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Clinico-pathological Features of Pediatric Spinal Cord Tumors:

Single Institution Experience for 32 years

소아 척수 종양의 임상적 병리학적 특징에 관한 고찰:

단일기관에서의 32년간 임상경험

2020년 2월

서울대학교 대학원

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최 호 용

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지도교수 김 승 기

이 논문을 의학석사 학위논문으로 제출함

2020년 1월

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Abstract

Clinico-pathological Features of Pediatric Spinal Cord Tumors: *Single Institution Experience for 32 years*

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Purpose: Because of the rare incidence and various pathological presentation, there exist few literatures for primary spinal cord tumors (PSCTs) in pediatric patients. The purpose of this study was to perform descriptive analysis and detailed survival analysis for pediatric patients who underwent surgery for PSCTs.

Methods: Between October 1985 and December 2017, a total of 126 pediatric patients

with PSCTs underwent surgery in a single institution. We retrospectively analyzed data regarding patients' demographics, tumor characteristics, surgical outcomes, and survival statistics. We performed detailed subgroup analysis for the intramedullary (IM) tumors and extradural (ED) tumors, separately.

Results: There were 56 males and 70 females with mean age of 6.4 ± 5.04 years. The mean follow-up period was 100.7 ± 91.60 months. The most common presenting symptom was motor weakness, and mean duration of symptom was 9.3 ± 21.61 months. The symptom duration was shorter in patients with malignant tumors. Patients with IM tumors had longer duration of symptom, and showed predominant motor symptom and spine deformity. Patients with ED tumors had shorter duration of symptom and were diagnosed by incidental radiographic abnormality with higher incidence. The most common level of tumor was thoracic level. The most common anatomical location of PSCTs was ED (n=57, 45.2%), followed by IM (n=43, 34.1%), and intradural extramedullary (IDEM; n=16, 12.7%), IDEM/ED (n=8, 6.3%), and IM/IDEM (n=2, 1.6%). About half of all PSCTs were malignant (n=69, 54.8%). Gross total removal was achieved in 50.0%, and most commonly performed surgical method was laminoplasty (55.6%). Regarding pathology, most common tumors were schwannomas (n=14) and neuroblastomas (n=14), followed by ganglioneuromas (n=12), Ewing sarcomas (n=10), diffuse astrotytomas (n=7), neurofibromas (n=7), and pilocytic astrocytomas (n=6). Preoperative McCormick scale was 2.75 ± 1.34, and improved to 2.19 ± 1.42, postoperatively (P=0.000). The amount of improvement of McCormick scale was not

different between IM tumors and ED tumors. Twenty-three patients (18.3%) died from disease, with a mean time of 23.1 ± 38.33 months. Thirty-nine patients (31.0%) suffered from disease progression. The mean period of progression was 36.8 ± 63.06 months. The 3-, 5-, 10-, and 20-year overall survival (OS) rates were 83%, 82%, 81% and 78%, respectively. The 3-, 5-, 10-, and 20-year progression-free survival (PFS) rates were 76%, 73%, 68% and 58%, respectively. Among patients with IM tumors, the 3-, 5-, 10-, and 20-year OS rates were 79%, 79%, 79% and 69%, respectively. The 3-, 5-, 10-, and 20-year PFS rates were 65%, 65%, 57% and 57%, respectively. In ED tumors, the 3-, 5-, 10-, and 20-year OS rates were 83%, 80%, 80% and 80%, respectively. The 3-, 5-, 10-, and 20-year PFS rates were 83%, 81%, 81% and 60%, respectively. Pathology of tumor and the extent of resection showed beneficial effect for OS for entire PSCTs, IM tumors, and ED tumors. Disease progression was mainly affected by extent of removal, rather than pathology in patients with entire PSCTs and ED tumors. In the contrast, pathology seems a main determinant on PFS whereas extent of removal had little effect on progression in patients with IM tumors.

Conclusion: PSCTs are uncommon pathology in pediatric patients. Malignant pathology comprises about half of all PSCTs. Most common anatomical location was ED, followed by IM, and IDEM. Schwannomas and neuroblastomas were the most common pathology. Both the pathology and extent of resection had a decisive effect on OS. In IM tumors, pathology was a main determinant on PFS whereas extent of removal had little effect. In ED tumors, however, the extent of removal showed an influence on PFS, rather than

pathology.

Keywords: Primary spinal cord tumor; Intraspinal tumor; Spinal cord; Pediatric; Outcome

Student number: 2010-23725

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List of abbreviations and symbols

PSCT: Primary spinal cord tumor

CNS: Central nervous system

NF: neurofibromatosis

MRI: Magnetic resonance imaging

IM: Intramedullary

IDEM: Intradural extramedullary

ED: Extradural

GTR: Gross total removal

STR: Subtotal removal

PR: Partial removal

WHO: World Health Organization

PFS: Progression-free survival

OS: Overall survival

MPNST: Malignant peripheral nerve sheath tumor

EWS: Ewing sarcoma

AT/RT: Atypical teratoid/rhabdoid tumor

Introduction

Primary spinal cord tumors (PSCTs) are one of the rarest categories of tumors, comprising 4-8% of all central nervous system (CNS) tumors[21 9, 13]. The incidence of pediatric PSCT (0.26 per 100,000 person-years) is even lower than that of adult (0.74 per 100,000 person-years)[23]. In addition to the rare incidence, the pathological presentation of pediatric PSCT varies widely. Because of these obstacles, there exist literatures comprised of small series of patients[5 3, 27] or larger series of multi-center study for specific tumor type[11, 19].

In the present study, we report a series of 126 pediatric patients with PSCTs who underwent surgery in a single institution. A descriptive analysis regarding symptomatology, tumor level, anatomical location, pathological diagnosis, and surgical outcomes was performed. In addition, we conducted detailed survival analysis according to particular anatomical location.

MATERIALS AND METHODS

Demographic of Patients

Between October 1985, the opening of the children's hospital of our institution, and December 2017, a total of 183 consecutive pediatric patients with spinal cord tumors were surgically treated, and their charts were retrospectively reviewed. The clinical presentation, radiographic imaging characteristics, surgical outcomes and pathological results were evaluated. Patients with metastatic lesion in spine, with missed radiographic or medical records were excluded from this study. Patients with multiple craniospinal tumors, usually associated with genetic syndromes such as neurofibromatosis (NF) or von Hippel-Lindau syndrome, were also excluded. Among patients with multiple lesions, most (26/27) patients were associated with NF (NF-1 in 9 patients, NF-2 in 14 patients, and undetermined type in 3 patients). Nonetheless, patients who have solitary spinal lesion in neuraxis were included in the study despite having genetic syndromes (n=5). Following medical chart and radiographic image review, 57 patients were excluded (metastasis in 25 patients, multiple craniospinal tumors in 27 patients, and incomplete data in 5 patients). Finally, a total number of 126 patients were evaluated for the present study. This study was approved by institute review board of Seoul national university hospital (H-1910-168-1074).

Radiographic assessment

The magnetic resonance imaging (MRI) was adopted at our institution in September 1987. Before the adoption of MRI, PSCTs were diagnosed using computed tomography-myelography. The number of involved segment, involved spinal level, and location of tumor were analyzed. The involved level of tumor was classified into cervical, cervico-thoracic, thoracic, thoraco-lumbar, lumbar, lumbo-sacral, and sacral. Tumor involving almost whole spinal cord was particularly classified to holocord tumor. Anatomical location was categorized into intramedullary (IM), intradural extramedullary (IDEM), and extradural (ED). Some ED tumors with extension to paravertebral space were also categorized into ED tumors. Tumors extending beyond one anatomical location were described including whole area of the tumors (IDEM/ED, for example).

Characteristics of tumor removal

The extent of tumor removal was categorized into gross total removal (GTR, >95% of tumor removal), subtotal removal (STR, >80% of tumor removal), partial removal (PR, <80% of tumor removal), and biopsy[7, 28]. The mode of bony removal was categorized into laminoplasty, laminectomy, (partial) hemilaminectomy, and corpectomy.

Pathologic assessment

All tumor specimens were inspected by neuro-pathologists. The classification of tumor was referred to the 2016 World Health Organization (WHO) Classification of Tumors of

the CNS[14]. Tumors coded /0, and /1 were classified to non-malignant tumors, whereas tumors coded /3 were classified to malignant tumors. ID tumors were classified by grading system. The old pathologic specimens were reviewed and molecular study was performed if possible.

Clinical assessment

Patient's neurological status was assessed preoperatively and post-operatively at three-month, using the modified McCormick scale (Table 1)[15]. Progression-free survival (PFS), defined as the absence of any clinical or radiographic sign of recurrence of the tumors, as well as overall survival (OS) were estimated. OS and PFS were evaluated for entire PSCT patients as well as IM and ED groups. Tumors spanning more than one anatomical location (such as IM/IDEM, IDEM/ED) were evaluated as entire group, only.

Statistical analysis

Statistical analysis was performed using IBM SPSS 22.0 software for Windows (IBM, Corp., Armonk, NY). The distributions of the variables were demonstrated as the mean value and standard deviation. Independent t-test and Paired t-test was used to compare parametric variables before and after operation. The degree of functional improvement after surgery was evaluated utilizing linear mixed model. Mann-Whitney test was utilized to analyze non-parametric independent variables. PFS and OS were assessed with the use

of Kaplan-Meier technique. Statistical significance was set at $P<0.05$.

RESULTS

Patients Demographics

There were 126 pediatric patients enrolled in this study (Table 2). The number of male patients and female patients was 56 and 70, respectively. The mean age of patients was 6.4 ± 5.04 years. The mean symptom duration was 9.3 ± 21.61 months. The symptom duration was significantly shorter in patients with malignant tumors, compared to patients with benign tumors (5.5 ± 17.42 months vs. 13.6 ± 25.27 months, P=0.038). In terms of sex and age, however, the symptom duration did not show statistical differences regarding malignancy. The mean follow-up period was 100.7 ± 91.60 months. The presenting symptoms were categorized into motor deficit, sensory disturbance, urinary symptom, spinal deformity, soft tissue mass, incidental radiographic finding, and miscellaneous. The most common presenting symptom was motor symptom (n=101, 80.2%). Among them, weakness on extremity (n=69) was most common motor symptom, followed by gait disturbance (n=28), neck motion limitation (n=3), and torticollis (n=1). Sensory disturbance was presented second most commonly (n=40, 31.7%). Pain was most common sensory disturbance (n=33), followed by hypesthesia (n=4), and tingling sense (n=3). Urinary disturbance was presented in 9 patients (7.1%). Ten patients (7.9%) were diagnosed to PSCTs during detailed imaging studies for evaluation of spinal deformity. Soft tissue mass was presented in two patients on their neck. Incidentally found mass on radiographic studies for irrelevant symptoms was found in 16 patients (12.7%). Other miscellaneous symptoms were comprised of extremity deformity (n=2), respiratory

difficulty (n=1), irritability (n=1), and hip dislocation (n=1).

Radiographic Outcomes

The mean number of involved segments was 5.4 ± 4.61 (Fig. 1). The most commonly involved level was thoracic spine (n=40, 31.7%), followed by cervical spine (n=23, 18.3%), cervico-thoracic spine (n=21, 16.7%), and thoraco-lumbar spine (n=15, 11.9%) The lumbar, lumbo-sacral, and sacral level were involved in 9 (7.1%), 7 (5.6%), and 2 (1.6%) patients. Holocord involvement of tumor was found in nine patients (7.1%).

Regarding anatomical location, the most common tumor location was ED (n=57, 45.2%), followed by IM (n=43, 34.1%), and IDEM (n=16, 12.7%). Among ED tumors, 12 cases (21.1%) were located exclusively epidural within spinal canal. The remainder (n=45, 78.9%) involved not only epidural space but also paravertebral space. Tumors spanning more than one anatomical location were as follows: IM/IDEM (n=2, 1.6%), IDEM/ED (n=8, 6.3%).

Characteristics of tumor removal

Regarding the extent of tumor removal, GTR was achieved in 63 patients (50.0%). STR, and PR were achieved in 41 (32.5%), and 14 (11.1%) patients, respectively. In 8 patients (6.3%), open biopsy was conducted.

Regarding operative methods, most commonly performed procedures were laminoplasty (n=70, 55.6%), and laminectomy (n=36, 28.6%). Partial hemilaminectomy was conducted in 7 patients (5.6%). In 3 patients (2.4%), corpectomy with instrumented fusion were done. Other approaches including thoracotomy, endoscopic surgery, or retroperitoneal approach were done in 10 patients (7.9%).

Tumor Pathology

Among total of 126 patients, malignant tumors consist 69 patients (54.8%, Table 3). The proportion of malignancy was highest in tumors located at ED (40/57, 70.2%), on the other hand, malignant tumors were absent in tumors located at IDEM (0/16). Among IM tumors (n=43), high grade tumors were confirmed in 11 patients (25.6%).

Regarding WHO classification of CNS tumor, 95 out of 126 tumors (75.4%) were able to be classified into CNS tumors. Among them, the most common type was tumors of the paraspinal nerves (n=23, 18.3%) including schwannomas (n=14), neurofibromas (n=7), and malignant peripheral nerve sheath tumors (MPNST, n=2). The second most common type of tumors was mesenchymal, non-meningothelial tumors, which was confirmed in 19 patients (15.1%). Among them, Ewing sarcomas (EWS) were the most common (n=10). Regarding 6 specimens of EWS which were able to conduct genetic study, all specimens revealed EWS translocation. Other mesenchymal, non-meningothelial tumors included lipomas (n=3), hemangiomas (n=3), peripheral neuroepithelioma (n=1),

hemangioblastoma (n=1), and myofibroblastomatosis (n=1). Diffuse astrocytic and oligodendroglial tumors were identified in 17 patients (13.5%), including diffuse astrocytomas (n=7), anaplastic astrocytomas (n=4), glioblastomas (n=3), oligodendrogliomas (n=2), and anaplastic oligodendroglioma (n=1). Among 7 patients with diffuse astrocytomas, 2 patients were reviewed with molecular study, and confirmed to diffuse astrocytoma, IDH-wildtype. All 3 patients with glioblastomas confirmed to glioblastoma, IDH-wildtype. There was no case of diffuse midline glioma, characterized by K27M mutations in the histone H3 gene, *H3F3A*. Pilocytic astrocytomas, which were separately categorized as other astrocytic tumors, were found in 6 patients (4.8%). In 9 patients (7.1%), neuronal and mixed neuronal-glial tumors were found, including gangliogliomas (n=5), gangliocytoma (n=1), anaplastic ganglioglioma (n=1), papillary glioneuronal tumor (n=1), and atypical glioneuronal tumor (n=1). Ependymal tumors were confirmed in 5 patients (4.0%), which were consist of myxopapillary ependymomas (n=3) and ependymomas (n=2). CNS embryonal tumors were identified in 5 patients (4.0%): atypical teratoid/rhabdoid tumors (AT/RT) in 3 patients, all of them revealed *INI1* alteration, and CNS embryonal tumor with rhabdoid features in 2 patients. CNS lymphomas and histiocytic tumors were identified in 4 (3.2%) and 3 (2.4%) patients, respectively. Germ cell tumors were found in 4 patients (3.2%); mature teratoma in one patient, immature teratoma in one patient, and other germ cell tumors in 2 patients.

For 31 out of 126 tumors (24.6%), which could not be classified into CNS tumors. These tumors were peripheral neuroblastic tumors, including neuroblastomas (n=14), ganglioneuromas (n=12), and ganglioneuroblastomas (n=5).

Clinical Outcomes

Preoperative McCormick scale was 2.75 ± 1.34, and improved to 2.19 ± 1.42, postoperatively (P=0.000). Postoperative McCormick scale was improved in 55 patients (43.7%), compared to preoperative condition. On the other hand, McCormick scale was worsened postoperatively in 13 patients (10.3%). In 56 patients (44.4%), perioperative McCormick scale remained unchanged. McCormick scale could not be assessed in 2 patients.

Twenty-three patients (18.3%) died from disease. The mean time for death was 23.1 ± 38.33 months. Most pathology of patients who died from disease was malignant tumors (22/23, 95.7%): EWS (n=7), anaplastic astrocytoma (n=3), CNS embryonal tumor with rhabdoid features (n=2), AT/RT (n=2), glioblastoma (n=2), diffuse astrocytoma (n=1), oligodendroglioma (n=1), lymphoma (n=1), neuroblastoma (n=1), peripheral neuroepithelioma (n=1), and MPNST (n=1). There was one patient with benign tumor who died from the disease. The patient underwent PR (total resection of intraspinal portion) of ED neurofibroma with huge extraspinal involvement. After 5 years, he was diagnosed malignant transformation of neurofibroma (MPNST), and died from the disease (survival period of 66 months). Patients who died from disease had significant shorter duration of symptom presentation until diagnosis (2.1 ± 2.99 months vs. 11.1 ± 23.88 months, P=0.000), worse preoperative McCormick scale (3.57 ± 1.47 vs. 2.53 ± 1.27, P=0.001), and worse postoperative McCormick scale (3.57 ± 1.47 vs. 1.84 ± 1.19,

P=0.000) compared to those survived. The age, sex, and number of involved segment did not show statistical significance between patients who died and survived.

Postoperatively, 39 patients (31.0%) suffered from disease progression. The mean period of progression was 36.8 ± 63.06 months. Patients who showed disease progression had significant shorter symptom duration, compared to patients without progression (2.7 ± 3.91 months vs. 12.6 ± 25.81 months, P=0.001). There was no statistical significance between patients with disease progression and without, in terms of age, sex, and number of involved segments. Among patients with disease progression, 17 patients (43.6%) underwent revision surgery. After revision surgery, three patients received both chemotherapy and radiotherapy, two patient received chemotherapy, and one patient underwent proton therapy for recurrent myxopapillary ependymoma. Five patients (12.8%) were treated by chemotherapy, radiotherapy, or both without revision surgery. Seventeen patients (43.6%) did not receive any treatment for disease progression. Seven patients could not take additional treatment because of rapid disease progression or poor general condition. Five patients rejected to receive any treatment and took hospice care. Two patients were undergoing imaging follow-up for slow progression. Three patients lost their follow-ups.

OS and PFS

The OS and PFS curves for the entire group are shown in Fig. 2. The 3-, 5-, 10-, and 20-

year OS rates were 83%, 82%, 81%, and 78%, respectively. The 3-, 5-, 10-, and 20-year PFS rates were 76%, 73%, 68%, and 58%, respectively.

Regarding malignant tumors, the 3-, 5-, 10-, and 20-year OS rates were 68%, 66%, 66%, and 61%, respectively. Whereas, the OS rates of benign tumors were 100%, 100%, 97%, and 97%, respectively. Patients with malignant tumors showed significant worse survival statistics compared to patients with benign tumors (P = 0.000). The 3-, 5-, 10-, and 20-year PFS rates in patients with malignant tumors were 65%, 63%, 61%, and 61%, respectively. The 3-, 5-, 10-, and 20-year PFS rates in patients with benign tumors were 89%, 85%, 71%, and 55%, respectively. The PFS statistics were superior in patients with benign tumors until 15-year, however, the curve showed crossed thereafter, because of the benign tumors with late progression (schwannomas at 187 months and 218 months, lipoma at 272 months). Finally, the PFS did not show statistical significance in terms of pathology (P = 0.101).

In terms of extent of tumor removal, patients with GTR showed the 3, 5, 10, and 20 year OS of 98%, 96%, 96%, and 96%, respectively. On the other hand, patients without GTR showed 68%, 68%, 66%, and 62% OS at the 3, 5, 10, and 20 year, respectively. The patients with GTR showed a significant better survival curve compared to those without GTR (P=0.000). The 3-, 5-, 10-, and 20-year PFS rates in patients with GTR were 90%, 83%, 78%, and 78%, respectively. The 3-, 5-, 10-, and 20-year PFS rates in patients without GTR were 64%, 64%, 55%, and 42%, respectively. The PFS was also better in patients with GTR than patients without GTR (P = 0.001).

IM tumors

In 43 patients with IM tumors (male:female = 16:27), the mean age of patients was 6.9 ± 5.18 years (Table 4). The mean period of symptom duration until diagnosis was significantly longer compared to patients without IM tumors (17.5 ± 32.50 months vs. 4.4 ± 7.68 months, P=0.014). The mean follow-up period was 93.6 ± 96.32 months.

Motor symptoms presented more dominantly in patients with IM tumors compared to patients without IM mores (97.7%% vs. 71.1%, P=0.000). Also, there were significantly more patients presenting with spinal deformity in IM tumors than those without IM tumors (16.3% vs. 3.6%, P=0.008).

The IM tumors involved significantly more segments compared to tumor with other location (8.5 ± 5.69 vs. 3.8 ± 2.87, P=0.000). The most commonly involved level was cervico-thoracic spine (n=12, 27.9%), followed by cervical spine (n=9, 20.9%), thoracic spine (n=9, 20.9%), and thoraco-lumbar spine (n=5, 11.6%). Holocord involvement of tumor (18.6%) was significantly predominant in IM tumors compared to tumors with other location (8/43 vs. 1/83, P=0.001).

In patients with IM tumors, GTR and STR was achieved in 16 patients (37.2%) each. PR were achieved in 6 patients (14.0%). In 6 patients (14.0%), only biopsy was performed for IM tumors. Regarding surgical methods, majority of patients underwent laminoplasty (n=28, 65.1%), followed by laminectomy (n=15, 34.9%).

Pathologic classification of IM tumors was summarized in Table 5. The most common tumor type was diffuse astrocytic and oligodendroglial tumors (n=17, 39.5%), including diffuse astrocytomas (n=7), anaplastic astrocytomas (n=4), glioblastomas (n=3), oligodendrogliomas (n=2), and anaplastic oligodendroglioma (n=1). Pilocytic astrocytomas, categorized as other astrocytic tumors, were found in 6 patients (14.0%). Ependymal tumors were confirmed in 3 patients (7.0%), which were consist of myxopapillary ependymoma (n=1) and ependymomas (n=2). In 9 patients (20.9%), neuronal and mixed neuronal-glial tumors were found, including gangliogliomas (n=5), gangliocytoma (n=1), anaplastic ganglioglioma (n=1), papillary glioneuronal tumor (n=1), and atypical glioneuronal tumor (n=1). There were 6 cases (14.0%) of mesenchymal, non-meningothelial tumors including EWS (n=1), lipomas (n=2), hemangiomas (n=2), and hemangioblastoma (n=1). Lymphoma and germ cell tumor (immature teratoma) were found in one case each.

Regarding functional status, postoperative McCormick scale was significantly improved compared to preoperative McCormick scale (2.65 ± 1.31 vs. 3.05 ± 1.21, P=0.007). In patients with IM tumors, preoperative functional status, utilizing McCormick scale, showed a trend toward worse than patients without IM tumors (3.05 ± 1.21 vs. 2.59 ± 1.39), without statistical significance (P=0.071). Regarding postoperative McCormick scale, which of patients with IM tumor was significantly worse than patients without IM tumor (2.65 ± 1.31 vs. 1.95 ± 1.42, P=0.008). The degree of improvement of McCormick scale after surgery showed no significant difference between patients with and without IM tumors (P=0.301).

Nine patients (20.9%) died from the disease progression. The median time for death was 13 months (20 days ~ 184 months). The majority of diagnosis of patients who died were high grade tumors, except two patients: anaplastic astrocytomas (n=3), glioblastomas (n=2), EWS (n=1), malignant lymphoma (n=1), diffuse astrocytoma (grade II, n=1), and oligodendroglioma (grade II, n=1). Most of survival period of the dead was less than 2 years, except one patient. One patient who died of diffuse astrocytoma expired after 184 months after diagnosis. Because the patient did not undergo additional operation or detailed radiographic studies, we could not find out whether malignant transformation occurred.

Sixteen patients (37.2%) suffered from disease progression. The median period of progression was 7.5 months (20 days ~ 114 months). Most of disease progression occurred within 2 years, except two patients. One patient with diffuse astrocytoma, described above, showed disease progression at 72 months. Another patient with myxopapillary ependymoma showed radiographic recurrence at 114 months. She underwent revision surgery with subtotal resection of tumor, and has continued regular follow-up. Among patients with disease progression, 8 patients (50.0%) received additional treatment including surgery, chemotherapy, or radiotherapy, 5 patients (31.3%) took only supportive care, one patient (6.3%) are on regular imaging follow-up, and 2 patients (12.5%) lost follow-ups.

Among patients with IM tumors, the 3-, 5-, 10-, and 20-year OS rates were 79%, 79%, 79%, and 69%, respectively (Fig. 4). The 3-, 5-, 10-, and 20-year PFS rates were 65%,

65%, 57%, and 57%, respectively. In patients with high grade IM tumors, the 3-, 5-, and 10-year OS rates were sustained to 32% (not available 20-year data), whereas, the 3-, 5-, 10- and 20-year OS rates in low grade IM tumors were 96%, 96%, 96%, and 84%, respectively (P=0.000). Tumor grade also showed significant differences on PFS (P=0.000): the 3-, 5-, and 10-year PFS rates in high grade tumors were 24%, 24%, and 24% vs. the 3-, 5-, 10- and 20-year PFS rates in low grade tumors were 79%, 79%, 68%, and 68%. In terms of extent of resection, all patients who achieved GTR of IM tumors survived. Whereas, the OS rates in patients without GTR were 68%, 68%, 68%, and 57% at 3-, 5-, 10-, and 20-year (P=0.021). The PFS in patients with IM tumors, however, did not show significant difference regarding the extent of resection (P=0.641).

ED tumors

In 57 patients with ED tumors (male:female = 26:31), the mean age of patients was 5.7 ± 5.10 years (Table 6). The mean period of symptom duration until diagnosis was significantly shorter compared to patients without ED tumors (2.2 ± 4.12 months vs. 14.1 ± 26.76 months, P=0.001). The mean period of follow-up was 100.9 ± 85.18 months.

Like tumors with other locations, the most common presenting symptom was motor symptoms, however, the proportion was lower compared to tumors with other locations (59.6% vs. 97.1%, P=0.001). Rather, proportion of patients diagnosed with incidentally found mass on radiographs was significantly higher in ED tumor (26.3% vs. 1.4%,

P=0.000).

The ED tumor involved significantly shorter segments compared to tumor with other location (3.8 ± 3.03 vs. 6.8 ± 5.24, P=0.000. The most commonly involved level was thoracic spine (n=30, 52.6%), followed by thoraco-lumbar spine (n=8, 14.0%), and lumbo-sacral spine (n=5, 8.8%).

In patients with ED tumors, GTR was achieved in 33 patients (57.9%) and STR in 17 patients (29.8%). PR and biopsy were achieved in 4 patients (7.0%) and 3 patients (5.3%). Most common method of bony removal was laminoplasty (n=24, 42.1%), followed by laminectomy (n=14, 24.6%), partial hemilaminectomy (n=6, 10.5%), and corpectomy (n=3, 5.3%). Other approaches including thoracotomy or thoracoscopy were utilized in 10 patients (17.5%).

Pathologic classification of ED tumors was summarized in Table 7. The most common type was ED tumors were peripheral neuroblastic tumors (n=31, 54.4%): neuroblastomas (n=14), ganglioneuromas (n=12), and ganglioneuroblastoas (n=5). CNS embryonal tumors, CNS embryonal tumors with rhabdoid features, were present in 2 patients (3.5%). There were 6 cases (10.5%) of tumors of the paraspinal nerves including schwannomas (n=3), neurofibroma (n=1), and MPNSTs (n=2). Mesenchymal, non-meningothelial tumors were second most common type of ED tumors (n=10, 17.5%), consist of EWS (n=9) and hemangioma (n=1). Besides, there were lymphomas (n=3, 5.3%), histiocytic tumors (n=3, 5.3%), and germ cell tumors (n=2, 3.5%).

Regarding functional status, postoperative McCormick scale was significantly improved compared to preoperative McCormick scale (1.77 ± 1.36 vs. 2.54 ± 1.49, P=0.000). In patients with ED tumors, preoperative functional status did not show significant difference from patients without ED tumors (2.54 ± 1.49 vs. 2.91 ± 1.20, P=0.125). However, postoperative McCormick scale was significantly better in patients with ED tumor compared to patients without ED tumor (1.77 ± 1.36 vs. 2.54 ± 1.38, P=0.002). The degree of improvement of McCormick scale after surgery showed no significant difference between patients with and without ED tumor (P=0.200).

Ten patients (17.5%) died from disease. The mean time for death was 17.1 ± 13.70 months. The pathology of patients who died were all malignant tumors, including EWS (n=6), CNS embryonal tumor with rhabdoid features (n=2), neuroblastoma (n=1), and MPNST (n=1). Most of death occurred within 2 years, except one patient (50 months).

Eleven patients (19.3%) suffered from disease progression. The median period of progression was 12 months (13 days ~ 218 months). Most of disease progression occurred within 4 years, however, there existed one patient with late progression of schwannoma beyond 15 years after first operation (218 months). Among patients with disease progression, seven patients (63.6%) were treated with surgery and/or chemotherapy. Three patents (27.3%) did not receive any treatment because of poor general condition or refusal of treatment, and one patient lost follow-up.

Among patients with ED tumors, the 3-, 5-, 10-, and 20-year OS rates were 83%, 80%, 80%, and 80%, respectively (Fig. 5). The 3-, 5-, 10-, and 20-year PFS rates were 83%,

81%, 81%, and 60%, respectively. In patients with malignant tumors, the 3-, 5-, 10- and 20-year OS rates were 75%, 72%, 72%, and 72%, whereas, the 3-, 5-, 10- and 20-year OS rates in benign tumors were sustained to 100% (P=0.024). Regarding disease progression, the 3-, 5-, 10- and 20-year PFS rates in malignant tumors were 74%, 71%, 71%, and 71%, whereas the 3-, 5-, 10- and 20-year PFS rates in benign tumor were 100%, 100%, 100% and 0% (P=0.072). The PFS rates were superior in patients with benign tumors until about 20 years, however, the curve showed crossed thereafter, because of a benign tumor with late progression (schwannoma at 218 months). In terms of extent of resection, the 3-, 5-, 10- and 20-year OS rates in patients who achieved GTR of ED tumors were 97%, 93%, 93%, and 93%. Whereas, the OS rates in patients without GTR were sustained to 65% at 3-, 5-, 10-, and 20-year (P=0.007). The 3-, 5-, 10- and 20-year PFS rates in patients with GTR of tumors were 97%, 93%, 93%, and 93%, and those without GTR were 63%, 63%, 63%, and 0% (P=0.002). Because of a patient with schwannoma who showed late progression after PR (at 218 months), the PFS rate dropped to 0% at 20-year.

DISCUSSION

In the present study, we reviewed 32-year experiences of surgical management of pediatric PSCT in a single institution. Although there exist several literatures comprising large number of pediatric patients with IM PSCTs, studies regarding tumors involving entire spinal columns are quite sparse[27]. To the best of our knowledge, the present study is the largest series comprising all primary neoplasms of spinal axis with evaluation of detailed survival analysis.

The mean duration of symptom was 9.3 months in the present study. It is similar to most previous studies ranging from 6 to 12 months[5, 7, 8, 11, 12, 24]. As Houten et al. described, the symptom duration was significantly shorter in malignant tumors in our study [11]. It is noteworthy that the symptom duration was much shorter in ED tumors (2.2 months) and longer in IM tumors (17.5 months), compared to total study population. These differences might result from the high proportion of malignancy in ED tumors (70.2%), and predominance of lower grade tumors in IM location (74.4%).

Majority of children diagnosed with PSCT presented with some type of symptoms. Among them, motor weakness (80.2%) including gait disturbance presented most commonly. This is on the contrary to some previous studies, which described most common presenting symptomatology was neck or back pain[8, 11, 24, 25]. However, others described that motor weakness was the most common symptom[5, 7, 12, 16]. Despite of the

discrepancy of dominant symptoms, the point is that the sensory symptom in pediatric patients with spinal cord tumor is not as predominant as in adult patients[5, 18]. This may be because pediatric patients often cannot be aware or complain of sensory change, while adolescent or adult can[5]. Among the patients presenting with spinal deformity, most of them (7/10) had IM tumors. The proportion of spinal deformity in patients with IM tumors (7/43, 16.3%) was similar to previous literature[1, 27, 28]. As described earlier, spinal deformity was more evident in IM tumors than tumors in other locations, because of the inequality between signaling to both sides of the spine and paraspinal muscles[2]. There have been increasing issues about postoperative progressive spinal deformity following laminectomy and irradiation[22, 27, 28]. Post-laminectomy kyphoscoliosis is beyond the scope of the present study, however, further studies would be necessary. In ED tumors, the proportion of incidentally found mass on radiographic examination was significantly higher than tumors with other locations (26.3% vs. 1.4%, P=0.000). The high incidence of peripheral neuroblastic tumors in ED tumors characterized by huge mediastinal or retroperitoneal mass could be the explanation for the incidental findings.

On the contrary to the adult type, pediatric PSCTs tend to extend multiple levels[17, 25]. In the present study, about half (56.3%) of patients had tumors involving more than three levels, and nine patients (7.1%) revealed holocord tumors, which was similar with previous literatures[25]. Regarding anatomical location, ED tumors were most common (45.2%), followed by IM tumors (34.1%), and IDEM tumors (12.7%) in the present study. The anatomical distribution of PSCTs was quite similar to previous studies. Spacca et al. reported in their study consisted of 134 patients that tumor location was ED in 39.5%, IM

in 34.3%[25]. Wetjen and Raffel reported ED tumors were 34.5% and IM tumors were 29.7% by collecting and calculating 10 studies[26]. Although some studies reported IM location was most common, it seems obvious that, unlike adult counterpart, IDEM tumors constitute small part among all PSCTs[2, 8].

Regarding pathologic presentation, malignant tumors comprise a half of all tumors. However, the proportion of malignancy significantly differ in terms of anatomical location. Although malignant tumor consists about half in IM tumors (tumors coded /3), about 70% of ED tumors were malignant. There was no malignant tumor in IDEM location. These findings imply PSCTs have distinct behavioral characteristics according to anatomical location, and should be assessed separately. Similar to previous studies, most common type of tumors were nerve sheath tumors (n=23), low grade gliomas including pilocytic astrocytomas, diffuse astrocytomas, oligodendrogliomas, and ependymal tumors (n=20), and neuroblastomas (n=14). And astrocytic tumors such as pilocytic astrocytomas, diffuse astrocytomas, anaplastic astrocytomas, and glioblastomas were dominant pathologies in IM tumors (46.5%)[7, 25].

It is of note that pathologic composition of pediatric spinal cord tumors is far different from those of adult ones. First, majority of spinal cord tumor in adult is metastatic tumors. In the present study, however, about a quarter (36/126) of all tumors were embryonal tumors (CNS or peripheral origin), and there were only 25 patients out of 183 patients on registry (before exclusion) with metastatic lesion (13.7%). Moreover, majority of cases of metastatic lesions were drop metastasis from brain, not from solid organ. Second,

meningiomas are encountered very rarely, in contrast to adult in which meningiomas are one of the most common tumors[23]. There was no case of meningioma in the present study after exclusion of one patient with atypical meningioma because of multiple neuraxis tumors associated with NF-2. Furthermore, summing up all cases of meningiomas in literatures about pediatric PSCT, there were only 3 cases among 255 patients (1.2%)[5, 8, 25, 27]. Although the old research by Fortuna et al. stated that meningiomas comprised 4.3% of childhood spinal tumors (sporadic in 21 cases, NF-associated in 5 cases), it seems much rarer than previously reported[10]. Third, the histologic proportion in IM tumors also differ from adult ones. Astrocytomas predominate over ependymomas especially in younger children, gangliogliomas are more prevalent, and hemangiomblastomas are found very rarely in pediatric population[11 6 20]. Our study regarding IM tumors was also consistent with previous literatures. Nonetheless, the proportion of ependymomas (including IM myxopapillary type) in IM tumors was very low (n=3, 7.0%) in the present study. Spinal cord ependymomas are known to be associated with NF-2 in pediatric population, and mutation on NF-2 transcript is frequently found even in sporadic case[2, 4]. There were 8 cases of IM ependymomas before exclusion, which was second most common IM tumors, like previously reported[2, 7, 8, 25]. However, five cases of ependymomas were excluded from the study because of multiple lesions associated with NF-2 (n=4) and incomplete date (n=1).

Regarding clinical outcomes, 39 patients (31.0%) suffered disease progression and 23 patients (18.3%) died from disease. According previous literatures, progression rates and mortality rates of pediatric PSCTs range 18.5 ~ 37.4% and 8.8 ~ 40.0%, respectively[3, 5, 24,

[25]. The clinical outcomes of our study were in general agreement with previous studies. Because of the great diversity of spinal cord pathology, literatures with detailed survival statistics were hardly found. In the present study, we conducted survival analysis for entire group, and subgroup analysis for IM and ED tumors. The major finding in the survival analysis were patients with benign pathology and who achieved GTR of tumors showed significant better OS rates for entire group, IM tumors, and ED tumors, altogether.

In terms of disease progression, however, the PFS curve showed somewhat complicated results. The PFS curve seemed similar between entire tumors and ED tumors, however, which demonstrated significantly different pattern in IM tumors. The earlier statistical benefit of benign tumors for disease progression disappeared in about 20 years, because the late progression of benign tumors with PR. This disappearance of benefit (intersection of PFS curve) was also observed in ED tumors. These benign tumors, which were not completely removed before, could progress in very long-term follow up. The impact of extent of resection on PFS seemed opposite to that of pathology. GTR of tumor in entire PSCTs and ED group showed significantly beneficial effect on PFS. Therefore, for ED tumors, disease progression was mainly affected by extent of removal, rather than pathology. Regarding IM tumors, the beneficial effect of low grade pathology on PFS continued throughout the follow up. On the other hand, the impact of extent of removal did not show significant difference regarding disease progression. According to previous literatures, the pathological composition is the main determinant for patient survival and tumor progression for pediatric IM tumors[7]. Whereas, the effect on OS and PFS of radical resection of IM tumor seems less clear[7, 11, 12], although some researchers advocated

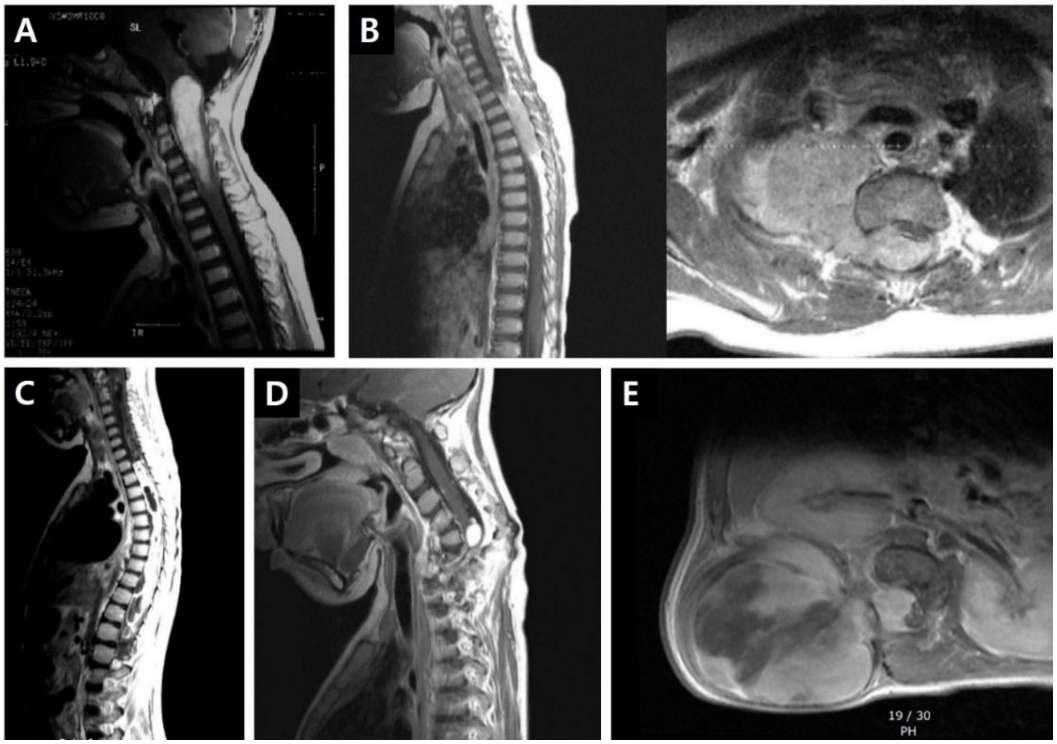
beneficial effect of total excision of tumor[5, 8]. Constantini et al. reported that long-term PFS did not show difference between groups with GTR and STR beyond 3-year postoperatively [7]. These findings were similar with the present study. Therefore, for IM tumors, tumor grade seems a main determinant on disease progression whereas extent of removal had little effect.

There are some limitations to be documented in the present study. The main limitation is the heterogeneity of pathology. This heterogeneity is inherent to pediatric PSCTs due to the rarity of this type of tumors, which is the main obstacle to the establishment of treatment protocol. To overcome this limitation, we categorized and evaluated the tumors according to particular anatomical location. Second, there exist numbers of patients excluded from the study. Representatively, we excluded patients with multiple lesions along craniospinal axis, because decision of recurrence or cause of death may be confusing in those patients. Twenty-six patients with NF diagnosed to neurofibromas (n=10), schwannomas (n=8), and ependymomas (n=5), MPNSTs (n=2), and meningioma (n=1), and one patient with von Hippel-Lindau syndrome were excluded for this reason. We suppose these patients would have worse clinical outcomes than patients with solitary lesion. It would be beneficial to evaluate the syndromic patients with multiple lesions separately afterward. In addition, there exist missed data due to loss of medical chart or radiographic images before the installation of electronic medical records and picture archiving and communication system in our institution. The lost data could result in bias in the evaluation. Third, because of some old data before the era of practical use of MRI, in-depth radiographic analysis was not possible.

CONCLUSION

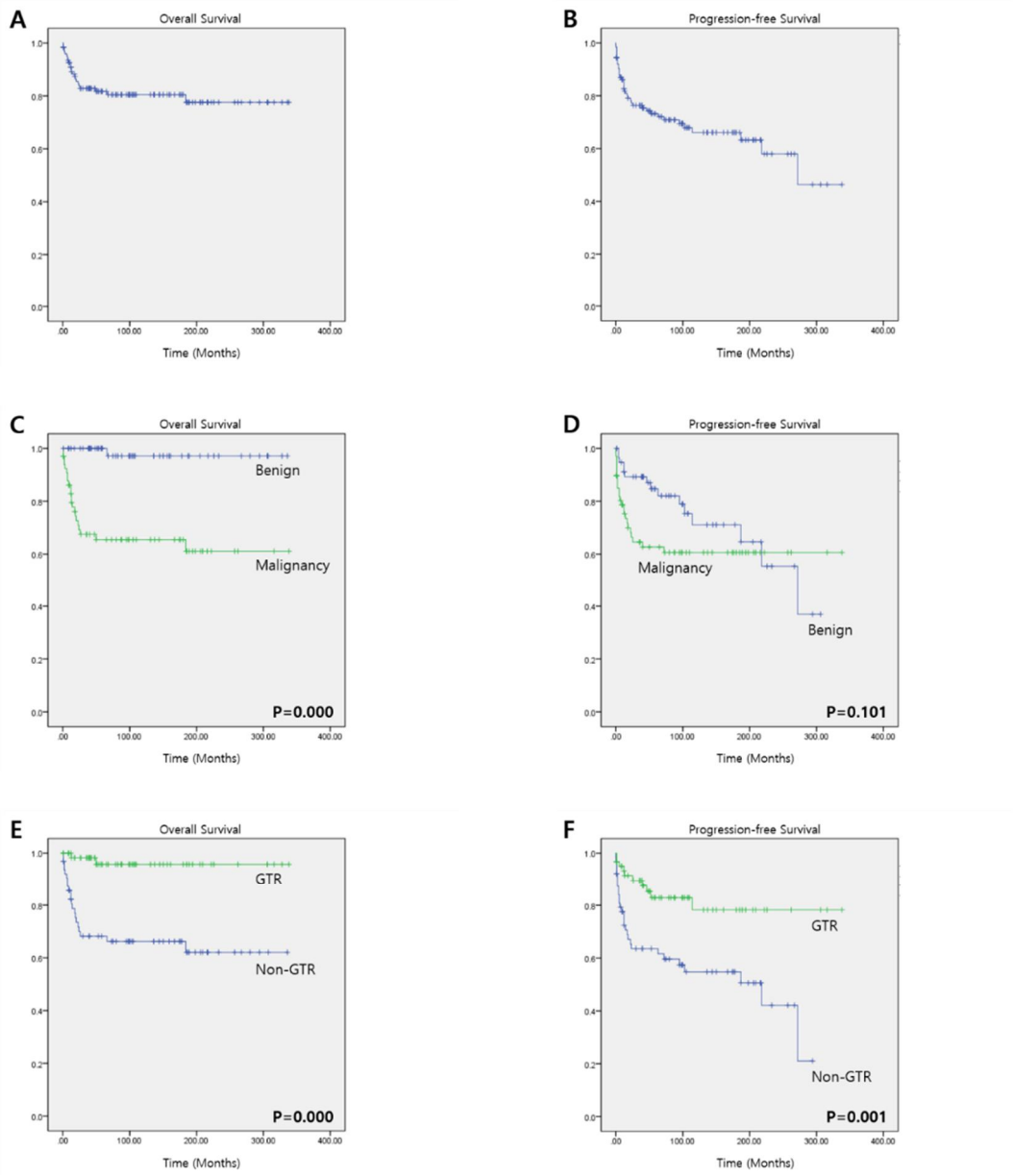
PSCTs are uncommon pathology in pediatric patients. The most common symptomatology was motor weakness, and symptom duration was shorter in patients with malignant tumors. Malignancy comprises about half of all tumors and the proportion of which was different by anatomical location. Most common anatomical location was ED, followed by IM, and IDEM. Most common tumors were schwannomas (n=14) and neuroblastomas (n=14), followed by ganglioneuromas (n=12), Ewing sarcomas (n=10), diffuse astrotytomas (n=7), neurofibromas (n=7), and pilocytic astrocytomas (n=6). Both the pathology and extent of resection had a decisive effect on OS. In IM tumors, pathology seems a main determinant on PFS whereas extent of removal had little effect. In ED tumor, however, the extent of removal showed an influence on PFS, rather than pathology. For the rarity and heterogeneity of pediatric PSCTs, which could act as an obstacle to detailed evaluation, future multi-center study would be needed.

Fig. 1. Magnetic resonance imaging of pediatric primary spinal cord tumors



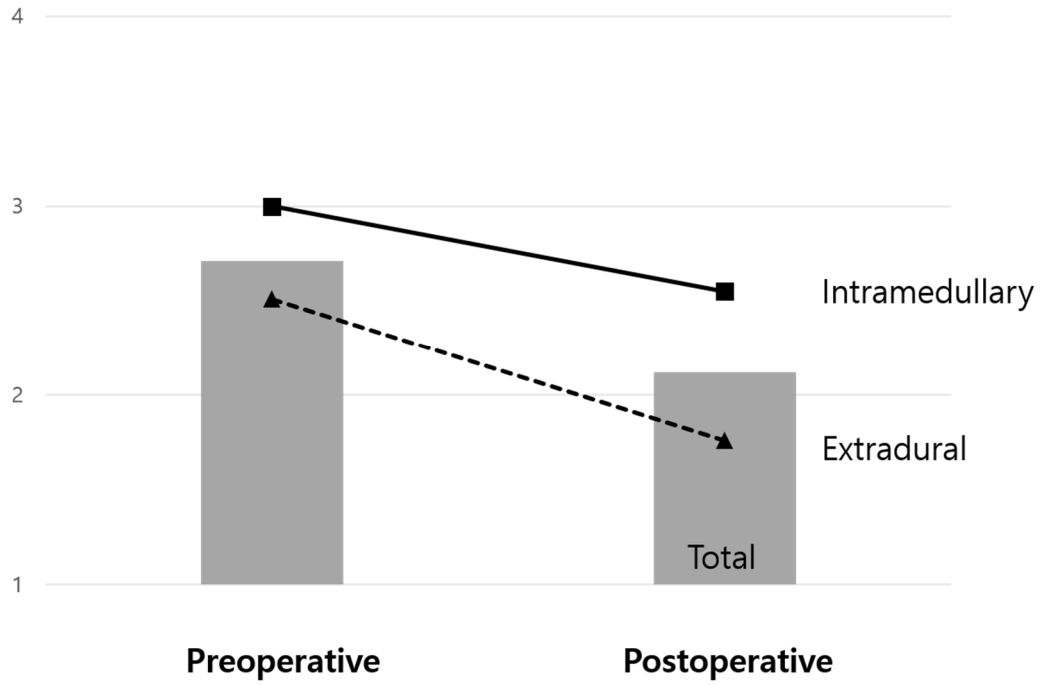
A. Intramedullary (IM) diffuse astrocytoma. **B.** Extradural (ED) neuroblastoma with extraspinal extension. **C.** IM gangliocytoma. **D.** Intradural extramedullary neurofibroma in neufofibromatosis type 1 patients. Note associated severe kyphoscoliosis. **E.** ED Ewing sarcoma with extraspinal extension.

Figure 2. Overall survival and progression-free survival for pediatric patients with primary spinal cord tumors



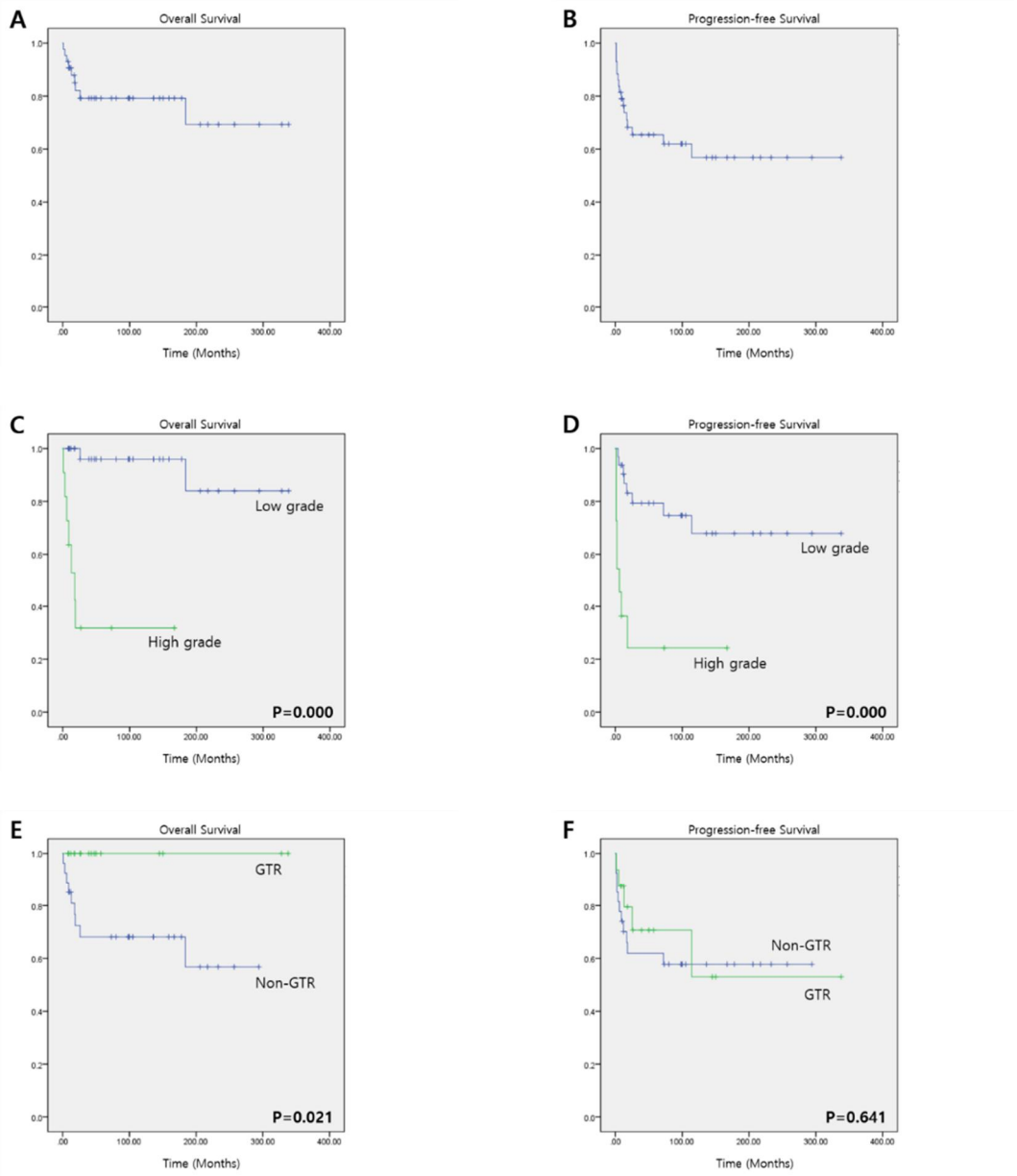
A and **B.** Overall survival (OS) and progression-free survival (PFS) for pediatric patients with primary spinal cord tumors (PSCTs). In contrast to OS curve, PFS statistics showed continuous decline after early rapid descent. **C.** OS of PSCTs regarding malignancy. OS rates were significant lower in patients with malignant tumors (P=0.000). **D.** However, PFS according malignancy did not show meaningful results (P=0.101). In benign tumors, there existed late progressions following surgery. **E.** In gross total resection (GTR) group, OS rates were superior to non-GTR groups (P=0.000). **F.** PFS was significantly higher in patients with GTR compared to those without GTR (P=0.001).

Figure 3. Perioperative functional outcomes



Postoperative McCormick scale improved after operation in all three groups (entire group, intramedullary group, and extradural group). The amount of improvement did not show significant difference among groups.

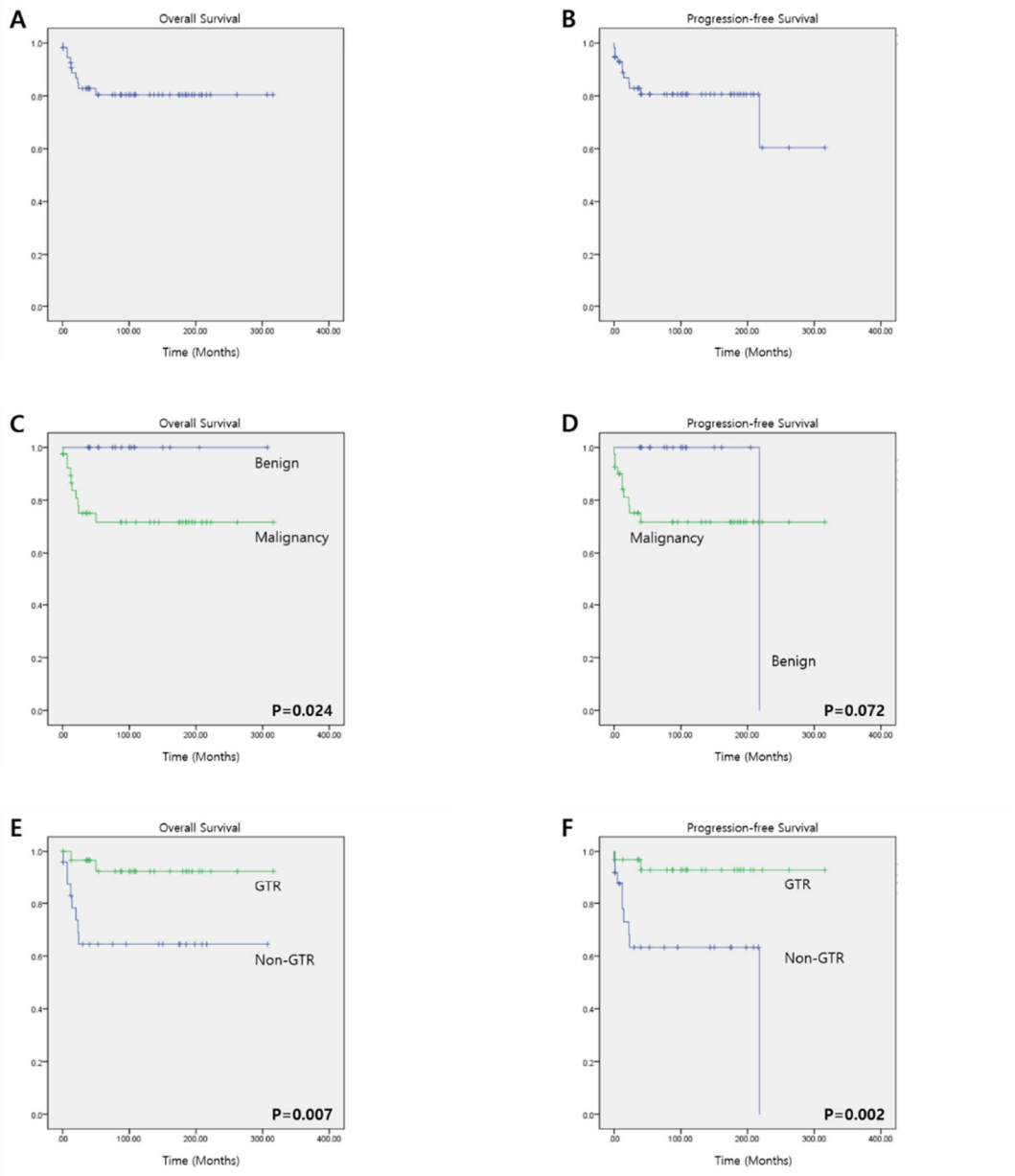
Figure 4. Overall survival and progression-free survival for pediatric patients with intramedullary tumors



A and **B.** Overall survival (OS) and progression-free survival (PFS) for pediatric

patients with intramedullary (IM) spinal cord tumors. **C.** In high grade IM tumors, OS rates were worse than in low grade IM tumors (P=0.000). **D.** PFS rates were also significantly different between groups with high grade IM tumors and low grade tumors (P = 0.000). **E.** IM tumors with gross total resection (GTR) showed higher OS rates than those without GTR (0.021). **F.** Regarding PFS, the results were inconclusive between groups with GTR and non-GTR (P=0.641).

Figure 5. Overall survival and progression-free survival for pediatric patients with extradural tumors



A and B. Overall survival (OS) and progression-free survival (PFS) for pediatric

patients with Extradural (ED) spinal cord tumors. **C.** In malignant ED tumors, OS rates were worse than in benign ED tumor (P=0.024). **D.** Regarding PFS, the results were inconclusive between groups with malignant and benign tumors, because of a late progression of benign tumor (P=0.072). **E.** ED tumors with gross total resection (GTR) showed higher OS rates than those without GTR (P=0.007). **F.** PFS was also significantly different between groups with GTR and non-GTR (P = 0.002).

Table 1. Modified McCormick Scale for Functional Evaluation of Patients

Grade	Explanation
I	Neurologically intact, ambulates normally, may have minimal dysesthesia
II	Mild motor or sensory deficit, patient maintains functional independence
III	Moderate deficit, limitation of function, independent with external aid
IV	Severe motor or sensory deficit, limit of function with a dependent patient
V	Paraplegia or quadriplegia, even if there is flickering movement

Table 2. Characteristics of Patients with Primary Spinal Cord Tumors

Variable	Value
Sex	M:F = 56:70
Age (year)	6.4 ± 5.04
Symptom duration (month)	9.3 ± 21.61
Follow-up period (month)	100.7 ± 91.60
Symptom	
Motor	101 (80.2%)
weakness	69
gait disturbance	28
neck motion limitation	3
torticollis	1
Sensory	40 (31.7%)
pain	33
hypesthesia	4
tingling sense	3
Urinary disturbance	9 (7.1%)
Spinal deformity	10 (7.9%)
Soft tissue mass	2 (1.6%)
Radiographic finding	16 (12.7%)
Other	5 (4.0%)
extremity deformity	2
respiratory difficulty	1
irritability	1

hip dislocation	1
Number of involved segments	5.4 ± 4.61
Level	
Cervical	23 (18.3%)
Cervico-thoracic	21 (16.7%)
Thoracic	40 (31.7%)
Thoraco-lumbar	15 (11.9%)
Lumbar	9 (7.1%)
Lumbo-sacral	7 (5.6%)
Sacral	2 (1.6%)
Holocord	9 (7.1%)
Location	
IM	43 (34.1%)
IM/IDEM	2 (1.6%)
IDEM	16 (12.7%)
IDEM/ED	8 (6.3%)
ED	57 (45.2%)
Extent of tumor removal	
Gross total removal	63 (50.0%)
Subtotal removal	41 (32.5%)
Partial removal	14 (11.1%)
Biopsy	8 (6.3%)

Surgical method	
Laminoplasty	70 (55.6%)
Laminectomy	36 (28.6%)
Partial hemi/Hemi-laminectomy	7 (5.6%)
Corpectomy	3 (2.4%)
Other	10 (7.9%)

IM, intramedullary; IDEM, intradural extramedullary; ED, extradural

Table 3. Pathological Diagnosis of Primary Spinal Cord Tumors

Classification	Value	Location
Diffuse astrocytic and oligodendroglial tumors	17 (13.5%)	
Diffuse astrocytoma	7	IM (7)
Anaplastic astrocytoma	4	IM (4)
Glioblastoma	3	IM (3)
Oligodendroglioma	2	IM (2)
Anaplastic oligodendroglioma	1	IM (1)
Other astrocytic tumors	6 (4.8%)	
Pilocytic astrocytoma	6	IM (6)
Ependymal tumors	5 (4.0%)	
Myxopapillary ependymoma	3	IDEM (2), IM (1)
Ependymoma	2	IM (2)
Neuronal and mixed neuronal-glial tumors	9 (7.1%)	
Ganglioglioma	5	IM (5)
Gangliocytoma	1	IM (1)
Anaplastic ganglioglioma	1	IM (1)
Papillary glioneuronal tumor	1	IM (1)
Atypical glioneuronal tumor	1	IM (1)
Embryonal tumors	5 (4.0%)	
Atypical teratoid/rhabdoid tumor	3	IDEM/ED (3)
CNS embryonal tumor with rhabdoid features	2	ED (2)
Tumors of the cranial and paraspinal nerves	23 (18.3%)	
Schwannoma	14	IDEM (8), ED (3), IDEM/ED (2), IM/IDEM (1)
Neurofibroma	7	IDEM (4), IDEM/ED (2), ED (1)

Malignant peripheral nerve sheath tumor	2	ED (2)
Mesenchymal, non-meningothelial tumors	19 (15.1%)	
Ewing sarcoma	10	ED (9), IM (1)
Lipoma	3	IM (2), IM/IDEM (1)
Hemangioma	3	IM (2), ED (1)
Peripheral neuroepithelioma	1	IDEM/ED (1)
Hemangioblastoma	1	IM (1)
Myofibroblastomatosis	1	IDEM (1)
Lymphomas	4 (3.2%)	ED (3), IM (1)
Histiocytic tumors	3 (2.4%)	ED (3)
Germ cell tumors	4 (3.2%)	
Germinoma	1	ED (1)
Mature teratoma	1	IDEM (1)
Immature teratoma	1	IM (1)
other	1	ED (1)
Peripheral neuroblastic tumors	31 (24.6%)	
Neuroblastoma	14	ED (14)
Ganglioneuroma	12	ED (12)
Ganglioneuroblastoma	5	ED (5)

CNS, central nervous system; IM, intramedullary; IDEM, intradural extramedullary; ED, extradural

Table 4. Characteristics of Patients with Intramedullary Tumors

Variable	Value
Sex	M:F = 16:27
Age (year)	6.9 ± 5.18
Symptom duration (month)	17.5 ± 32.50
Follow-up period (month)	93.6 ± 96.32
Symptom	
Motor	42 (97.7%)
weakness	29
gait disturbance	10
neck motion limitation	2
torticollis	1
Sensory	10 (23.3%)
pain	7
hypesthesia	2
tingling sense	1
Urinary disturbance	2 (4.7%)
Spinal deformity	7 (16.3%)
Other	2 (4.7%)
extremity deformity	2
Number of involved segments	8.5 ± 5.69
Level	

Cervical	9 (20.9%)
Cervico-thoracic	12 (27.9%)
Thoracic	9 (20.9%)
Thoraco-lumbar	5 (11.6%)
Lumbar	0 (0%)
Holocord	8 (18.6%)
Extent of tumor removal	
Gross total removal	16 (37.2%)
Subtotal removal	16 (37.2%)
Partial removal	6 (14.0%)
Biopsy	5 (11.6%)
Surgical method	
Laminoplasty	28 (65.1%)
Laminectomy	15 (34.9%)

Table 5. Pathological Diagnosis of Intramedullary Tumors

Classification	Value
Diffuse astrocytic and oligodendroglial tumors	17 (39.5%)
Diffuse astrocytoma	7
Anaplastic astrocytoma	4
Glioblastoma	3
Oligodendroglioma	2
Anaplastic oligodendroglioma	1
Other astrocytic tumors	6 (14.0%)
Pilocytic astrocytoma	6
Ependymal tumors	3 (7.0%)
Myxopapillary ependymoma	1
Ependymoma	2
Neuronal and mixed neuronal-glial tumors	9 (20.9%)
Ganglioglioma	5
Gangliocytoma	1
Anaplastic ganglioglioma	1
Papillary glioneuronal tumor	1
Atypical glioneuronal tumor	1
Mesenchymal, non-meningothelial tumors	6 (14.0%)
Ewing sarcoma	1
Lipoma	2
Hemangioma	2
Hemangioblastoma	1

Lymphomas	1 (2.3%)
Germ cell tumors	1 (2.3%)
Immature teratoma	1

Table 6. Characteristics of Patients with Extradural Tumors

Variable	Value
Sex	M:F = 26:31
Age (year)	5.7 ± 5.10
Symptom duration (month)	2.2 ± 4.12
Follow-up period (month)	100.9 ± 85.18
Symptom	
Motor	34 (59.6%)
weakness	24
gait disturbance	10
Sensory	17 (29.8%)
pain	15
tingling sense	2
Urinary disturbance	6 (10.5%)
Soft tissue mass	2 (3.5%)
Radiographic finding	15 (26.3%)
Other	1 (1.8%)
irritability	1
Number of involved segments	3.8 ± 3.03
Level	
Cervical	5 (8.8%)
Cervico-thoracic	3 (5.3%)

Thoracic	30 (52.6%)
Thoraco-lumbar	8 (14.0%)
Lumbar	3 (5.3%)
Lumbo-sacral	5 (8.8%)
Sacral	2 (3.5%)
Holocord	1 (1.8%)
Extent of tumor removal	
Gross total removal	33 (57.9%)
Subtotal removal	17 (29.8%)
Partial removal	4 (7.0%)
Biopsy	3 (5.3%)
Surgical method	
Laminoplasty	24 (42.1%)
Laminectomy	14 (24.6%)
Partial hemi/Hemi-laminectomy	6 (10.5%)
Corpectomy	3 (5.3%)
Other	10 (17.5%)

Table 7. Pathological Diagnosis of Extradural Tumors

Classification	Value
Embryonal tumors	2 (3.5%)
CNS embryonal tumor with rhabdoid features	2
Tumors of the cranial and paraspinal nerves	6 (10.5%)
Schwannoma	3
Neurofibroma	1
Malignant peripheral nerve sheath tumor	2
Mesenchymal, non-meningothelial tumors	10 (17.5%)
Ewing sarcoma	9
Hemangioma	1
Lymphomas	3 (5.3%)
Histiocytic tumors	3 (5.3%)
Germ cell tumors	2 (3.5%)
Germinoma	1
other	1
Peripheral neuroblastic tumors	31 (54.4%)
Neuroblastoma	14
Ganglioneuroma	12
Ganglioneuroblastoma	5

CNS, central nervous system

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국 문 초 록

목적: 소아의 원발성 척수 종양은 낮은 발병률과 진단의 다양성으로 인하여 연구된 바가 많지 않다. 본 논문의 목적은 원발성 척수 종양으로 수술받은 소아환자들에 대한 단일기관 연구로서 기술적 분석 및 생존 분석을 시행하고자 하였다.

방법: 1984년 8월부터 2008년 12월까지 단일기관에서 수술을 받은 소아의 원발성 척수종양 126례에 대하여 조사하였다. 환자의 인구통계학적 특성, 종양의 특질, 수술 및 임상 결과, 생존분석에 대해 조사하였다. 또한 수질내 종양 및 경막외 종양에 대하여 별도로 분석을 시행하였다.

결과: 남자와 여자 환자는 각각 56명, 70명으로 총 126명이었다. 평균 연령은 6.4 ± 5.04 세였으며, 평균 추적관찰 기간은 100.7 ± 91.60 개월이었다. 환자가 호소하는 가장 흔한 증상은 위약이었으며, 증상의 평균 발현기간은 9.3 ± 21.61 개월이었다. 수질내 종양 환자의 경우 증상의 발현기간이 가장 길었으며 위약 및 척추 변형의 빈도가 높았다. 경막외 종양 환자의 경우 증상의 발현 기간이 가장 짧았으며, 영상의학적 이상으로 진단된 비율이 높았다. 종양의 분포 부위는 흉추가 가장 흔했다.

종양의 해부학적 위치로는 경막외가 가장 흔했으며 (57례, 45.2%), 그 다음은

수질내 (43례, 34.1%), 경막내수질외 (16례, 12.7%), 경막내수질외/경막외 (8례, 6.3%), 수질내/경막내수질외 (2례, 1.6%) 순이었다. 소아 원발성 척수종양의 절반 정도 (69례, 54.8%)가 조직학적으로 악성이었다. 55.6%의 환자에서 종양의 전적출이 가능하였으며, 가장 흔히 시행된 술식은 후궁성형술이었다 (55.6%). 병리학적 진단으로는 신경초종 (14례)과 신경아세포종 (14례)이 가장 흔했으며, 신경절신경종 (12례), Ewing 육종 (10례), 미만성 별아교세포종 (7례), 신경섬유종 (7례), 털모양 별아교세포종 (6례)가 다음으로 많았다. 수술 전 McCormick 등급은 2.75 ± 1.34, 수술 후 McCormick 등급은 2.19 ± 1.42 였다 (P=0.000). 수술 전후 McCormick 등급의 호전 정도는 수질내 종양과 경막외 종양에서 차이가 없었다. 23명 (18.3%)의 환자가 종양 진행으로 사망하였으며 평균 생존 기간은 23.1 ± 38.33 개월이었다. 39명 (31.0%)의 환자에게서 종양의 진행이 확인되었으며 진행까지의 평균 기간은 36.8 ± 63.06 개월이었다. 3, 5, 10, 20년 전체 생존율은 83%, 82%, 81%, 78% 였으며 3, 5, 10, 20년 무진행 생존율은 76%, 73%, 68%, 58% 였다. 수질내 종양의 경우, 3, 5, 10, 20년 전체 생존율은 79%, 79%, 79%, 69% 였으며, 3, 5, 10, 20년 무진행 생존율은 65%, 65%, 57%, 57% 였다. 경막외 종양의 경우 3, 5, 10, 20년 전체 생존율은 83%, 80%, 80%, 80% 였으며, 무진행 생존율은 83%, 81%, 81%, 60% 였다. 전제 환자, 수질내 종양 환자 및 경막외 환자 모두에서 종양의 조직학적 소견과 절제 정도가 전체 생존율에 유익한 효과가 있었다. 전체

종양 환자 및 경막외 종양 환자에게서 종양의 절제 정도가 무진행 생존율에 유익한 효과가 있었으나, 조직학적 소견의 영향은 명확하지 않았다. 반대로, 수질내 종양 환자에게서는 종양의 조직학적 소견이 종양의 진행에 유익한 효과가 있었으나, 종양의 절제 정도는 효과가 명백하지 않았다,

결론: 소아 환자의 원발성 척수 종양은 드문 질환으로서 절반 정도가 조직학적으로 악성이었다. 가장 흔한 발생 위치는 경막외 종양이고 수질내 종양과 경막내수질외 종양이 그 다음 순이었다. 신경초종과 신경아세포종이 가장 흔한 병리학적 진단이었다. 종양의 병리학적 소견 및 절제 정도가 전체 생존율에 영향을 미치는 인자였다. 수질내 종양의 경우 종양의 절제 정도보다는 조직학적 소견이 종양의 진행에 영향을 미치는 인자였고, 경막외 종양의 경우 종양의 조직학적 특성 보다는 절제 정도가 종양의 진행에 영향을 미치는 인자였다.

주요어: 원발성 척수 종양, 척추내 종양, 척수, 소아, 치료 결과

학번: 2010-23725