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ORIGINAL ARTICLE

Primary spinal cord tumors: review of 678 surgically treated patients in Japan. A multicenter study

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Abstract
Purpose To clarify the relative frequency of various histopathological primary spinal cord tumors and their features in Japanese people and to compare this data with other reports.
Methods Primary spinal cord tumor surgical cases from 2000 to 2009, which were registered in our affiliated hospital database were collected. We examined age at surgery, sex, anatomical location, vertebral level of the tumor, and pathological diagnosis in each case.
Results Of the 678 patients in our study, 377 patients (55.6 %) were males and 301 patients (44.4 %) were females (male/female ratio 1.25). The mean age at surgery was 52.4 years. Of these tumors, 123 cases (18.1 %) were intramedullary, 371 cases (54.7 %) were intradural extramedullary, 28 cases (4.1 %) were epidural, and 155 cases (22.9 %) were dumbbell tumors. The pathological diagnoses included 388 schwannomas (57.2 %), 79 meningiomas (11.6 %), 54 ependymomas (8.0 %), 27 hemangiomas (4.0 %), 23 hemangioblastomas (3.4 %), 23 neurofibromas (3.4 %), and 9 astrocytomas (1.3 %). The male/female ratios for schwannomas, meningiomas, ependymomas,

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hemangiomas, hemangioblastomas, neurofibromas, malignant lymphomas, and lipomas are 1.4, 0.34, 1.3, 1.5, 2.3, 1.3, 2.7 and 2.3, respectively.

Conclusion This is the first published research in English on the epidemiology of primary spinal cord tumors in Japanese people. Similar to other reports from Asian countries, our data indicates a higher male/female ratio overall for spinal cord tumors, a higher proportion of nerve sheath cell tumors, and a lower proportion of meningiomas and neuroepithelial tumors compared to reports from non-Asian countries. Data in the current study represent the characteristics of primary spinal cord tumors in Asian countries.

Keywords Spinal cord tumor · Epidemiology · Tumor location · Schwannoma · Meningioma

Introduction

Primary spinal cord tumors are one of the rarest categories of tumors, representing about 4–16 % of all tumors arising from the central nervous systems (CNS) according to previous reports [1–13]. Because of variation in population sizes studied and classification of tumors, the frequencies of different spinal cord tumors vary among these reports. Although there are many reports on the epidemiology of all CNS tumors (including brain and spinal cord or brain only), there are less reports focusing upon epidemiology of spinal cord tumors alone [2, 10, 14–18]; as far as we know, there is no report in the English literature which focuses on the epidemiology of spinal cord tumors from Japan. The occurrence rate of spinal cord tumors in a population, frequency by sex or age, and frequency by pathology vary among races and regions. Comparing the relative incidence of various neoplastic entities within different nations and ethnic groups might provide relevant clues as to etiology.

The aims of this study are to review surgically treated cases of primary spinal cord tumors, and to clarify the relative frequencies of these tumors in Japanese people as classified by histological type, anatomical location and vertebral level at which they are found. By describing features of spinal cord tumors in Japanese people, we can determine the similarities and differences of spinal cord tumors in populations from other countries (such as pathology, race and sex), suggesting the role that environmental, genetic, and hormonal factors may play in the etiology of spinal cord tumors.

Materials and methods

Hospitals of the Nagoya Spine Group (NSG) have registered their spine surgery cases in the NSG database annually since 2000. In the database, 25,720 spine surgical cases have been registered for 10 years. The participant hospitals in the database are all associated hospitals with Department of Orthopaedic Surgery of Nagoya University. At these 12 hospitals in Central Japan, orthopedic spine surgeons perform spine and spinal cord surgery. From this database, we collected cases with primary spinal cord tumors that were treated surgically between January 2000 and December 2009. We excluded metastatic and spinal bone tumors from this study. The study protocol was approved by the Committee on Ethics in Human Research of Nagoya University.

In each case, we determined age at surgery, sex, the anatomical location of tumors (intramedullary, intradural extramedullary, epidural and dumbbell), the vertebral level location (cervical, cervicothoracic, thoracic, thoracolumbar, lumbar, lumbosacral and sacral) and pathological diagnosis. Data were analyzed using SPSS statistical software (SPSS Inc.). Statistical significance was assessed using the One-way ANOVA and post hoc Scheffe for analyzing age and the histopathological type of tumor. Probability values of less than 0.05 were considered to be statistically significant.

Results

Patient demographics

There were 678 patients with primary spinal cord tumors surgically treated during the period of this study. Of the 678 patients, 55.6 % were male (377 patients) and 44.4 % were female (301 patients). The mean age at surgery was 52.4 years (range, 2 months to 92 years, Fig. 1). When

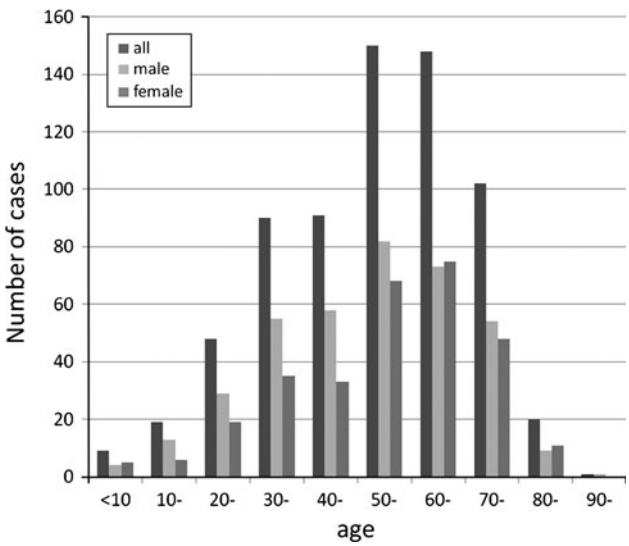

Fig. 1 Age and sex distributions of patients with primary spinal cord tumors (*bar graph*)

stratified by patient age in 10-year intervals, the patient groups aged 50–59 years and 60–69 years encompassed the largest number of patients with primary spinal cord tumors; only 4.1 % of patients were under 20 years of age.

There were 124 patients (18.3 %) with intramedullary tumors, 371 patients (54.7 %), with intradural extramedullary tumors, 27 patients (4.0 %) with epidural tumors, and 155 patients (22.9 %) with dumbbell tumors (Fig. 2). The vertebral levels of the tumors were evenly distributed (Fig. 3). The pathological diagnoses of the primary spinal cord tumors are shown in Table 1.

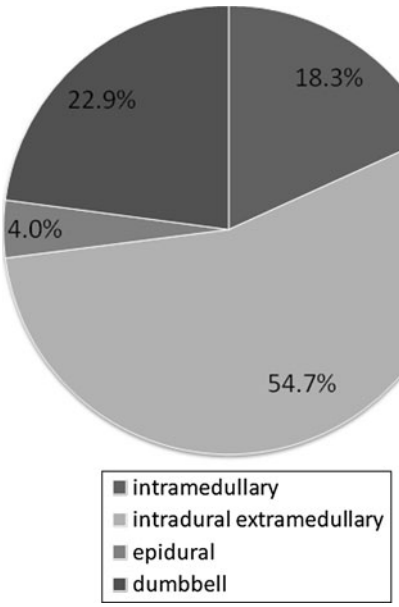

Fig. 2 Anatomical locations of primary spinal cord tumors (*circle graph*)

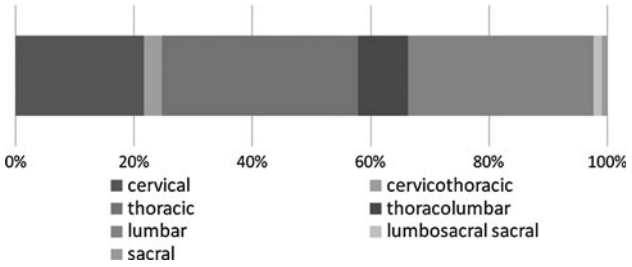

Fig. 3 Vertebral level distribution of primary spinal cord tumors (*bar graph*)

Histological type of tumors

Schwannoma

Of the 388 patients with schwannomas, males predominated (228 males and 160 females). These tumors included 2 intramedullary tumors (0.5 %), 253 intradural extramedullary tumors (65.2 %), 5 epidural tumors (1.3 %) and 128 dumbbell tumors (33.0 %). With respect to the vertebral level where these tumors were located, they occurred mainly at the level of the lumbar spine (25.5 %) (Table 2). They were diagnosed typically after the age of 30, and the peak incidence for schwannomas was found in a range from 50 to 59 years of age (Fig. 4).

Meningioma

Seventy-nine patients with meningiomas were treated, with females outnumbering males almost 3 to 1 (20 males and 59 females). These tumors included 3 intramedullary tumors (3.8 %), 75 intradural extramedullary tumors (94.9 %) and 1 dumbbell tumor (1.3 %). Meningiomas were found predominantly at the level of the thoracic spine (73.4 %) (Table 2). They occurred mainly after the age of 50, and the peak incidence for meningiomas was found in a range from 60 to 69 years of age (Fig. 5).

Ependymoma

There were 54 patients with ependymomas, including 31 males and 23 females. These tumors included 41 intramedullary tumors (75.9 %) and 13 intradural extramedullary tumors (24.1 %). We also included 15 myxopapillary ependymomas. Ependymomas seemed to be evenly distributed at all spinal levels (Table 2). The typical age of a patient with an ependymoma was greater than 20 years, and the incidence peaked between 30 and 39 and 60 and 69 years old (Fig. 6).

Hemangioma

There were 27 patients with hemangiomas, including 16 males and 11 females. These tumors included 19 intramedullary tumors (70.4 %), 3 intradural extramedullary tumors (11.1 %), 3 epidural tumors (11.1 %) and 2 dumbbell tumors (7.4 %). Hemangiomas predominated at the cervical and thoracic spinal levels (66.7 %) (Table 2) and were seen mainly after the age of 50 (Fig. 7).

Hemangioblastoma

Of the 23 patients with hemangioblastomas, including 16 males and 7 females, there were 21 intramedullary tumors (91.3 %) and 2 intradural extramedullary tumors (8.7 %). Nine patients (39.1 %) were also diagnosed with von Hippel-Lindau disease. Hemangioblastomas were mainly found at the cervical and thoracic levels (87.0 %) (Table 2) and occurred after the age of 20 with a peak incidence ranging from 30 to 39 years of age (Fig. 8).

Table 1 Primary spinal cord tumors by histology and sex

	Number (% of total)	Male	Female	Male/female ratio
Histology				
Schwannoma	388 (57.2)	228	160	1.4
Meningioma	79 (11.7)	20	59	0.34
Ependymoma	54 (8.0)	31	23	1.3
Hemangioma	27 (4.0)	16	11	1.5
Hemangioblastoma	23 (3.4)	16	7	2.3
Neurofibroma	23 (3.4)	13	10	1.3
Malignant lymphoma	11 (1.6)	8	3	2.7
Lipoma	10 (1.5)	7	3	2.3
Astrocytoma	9 (1.3)	4	5	0.8
Others	56	34	20	1.7
Total	678	377	301	1.3

Table 2 Vertebral level distribution of each type of tumor (%)

Tumor type	Cervical	Cervicothoracic	Thoracic	Thoracolumbar	Lumbar	Lumbosacral	Sacral
Schwannoma	19.1	1.3	23.5	8.5	44.6	1.8	1.3
Meningioma	13.9	8.9	73.4	–	1.3	–	–
Ependymoma	27.8	5.6	29.6	14.8	22.2	–	–
Hemangioma	22.2	–	44.4	18.5	14.8	–	–
Hemangioblastoma	33.3	–	50.0	8.3	4.2	–	–
Neurofibroma	43.5	–	21.7	13.0	17.4	4.3	–

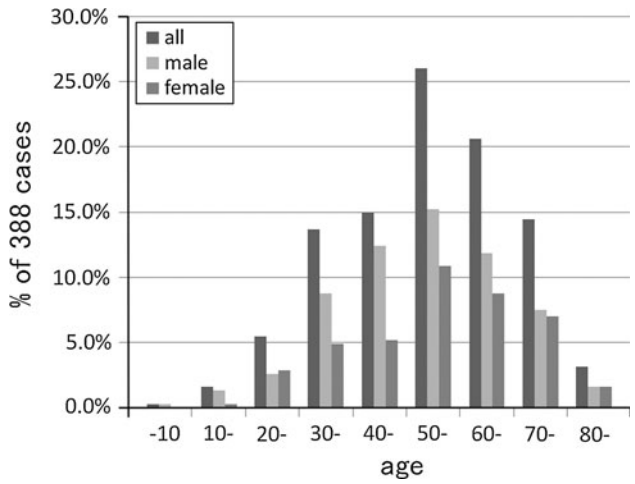

Fig. 4 The characteristics of schwannomas. Age and sex distributions (*histogram*)

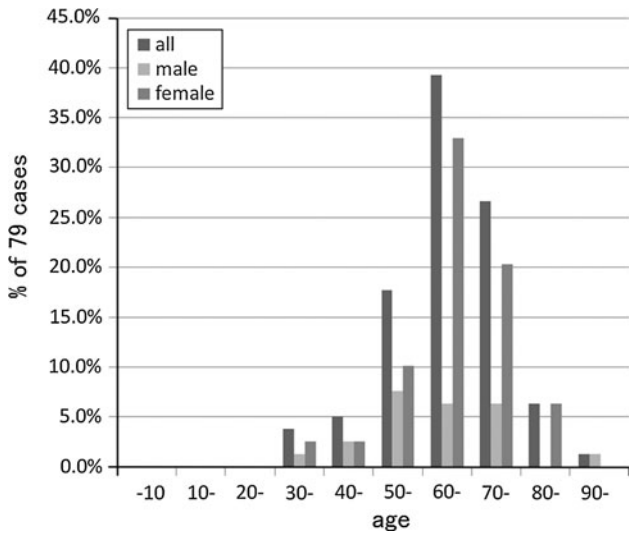

Fig. 5 The characteristics of meningiomas. Age and sex distributions (*histogram*)

Neurofibroma

There were 23 patients with neurofibromas, 13 males and 10 females, and these included 10 intradural extramedullary tumors (43.5 %) and 13 dumbbell tumors (56.5 %). Twelve of these patients (52.2 %) were diagnosed with von Recklinghausen disease. Neurofibromas predominated at the cervical level of the spine (43.5 %) (Table 2) and occurred after the age of 10.

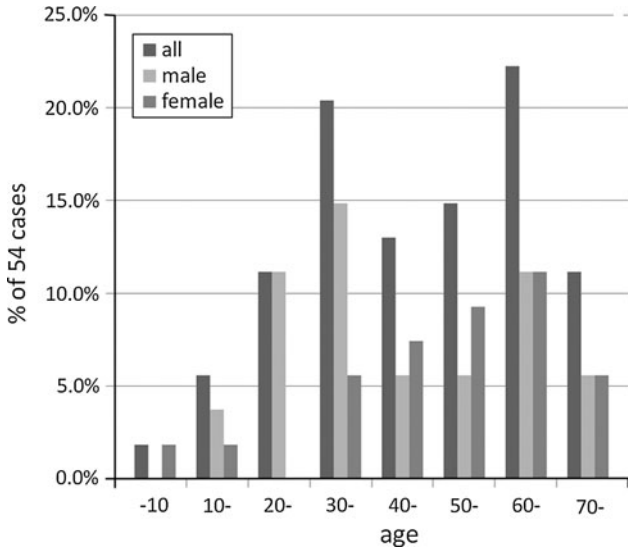

Fig. 6 The characteristics of ependymomas. Age and sex distributions (*histogram*)

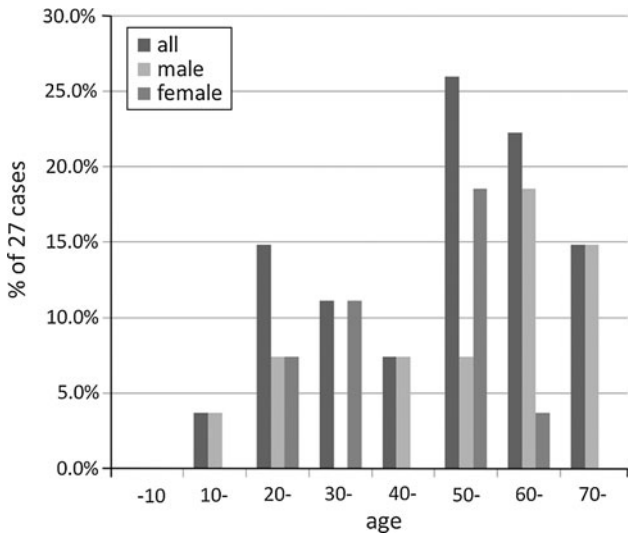

Fig. 7 The characteristics of hemangiomas. Age and sex distributions (*histogram*)

Tumor location

Analysis of primary spinal cord tumors from the aspect of anatomical location is shown in Table 3.

Age at surgery

There were significant differences between the three major tumor types (schwannoma, meningioma, and ependymoma) with respect to the age of patients in our current study ($p < 0.01$; Figs. 4, 5, 6). Patients with meningiomas (mean age 64.7 ± 11.4 years) were significantly older than patients with Schwannomas (mean age 53.5 ± 15.8 years),

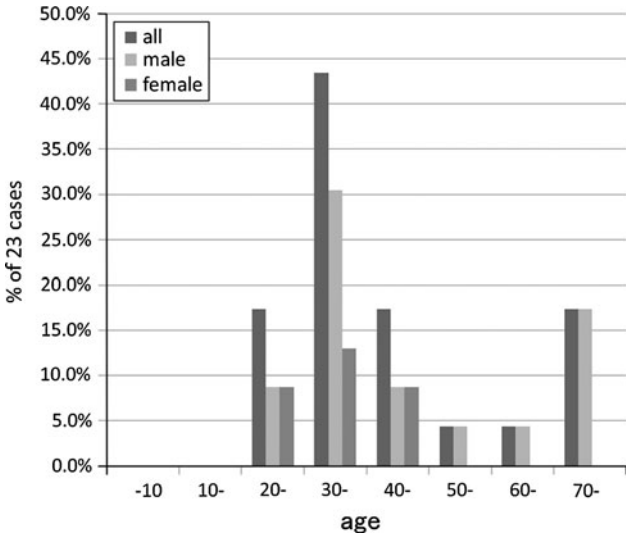

Fig. 8 The characteristics of hemangioblastomas. Age and sex distributions (*histogram*)

who were significantly older than patients with ependymomas (mean age 46.6 ± 18.1).

Discussion

This study evaluates one of the largest series of cases of primary spinal cord tumors in the world, and it is the first from Japan detailed in the English literature. Our study uses a spine surgery registry to retrospectively analyze primary spinal cord tumor cases and collect detailed data about patients' age at surgery, sex, anatomical location of tumors, vertebral level of tumors and pathological diagnoses.

To confirm that our data represent the characteristics of primary spinal cord tumors in Japan, we compared our data with other report [19] from Japan. The literature (written in Japanese language) describes the number and type of spinal cord tumors found in the Japanese population but does not detail the patient demographics for each type of tumor. In that study of 642 spinal cord tumors, 47 % were schwannomas, 13 % meningiomas, 8 % ependymomas, 11 % vascular tumors, 5 % astrocytomas, and 4 % were neurofibromas. We found a similar trend in the frequencies of these six major tumor types in our current study (Table 2; 57.2, 11.7, 8.0, 7.4, 1.3 and 3.4 %, respectively). In general, the data from our study approximates the other Japanese reports.

The incidence of primary spinal cord tumors in various series is listed in Table 4. Compared with reports from other parts of the world, there are evident differences in the frequencies of nerve sheath cell tumors (NSCTs: schwannomas and neurofibromas) and meningiomas. In Asian countries [2, 11–15, 20], including what we found in the current study, the frequency of NSCTs is higher than that

Table 3 Histological types of spinal cord tumors at anatomical locations

Histology	No. of cases (% of total)
Intramedullary	
Ependymoma	41 (33.1)
Hemangioblastoma	21 (16.9)
Hemangioma	19 (15.3)
Astrocytoma	9 (7.3)
Lipoma	9 (7.3)
Other tumors	25 (20.2)
Total	124
Intradural extramedullary	
Schwannoma	254 (68.5)
Meningioma	75 (20.2)
Ependymoma	13 (3.5)
Neurofibroma	10 (2.7)
Other tumors	19 (5.1)
Total	371
Epidural	
Malignant lymphoma	9 (33.3)
Schwannoma	6 (22.2)
Hemangioma	3 (11.1)
Ganglioneuroma	2 (7.4)
Neuroblastoma	2 (7.4)
Other tumors	5 (18.5)
Total	27
Dumbbell	
Schwannoma	125 (82.6)
Neurofibroma	13 (8.4)
Hemangioma	2 (1.3)
MPNST	2 (1.3)
Malignant lymphoma	2 (1.3)
Other tumors	11 (7.1)
Total	155

MPNST malignant peripheral nerve sheath tumor

of meningiomas. This tendency is even stronger in eastern Asia [2, 11–13, 15]. On the other hand, the incidence of meningiomas in non-Asian countries (USA, Europe, Australia), is equal to or higher than that of NSCTs [8, 10, 16, 17, 21] with the exception of only one report [18]. In the series from Germany [18], authors counted multiple tumors in one patient (probably, neurofibromatosis or schwannomatosis). Therefore, NSCTs outnumbered meningiomas in their series. Neuroepithelial tumors seem to occur less frequently in Asian countries than in non-Asian countries. The frequency of vascular tumors seems to vary less among countries studied. Our results confirm previous reports [2, 13–15] which demonstrate different frequencies of NSCTs, meningiomas, and neuroepithelial tumors between Asian countries and other parts of the world.

According to previous studies [10, 13, 15–17, 21], the male/female ratios for patients with primary spinal cord tumors vary among countries from 40 % male/60 % female in the USA [10] to 60.3 % male/39.7 % female in China [13] (Table 5). In our current study in Japan, of 678 primary spinal cord tumors 55.6 % were male and 44.4 % were female. Briefly, in Asian countries spinal cord tumors predominantly occur in men, whereas in non-Asian countries they predominantly occur in women. Furthermore, previous studies [8, 10, 17, 21, 22] have reported that one type of spinal cord tumor, spinal meningioma, occurs much more frequently in women than in men. The female preponderance for spinal meningiomas is universal; as we found in our study, the male/female ratio for meningiomas is 0.339. As Engelhard et al. [21] pointed out the female preponderance in meningiomas alone is enough to change male/female ratios for entire spinal cord tumor series (in non-Asian countries). However, in Asian countries, where the frequencies of spinal meningiomas overall are lower than in non-Asian countries, the male/female ratio for an entire series might not be affected by the male/female ratio for meningiomas. Engelhard et al. [21] have pointed out that there would be a slight male preponderance for primary intraspinal tumors if meningiomas were not included. Our current series confirms this finding (Table 1); there was a male preponderance in schwannomas, ependymomas, hemangiomas, hemangioblastomas, neurofibromas, malignant lymphomas, and lipomas.

Authors of previous studies [8, 10, 16, 17, 23] have noted that astrocytomas are much more common in children than in adults. In the current series, the frequency of astrocytomas (1.3 % of the entire series) is lower than in other series studied: 9.5 % in the USA [21], 6.0 % in Germany [18], 6.0 % in Norway [16], 4.6 % in Iran [14], 6.4 % in China [2], 5.3 % in Korea [12], 2.5 % in Thailand [11]. One of the reasons for our low percentage of astrocytomas may be that only 4.1 % of patients were under 20 years of age in the current study. In Japan, children with spinal cord tumors are more likely to be treated by neurosurgeons than by orthopedic spine surgeons. It is important to note that previous reports [17, 24, 25] indicate that in children, astrocytomas are 3–4 times more frequent than ependymomas. Another reason for our low percentage of astrocytomas is that when obviously malignant grade tumors as judged from imaging studies or clinical course were identified in our institutes, they were typically treated with radiation or chemotherapy, not surgically. This would place a lower number of children with malignant gliomas into our surgical spinal cord tumor series.

Previous literature [21] has reported that ependymomas and schwannomas are more commonly found in middle-

Table 4 Incidence of primary spinal cord tumors by series

References	Country	No. of cases	Date	NSCTs (%)	Meningioma (%)	Neuroepithelial tumors (%)	Vascular tumors (%)
Schellinger et al. [17]	USA	3,226	1998–2002	24.4	28.9	29.2	–
Preston-Martin [10]	USA	462	1972–1985	22.3	42.9	28.4	–
Engelhard et al. [21]	USA	430	2000	22.6	24.2	39.3	1.6
Klekamp and Samii [18]	Germany	1,081	1978–2003	26.9	16.7	17.1	3.4
Helseth et al. [6]	Norway	415	1955–1986	10.8	46.7	32.0	4.1
Kaye et al. [8]	Australia	266	1986–1988	32.3	29.7	24.4	–
Ardehali [14]	Iran	108	1962–1986	40.7	33.3	16.7	3.7
Lalitha and Dastur [20]	India	326	Before 1980	39.9	25.5	20.9	5.8
Shuangsh and Panyatha [11]	Thailand	120	1956–1973	65.8	14.2	12.5	1.7
Cheang et al. [15]	Taiwan	92	1988–1995	52.2	15.2	10.9	3.3
Wen-Qing et al. [13]	China	2,245	Before 1982	49.4	14.7	11.4	4.7
Cheng [2]	China	1,549	Before 1982	49.5	13.2	10.7	6.3
Suh et al. [12]	Korea	141	1997–1998	39.7	25.5	19.1	6.4
Present study	Japan	678	2000–2009	60.6	11.7	9.4	7.4

NSCTs nerve sheath cell tumors

Table 5 Male/female ratios for patients with primary spinal cord tumors by series

References	Country	No. of cases	Date	Male (%)	Female (%)
Schellinger et al. [17]	USA	3,226	1998–2002	45.0	55.0
Preston-Martin [10]	USA	462	1972–1985	40.0	60.0
Engelhard et al. [21]	USA	430	2000	43.3	56.7
Helseth et al. [6]	Norway	415	1955–1986	37.0	63.0
Cheang et al. [15]	Taiwan	92	1988–1995	56.5	43.5
Wen-Qing et al. [13]	China	2,245	Before 1982	60.3	39.7
Present study	Japan	678	2000–2009	55.6	44.4

aged patients, while meningiomas are found in middle-aged and older patients. Still other reports [2, 14, 15] indicate that the most common primary spinal cord tumor in patients older than 60 years is meningioma, with a higher incidence than schwannomas. In the current study, the average age of patients with meningiomas (64.7 years) was significantly higher than that of schwannomas (53.5 years) and ependymomas (46.6 years), and the average age for ependymomas was significantly younger than for schwannomas. Our study confirms previous findings [2, 14, 15, 21] that meningiomas predominantly occur in elderly patients. As far as we know, this is the first report to indicate that, of the three major spinal cord tumors (schwannomas, meningiomas and ependymomas), ependymomas occur in the youngest patients.

As mentioned above, there are dissimilarities in the relative frequencies of spinal cord tumors among various reports (Table 4). While some of these discrepancies are due to differences in the actual rate of occurrence of these tumors, others might result from different ways in which data are obtained. For various reasons, the comparison of data from different sources in various communities might not reveal real differences among the communities. Moreover, the diversity in the types of tumors included, and the classification used in different series further complicates the collation of statistics. However, despite dissimilarities in the materials and methods, comparing these series might reveal important points on the relative frequency of spinal cord tumors in different parts of the world, suggesting the possible roles of environmental, genetic, and hormonal factors in the etiology of spinal cord tumors. For surgeons, it is very useful to recognize what type of tumor is likely to be encountered, based not only on preoperative imaging characteristics such as magnetic resonance imaging (MRI), but also on the reported incidence of the various tumors in each country or region.

There were potential limitations in the current study. Since this was a non-population-based study, and we dealt

only with surgical cases, we could not determine the actual frequency of spinal cord tumors occurring within the Japanese population. That is, we did not include asymptomatic cases or cases in which the spinal cord tumors were diagnosed with imaging and treated conservatively. We learned the relative frequencies of different spinal cord tumors which were treated surgically with this study. A population-based study on primary spinal cord tumors should be planned in Japan, similar to broad-based studies from other countries.

Conclusions

This is the first published research in English on primary spinal cord tumors describing the demographic characteristics, histopathological features, anatomical location, and vertebral level of these tumors treated surgically in Japanese people. Similar to other reports from Asian countries, there is a higher male/female ratio for all spinal cord tumors as a group. There is also a higher proportion of NSCTs, and a lower proportion of meningiomas and neuroepithelial tumors compared with reports from non-Asian countries. Data in the current study represent the characteristics of primary spinal cord tumors in Asian countries.

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Conflict of interest The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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