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Original Article

Assessment of the Concordance Rate between Intraoperative Pathological Diagnosis and the Final Pathological Diagnosis of Spinal Cord Tumors

Sosuke Muraoka[a], Kentaro Yamane[b]*, Haruo Misawa[c], Tomoyuki Takigawa[c], Tomoko Tetsunaga[c], Yoshiaki Oda[c], Kazuo Nakanishi[d], Toshifumi Ozaki[a], and Takehiro Tanaka[e]

Departments of [a]Orthopaedic Surgery, [b]Intelligent Orthopaedic Surgery, [e]Pathology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, [c]Department of Orthopaedic Surgery, Okayama University Hospital, Okayama 700-8558, Japan, [d]Department of Orthopaedic Surgery, Kawasaki Medical School Hospital, Kurashiki, Okayama 701-0192, Japan

The intraoperative pathological diagnosis (IPD) plays an important role in determining the optimal surgical treatment for spinal cord tumors. The final pathological diagnosis (FPD) is sometimes different from the IPD. Here, we sought to identify the accuracy of the IPD of spinal cord tumors compared to the FPD. We retrospectively analyzed the cases of 108 patients with spinal cord tumors treated surgically in our institute; the IPD, FPD, mismatched cases, and concordance rate between the IPD and FPD were investigated. Five cases involved a mismatch between the IPD and FPD. The overall concordance rate was 95.4%, with 90.9% for extradural lesions, 98.5% for intradural extramedullary lesions, 84.2% for intramedullary lesions, and 100% for dumbbell-type tumors. The concordance rate of intramedullary lesions tended to be lower than that of other lesions ($p = 0.096$). A lower concordance rate was revealed for intramedullary lesions compared to the other lesions. Despite the IPD clearly remaining a valuable tool during operative procedures, surgeons should recognize the limitations of IPDs and make comprehensive decisions about surgical treatments.

Key words: spinal cord tumor, intraoperative pathological diagnosis, final pathological diagnosis, concordance rate

For the determination of a definite diagnosis of a spinal cord tumor, pathological findings are the most important type of findings. A surgical resection of a spinal cord tumor is commonly performed, but variables related to the surgical method (*e.g.*, the excision range) can be changed according to the pathological findings. Imaging modalities such as magnetic resonance imaging (MRI) and computed tomography (CT) are applied to determine the types of spinal cord tumor [1, 2]. The information of tumor locality, signal intensity, shape, enhancement effect, and calcification enables the establishment of differential diagnoses. However, it is impossible to determine the exact type of spinal tumor based on only imaging findings. A definitive diagnosis cannot be established without pathological findings.

A needle biopsy is a relatively simple, minimally invasive procedure that can be performed for many lesions (*e.g.*, bone tumors and soft-tissue tumors) [3]. However, it is often difficult to perform a needle biopsy in patients with spinal cord tumors because of risks such as iatrogenic nerve damage close to the tumor and the presence of a hematoma around the spinal cord. An

Received January 4, 2021; accepted February 22, 2021.
*Corresponding author. Phone: +81-86-235-7273; Fax: +81-86-223-9727
E-mail: woodblocks0311@gmail.com (K. Yamane)

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incisional biopsy or resection is thus performed more frequently in cases of spinal cord tumors. Additional treatments are sometimes needed postoperatively based on the results of the FPD [4].

The intraoperative pathological diagnosis (IPD) provides useful information to support surgeons' decision-making, especially for cases in which reaching a definite diagnosis based on preoperative imaging or to help the surgeon determine whether a tumor is benign or malignant. However, the accuracy of IPDs is limited by the characteristics of this procedure, which can only use simple fixing and staining protocols in a short period. Some reports have described the concordance rates between the IPD and FPD in other types of surgery [5,6]; however, there are few similar reports of spinal cord tumors [7]. We performed the present study to identify the concordance rate between the IPD and FPD in patients who have undergone the surgical management of spinal cord tumors at our institute.

Patients and Methods

Between 2004 and 2017, 151 surgeries for spinal cord tumors were performed at our institute. Of these, 43 surgeries were performed without an IPD. An IPD was obtained during the surgery for a total of 108 patients. The patients were 50 males and 58 females, aged 13-87 years (mean 56 years). The tumors were located in the cervical area (n = 29, 27%), the thoracic area (n = 47, 43%), and the lumbosacral area (30%, n = 32). The tumors were extradural (n = 11), intradural-extramedullary (n = 67), intramedullary (n = 19), or dumbbell-type (n = 11). All of the IPDs and FPDs were performed by pathologists in our hospital.

The IPD procedure in each case was performed as follows. The specimen was placed in a cup and delivered to the pathology department. The tissue and compound in the cryomold were frozen by soaking in −70° acetone for 5-10 sec. The tissue block was sectioned at a thickness of 5-10 μm using a cryostat and adhered to the slide glass. The sample was fixed using alcohol and formalin, stained with hematoxylin and eosin (H&E), and cleared using xylene. A single pathologist confirmed the diagnosis. The pathologist who confirmed the IPD was not necessarily the same as the pathologist who confirmed the FPD.

We determined the concordance rates between the IPD and FPD for these 108 cases. When the IPD and FPD were the same, the diagnosis was defined as a "match." When the two were different, the diagnosis was defined as a "mismatch." The statistical analysis was performed using Fisher's exact test with Statcel, the useful add-in form on Microsoft Excel, 4th ed. Probability (p)-values < 0.05 were considered significant. The study was approved by the university's Research Ethics Committee.

Results

Mismatched cases. The IPD and FPD results are summarized in Table 1 and Table 2. A total of five cases involved a mismatch between the IPD and the FPD. The 5 cases of hemangioblastoma, astrocytoma, malig-

Table 1 The results of the intraoperative pathological diagnoses (IPDs)

Intraoperative pathological diagnosis	Number of cases (%)
Schwannoma	62 (57.4)
Meningioma	14 (13)
Ependymoma	8 (7.4)
Astrocytoma	6 (5.6)
Hemangioma	5 (4.6)
Unknown condition	4 (3.7)
Hemangioblastoma	3 (2.8)
Neurofibroma	2 (1.9)
Angiolipoma	1 (0.9)
Malignant lymphoma	1 (0.9)
Metastatic adenocarcinoma	1 (0.9)
Sarcoidosis	1 (0.9)
Total	108 (100)

Table 2 The results of the final pathological diagnoses (FPDs)

Final pathological diagnosis	Number of cases (%)
Schwannoma	61 (56.5)
Meningioma	14 (13)
Ependymoma	10 (9.3)
Hemangioma	6 (5.6)
Astrocytoma	5 (4.6)
Unknown condition	4 (3.7)
Hemangioblastoma	2 (1.9)
Neurofibroma	2 (1.9)
Angiolipoma	1 (0.9)
Malignant peripheral nerve sheath tumor	1 (0.9)
Metastatic adenocarcinoma	1 (0.9)
Sarcoidosis	1 (0.9)
Total	108 (100)

nant lymphoma, schwannoma, and an unknown condition based on the IPD were later identified as ependymoma, ependymoma, no evidence of malignant lymphoma, malignant peripheral nerve sheath tumor, and hemangioma based on the FPD, respectively (Table 3).

Concordance rates between the IPDs and FPDs. The concordance rate was 95.4% (103/108) for all of the cases, 90.9% (10/11) for the extradural lesions, 98.5% (66/67) for the intradural extramedullary lesions, 84.2% (16/19) for the intramedullary lesions, and 100% (11/11) for the dumbbell-type lesions (Fig. 1). The concordance rate of the intramedullary lesions tended to be lower than those of the other lesions ($p = 0.096$).

Case Reports

Case 1. A 39-year-old woman presented with right-limb numbness. MRI revealed an intramedullary spinal cord tumor at the level of C2, showing a low-intensity signal on T1-weighted images, a high-intensity signal on T2-weighted images, and partial enhancement on gadolinium-diethylenetriaminepentaacetate (Gd-DTPA)-enhanced images (Fig. 2A-C). An intralesional resection of the tumor was performed. The IPD was hemangioblastoma (Fig. 2D), whereas the FPD was ependymoma (World Health Organization [WHO] grade II) (Fig. 2E). The mismatch between the IPD and FPD might have occurred because of time constraints and sampling limitations.

Case 2. A 26-year-old woman presented with gait disturbance. MRI revealed an intramedullary spinal cord tumor originating at the C2-C7 level, showing iso-intensity on both T1-weighted images and T2-weighted images and heterogeneous enhancement on Gd-DTPA-enhanced images (Fig. 3A-C). Syringomyelia was present in the thoracic spinal cord. An incisional biopsy was performed. The IPD was astrocytoma (WHO grade II) (Fig. 3D). The FPD of the sample of the incisional biopsy was also astrocytoma (WHO grade II). Gross total resection of the tumor was performed. The last FPD was ependymoma (WHO grade II) (Fig. 3E). Gliosis was observed around the tumor in the sample acquired during the second surgery (Fig. 3F). The sample from the incisional biopsy consisted of only the area of gliosis. The small sample size could have led to the mismatch between the IPD and FPD.

Case 3. A 71-year-old woman developed numbness and pain of the upper limbs. MRI revealed an intramedullary spinal cord tumor originating at the C5-C7 level, showing iso-intensity on T1-weighted images, iso-high signal intensity on T2-weighted images, and partial enhancement on Gd-DTPA-enhanced images (Fig. 4A-C). An incisional biopsy was performed; the IPD was malignant lymphoma (Fig. 4D).

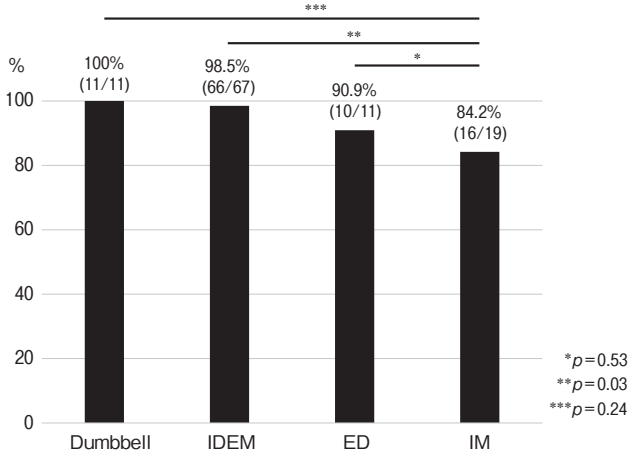

Fig. 1 Comparison of the concordance rates between the IPD and FPD: 100% for dumbbell-type lesions, 98.5% for intradural extramedullary (IDEM) lesions, 90.9% for extradural (ED) lesions, and 84.2% for intramedullary (IM) lesions.

Table 3 Mismatched cases between the IPD and FPD

Case	Location	Localization	IPD	FPD
1	Cervical	IM	Hemangioblastoma	Ependymoma
2	Cervical	IM	Astrocytoma	Ependymoma
3	Cervical	IM	Malignant lymphoma	No evidence of malignant lymphoma
4	Cervical	IDEM	Schwannoma	Malignant peripheral nerve sheath tumor
5	Thoracic	ED	Unknown condition	Hemangioma

IM, intramedullary; IDEM, intradural extramedullary; ED, extradural; IPD, intraoperative pathological diagnosis; FPD, final pathological diagnosis.

Immunostaining of the tissue revealed positive staining for cluster of differentiation (CD)3, CD20, and CD138, with negative staining for cyclin D1 (Fig. 4F-I). The FPD was based on the absence of evidence of malignant lymphoma (Fig. 4E). The small sample size and staining limitations might have been associated with the mismatch between the IPD and FPD.

Discussion

The overall concordance rate between the IPD and FPD of spinal cord tumors was 95.4% in this study of 108 cases. Based on the location of the tumor, the concordance rates were 90.9% for extradural lesions, 98.5% for intradural extramedullary lesions, 84.2% for intramedullary lesions, and 100% for dumbbell-type lesions. The concordance rate for intramedullary lesions tended

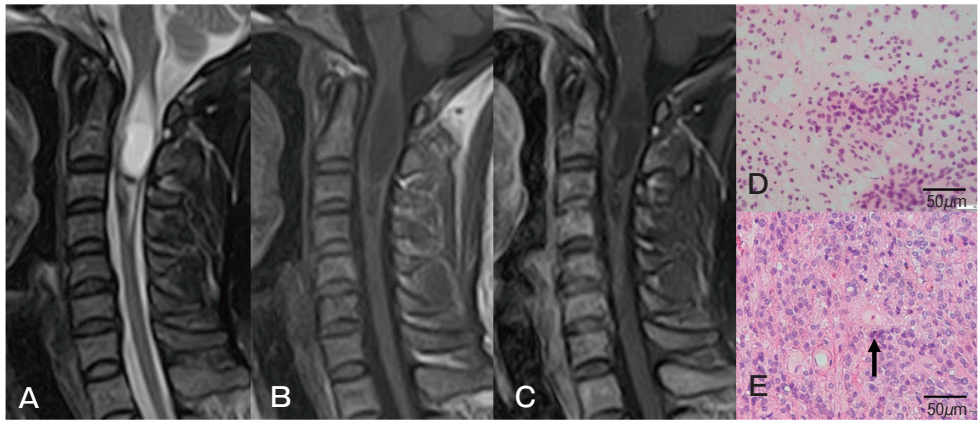

Fig. 2 Case 1. High-signal-intensity T2-weighted MRI (A), low-signal-intensity T1-weighted MRI (B), and partially Gd-DTPA-enhanced lesions around the tumor (C). IPD: luminal structure, homogeneous nuclei, clear cytoplasm (hemangioblastoma) (D). FPD: circular nuclei and true rosettes (ependymoma) (*arrow*) (E).

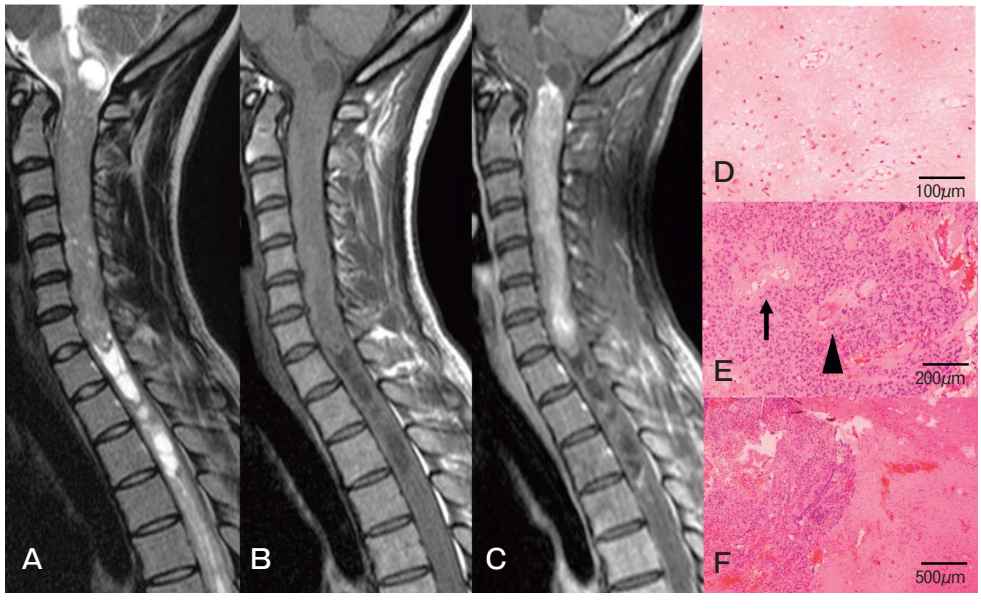

Fig. 3 Case 2. Low-signal-intensity T2-weighted MRI (A), high-signal-intensity T1-weighted MRI (B), and Gd-DTPA-enhanced tumor (C). IPD based on the biopsy: small glial cells containing homogeneous nuclei (astrocytoma) (D). FPD based on the final resection: true rosettes (*arrow*) and perivascular pseudorosettes (*arrowhead*) (E). Gliosis around the ependymoma (F).

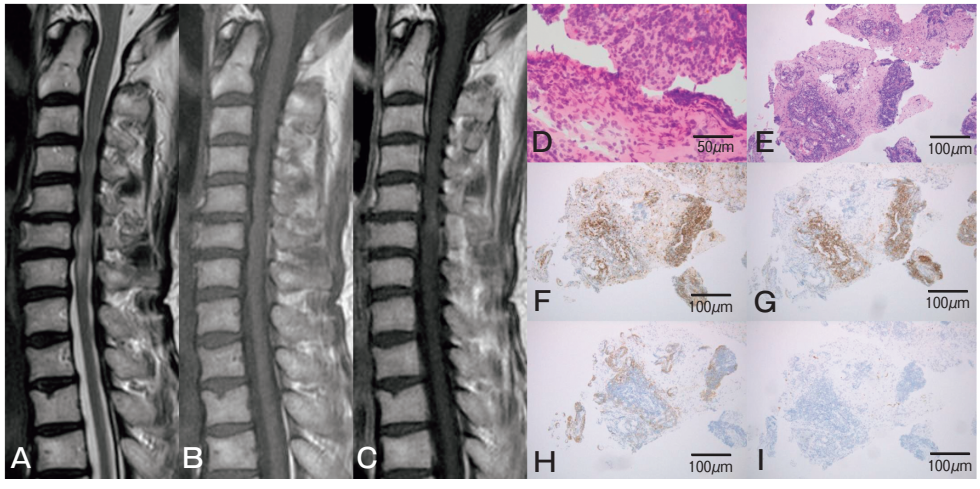

Fig. 4 Case 3. High-signal-intensity T2-weighted MRI (**A**), iso-signal-intensity T1-weighted MRI (**B**), and Gd-DTPA-enhanced tumor (**C**). IPD: high nucleus-to-cytoplasmic ratio (malignant lymphoma) (**D**). FPD: No evidence of malignant lymphoma (**E**), Cluster of differentiation CD3+ (**F**), CD20+ (**G**), CD138+ (**H**), cyclin D1− (**I**).

to be lower than those for the other lesions.

The reported concordance rate between IPDs and FPDs varies from 88.8% to 97.3% for various types of tumors [5-14]. There have been few studies of the concordance rate between the IPD and FPD of spinal cord tumors. Kobayashi *et al.* reported that the overall concordance rate between the IPD and FPD of spinal cord tumors was 86.8% (58/67), with 100% (13/13) for extradural lesions, 96% (26/27) for intradural extramedullary lesions, and 70% (19/27) for intramedullary lesions; the concordance rate of the intramedullary lesions is significantly lower than that of the other lesions [7]. In other reports, the concordance rates of the IPDs and FPDs of intramedullary tumors range from 58.1% to 80.4% [7-9]. Although it was not significant in our series, the finding of a low concordance rate for intramedullary lesions is consistent with the previous reports.

Several reasons may contribute to the low concordance rate of intramedullary tumors. Intramedullary tumors are smaller than the tumor sizes observed on imaging because of local tissue reactions such as edema or inflammation surrounding the tumor. The sample tissues for an IPD may be collected from the boundary between the actual tumor and the reactive tissue.

There have been some reports of concordance rates between needle-biopsy findings and the final histological diagnosis [3,15-17]. Kubo *et al.* conducted a meta-analysis of the diagnostic accuracy of core needle biopsies and surgical biopsies in the field of musculoskeletal lesions; the concordance rate between the results of these 2 types of biopsy was 84% [15]. The diagnostic accuracy of a core needle biopsy is significantly lower than that of a surgical biopsy. These findings confirm that appropriate tissue collection and a sufficient sample volume are essential for an accurate diagnosis. Moreover, intramedullary spinal cord tumors are associated with more differential diagnoses than tumors at other locations [8,18]. The limitation of the minimum simple staining due to time constraints makes achieving the differential diagnosis more difficult. Our mismatched cases may also have been affected by these factors or limitations.

There are reports of several types of tumors that are easily misdiagnosed. In the field of brain tumors, glioblastoma may be misdiagnosed as a metastatic tumor or non-glial tumor [10]. A cytodiagnosis using the squash method is useful to differentiate between a glioma and a non-glial tumor. Nasir *et al.* reported that nonglial neoplasms such as neurocytoma, hemangioblastoma, atypical meningioma, and lymphoma are sometimes misdiagnosed as glioma based on an IPD [19]. A meningioma is also easily misdiagnosed as a different type of spindle cell tumor (*e.g.*, schwannoma) when the tissues lack the typical features of meningioma represented by whorls and psammoma bodies [10,12]. Low-grade astrocytoma and gliosis are sometimes difficult to differentiate [11], which may be relevant to our present

Case 2. Sato *et al.* described 2 of 6 cases involving a diagnosis of astrocytoma based on the IPD that turned out to be ependymoma on the FPD [8].

This study had several limitations. The number of patients was relatively small (n = 108). The data used in this study originated from one source, and the concordance rate between the IPDs and FPDs was thus slightly different from those of previous studies. Factors such as the IPD procedure and the pathologists conducting the diagnostic procedure may have affected the outcomes. Despite these limitations, we believe that this study provides important information for surgeons.

In conclusion, we investigated the concordance rate between the IPD and FPD in patients who underwent surgery for a spinal cord tumor. The overall concordance rate between the IPDs and FPDs was 95.4%, which indicates that the IPD is a highly reliable procedure to decide on the operative methods to implement during surgeries. However, the accuracy of IPDs for intramedullary spinal cord tumors tends to be lower than that for other sites of spinal cord tumors. Surgeons should consider that there are limitations in the use of IPDs and make comprehensive decisions about surgical methods by referring to other information such as preoperative imaging findings and the tumor's appearance during the surgery.

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