Clinical Research

Comparisons of Intradural Ekstramedullary and Intramedullary Spinal Tumors

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ABSTRACT

Objective: Intradural spinal tumors present with back and extremity pain due to neuropatic pain and / or neurologic deficits. We aimed to compare the outcomes of the operated spinal intradural extramedullary and intramedullary tumors with or without using intraoperative neuromonitor (IONM).

Material and Methods: 82 patients, having undergone surgical excision of intradural spinal tumors, were included. Demographic datas, neuropatic pain VAS scores, neurologic deficits charted via Motor Muscle Strength Scale preoperatively and postoperatively, the anatomical location of tumors (extramedullary / intramedullary), histopathology, and use of intraoperative neurophysiologic monitoring were collected. Statistical significance was assessed by One-way ANOVA and post hoc Scheffe tests.

Results: 59 patients were operated for extramedullary tumor. The most common histologies were NSCT (schwannoma / neurofibroma), and menengioma. 23 patients were operated for intramedullary tumor. The commenest histopathologies were epandimoma and astrocytoma. Statistically significant postoperative neuropatic pain and neurologic defisit improvements were seen in extramedullary and intramedullary tumors except intramedullary astrocytomas. Using of IONM made a contribution by intramedullary tumors. However there was no significant difference determined for extramedullary tumors.

Conclusion: Gross-total resection frequently can be applied in extramedullary tumors, it also should be aimed for intramedullary tumors. But if they are infiltrative, surgeons have to go for sub-total resection for achievement of neurologic detoriations. Postoperative improvements of neuropatic pains and neurologic deficits are high in extramedullary and intramedullary tumors, except intramedullary astrocytomas because of their invasive character. The effects of IONM on the results made a contribution on intramedullary astrocytomas. However there was no significant difference determined for extramedullary tumors.

Keywords: Extramedullary tumors, Intramedullary tumors, Intraoperative Neuromonitorization, Neuropathic Pain, Neurologic Deficits, Spinal Tumors.

ÖZ

İntradural Ekstramedüller ve İntramedüller Spinal Tümörlerin Karşılaştırılması

Amaç: İntradural spinal tümörler nöropatik ağrı ve/veya nörolojik defisitlere bağlı sırt ve ekstremite ağrısı ile kendini gösterir. İntraoperatif noromonitör (İONM) kullanılarak veya kullanılmadan ameliyat edilen spinal intradural ekstramedüller ve intramedüller tümörlerin sonuçlarını karşılaştırmayı amaçladık.

Gereç ve Yöntem: İntradural spinal tümörlerin cerrahi eksizyonu yapılan 82 hasta çalışmaya dahil edilmiştir. Demografik veriler, nöropatik ağrı VAS skorları, ameliyat öncesi ve sonrası Motor Kas Gücü Ölçeği ile kaydedilen nörolojik defisitler, tümörlerin anatomik yerleşimi (ekstramedüller / intramedüller), histopatoloji ve intraoperatif nörofizyolojik monitörizasyon kullanımı toplandı. İstatistiksel anlamlılık Tek Yönlü ANOVA ve post hoc Scheffe testleri ile değerlendirilmiştir.

Bulgular: 59 hasta ekstramedüller tümör nedeniyle ameliyat edildi. En sık görülen histolojiler periferik sinir kılıfı tümörü (schwannoma / nörofibroma) ve menenjiyomdu. 23 hasta intramedüller tümör nedeniyle ameliyat edildi. En sık görülen histopatolojiler epandimom ve astrositomdu. İntramedüller astrositomlar hariç ekstramedüller ve intramedüller tümörlerde postoperatif nöropatik ağrı ve nörolojik defisitte istatistiksel olarak anlamlı iyileşmeler görüldü. İONM kullanımı intramedüller tümörler için katkı sağlamıştır. Ancak ekstramedüller tümörler için anlamlı bir fark saptanmadı.
Sonuç: Gross-total rezeksiyon sıklıkla ekstramedüller tümörlerde uygulanabilir, intramedüller tümörler için de hedeflenmelidir. Ancak infiltratif olmaları durumunda cerrahlar nörolojik detorsiyonun sağlanması için sub-total rezeksiyonu tercih etmek zorundadırlar. İnvaziv karakterleri nedeniyle intramedüller astrositomlar hariç, ekstramedüller ve intramedüller tümörlerde nöropatik ağrılarda ve nörolojik defisitlerde postoperatif düzelme yüksektir. İONM'nin sonuçlara etkisi intramedüller astrositomlar için katkıda bulunmuştur. Ancak ekstramedüller tümörler için anlamlı bir fark tespit edilmemiştir.

Anahtar Sözcükler: Ekstramedüller tümörler, İntramedüller tümörler, İntraoperatif Nöromonitörizasyon, Nöropatik Ağrı, Nörolojik Defisit, Spinal Tümörler.
Bu makale atıfta nasıl kullanılır: Akgün B, Akçin İ, Ertuğrul B, İbragimov S, Erol FS. İntradural Ekstramedüller ve İntramedüller Spinal Tümörlerin Karşılaştırılması. Fırat Tıp Dergisi 2025; 30(1): 55-61.
How to cite this article: Akgun B, Akcin I, Ertugrul B, Ibragimov S, Erol FS. Comparisons of Intradural Ekstramedullary and Intramedullary Spinal Tumors. Firat Med J 2025; 30(1): 55-61.

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Geliş Tarihi/Received: 27.09.2024 Kabul Tarihi/Accepted: 07.11.2024

Spinal tumors are uncommon lesions, comprise 5-15% of all CNS tumors. However, these lesions can cause significant morbidity in terms of extremity motor and /or sensorial dysfunction, serious pain and can be associated with mortality as well. Anatomically, spinal tumors can be classified as extradural tumors, intradural extramedullary tumors, and intramedullary tumors by their relation with the dura and spinal cord (1,2). Most common spinal tumor location is extradural, where cancer metastasis to spine leads the way. Primary vertebral bone tumors also can be seen in the extradural region. Intradural spinal tumors are rare and can be classified into extramedullary or intramedullary. They are frequently benign tumors. They commonly present with symptoms such as intractable back pain or neurologic deficits. These tumors produce pain syndroms, a variety of neurological symptoms; motor, sensory, sphincter or a combination of thereof. All spinal levels may be involved (2). Magnetic resonance (MR) imaging, which plays very important role in the imaging of spinal tumors, easily allows tumors to be classified as extradural, intradural–extramedullary or intramedullary (3). Preferred treatment is the microsurgical radical resection. Perioperative mortality is very low as is serious morbidity. Recent advances in microsurgical procedures, instrumentation, and perioperative management by intraoperative noromonitor (İONM) using are very important in grostotal (GTR) or subtotal resection (STR) of intradural tumors (4).

In this report, we present our single institution's surgical experience and clinical outcomes on patients who have undergone surgical excision for intradural spinal tumors. We herein discuss various aspects of presenting symptomatology, neuropatic pain, neurologic defist, and the effects of IONM using.

MATERIAL AND METHOD

We retrospectively reviewed all patients who had undergone surgical excision of solitary intradural spinal tumors in our unit from May 2013 to May 2023 (Figure 1 and Figure 2). Data on age, gender, most common presenting symptoms of pain charted via VAS score and neurolgic defisit charted via Motor Muscle Strength Scale and American Spinal Injury Association score preoperatively and postoperatively, the anatomical location of tumors (extramedullary or intramedullary), the vertebral level location (cervical, cervicothoracic, thoracic, thoracolumbar, lumbar, lumbosacral and sacral), histopathology, extent of resection, and use of intraoperative neurophysiologic monitoring (IONM) were collected. Patients with extradural and or multiple intradural tumors or those with illness-limiting surgical interventions and patients who were lost to follow-up were excluded from the study.

Written and Informed consent was obtained from all patients and their representatives regarding their willingness to be a part of the study and the follow-up process. All patients underwent preoperative and postoperative 1st month magnetic resonance imaging of the spinal cord to determine the extent of tumor resection, and also after one year of surgery to look for recurrence, except one patient. MRI was contrendicated for that patient, because of his cardiac pacemaker. A large dumbbell shape tumor which also eroded and remodeled intravertebral foramen, caused scalloping of the posterior aspect of the vertebral body in lomber 3 vertebra level, reported as nerve sheat tumor, was detected in his lomber CT.

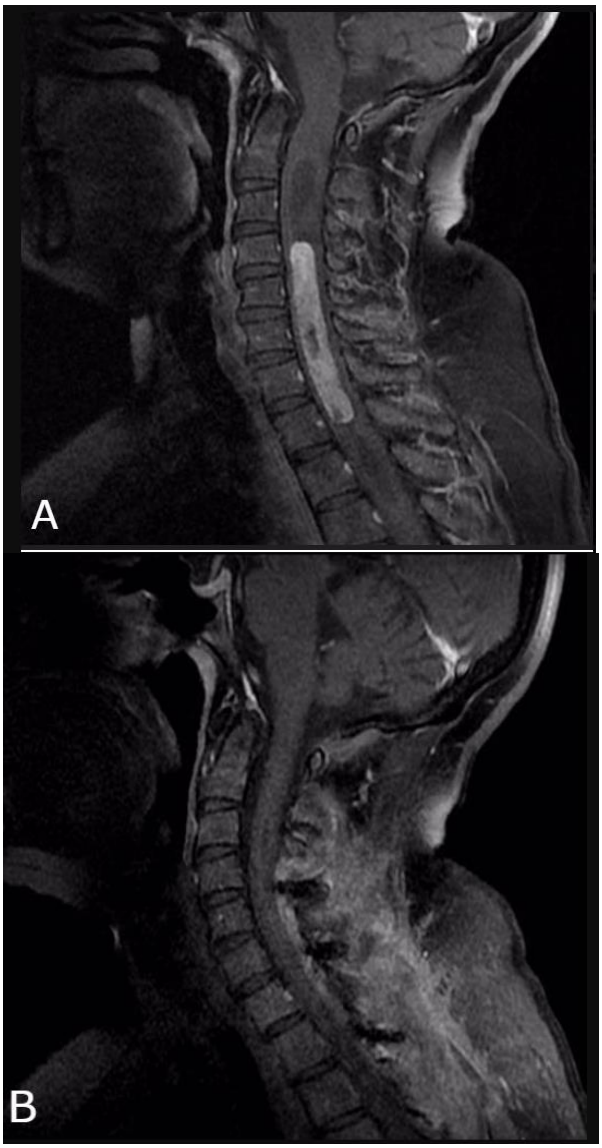

Figure 1: (A) *Preoperative sagittal MRI, and* ***(B)*** *Postoperative sagittal MRI with contrast enhancement sections of a 39-year-old female patient was included to our study, was operated due to intradural extramedullary tumor (neurofibroma), and total excision was achieved.*

Data were analyzed using SPSS statistical soft- ware (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.

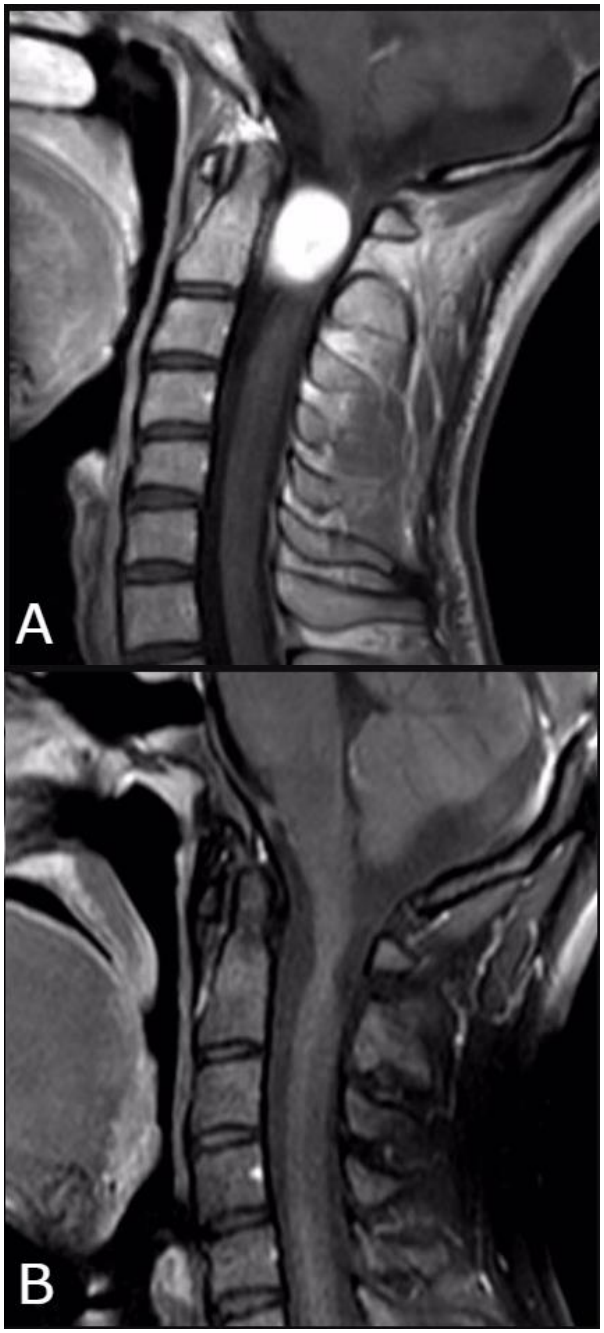

Figure 2: (A) *Preoperative sagittal MRI, and* ***(B)*** *Postoperative sagittal MRI with contrast enhancement sections of a 47-year-old female patient, was included to our study, operated due to intradural intramedullary tumor (epandimoma), total excision was achieved*.

RESULTS

59 patients were operated for extramedullary tumor. The most common histology was NSCT (schwannoma / neurofibroma), the second common extramedullary tumor was menengioma. Twenty-three patients were operated for intramedullary tumor. The most common histopathologies were epandimoma and astrocytoma (Table 1).

Table 1: *Diagnosis, frequencis, demographic features and locations of the tumors.*

Tumors	Frequency	Female/Male Ratio	Age (Average)	Location
Intradural Extramedullary Tumors				
Nerve Sheath Tumor	% 48	1/1	47	%45 cervical vertebrae, %50 lumbar vertebrae
Meningioma	% 42	5/1	64	%85 thoracic vertebrae
Other (Epidermoid, teratoma, lipoma)	% 10			
Intradural Intramedullary Tumors				
Ependymoma	% 42	1/2	46	%50 cervical vertebrae
Astrocytoma	% 39	1/2	37	%50 cervical vertebrae
Other (hemangioblastoma, ganglioglioma, metastasis, cavernoma)	% 19			

Statistically significant postoperative neuropatic pain improvements with VAS scores were seen in extramedullary tumor group. However in intramedullary group, significant postoperative neuropatic pain improvements were not detected in astrocytoma patients, regardless of GTR or STR. However significant postoperative neuropatic pain improvements were obtained in other intramedullary tumors (ependimoma, gangliogliom, cavernoma). Also small amounts of benefits of IONM using was detected in extramedullary tumors, but not statistically significant. However significantly contributions of IONM using was seen in intramedullary tumors (Table 2).

Table 2: *Postoperative VAS scores improvements.*

Tumors	Average increase in Vas scores
Used IONM*	
Extramedullary Tumors	3.8
Intramedullary astrocytoma	2.5
Intramedullary (ependymoma and other)	3.4
IONM not used	
Extramedullary Tumors	3.6
Intramedullary astrocytoma	1.9
Intramedullary (ependymoma and other)	3.2

**IONM: Intraoperative Neuromonitoring*

Postoperative improvements of neurologic deficits and neuropathic pain are high in extramedullary and intramedullary tumors, except intramedullary astrocytomas. There were conributions of the IONM using to the results for improving the neurologic outcome in intramedullary astrocytomas was detected (Table 3).

Table 3: *Deterioration of postoperative neurological deficit and neuropathic pain.*

Tumors	Patient Count (n)	Increase in post-op neurological deficit (n)	Post-op increase in neuropathic pain (n)
Used IONM			
Extramedullary Tumors	34	1	1
Intramedullary astrocytoma	5	2	2
Intramedullary (ependymoma and other)	8	0	0
IONM not used			
Extramedullary Tumors	25	1	1
Intramedullary astrocytoma	4	2	2
Intramedullary (ependymoma and other)	6	0	0

DISCUSSION

The incidence of primary spinal cord tumors in different series was variable. In Asian countries, especially eastern Asia, the frequency of NSCTs is higher than meningiomas. On the other hand, the incidence of meningiomas in western countries (USA and, Europe), is equal to or higher than NSCTs (5). In our series NSCTs, were seen little higher than meningiomas, but no significant difference was determined. The incidances of both types of tumors are close to each other.

According to literature, the male/female ratios for patients with primary spinal cord tumors vary among countries. Briefly, in eastern Asian countries spinal cord tumors predominantly occur in men except menengiomas, whereas in non-Asian countries they predominantly occur in women. Furthermore, a lot of studies from both western and eastern countries, have reported that, spinal meningiomas occur much more frequently in women than in men. The female preponderance for spinal meningiomas is also universal (5). In our current study, we detected; female predominancy for menengiomas, approximately equal ratios for NSCTs, but male predominancy for intramedullary epandimomas and astrocytomas.

In the ligth of the literature, the most common primary spinal cord tumor in patients older than 60 years is meningioma. Ependymomas and schwannomas are more commonly found in middle-aged patients (5). For this series, the average age of patients with meningiomas (64.5 years) was significantly higher than that of schwannomas (53 years) and ependymomas (46.5 years).

GTR is the treatment of choice for spinal meningiomas. Surgical treatment of spinal meningiomas has a favorable outcome in the majority of cases. When the tumor resected completely, functional outcome is excellent and recurrence rates are low. Yoon et al. reported the Simpson Grade of resection as a good predictor for recurrence. They emphasized that no recurrent disease seen in their series after Simpson Grade I to III resections (6). The most commonly reported sufficient surgical procedure is a single-level posterior laminectomy to access the thecal sac and spinal cord for tumor resection; however, laminoplasty or multilevel laminectomy with or without spinal fusion can be other options in suitable cases when necessary. An analysis of 80 patients with spinal meningioma treated surgically with intraoperative monitoring (IOM) by Setzer et al. showed a good outcome with improved or unchanged neurological status in 93.5% of patients. Other studies also showed positive outcomes in over 90% of patients (7**).** Radiotherapy is not a curative treatment for spinal meningiomas; nonetheless, conventional radiotherapy or stereotactic radiosurgery (cyberknife) have been both employed for recurrent meningiomas, large rezidual tumors with atypical or malignant behavior (8**) .**

Schwannomas and / or Neurofibromas (Nerve Sheet Tumors) are slow-growing lesions that arise from the sensory dorsal rootlets in most cases. The majority of lesions are intradural but they can also grow extradurally (10%) or combined intra-extradurally (10–15%). Schwannomas tend to develop an hourglass / dumbell shape due to bony impression at the neural foramen. They present with radicular pain and / or in motor deficits. They are also primarily treated surgically in most cases. The recurrence rate after surgical excision is low. Nerve sheath tumors can be removed effectively due to microsurgical developments. Fernandes et al. reported a GTR rate of 96% and a recurrence rate of 3.3% (9). Large tumors with extraforaminal extension may require more extensive approaches and sometimes even stabilization (10). In the rare case of intramedullary schwannomas, surgery is the treatment of choice and results in good outcomes if GTR is achieved (11). Malignant NSTs are very rare (2.5%). In this study intramedullary schwannoma or neurofibroma and malignant NST were not seen. All of the NSTs were located intradural-extramedullary. Surgery has minimal morbidity, improves symptoms, and may be curative. No adjuvant therapy is recommended and incompletely resected tumors should be followed given the benign growth of the majority of these tumors. Stereotactic radiosurgery is an option for poor surgical candidates (12). Malignant schwannoma should be treated with postoperative radiotherapy, even if total resection was achieved.

Ependymomas are the most frequent IMSCTs in adults (13). They are mostly benign tumors (WHO Grade II), which are most likely found in the cervical spine. They are slightly more frequent in males and occur during the 3rd and 6th decade. Histopathologically, ependymomas can be classified as myxopapillary (WHO grade 1), papillary, cellular, epithelial, and mixed. WHO

Grade III intramedullary ependymomas are very rare (14). Cellular (classic) ependymoma arises from the intraspinal canal of the cervical and thoracic cord. Myxopapillary ependymomas arise from the filum terminale and occur almost exclusively at the conus medullaris. The treatment and prognosis for spinal cord ependymomas is often excellent as these tumors may be resected completely and in such instances manifest a low recurrence risk. Ependymomas by MRI appear as a focal enlargement of the cord and hyperintense on T2W and FLAIR images and hypo- or isointense to normal spinal cord on T1W images with heterogeneous contrast enhancement (15). These tumors may also be associated with cystic changes, hemosiderin suggestive of previous hemorrhage, and syrinx. Surgery is the most effective treatment with complete surgical resection yielding reported local control rates of 90% to 100% (16). Intraoperative monitoring of motor and somatosensory-evoked potentials is often used to assist in achieving a more safe and complete resection (17). Even if lower the risk of dissemination, en bloc resection whenever safely possible was recommended (18). Post-operative radiotherapy has been shown to result in superior outcomes for ependymoma: whilst there is general consensus of its benefit in STR, radiotherapy after GTR is contentious (19). Especially, WHO grade II ependimomas have a good survey, without RT, if en bloc resection was carried out. Involved- field external beam radiotherapy at a dose of 45 to 54 Gy is indicated and suggested by some authors for partially resected WHO grade 2 ependymomas or malignant WHO grade 3 tumors (20). Sgouros et al. (21) failed to detect a significant effect of radiotherapy on progression or recurrence, and Tarapore et al. (22) identified a negative effect of radiotherapy on survival after STR. Therefore, reoperation in case of the first recurrence should be considered. Radiotherapy may be indicated in case of a repeated STR, thus reducing the long-term risks of radiation myelopathy especially in children and young adults. Chemotherapy for ependymomas outside of a clinical trial is therefore reserved for patients in whom surgery or radiotherapy is not an option or has been previously administered (18).

Approximately 40% of IMSCTs are astrocytomas. Astrocytomas develop in childhood or later in adulthood within the 3rd and 5th decade with a slight male predominance (1.5:1). Their dominant location is the thoracic spine. Spinal astrocytomas in children are mostly benign while those in adults can be more commonly WHO Grade III and IV lesions (18). The majority (75%) are low-grade (WHO grade 2) fibrillary astrocytomas with 5-year survivorship exceeding 70%. Histology is the most important prognostic variable (23). High-grade spinal cord gliomas (WHO grades 3 and 4; 25%) are less common and associated with a poor survival. Regardless of WHO grade, spinal cord astrocytomas are infiltrative. Astrocytomas appear on MRI as fusiform expansion of the cord and occasionally a cystic component (24). Associated edema or syrinx (seen in 40%) may be present. The tumor is hypo- to isointense on T1W images, hyperintense on T2W and FLAIR images, with variable contrast enhancement. In general, the distinction between astrocytomas and ependymomas by magnetic resonance (MR) is not possible (25). Initial treatment consists of maximal safe surgical resection or biopsy followed by observation or external beam radiotherapy. Because spinal cord gliomas are infiltrative, gross total resection is rarely accomplished, complete surgical resection is seldom possible and the recurrence rate is as high as 50% over 5 years. Some authors favor biopsy and radiation because surgery carries a risk of neurological deficits and has limited survival benefit even after aggressive resection, but advances in surgical techniques and intraoperative monitoring have improved outcomes (26). Tumor histology, extent of resection, and functional status at time of presentation appear to be the primary determinants of outcome (27). In general, factors suggestive of need for radiotherapy and/or chemotherapy are higher tumour grade, biopsied-only tumors, and those with progressive disease. At recurrence, radiotherapy is the preferred treatment if not already utilized. Chemotherapy is reserved for patients with progression of disease following surgery and radiotherapy with no other treatment options. Literature regarding chemotherapy for recurrent astrocytomas is extremely limited (25)**.** In spinal astrocytomas, histological type is the main prognostic factor for outcome. Tumor histology affects its biological behaviour (WHO grade) as well as the probability of finding a plane of dissection and thereby the potential for GTR (e.g. the behavior of pilocytic astrocytoma versus diffuse astrocytoma) (26). Low-grade tumors have low surgery-related complication rates and a good long-term outcome when operated early. In most high-grade tumors, GTR is hardly possible and STR or biopsy followed by radiation and chemotherapy is the recommended standard treatment. Because high grade astrocytomas have more invasive nature than epandimomas (18).

Where safe and feasible, GTR is the optimal surgical strategy for IMSCTs due to maximal tumour clearance and lower risk of recurrence. Feasibility of GTR depends on tumour histology and subtype, as well as individual patient anatomy and intra-operative findings. When creating the surgical ‘corridor’ through the spinal cord to access intramedullary tumours, a path that is least destructive to vertical tracts is used. The majority of IMSCT excisions are undertaken via midline myelotomy, which represents the ‘workhorse’ approach due to minimal long-tract disruption and its versatility amongst IMSCTs with a significant central component: in tumours with an eccentric distribution, a number of lateral approaches (e.g. dorsal root entry zone or far-lateral) may be used (28). We performed midline myelotomy in our all IMSCT cases.

In recent years, IONM has become increasingly important for spinal surgeries, especially in intradural spinal tumors where the risk of spinal cord injury is high (18,28). The use IONM did not become routine for all spinal surgeries in the whole world. Also the use of

IONM was left to the discretion of the primary surgeon. But some benefits shown for IONM, as it serves to guide the surgeon if there is any early compromise to the spinal cord or nerves and prompts the surgeon to alter his or her technique to prevent worsening neurologic injury. In our results; 34 extramedullary tumor patients were operated with IONM. Only one of these patients had a postoperative worsening of neurological deficit and an increase in neurotic pain. Twenty-five patients with extramedullary tumours underwent surgery without IONM. Only one of these patients had worsening neurological deficit and increased neuropathic pain postoperatively. In 8 intramedullary epandimoma patients operated with IONM, and in 6 intramedullary epandimoma patients operated without IONM; we did not see any neurological deterioration and a 100% success was shown. We did not find a significant difference in neurologic outcomes with the use of IONM for excision of intradural extramedullary tumors and intramedullary epandimomas compared with those without IONM. Five intramedullary astrositoma patients were operated with IONM and 4 intramedullary astrositoma patients were operated without IONM. A 60% success rate in IONM group and 50% success rate in non-IONM used patients was achived. These low success rates were due to invasive character of the astrocytomas. According to these results; IONM using may contribute in astrocytomas. IONM can warn the surgeon in the infiltrative parts of the astrocytomas. Also surgeon can be careful in the manuplations of the invasive parts.

This retrospective series showed that good neurologic outcomes and low complication rates after surgery can be achieved in both extramedullary and intramedullary tumors except astrocytomas, especially in high grade astrocytomas. Successfull neuropatic pain and neurologic defisit improvements were not seen in intramedullary astrocytoma patients because of the invasive character of them. Also complete resections of tumors are associated with better outcomes, it is not easy to perform complete excision without causing any neurologic deficit in intramedullary astrocytomas.

CONCLUSION

This retrospective series showed that good neurologic outcomes and low complication rates after surgery can be achieved equally in both extramedullary and intramedullary spinal tumors except intramedullary astrocitomas. Pain and the neurologic deficits are the predominant symptoms of spinal cord tumors and frequently persist after treatment. Primary treatment of primary spinal cord tumors is surgical resection and predictors of outcome include preoperative functional status of neuropathic pain and neurologic defisits, histologic grade of tumor (lower grade predicts for improved survival), tumor type (astrocitomas have worse prognosis) and extent of surgical resection (image-verified complete resection improves survival). GTR can be applied in extramedullary tumors, and also mostly intramedullary tumors except astrositomas. Mostly astrocitomas have invasive character, so surgeons have to prefer STR for achievement of neurologic deteriorations. Postoperative improvements of neuropatic pain and neurologic deficits are high in extramedullary and intramedullary tumors, except intramedullary astrocytomas. The effects of IONM on the results were contributed for improving the neurologic outcome in intramedullary astrocytomas, because protection of spinal cord or nerve fibers is more difficult. However there was no significant difference determined for extramedullary tumors.

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