Study Design: Retrospective clinical study

Objective: The objective of this study is to evaluate MR imaging and pathological features of spinal schwannomas (SCHs) and myxopapillary ependymomas (MPEs) with focus on differentiating two disease entities.

Summary of Background Data: Few studies have reported on the differentiation of SCHs and MPEs.

Methods: 53 patients were retrospectively reviewed with histologically confirmed spinal SCHs (41 patients) or MPEs (12 patients) of the *cauda equina* and/or conus medullaris. We evaluated neurologic deterioration after surgery in association with the intraoperative findings of the tumor, as well as with the preoperative MRI and postoperative histologic findings.

Results: Patients in the SCH group had a greater mean age at surgery, and a greater mean disease duration. In the SCH group, all 24 tumors which were homogeneously hyperintense on the T2W images showed rim enhancement on the postcontrast T1W images. Moreover, all 14 of the SCHs with homogeneous enhancement on the postcontrast T1W images were isointense on the T2W images. However, in the MPE group, all 8 of the tumors which were homogeneously hyperintense on T2W images showed homogeneous enhancement on their postcontrast T1W images.

Conclusions: It is very important to differentiate SCHs and MPEs before surgery because there are reported cases of dissemination of MPEs via cerebrospinal fluid throughout the neuraxis; the tumor must be removed en block to prevent this. Although MPEs and SCHs may have similar imaging characteristics, detailed examination of the MR T2W image and postcontrast T1W image facilitates their differentiation.

Key words

MR imaging Pathological features spinal Schwannomas Myxopapillary ependymomas Differentiation

Introduction

Schwannomas (SCHs), which are considered benign tumors (WHO grade I), are the most common intradural extramedullary spinal lesion.[1] There are reports on differentiating spinal SCHs from meningiomas;[7,15,17] SCHs are usually located on the conus and cauda regions where meningiomas rarely exist.[15] Surgery for spinal SCHs usually results in good postoperative functional outcomes.[12]

Myxopapillary ependymoma (MPE) is a highly vascular subtype of ependymoma

that arises almost exclusively from the filum terminale and conus medullaris and accounts for 30-80% of ependymomas in these regions.[4,20] MPEs are also classified as WHO grade I, and usually arise from the cauda equina with occasional extension into the conus medullaris.[16] There are reported cases of dissemination via cerebrospinal fluid throughout the neuraxis, although this is uncommon. Like SCHs, most MPEs grow slowly, circumscribed by a connective tissue capsule and a lack of firm attachment to or incorporation of surrounding spinal nerve root.[20] Thus, they are highly amenable to complete excision with a generally excellent postoperative outcome.[4,20] However, unlike SCHs, once the capsule breaks down, they infiltrate or adhere to the nerve roots of the *cauda equina* and/or conus medullaris and are then associated not only with a high recurrence rate,[4] but also with postoperative neurologic deficit.

MPEs and SCHs sometimes have a similar appearance with our imaging modalities[23] making presurgical differentiation difficult. Although accurately diagnosing these two disease entities prior to surgery is extremely important, there have been no previous reports focused on this. In our present study, we compared the magnetic resonance images (MRI) and pathological features of SCHs and MPEs retrospectively and evaluated features that would allow differentiation of these two tumors.

Materials and methods

Patient population

From 2001 to 2009, a total of 53 patients with histologically confirmed spinal SCHs or MPEs of the *cauda equina* and/or conus medullaris were surgically treated at our institution. The location of the tumors was strictly intradural-extramedullary. All cases received a histological review of tumor microsections stained with hematoxylin and eosin and were diagnosed as either spinal SCHs or MPEs. There were 41 patients in the SCH group and 12 patients in the MPE group. All patients underwent tumor resection using microscopic and intraoperative spinal cord monitoring. The extent of surgery was determined from the surgical reports and postoperative imaging studies. We used the Japanese Orthopedic Association scoring system for low back pain[3] to evaluate the operative results. The scoring system has a maximum of 29 points consisting of subjective symptoms, clinical signs, restriction of ordinary daily life, and urinary bladder function. The recovery rate was calculated using Hirabayashi's method based on the formula:[10]

recovery rate (%) = [(post-operative score - pre-operative score) × 100]/17 - pre-operative score).

We evaluated neurologic deterioration after surgery in association with the intraoperative findings of the tumor, as well as with the preoperative MRI and postoperative histologic findings.

MR imaging

All patients underwent MR imaging in the sagittal, coronal and axial planes with T1-weighted (T1W, TR, 400-700 ms; TE, 9-25ms), fast spin-echo (FSE) T2-weighted (T2W, TR, 3,000-5,000 ms; TE, 96-150ms), and postcontrast (0.1 mmol/kg Gd-DTPA) T1-weighted sequences. Two board-certified neurosurgeons reviewed all images. These neurosurgeons had worked mainly as spine surgeries and had interpreted spine MR images as their daily clinical and research practice. The two reviewers (A.M. and H.M.) identified and characterized the abnormalities by consensus. Neither neurosurgeon had received information pertaining to age, sex, clinical history, symptoms and/or histopathological results at the time of the interpretation. They identified each intradural tumor in the 53 patients and assessed its location, signal intensity characteristics and enhancement. Tumor size relative to the affected spinal segments was measured on the contrast-enhanced images. Furthermore, the precontrast signal characteristic on T1W images as isointense, hyperintense or hypointense was

classified relative to the spinal cord. The precontrast signal characteristic on T2W images was classified as isointense, homogeneous hyperintense or heterogeneous intense. The contrast enhancement pattern on post-contrast T1W images classified as homogeneous, rim enhancement when it was peripheral, or as heterogeneous.

Spinal tumors were classified as intramedullary or extramedullary based on their location with respect to the spinal cord and their morphologic characteristics. Besides SCHs and MPEs, other intradural-extramedullary tumors, e.g. meningioma (n=2), neurofibroma (n=1), paraganglioma (n=1), and perineurinoma (n=1), were observed on the conus and cauda regions. We did not consider them relevant to the study and therefore excluded them. Tumors with extraspinal extension such as dumbbell schwannomas were also excluded (n = 4). We particularly evaluated the signal intensity and contrast enhancement patterns with the T2W sagittal sequencing on MR imaging.

Statistical analysis

Data were analyzed using the Statistical Program for the Social Sciences (SPSS version 19 software package, Inc., Chicago, IL). The mean values are presented as mean ± SD. The Mann-Whitney U-test was used for analyzing differences between the 2 groups, and the $\chi 2$ test was used to assess measures of association in a frequency table,

with $p < 0.05$ considered statistically significant.

Results

Three tables summarize the clinical presentation and MR characteristics of the SCHs and MPEs.

Clinical manifestation

Table 1 shows gender, mean age at surgery, mean disease duration, pre- and postoperative JOA score, JOA recovery rate, and tumor size for each tumor group. In total, there were 32 male and 21 female patients with an age range from 8 to 86 years. The SCH group included 41 patients, 25 males and 16 females, with an age range from 29 to 86 years (mean age 51.6 years), and the MPE group had 12 patients, 7 males and 5 females, with an age range from 8 to 60 years (mean age 38.9 years). The follow-up period ranged from 2 to 10 years (median 73.6 months). Patients in the SCH group had a greater mean age at surgery (51.7 ± 16.3 years for SCH versus 38.9 ± 15.5 years for MPE), and a greater mean disease duration (13.0 ± 20.6 months for SCH versus 3.6 ± 1.8 months for MPE), whereas, the average number of affected spinal segments (tumor size) was slightly larger in the MPE group, although not significantly (1.2 ± 0.6 vertebrae for SCH versus 1.7 ± 1.0 vertebrae for MPE). There was no statistically

significant difference between the pre- and postoperative JOA scores or JOA recovery rates. Surgery was the initial treatment in all patients. Complete tumor excision was achieved on all SCHs and on 10 of the 12 MPEs (83.3%). Two patients (16.7%) in the MPE group received subtotal resection because of nerve root and conus involvement. These 2 patients received postoperative radiotherapy (40-45 Gy). Preoperatively, we suspected SCH in 8 (66.7%) of the MPE patients. There was neither tumor recurrence nor progression of the remaining tumors in either group. There were no deaths due to surgery.

MRI findings

On T1W images, all SCHs and MPEs were isointense. Of the 41 SCHs on T2W images, 14 (34.1%) were isointense, 24 (58.5%) were homogeneously hyperintense, and 3 (7.3%) were heterogeneously intense. Of the 12 MPEs, 1 (8.3%) was isointense, 8 (66.7%) were homogeneously hyperintense , and 3 (25.0%) were heterogeneously intense. Homogeneous hyperintensity on T2W images was the most frequent signal intensity in both groups. On the other hand, on postcontrast T1W images 24 (58.5%) of the 41 SCHs showed rim enhancement, 14 (34.1%) showed homogeneous enhancement, and 3 (7.3%) showed heterogeneous enhancement. Of the 12 MPEs, 9 (75.0%) showed

homogeneous enhancement, and 3 (25.0%) showed heterogeneous enhancement. More than half of the SCH group showed rim enhancement, while 75% of the MPE group showed homogeneous enhancement. In the axial plane, 32% of SCH were anterior or antero-lateral, 19.5% were lateral and 12.2% were central. Concerning MPE, 50% were central (Table 2).

The relationship between T2W and postcontrast T1W images,

In the SCH group, all 24 tumors which were homogeneously hyperintense on the T2W images showed rim enhancement on the postcontrast T1W images. Moreover, all 14 of the SCHs with homogeneous enhancement on the postcontrast T1W images were isointense on the T2W images (Fig. 1A). However, in the MPE group, all 8 of the tumors which were homogeneously hyperintense on T2W images showed homogeneous enhancement on their postcontrast T1W images of (Fig. 1B).

The relationship between MR imaging and pathology

The SCHs which were homogeneously hyperintense on their T2W images had hypocellular lesions and cystic degeneration, the Antoni type B tissue pattern. Those SCHs that were isointense on T2W images had highly cellular lesions, the Antoni type A tissue pattern (Figs. 2A, B, C). Moreover, the Antoni type A pattern, which was

isointense on T2W images, showed homogeneous enhancement on postcontrast T1W images (Figs. 3A, B, C).

In the MPE group, those tumors which were homogeneously hyperintense on T2W images had papillae with abundant areas of myxoid stroma containing capillary blood vessels. Those MPEs with homogeneous enhancement on postcontrast T1W images had these same pathologic features (Figs. 4A, B, C). MPEs that were isointense on T2W images and postcontrast T1W images had necrosis and intratumoral hemorrhage (Figs. 5A, B, C). In contrast, SCHs which were isointense on T2W images and enhanced on postcontrast T1W images were highly cellular on histopathology (Figs. 3A, B).

Discussion

Spinal SCHs are benign, mostly intradural-extramedullary tumors that are solitary, well-circumscribed, encapsulated, and located eccentrically on spinal nerve roots.[13] MPEs are usually histologically benign, often encapsulated, slow-growing tumors that mostly occur in the *cauda equina* and/or conus medullaris regions.[2] Of 62 consecutive spinal tumors we saw at our institution which occurred in the *cauda equina* and/or conus medullaris regions, SCH (n=45) was the most frequently seen and MPE (n=12)

was the second most frequent. Moreover, 8 patients in our study with MPEs were preoperatively suspected of having SCHs.

Surgical outcomes of most spinal SCH resections have been reported as good and without recurrence.[5] Unlike SCHs, the recurrence rate of MPEs after surgery varied with treatment. Celli et al. reviewed 271 cases and found that 4% (range 1%-10%) recurred after total excision and 28% (range 20%-40%) recurred after partial removal and radiotherapy.[4] Because of this difference in recurrence relative to the type of excision for MPEs, preoperative strategy for each tumor is very important. It is especially important for an encapsulated MPE to be removed intact because it may spread along the cauda equina and occupy the dural canal, eventually leading to CSF dissemination if the tumor perforates the capsule during surgery.[6,19,20] In the present study, there was no significant difference between the two tumor groups in their clinical manifestations including tumor size; MPEs tended to be larger than the SCHs, but not significantly.

In the axial plane, 50% of MPEs were central. The distribution of the roots of the cauda equina in the thecal sac also may help in distinguishing the tumors: An ependymoma of the filum pushes the roots to the periphery of the thecal sac, whereas a

schwannoma of the cauda more often pushes the roots together in an eccentric fashion. When the tumors are small, the observation of an origin from a root in the cauda equina, rather than the filum, may aid in distinguishing SCHs from MPEs.

SCHs' and MPEs' signal patterns on T1W images are concordant with other studies,[7,15,18] showing isointensity relative to the spinal cord. SCHs tend to be mild to markedly hyperintense on T2W images.[9] Focal areas of even greater hyperintensity on T2W images often correspond to cystic portions, whereas isointensity may represent hemorrhage, dense cellularity, or collagen deposition.[8] Moreover, Antoni B structures in the tumor, which correspond to a loose structure rich in free water, could increase the T2 value.[11] In the present study, there were 24 cases (58.5%) with homogeneous hyperintensity and 14 cases (34.1%) with isointensity on T2W images.

On the other hand, MPEs are unique for their intracellular and perivascular accumulation of mucin.[14] Mucin, which is proteinaceous, should be hyperintense on T2W images.[21] There were 8 cases (66.7%) in our study that were homogeneously hyperintense on T2W images. On postcontrast T1W images, all 24 of the SCHs with homogeneous hyperintensity on T2W images showed rim enhancement on postcontrast T1W images. All 14 SCHs that had homogeneous enhancement were isointense on

T2W images. However, all 8 of the MPE cases showing homogeneous hyperintensity on T2W images had homogeneous enhancement on postcontrast T1W images.

We evaluated lesion pathology in relation to intensity on T2W images. SCH tissue that was highly cellular and hypervascular, called Antoni type A, was also isointense on T2W images and enhanced on postcontrast T1W images (Figs. 2, 3). On the other hand, highly cellular areas with mucin appeared as homogeneous hyperintense lesions on T2W images and enhanced lesions on postcontrast T1W images (Fig. 4). It has been suggested that open gap junctions between endothelial cells of blood vessels are permeable to Gd-DTPA molecules, thus facilitating the movement of Gd-DTPA from vascular to extracellular spaces in SCHs.[22] This is likely the same process in MPEs.

It is difficult to differentiate SCHs and MPEs on T2W images because they are both heterogeneously intense. However, as we noted previously, the homogeneous hyperintense areas on T2W images were not enhanced on postcontrast T1W images, whereas, isointense areas of SCHs were enhanced on postcontrast T1W images (Figs. 6A, B), and homogeneous hyperintense areas of MPEs were enhanced on postcontrast T1W images (Figs. 6C, D). It may be possible to differentiate SCHs and MPEs of the inhomogeneous type on postcontrast T1W images.

In summary, it is very important to differentiate SCHs and MPEs before surgery because there are reported cases of dissemination of MPEs via cerebrospinal fluid throughout the neuraxis; the tumor must be removed en block to prevent this. Although MPEs and SCHs may have similar imaging characteristics, detailed examination of the MR T2W image and postcontrast T1W image facilitates their differentiation.

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TABLE 1: Clinical characteristics and tumour location of schwannoma and myxopapillary ependymoma

TABLE 2: MR imaging findings for schwannomas and myxopapillary ependymomas

Figure 1: The relationship between T2W and postcontrast T1W images A. SCHs, B. MPEs

Figure 2: The SCHs which were homogeneously hyperintense on their T2W images (A) and rim enhancement on postcontrast T1W images (B) had hypocellular lesions and cystic degeneration, the Antoni type B tissue pattern (C).

Figure 3: The SCHs which was isointense on T2W images (A), showed homogeneous enhancement on postcontrast T1W images (B), and the Antoni type A pattern (C),

Figure 4: The MPEs that were homogeneously hyperintense on T2W images (A) and homogeneous enhancement on postcontrast T1W (B) had papillae with abundant areas

of myxoid stroma containing capillary blood vessels (C).

Figure 5: MPE that was isointense on T2W images (A) and postcontrast T1W images (B) had necrosis and intratumoral hemorrhage (C).

Figure 6: The homogeneous hyperintense areas on T2W images were not enhanced on postcontrast T1W images, whereas, isointense areas of SCHs were enhanced on postcontrast T1W images (A, B), and homogeneous hyperintense areas of MPEs were enhanced on postcontrast T1W images (C, D).