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Surgical management of intradural spinal cord tumors in children and young adults: A single-center experience with 50 patients

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Abstract

Background: Intradural spinal cord tumors (IDSCTs) in children and young adults are rare diseases. This present study is aimed to demonstrate our experience with a large series of children and young adults with IDSCT.

Methods: A total of 50 patients aged <20 years with IDSCT treated in our department between 1990 and 2010 were included in the study. Clinical, histological, and radiological findings, treatment strategies, and clinical outcome were retrospectively assessed. Depending on the relation to the spinal cord, IDSCT were dichotomized into intramedullary SCT (IMSCT) and extramedullary SCT (EMSCT). The functional outcome was evaluated with the Frankel score assessing the longest available follow-up period.

Results: Mean age was 10.3 years (range 6 months–19 years). IDSCT surgery was performed in 44 patients (88%). A common first symptom in patients with EMSCT was neck and back pain (41%), whereas monoparesis of arms (43%) were often seen in patients with IMSCT. The main duration of the symptoms was longer in patients with IMSCT. The postoperative functional outcome was generally comparable to the preoperative functional condition, while better for EMSCT ($P < 0.01$). The functional outcome at last follow-up correlated significantly with the preoperative Frankel score ($P < 0.002$).

Conclusion: Due to the mostly mild impact of the surgery on the functional outcome, the surgical treatment of IDSCT in children and young patients can be uniquely advocated.

Key Words: Adolescence, intramedullary tumor in childhood, pediatric neurosurgery, pediatric spine, spinal cord tumor, spinal instrumentation

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INTRODUCTION

Spinal tumors are rare and compromise approximately 5–10% of all tumors of the central nervous system in children and young adults.[32] The annual incidence of these tumors varies between 0.9 and 2.6/100,000.[24]

Since the first successful removal of an intradural extramedullary fibromyxoma by Gowers and Horsley in 1888,[21] remarkable progress has been achieved in spinal

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cord tumor surgery. Advancements in diagnostics, surgical techniques equipment, and oncological treatment improved the outcome of these challenging tumors, in particular, with intramedullary involvement.[15,24,39] The development of modern neuroimaging procedures for surgical planning, as well as innovative technologies for intraoperative visualization and tumor resection, represent substantial developments which have contributed to the safety and efficacy of spinal cord surgery.[3,7,12,17,20,34,43,44]

The age-related peculiarities of the surgical treatment of spinal cord tumors in children and young adults lie in the body growth and different biological features of neoplastic lesions. However, there are still no specific guidelines or recommendations for the treatment of spinal cord tumors in children and young patients.[22]

Against this background, we present a large series of children and young adults with intradural spinal cord tumors (IDSCTs) treated at our department during a 20-year period and aimed to derive specific treatment recommendations for pediatric patients upon a single-center experience.

MATERIALS AND METHODS

Patient population

Data of 90 pediatric patients and young adults (younger than 20 years) with the diagnosis of a spinal cord lesion, who were treated at our Neurosurgical Department between January 1990 and December 2010, were retrospectively collected. Children and young adults with extradural spinal cord tumors and spinal abscesses, as well as intradural vascular lesions such as cavernous hemangiomas, arteriovenous fistulas, and arteriovenous malformations, were excluded from this study. Thus, a total of 50 patients fulfilling the inclusion criteria of IDSCTs were identified and enrolled into the study. The study was conducted in accordance with the Declaration of Helsinki and the Guideline for Good Clinical Practice. The study protocol was approved by the local ethic committee of the University of Duisburg-Essen, Germany.

Data management

The data on demographic, clinical, and radiological characteristics of the patients, intraoperative findings, and complications, as well as the parameters of the postoperative course were retrospectively collected. The neurological status was assessed using the Frankel score.[19] According to this score, the outcome was classified as poor (A + B), fair (C), and good (D + E).

All patients underwent the clinical examination pre- and post-operatively, as well as 3 months after the surgery. Radiological examination using magnetic resonance imaging (MRI) before and 3 months after surgery was also performed in all cases. Furthermore, depending on the histopathology and clinical status, patients underwent later clinical and MRI-controls (at 6 months and yearly) in certain cases. Therefore, the average follow-up period was 3.5 ± 3.2 years (range 3 months–10 years).

Surgical treatment was performed under standard microsurgical conditions and intraoperative electrophysiological monitoring (with obligatory use of sensory evoked potentials, as well as increasing the use of motor-evoked potentials and D-wave recordings in the recent years). The patients were positioned depending on the location of the tumor: A semi-sitting position was performed for tumors of the upper and middle cervical region and prone position for lesions of the lower cervical and thoracic region including the medullary conus. The extent of tumor resection was judged upon the operative report.

IDSCT were classified into two groups: Intramedullary SCT (IMSCT) and extramedullary SCT (EMSCT). There were 29 (58%) patients suffering from EMSCT and 21 (42%) from IMSCT. The functional outcome was correlated with the histological features, tumor location, and the extension of the tumor. Surgical mortality was referred to death from any cause within 30 days of surgery, whereas the IDSCT mortality was referred to the cases issuing from IDSCT progression.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 22 (IBM Corporation, USA). Interval-scaled data were expressed as mean and standard deviations and nominal data were expressed as absolute numbers and valid percent.

Correlation analyses were conducted using Spearman's Rho due to not normal distribution of the data. *P* value of ≤0.05 was considered as statistically significant.

RESULTS

Patient population

The investigated cohort consisted predominantly of males (n = 32, 64%), the mean age was 10.3 years (range 6 months–19 years). There were no differences in age and sex between patients with IMSCT and EMSCT.

Clinical presentation

The mean duration between the first symptoms and diagnosis was 2.8 months (from incidental finding up to 1 year) in patients with IMSCT and 8.1 ± 9.9 months (from incidental finding up to 3 years) in cases with EMSCT. The initial symptoms at the time of admission were also different between both groups. The most common symptom in patients who suffered from EMSCT was back or neck pain. Monoparesis was more often in patients with IMSCT (62%), compared to

only nine cases in the EMSCT-group (31%). The rates of gait disturbance were comparable in both groups with 19% and 21% for EMSCT and IMSCT, respectively. A detailed description of symptoms is shown in Table 1.

More often IMSCT were located in the cervical part of the spine, whereas EMSCT were more typical for lumbar spine. Tumor locations are presented in Figure 1.

Histopathology

Histological findings of IMSCT and EMSCT are shown in Table 2. The most common primary IMSCT were astrocytomas (12, 57%) followed by metastases arising from intracranial medulloblastomas (7 patients, 29%). In turn, neurinomas (10, 34%) and lipomas (9, 31%) represented the most frequent lesions of the intradural extramedullary compartment. Most tumors were benign (Grade I–II, 78%) and only 11 patients (22%) had high-grade tumors according to the World Health Organization (WHO)-classification.

Table 1: Symptoms at admission

Symptoms*	EMSCT (*n*=29)	IMSCT (*n*=21)
Pain/lumbargo	12 (41%)	4 (19%)
Sensory disorders	9 (31%)	3 (14%)
Motor deficits		
Monoparesis arms	0	9 (43%)
Monoparesis legs	9 (31%)	4 (19%)
Paraparesis	5 (17%)	1 (5%)
Tetraparesis	0	
Gait disturbance	6 (21%)	4 (19%)
Stiff neck/Wrynech	1	1
Headache/Nausea/Vomiting	3	4
Bladder and Bowl dysfunction	5	1
No neurological deficits	4	1

*More than one symptom possible. EMSCT: Extramedullary spinal cord tumors, IMSCT: Intramedullary spinal cord tumor

Table 2: Histopathology and medullary location of IDSCTs

Histopathology	IMSCT	EMSCT	Low Grade I-II	High Grade IV-V*	Total
Astrocytoma	12		9	3	12
Ependymoma	2	1	3		3
Metastasis	6	1		7	7
Intramedullary cyst	1		1		1
Meningioma		3	3		3
Neurinoma		10	9	1	10
Lipoma		9	9		9
Dermoid		2	2		2
Epidermoid		2	2		2
Arachnoid cyst		1	1		1
Total	21	29	39	11	50

*According to WHO Grade ≥III. EMSCT: Extramedullary spinal cord tumors, IMSCT: Intramedullary spinal cord tumor, WHO: World Health Organization, IDSCT: Intradural spinal cord tumor

Neurosurgical treatment

Forty-four patients (88%) underwent surgical treatment of IDSCT. In five cases with intramedullary metastases, intrathecal chemotherapy was administered through an Ommaya reservoir. One patient with intradural extramedullary lipoma underwent conservative management.

Laminoplasty was the standard surgical approach for intraspinal and intradural lesions (27 patients, 61%). Laminectomy was used in the early period of this study for intradural extramedullary tumors. Stabilization of the spine was necessary in only one case of a 14-year-old boy suffering from a spinal metastasis of a colon cancer.

Complete surgical removal was 71% for IMSCT and 59% for EMSCT, respectively.

The surgical morbidity rate was 2%. A postoperative wound infection was observed in one case, and a temporary percutaneous tracheotomy was necessary in 2 patients. Two patients developed pneumonia, which were treated successfully with antibiotic medication.

Illustrative case

A 14-year-old girl suffered from bilateral arm weakness for 1 year. Gait disturbances or other neurological deficits were not present. An MRI was performed revealing an IMSCT from C5 to C7 with cystic and solid tumor compartments without contrast enhancement. The tumor was removed via a laminotomy of the vertebral arch from C5 to C7 under intraoperative electrophysiological monitoring. The tumor was removed incompletely due to the lack of a clear plane of cleavage. Histopathological examination revealed a fibrillary astrocytoma according to the WHO Grade II. Sensory deficits in arms and legs were observed postoperatively, but improved until discharge and during the postoperative rehabilitation continuously [Figure 2].

Early postoperative outcome

In summary, 17 patients (38%) developed transitory neurological symptoms (new sensory deficits, paresis, or gait disturbances) directly after the surgery. However, these symptoms were mostly reversible, so that the

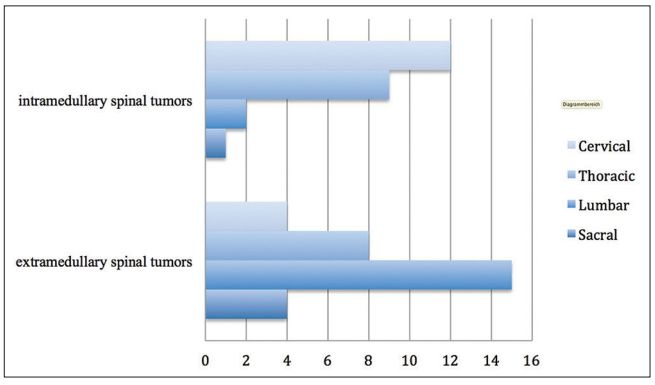

Figure 1: Level of lesion depended on tumor location

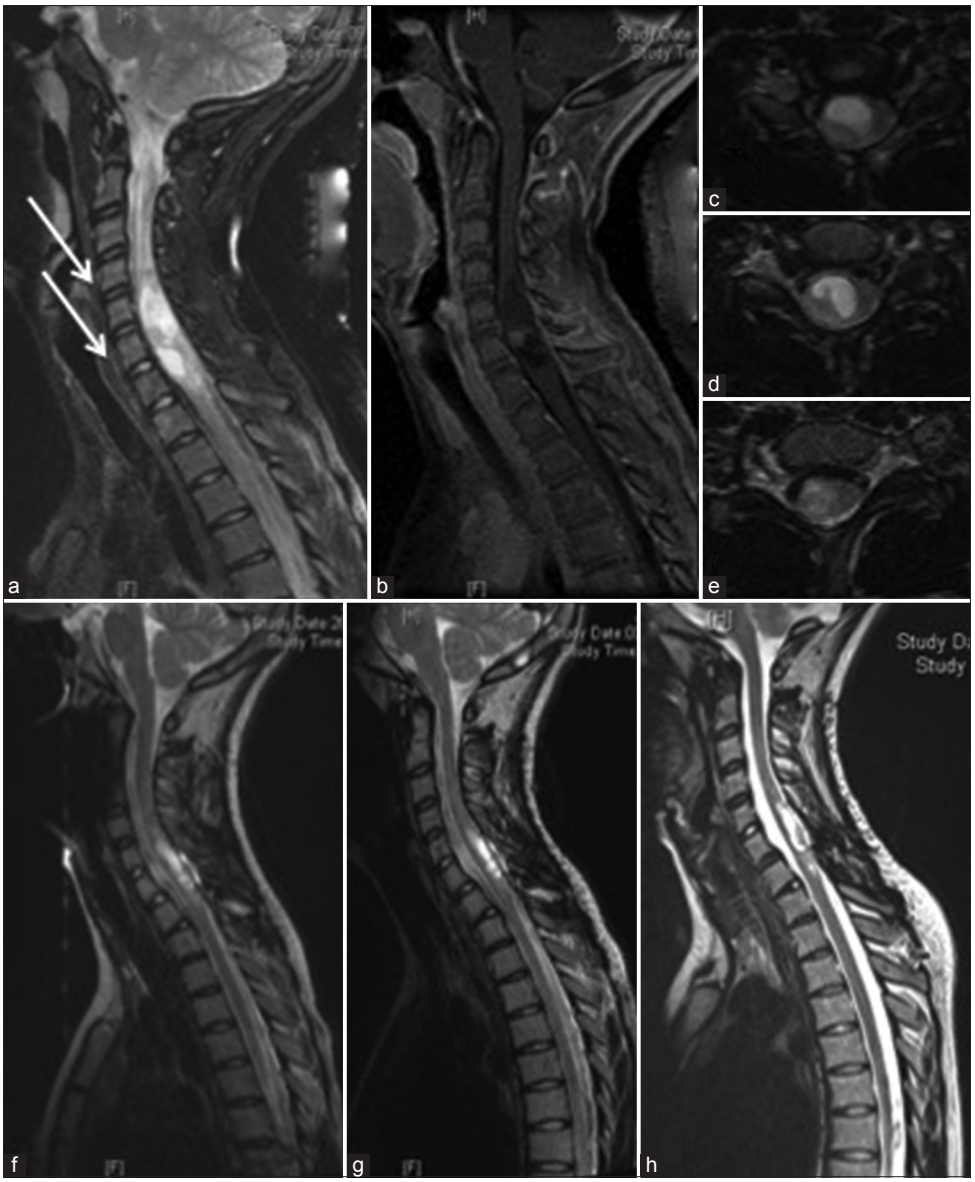

Figure 2: A 14-year-old girl with an intramedullary cystic fibrilar astrocytoma World Health Organization II from C5 to C7. (a and b) Preoperative T2 and T1 with contrast enhancement in sagittal view of the tumor and interestingly the vertebral body deformation from C3 to C6 due to the slow tumor growing (arrow), (c-e) T2 in axial view preoperatively, (f) 5 months after surgery with tumor rests in the apical and caudal part of the initial tumors, (g) T2 sagittal view 10 months after surgery and (h) 6 years after surgery, only the postoperative defect of the initial tumor were seen

postoperative Frankel score at discharge was comparable with the preoperative score.

Postoperative transitory neurological deterioration was predominantly observed in IMSCT patients (n = 12). Among them, only 1 patient with an IMSCT suffered from a persistent postoperative neurological deterioration from Fankel Grade E to C. In turn, EMSCT patients were more likely to improve in their neurological condition postoperatively [Table 3].

Follow-up

The mean duration of follow-up was 3.5 years (range 3 months–10 years). Spinal deformity after surgery was not detected except for 1 female patient after laminectomy. This patient had to be re-operated for spine stabilization using dorsal transpedicular screw and rod fixation. In other case with the removal of a spinal lipoma at the age of 1 year and 11 years later repeated surgery with detethering was required because of the development of a tethered cord.

Short-term follow-up at 12 months after discharge was available for 33 (66%) patients (18 with EMSCT, 15 with IMSCT). Nine (50%) patients with EMSCT recovered in this time up to the preoperative Frankel score. Among IMSCT patients, the complete recovery could be achieved in only 3 patients (20%).

At the 12 months follow-up, the Frankel score of the EMSCT-group was higher than the Frankel score of the IMSCT-group [Table 3].

The WHO grading of the tumor was significantly correlated with the functional outcome at discharge ($P = 0.017$) and at later follow-ups ($P = 0.02$). Moreover, there was a statistically significant positive correlation between the preoperative Frankel score and the last follow-up ($P = 0.002$) [Figure 3].

Recurrence

Tumor recurrence was seen in 7 (14%) patients during the whole observational time. In all of these cases, the initial tumor resection was performed subtotally. Four of them (57%) had IMSCT. The detailed description of the cases with recurrent IDSCT is given in Table 4.

Mortality

Five individuals (10%) died during the follow-up due to the tumor progress. These cases include two 14-year-old patients with intramedullary anaplastic astrocytoma (WHO Grade III) who died 2 and 5 years after the surgery, respectively. Two other patients died 1 and 3 years after surgery, suffering from metastasis from colon carcinoma and medulloblastoma. Finally, a 14-year-old male suffered from malignant peripheral nerve sheath tumor and died 2 months postoperatively.

Table 3: Functional outcome according to the Frankel classification grading system at different time points

Variable	Frankel-grade		
	Preoperative	Postoperative	At 12 months
Patients with EMSCT[a]	*n*=29 (%)	*n*=29 (%)	*n*=18 (%)
Poor (A + B)	3 (10.4)	1 (3.4)	-
Fair (C)	4 (13.8)	3 (10.4)	-
Good (D + E)	22 (75.9)	25 (86.2)	18 (62.1)
Patients with IMSCT[b]	*n*=21 (%)	*n*=21 (%)	*n*=15 (%)
Poor (A + B)	2 (9.5)	2 (9.5)	2 (13.3)
Fair (C)	2 (9.5)	3 (14.3)	-
Good (D + E)	17 (81.0)	16 (76.2)	13 (86.7)

Data are presented as frequency and valid percent. [a]EMSCT: Extramedullary spinal cord tumors; [b]IMSCT: Intramedullary spinal cord tumors

Table 4: Recurrences

Location	Tumor entity	WHO grading	Time until recurrence (years)	Treatment
IMSCT	Proteoplastic astrocytoma	III	5	Chemotherapy
	Atypic pilocytic astrocytoma	II	5	Radiotherapy
	Pilocytic astrocytoma	I	5	Radiotherapy
	Ependymoma		3	Surgery
EMSCT	Neurinoma	I	4	Surgery
	PNET		0.25 (3 months)	Surgery

EMSCT: Extramedullary spinal cord tumor, IMSCT: Intramedullary spinal cord tumor, PNET: Primitive neuroectodermal tumor, WHO: World Health Organization

DISCUSSION

After the implementation of a modern neuroradiological imaging and microsurgical techniques, better functional outcome after IDSCT surgery could be achieved, especially for IMSCT.[6]

The specific aspects of perioperative care for spinal tumors and spine trauma in the mature spine have been widely described in the modern literature.[3,6,11,17] In the present study, we addressed the challenges and clinical impact of modern microsurgery in the pediatric population with IDSCT.

Clinical presentation

The symptoms of IDSCT in children and young adults are attributed to spinal cord compression, and include pain and motor weakness of the extremities. The most common symptoms of patients with EMSCT were pain/back pain (41%). Patients suffering from IMSCT presented more common with the motor weakness of extremities (52%). Constantini *et al.*[7] have also reported the motor regression as the leading symptom in 65.2% of intramedullary tumors in children and young adults.

In our cohort, the mean duration of the symptoms before admission was 8.1 months for EMSCT and 2.8 months for IMSCT. Observation is partially based on spinal cord plasticity allowing considerable tumor progression without the development of meaningful neurological deficits.[11] Furthermore, the diagnostic delay which is common in pediatric malignancies,[33] could also have contributed to the longer duration of clinical symptoms in the preoperative stage in our cohort.

Such long clinical "tolerability" of IDSCT explain the fact that Dincer *et al.*[11] reported about 4.8% scoliosis as an initial symptom and emphasized that it could be related to delayed diagnosis. However, the deformities of the spine or scoliosis are not seen in the patients with IDSCT in our series. We agree with the most

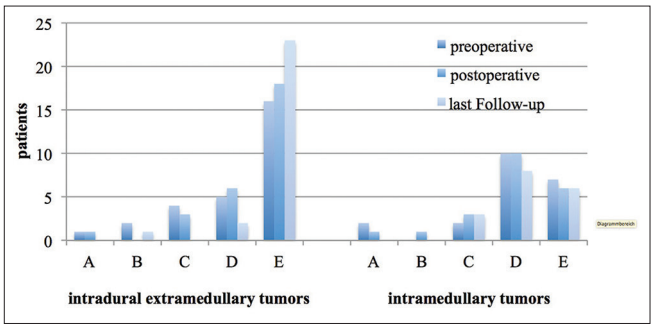

Figure 3: Frankel score in follow-up Exitus letalis in the extramedullay group: 2, intramedullary group: 4

of authors[6,7,13,16,26] who concluded that the residual disability after the treatment is rather attributed to the delay in the diagnosis, than due to the surgical technique or postoperative tumor progression.[11,35,36]

Surgery

Due to the high-risk of secondary spinal deformity in the pediatric patients,[10,28,41,42] the surgical approach remains a matter of debate in the treatment of IDSCT in children and young adults. The use of laminoplasty has not been proven to be superior with regard to the development of spinal deformity after surgery compared to laminectomy.[1,28,38,41,42] However, it seems to have a positive effect on wound healing and the reduction of cerebrospinal fluid leakages.[38] Furthermore, the pathogenesis of spinal deformity after IMSCT surgery is not only the result of the selected surgical approach, but rather an effect from the underlying neuromuscular dysfunction.[2]

On the other hand, the use of prophylactic fusion has certain challenges in the pediatric population, such as the risk of neuromuscular scoliosis and "crank-shaft"-deformity due to the continued growth of the anterior spine column, a high rate of pseudarthrosis and the difficulties of screw placement based on the small pedicles.[27,29]

In our opinion, the reposition of the posterior arches with micro plates may prevent the development of postoperative scare and, therefore, protects the nervous structures, but does not prevent the development of spinal deformities. Our current surgical strategy consists of the use of laminoplasty without prophylactic fusion and continuous clinical and radiological follow-up that may warrant the timely detection of the secondary spinal deformity in younger individuals.

The extension of the tumor resection depends on tumor histology and location of the tumor.[14,17] Although several authors reported a series with complete tumor removal and good postoperative functional outcome,[7,14,16,37] others pointed out the limitations of the surgery caused by the absence of a clear plane of cleavage, resulting in partial resection, decompression, or biopsy only for diagnosis.[26]

In our cohort, the majority of EMSCT were resected completely, except of lipomas and intradural extramedullary metastasis. Intradural meningiomas were completely resected, whereas in one case a Grade I meningioma was recurrent and, therefore, re-surgery was performed.

Astrocytomas are characterized as infiltrative growing tumors, without clear border to the spinal cord tissue and, therefore, often leading to an incomplete tumor removal.[4,18] Whereas ependymomas are tumors which are recognized as resectable lesions due to a clearly defined plane of dissection.[39] Safaee *et al.*[39] noted that the extent of resection of spinal ependymoma is an important prognostic factor. In our cohort, the complete removal of IMSCT has been achieved in 60% of the cases, whereat ependymomas were completely resected in 90%. Constantini *et al.*[7] reported in his large series about 164 patients with IMSCT (age between 6 months and 21 years). They observed that radical surgery for low-grade IMSCTs could be performed with an acceptable risk and moderate functional outcome. These findings correlated with our series. Furthermore, the postoperative functional performance is mainly determined by the preoperative deficits.[7] Therefore, IMSCTs are potentially excisable lesions, both at presentation and if they recur.[2,6-9,11,14,16,23,26,30,31] The treatment management of primary malignant spinal cord astrocytomas is not clearly determined in the current literature, neither for children nor in adults.[6,7,40]

Functional outcome

Functional outcome after surgery has correlated strongly with the preoperative neurological status, both in EMSCT and in IMSCT patients. Postoperative temporary worsening was seen more likely in patients with IMSCT. We agree with the hypothesis of Epstein,[14] that particularly the patients with large, long-standing IMSCT may be attributed to thinning of the spinal parenchyma.

Interestingly, at the time of admission the functional grade was good in 75% of EMSCT and 81% of IMSCT patients. Both groups resulted in an improvement or total functional recovery at discharge.

There was no surgery-related mortality in our study. The overall mortality from tumor progression was 10% (n = 8), mainly due to leptomeningeal metastases. Previous reports based upon intramedullary tumors described even higher rates of mortality due to tumor progression (up to 22%).[5,7] In addition, the overall recurrence rate of 14% in our study is also considerably lower, as compared to earlier series with recurrent intramedullary tumors in 35% of the patients.[11]

In summary, the postoperative functional outcome in the presented cohort is comparable with the previous reports.[3,4,14,18,25] The use of modern neurosurgical techniques, as well as advanced perioperative and neuro-oncological management may contribute to further improvement of the functional outcome of younger individuals with IDSCT.

Study limitations

This study presents a retrospective, single-institution analysis and, therefore, faces certain limitations. Retrospective analysis introduces recall bias and difficulty for controlling of confounders. However, randomized prospective studies are difficult for surgical diseases, particularly for pediatric IDSCTs. Then, the histopathological and age heterogeneity of the presented

data should also be mentioned as study limitations. Finally, due to the nonuniformly performed postoperative clinical and radiological follow-up, our data do not allow any assumption about the correlations between the surgical radicality and postoperative outcome.

CONCLUSION

IDSCTs are good candidates for radical surgical treatment. As to the surgical technique, we advocate laminotomy to reduce the secondary surgery-related complications. Multicenter prospective database may be helpful in the development of optimal surgical strategies in children and young adults with IDSCTs.

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Conflicts of interest
There are no conflicts of interest.

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