	II (n = 13) (%)	III (n = 3) (%)	
None	0 (0)	4 (31)	2 (67)	6 (32)
Focal nodular	1 (33)	4 (31)	0 (0)	5 (26)
Patchy	1 (33)	2 (15)	0 (0)	3 (16)
Inhomogeneous diffuse	1 (33)	3 (23)	1 (33)	5 (26)
Homogeneous diffuse	0 (0)	0 (0)	0 (0)	0 (0)

sion 1.5T, Magnetom Sonata 1.5T, and Magnetom Trio A Tim 3T, Siemens, Erlangen, Germany; Genesis Signa 1.5T, Excite 3T, GE Healthcare, Milwaukee, Wisconsin). All patients underwent transverse and sagittal T1-weighted spin-echo imaging and T2-weighted fast spin-echo imaging plus additional imaging as necessary. The parameters of the standard T1- and T2-weighted sequences were adjusted to each MR imaging system. Contrast-enhanced transverse and sagittal T1-weighted images were obtained immediately following intravenous Gd-DTPA (0.1 mmol/kg body weight) administration. The MR images were independently reviewed by 2 neuroradiologists (H.S.S., Y.H.L.). Following the initial viewing, they re-evaluated the images and reached a consensus for any remaining discrepancies.

The tumor-enhancement patterns were classified into the following categories according to the area of solid tumor enhancement and homogeneity: 1) no enhancement, 2) focal nodular enhancement, 3) patchy enhancement (enhancement of less than one-half of the solid portion of the tumor), 4) inhomogeneous diffuse enhancement (inhomogeneous enhancement of one-half or more of the solid portion of the tumor), and 5) homogeneous diffuse enhancement (homogeneous enhancement of one-half or more of the solid portion of the tumor). In addition to the enhancement pattern, intramedullary astrocytomas were assessed with respect to axial location (central, eccentric), longitudinal location (cervical, thoracic, lumbar), size (longitudinal length and number of vertebral segments involving tumor), T1 and T2 signals relative to the spinal cord (hypointense, isointense, hyperintense) as well as the presence of edema, peritumoral or intratumoral cysts, syringohydromyelia, hemorrhage, and periapical cap (a rim of extreme hypointensity at the poles of the tumor on T2-weighted imaging).

Literature Review

PubMed was searched for articles regarding nonenhancing intramedullary astrocytomas with the use of combinations of the search terms: “spinal cord,” “astrocytoma,” and “MR.” The search identified a total of 52 articles published between 1984 and 2008, including 40 English-

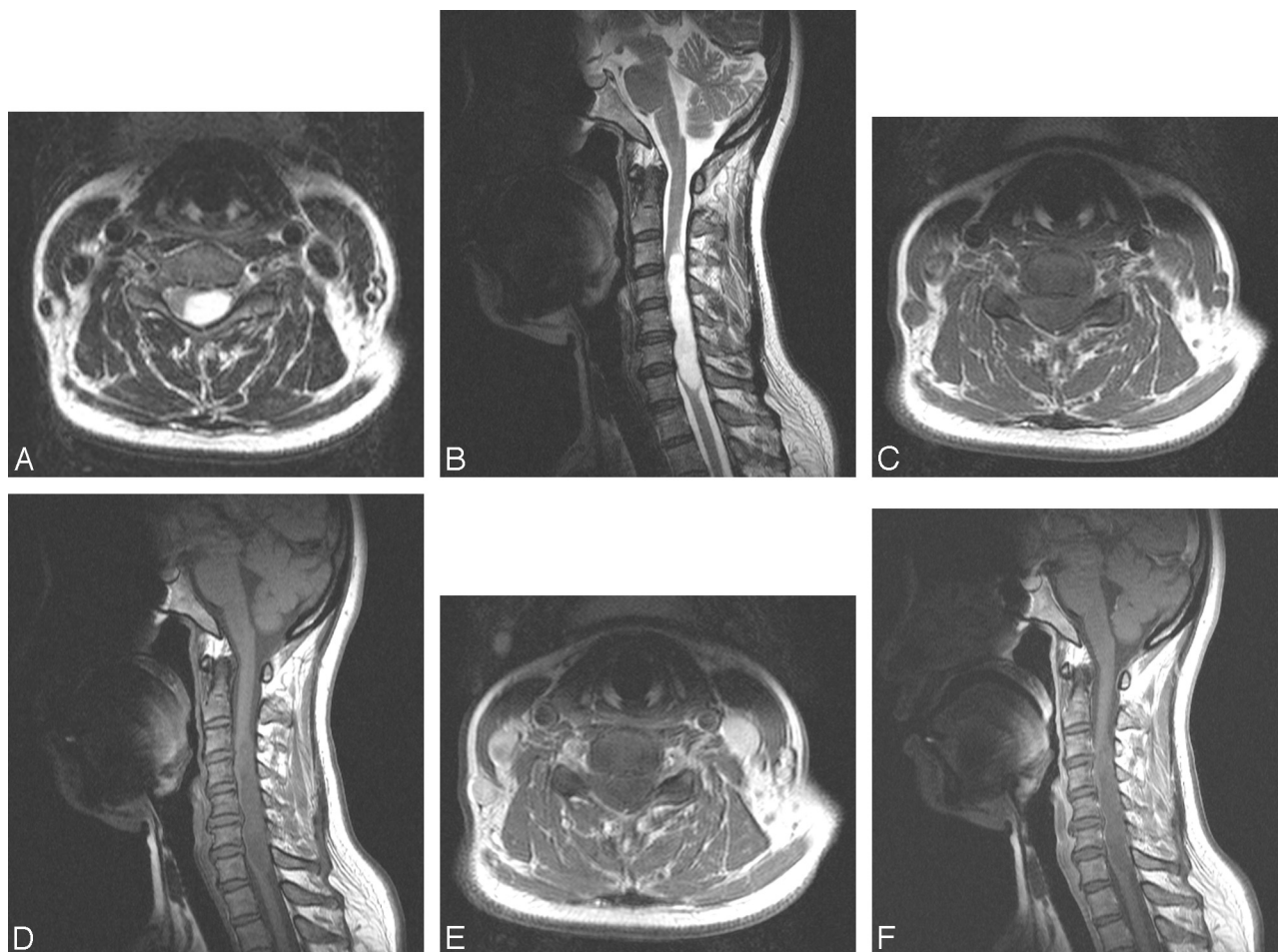


Fig 1. A 50-year-old woman with nonenhancing WHO grade II diffuse astrocytoma. Her symptoms were progressive left-handed weakness, hypoesthesia, and lower right-legged paresthesia starting 5 months earlier. *A* and *B*, Axial and sagittal T2-weighted MR images show a well-demarcated hyperintense intramedullary mass at the cervical spinal cord. The mass is slightly eccentric to the left side from the spinal cord center on the axial image. There is no peritumoral edema, periapical cap, or hemorrhage. *C* and *D*, The mass is hypointense on axial and sagittal T1-weighted images. *E* and *F*, Contrast enhanced T1-weighted images show that the mass is not enhanced at all.

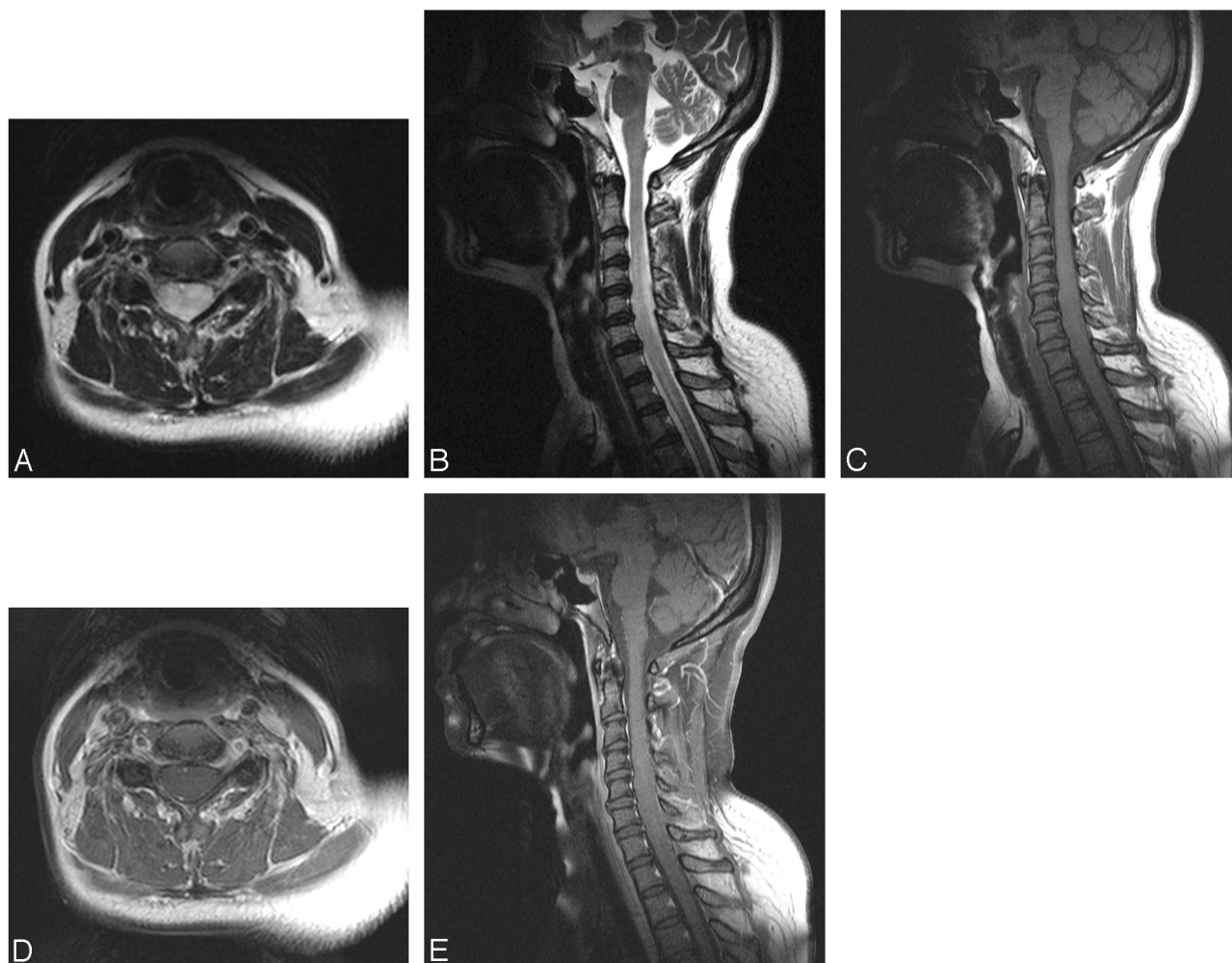


Fig 2. A 47-year-old woman with a nonenhancing WHO grade III anaplastic astrocytoma. Her chief symptoms were a left upper extremity tingling sense and weakness, which had gradually extended from the distal to the proximal portion. Thereafter, the same symptoms occurred in both lower extremities. *A* and *B*, Axial and sagittal T2-weighted MR images show an ill-defined slightly hyperintense mass at cervical spinal cord. *C*, The mass is isointense to the spinal cord on sagittal T1-weighted images. *D* and *E*, Contrast-enhanced axial and sagittal T1-weighted images show a nonenhanced mass.

language articles when we searched in April 2009. Abstracts of the identified publications were reviewed.

Seven articles including MR imaging enhancement studies of intramedullary astrocytomas were eligible for this literature review.⁷⁻¹³ The full text from 6 English articles was reviewed and 1 article written in Chinese was reviewed by abstract alone. Literature review was performed by 1 author (H.S.S.).

Results

Retrospective Study

The enhancement patterns of intramedullary astrocytomas were varied (Table 1). Six astrocytomas (32%), including 2 anaplastic astrocytomas, did not enhance at all (Figs 1–3). Thirteen of 19 astrocytomas (68%) demonstrated enhancement. Focal nodular enhancement was identified in 5 astrocytomas (26%), patchy enhancement in 3 (16%), and inhomogeneous diffuse enhancement in 5 (26%). There was no intramedullary astrocytoma with homogeneous diffuse enhancement.

Most intramedullary astrocytomas were iso- ($n = 7$, 37%) or hypointense ($n = 11$, 58%) relative to the spinal cord on

T1-weighted imaging (Table 2). In 1 patient, the tumor manifested as a hyperintense mass, most likely due to hemorrhage. On T2-weighted imaging, most tumors were hyperintense ($n = 18$, 95%) relative to the spinal cord, with the exception of isointense grade II astrocytoma (Table 3).

Thirteen astrocytomas (68%) were centrally located in the axial spinal cord, and 6 (32%) were eccentric (Tables 2 and 3). Intramedullary astrocytomas occurred most commonly in the cervical region ($n = 13$, 69%), with 2 extending into the upper thoracic region and 1 involving the whole spinal cord. Five astrocytomas (26%) were located solely in the thoracic cord, and 1 (5%) involved the distal thoracic cord and the conus medullaris. The mean tumor size was 7.3 ± 8.2 cm, and the average number of vertebral segments involved was 4.2 ± 4.7 .

Seven astrocytomas (37%) were associated with surrounding edema (Tables 2 and 3). Intratumoral cysts appeared in 4 astrocytomas (21%), and peritumoral cysts appeared in 3 (16%) patients. Syringohydromyelia was not associated with any astrocytoma. Two astrocytomas (11%) showed evidence of hemorrhage. One astrocytoma demonstrated a periapical cap at its poles on T2-weighted imaging.

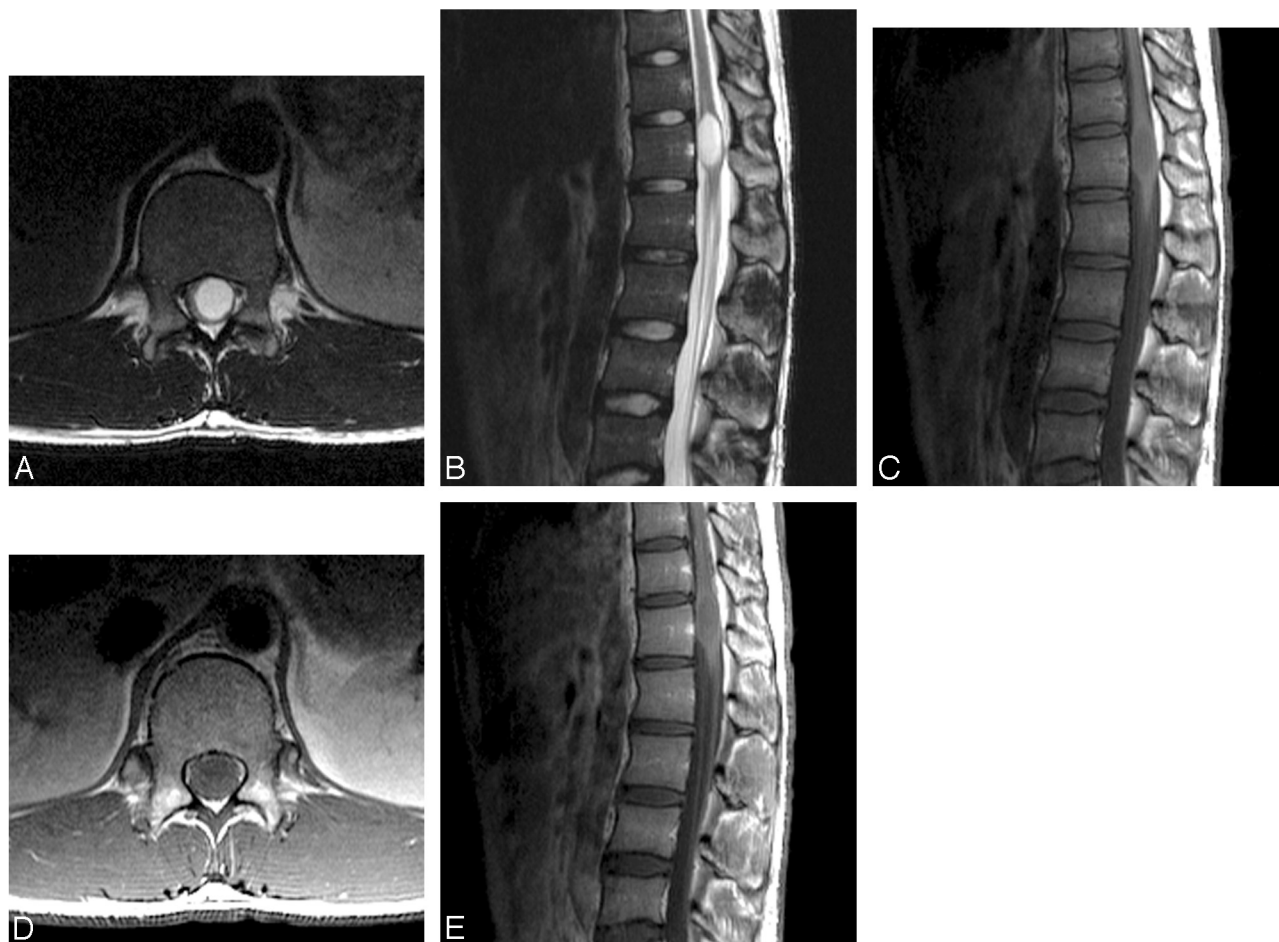


Fig 3. A 19-year-old man with a nonenhancing WHO grade III anaplastic astrocytoma. His chief symptoms were left lower extremity weakness, hypoesthesia, and lower back pain starting 6 months earlier. *A* and *B*, Axial and sagittal T2-weighted MR images show a well-demarcated hyperintense mass at the center of the conus medullaris. *C*, The mass is hypointense on the sagittal T1-weighted image. *D* and *E*, Contrast-enhanced axial and sagittal T1-weighted images show that the mass is not enhanced at all.

Table 2: T1 MR imaging features of intramedullary astrocytomas	
T1 Signal	Cases (%)
Hypointense	11 (58)
Isointense	7 (37)
Hyperintense	1 (5)
Axial Location	
Central	13 (68)
Eccentric	6 (32)
Other Findings	
Edema	7 (37)
Intratumoral cyst	4 (21)
Peritumoral cyst	3 (16)

Literature Review

The results of the literature review are summarized in Table 4. The frequency of nonenhancing intramedullary astrocytomas was 14 of 76 (18%), including 2 anaplastic astrocytomas. The range of frequency was wide (0%–50%). Unfortunately, 5 of the 7 studies failed to provide any surgical history with respect to the tumors. In the remaining 2 studies, all of the 8 recurrent intramedullary astrocytomas demonstrated enhancement.^{8,9} Although the enhancement patterns were classified in different ways, 5 studies described the enhancement pattern and the frequency of nonenhancing astrocytomas.^{8,9,11–13} With the exception of 4 nonenhancing astrocytomas of a total of 34 cases, 12 enhanced diffusely; 9, inhomogeneously; 2, homogeneous-

Table 3: T2 MR imaging features of intramedullary astrocytomas	
T2 Signal	Cases (%)
Hyperintense	18 (95)
Isointense	1 (5)
Longitudinal Location	
Cervical	10 (53)
Thoracic	5 (26)
Cervical/thoracic	2 (11)
Thoracic/lumbar	1 (5)
Cervical/thoracic/lumbar	1 (5)
Other Findings	
Syrinx	0 (0)
Hemorrhage	2 (11)

ly; 2, markedly; and 1 each had moderately, patchy, minimally, well-delineated, and cord surface enhancement.

Discussion

Approximately one-third of the intramedullary astrocytomas did not enhance at all in this multicenter retrospective study (Figs 1–3), and the frequency of nonenhancing intramedullary astrocytomas was 18% in a literature review of 7 articles. These results are in contrast to the widely accepted near-invariable enhancement of intramedullary astrocytomas.^{3,5,6}

Although astrocytomas represent approximately 30% of spinal cord tumors, intramedullary astrocytomas are rare be-

Table 4: Literature review

Study	Year	Total No.	No. Enhanced (%)	Comment
White et al. ⁷	2007	35	10 (29)	Includes 2 nonenhancing anaplastic astrocytomas
Lin and Zhang ¹³	2004	4	2 (50)	
Patel et al. ¹¹	1998	15	1 (7)	
Breger et al. ¹²	1989	3	0 (0)	
Parizel et al. ¹⁰	1989	7	0 (0)	Includes 1 pilocytic and 6 low-grade astrocytomas
Dillon et al. ⁹	1989	6	0 (0)	Includes 6 recurrent astrocytomas
Sze et al. ⁸	1988	6	1 (17)	Includes 4 primary and 2 recurrent astrocytomas
Total		76	14 (18)	

cause spinal cord tumor accounts for 4%–10% of central nervous system tumors.³ As such, most articles regarding the MR imaging findings of intramedullary astrocytomas were limited with respect to the number of patients; therefore, the frequency of nonenhancing astrocytomas varied from 0% to 50%.^{7–13} However, the largest scale study showed that nonenhancing intramedullary astrocytomas were present in 29% of 35 patients with spinal cord tumors,⁷ similar to those in the present study.

Tumor contrast enhancement is caused by a breakdown of the blood-brain barrier. The barrier remains relatively intact in low-grade astrocytomas, while high-grade astrocytomas are pathologically characterized by their exponential growth and neovascularization, and contrast materials are able to pass through the barrier breakdown.^{14,15} In spinal cords possessing an intact blood-brain barrier, nearly all anaplastic intramedullary astrocytomas were expected to enhance, as supported by a small-scale study of malignant intramedullary astrocytomas in children.¹⁶ However, nonenhancing intramedullary tumors were found in 2 of 3 anaplastic astrocytomas in this retrospective study (Figs 2 and 3) and in 2 anaplastic astrocytomas in the literature review.⁷ Although further study regarding the enhancement of anaplastic astrocytoma is required to compensate for the limited number of cases, enhancement of anaplastic intramedullary astrocytomas on MR imaging is unexpected.

Pilocytic astrocytomas of the spinal cord are categorized histologically as WHO grade I and are known to be always enhancing,¹ like those in the brain.² In this study, all 3 pilocytic astrocytomas were enhanced and their enhancement patterns varied from focal to diffuse. However, a nonenhancing pilocytic astrocytoma of the spinal cord has been documented in 1 case report.¹⁷

Previously, most intramedullary neoplasms were considered to demonstrate at least minimal enhancement, and neoplasms were often excluded for nonenhancing intramedullary lesions.¹⁸ Nonenhancing neoplasms of the spinal cord may be difficult to differentiate from non-neoplastic lesions, including demyelinating disease, myelitis, sarcoidosis, etc. However, the nonenhancing intramedullary astrocytomas reviewed for the present study demonstrated prominent mass effects or cord expansion, thus meeting the criteria for a neoplasm (Figs 1–3).

The enhancement patterns of the intramedullary astrocytomas, with the exception of the nonenhancing astrocytomas, were evenly distributed with focal nodular, patchy, and inhomogeneous diffuse enhancement; however, none demonstrated a homogeneously diffuse enhancing pattern. These

patchy or irregular enhancements are one of the MR imaging characteristics of astrocytomas, differentiating them from ependymoma³ and are supposedly the result of the pathologic features of astrocytomas that tend to have an infiltrative nature extending far beyond the gross tumor margin.¹⁹ Therefore, patients with astrocytomas have a worse prognosis and survival rate than those with ependymomas.²⁰

On noncontrast MR imaging, most astrocytomas were isointense or hypointense relative to the spinal cord on T1-weighted imaging and hyperintense on T2-weighted imaging, as described in previous studies.^{1,3} When located in the axial spinal cord, most astrocytomas were central or involved the entire cord. Only 30% were located eccentrically; this finding is another characteristic distinguishing astrocytoma and ependymoma (Fig 1).^{1,3} With respect to longitudinal location, Baleriaux²¹ reported that most astrocytomas reside in the thoracic region. However, in the present study, most ($n = 13$, 69%) of intramedullary astrocytomas were located only in the cervical region (Figs 1 and 2).

The frequency of peritumoral edema was <50% and was typically small in quantity. Intratumoral or peritumoral cysts and hemorrhage in and around the tumor were uncommon. Syringohydromyelia was not found in any case. None of the aforementioned MR imaging features are necessarily specific findings of intramedullary astrocytoma.

Because of the rarity of intramedullary astrocytoma, this retrospective study included a small number of patients. Another limitation of this study was the use of variable MR imaging systems, ranging between 1T and 3T, because MR imaging studies were performed at several centers over the course of a decade. However, all except 4 studies were performed by using 1.5T MR imaging systems, and the MR imaging studies from 3 patients performed at 1T were of good quality. In the literature review, in most studies the number of patients was also limited, and recurrent astrocytomas following surgical removal and radiation therapy were reported in 2 studies.^{8,9}

Conclusions

Nonenhancing intramedullary astrocytomas are not uncommon and comprise between 20% and 30% of intramedullary astrocytomas. Therefore, astrocytoma must remain in the differential diagnosis of nonenhancing intramedullary lesions, particularly if the lesion demonstrates a prominent mass effect or cord expansion. Most intramedullary astrocytomas appear to be hyperintense on T2-weighted images; however, other MR imaging features are variable.

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