Original Article

Epidemiology study on the prognostic factors of intradural extramedullary spinal tumors

ABSTRACT

Introduction: Intradural extramedullary (IDEM) tumors are rare tumors of the spinal cord. Currently, there is no evidence on the factors that predict poor outcomes in the patients. The objective of this study was to determine the prognostic factors that are associated with poor outcomes in IDEM tumors.

Materials and Methods: Patients 18 years and older with IDEM tumors who underwent surgery at our institute were identified and retrospectively reviewed. The patient's demographic data, risk factors, and modified McCormick Scale score were collected.

Results: A total of 129 patients with IDEM were included in this study. The age ranged from 19 to 79 years (mean 51.3 years), with a predominantly female population (85 patients, 65.9%). Eighty-nine (68.9%) patients had a good outcome, while 40 (31.0%) patients had a poor outcome. The significant factors for poor outcomes included the number of vertebral levels removed for tumor access (adjusted odds ratio [OR] = 3.80, 95% confidence interval [CI] =1.30–11.08, $P = 0.013$); pathology other than meningioma, schwannoma, and neurofibroma (adjusted OR = 18.86, 95% CI = 2.16–164.49, $P = 0.007$); and bowel/bladder involvement (adjusted OR = 3.47, 95% CI = 1.15–10.39, $P = 0.027$).

Conclusion: We found that the factors for poor outcomes included bowel/bladder involvement, number of vertebral levels removed for tumor access, and pathology other than meningioma, schwannoma, and neurofibroma.

Keywords: Functional outcome, modified McCormick Scale, spinal intradural extramedullary tumors

INTRODUCTION

Intradural extramedullary (IDEM) tumors are rare, with reports of the incidence ranging from 0.74 per 100,000 person-years to 1.11 per 100,000 person-years.[1,2] In Thailand, once diagnosed, most patients are referred to tertiary care centers to be treated by spine specialists.

IDEM tumors usually manifest as signs of cord and nerve root compression, such as motor, sensory, and bowel/bladder deficits, in a nonmutually exclusive manner.[3-5] The patient's history and physical examination may be used to infer the tumor's presence and location, which is then confirmed with spinal imaging.

The Medical Research Council grading for muscle power is a universally accepted scale for assessing muscle power, with different discrete grades indicating a certain amount of muscle activity. Sensory deficits, on the other hand, are difficult to quantify. Functional grading scales such as the Modified McCormick Scale more holistically evaluate the patient's status and provide a means of assessment that unites both motor and sensory aspects.[5-8]

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There have been studies examining the factors that are associated with a poor outcome after surgical resection of IDEM. However, the results are inconsistent, probably attributable to the fact that each study did not examine the same factors, had a rather small sample size, and had different definitions of what a poor outcome is supposed to be.

To the best of the author's knowledge, none of the studies in the literature have been able to identify predictive factors for an unfavorable outcome. This study aims to determine prognostic factors for the surgery of IDEM tumors.

MATERIALS AND METHODS

A retrospective review was performed to identify patients with IDEM tumors who were operated on between 2003 and 2019 in Srinagarind Hospital, Khon Kaen, Thailand. The study was approved by the Khon Kaen University Ethics Committee (ID: HE621228).

Inclusion criteria

All patients who were 18 years old and above at the time of operation with available gadolinium-enhanced magnetic resonance imaging (MRI) inside the database were selected.

Exclusion criteria

Patients with foramen magnum tumors, coagulopathy, multiple spine pathologies, and those under the age of 18 years were excluded. Patients who were lost to follow-up before 1 year were also excluded.

Patients

A total of 129 patients who were diagnosed with IDEM tumors and received surgery were identified through the hospital's electronic patient record system. All patients had a preoperative MRI and received routine follow-up for at least 1 year.

Demographic information such as age, sex, smoking, and underlying diseases were recorded. Information about the particular inpatient visit was obtained: symptom duration before surgery, symptoms present, the number of levels of bone removed to access the tumor, total or subtotal tumor removal, tumor configuration in relation to the spinal cord, pathology, operation, and whether or not the bony removal covered the C-T, T-L, L-S junctions. Preoperative and postoperative modified McCormick scores were assessed by the patients' respective surgeons.

Tumor configuration (anterior, lateral, and posterior) was determined by dividing the spinal cord into four quadrants. A tumor was defined as anterior if the majority of the tumor base involves the anterior quadrant and, similarly, lateral and posterior for the other quadrants. This information was obtained from operative notes and confirmed with preoperative MRI. There were no discordant findings. Tumor configuration was determined exclusively from the preoperative MRI if it is not described in the operative note.

The extent of tumor resection was also obtained from the operative note. All of the operations were done with the posterior approach. There were two main operations used to access the tumor: laminectomy, defined as the removal of the posterior ligaments, the spinous process and lamina, and laminoplasty, defined as elevating the spinous process and lamina in one piece and then subsequently fixing them back using plates and screws. There did not seem to be any set guidelines for spinal fixation, and they were done according to the surgeon's judgment at the time.

Outcome

The modified McCormick score of each patient was recorded at the 1-year follow-up outpatient visit. If the patient is Grade 1 or 2 initially, a poor outcome is defined as having a lower grade postoperatively. For patients with Grades 3, 4, and 5, a poor outcome is defined as having a decrease in postoperative modified McCormick grade.

Statistical analysis

Data are reported as counts and percentages, which were then analyzed with the software Stata version 10.1 (Stata Corp., Texas, USA). Pearson's Chi-square and Fisher's exact tests were used to determine the association between the variables and the outcome for normally distributed continuous variables, and the Mann–Whitney *U*-test for nonparametric continuous variables. Binary logistic regression was then used in univariate analysis to identify potential factors to be entered into a logistic regression model. Multivariable logistic regression models were then constructed to calculate the adjusted odds ratios (ORs) and the 95% confidence intervals (CIs) for the predictive effect of the multiple variables on the outcome. The model's goodness of fit was assessed by the Hosmer and Lemeshow test. $P \leq 0.05$ was interpreted as statistically significant.

RESULTS

A total of 129 patients were identified. The age ranged from 19 to 79 years (mean 51.3 years), with a predominantly female population (85 patients, 65.9%). Eighty-nine (68.9%) patients had a good outcome, while 40 (31.0%) patients had a poor outcome.

For the majority, the duration of the first noticed onset of symptoms was more than 90 days (112 patients,

86.7%), with motor symptoms being the most prevalent (101 patients, 78.2%). The most common pathological diagnosis was schwannoma (64 patients), followed by meningioma (54 patients). Other pathologies included ossifying fibroma (1 patient), arachnoid cyst (2 patients), hemangiopericytoma (1 patient), capillary hemangioma (1 patient), myxopapillary ependymoma (1 patient), low-grade spindle cell tumor (1 patient), and lipoma (1 patient).

Gross total tumor removal was achieved in 111 (86.05%) patients. Laminectomy was the preferred operation to access the tumor (101 patients), and 30 operations involved spinal junctions [Table 1].

The significant factors for poor outcomes included the number of vertebral levels removed for tumor access (adjusted OR = 3.80, 95% CI = 1.30–11.08, $P = 0.013$), arachnoid cyst and other pathologies (adjusted OR = 18.86, 95% CI = 2.16–164.49, $P = 0.007$), and bowel/bladder involvement (adjusted OR = 3.47, 95% CI = 1.15–10.39, $P = 0.027$) [Table 2].

DISCUSSION

IDEM tumors were found to have a good prognosis, with remarkable rates of gross total tumor removal.[4,5,9,10] This is reflected in this study with 71.3% good prognosis and 86.8% gross total tumor removal. Patel *et al*. found that 27/34 (79.4%) patients had an improvement in the Frankel score at 1-year follow-up, and 100% had an improvement in Nurick grade.[11] In Subramanian *et al*.'s case series,[12] IDEM tumors were found to have a mostly good prognosis, with 63/66 (95.4%) patients improving on the Nurick grade postoperatively. Kobayashi *et al*. reported that neurological function had improved in 73 (63%) patients, was stable in 34 (29%), and had worsened in 9 (8%).[9] Fachrisal *et al*. reported a case series with a mean postoperative Karnofsky Performance Status (KPS) score of 74.[13] Mehta *et al*. reported a 90.6% functional improvement,[10] while Sandalcioglu *et al*. reported

Table 1: Patient demographics and clinical characteristics

	Good outcome ($n=89$), *n* (%)	Poor outcome ($n=40$), *n* (%)	*P*[a]
Age >60	27 (29.35)	7 (18.92)	0.126
Sex, male	62 (69.66)	23 (57.50)	0.178
DM	17 (19.10)	9 (22.50)	0.928
Smoking	15 (16.85)	7 (17.50)	0.656
Duration of symptoms before surgery (days)			
<30	5 (5.43)	2 (5.41)	0.811
31–90	6 (6.74)	4 (10.0)	
>91	78 (87.64)	34 (85.0)	
Number of vertebral levels removed for tumor access			
1–2	53 (59.55)	53 (59.55)	0.256
3–6	36 (40.45)	36 (40.45)	
Extent of tumor removal			
Subtotal	11 (12.36)	6 (15.0)	0.682
Gross total	78 (87.64)	34 (85.0)	
Tumor configuration			
Anterior	14 (16.28)	10 (26.32)	0.183
Lateral	60 (69.77)	20 (52.63)	
Posterior	12 (13.95)	8 (21.05)	
Pathology			
Meningioma	38 (42.70)	16 (40.0)	0.137
Schwannoma and neurofibroma	48 (53.93)	19 (47.50)	
Arachnoid cyst and others	3 (3.37)	5 (12.50)	
Presence of pain	51 (57.30)	18 (45.0)	0.195
Presence of numbness	44 (49.44)	27 (67.50)	0.056
Presence of weakness	68 (76.40)	33 (82.50)	0.437
Bowel/bladder involvement	24 (26.97)	16 (40.0)	0.139
Operation			
Laminectomy	71 (79.78)	31 (77.50)	0.706
Laminoplasty	16 (17.98)	7 (17.50)	
Laminectomy with fixation	2 (2.25)	2 (5.0)	
Involvement of junction	23 (25.84)	7 (17.50)	0.328

[a]Chi-square test. DM - Diabetes mellitus

Table 2: Odds ratio for poor outcomes

Factors	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P*	Adjusted OR	95% CI	*P*
Age >60	0.48	0.19–1.23	0.131	0.38	0.11–1.26	0.119
Sex, male	0.53	0.27–1.27	0.180	0.42	0.14–1.27	0.124
DM	0.48	0.19–1.23	0.13	0.38	0.11–1.26	0.943
Smoking	1.04	0.39–2.80	0.928	0.96	0.24–3.72	0.806
Duration of symptoms before surgery (days)						
<30	1			1		
31–90	1.66	0.21–13.22	0.629	2.04	0.13–31.86	0.612
>91	1.08	0.20–5.89	0.921	2.33	0.23–22.69	0.466
Number of vertebral levels removed for tumor access						
1–2	1			1		
3–6	0.63	0.28–1.40	0.258	3.80	1.30–11.08	0.013*
Extent of tumor removal						
Subtotal	1			1		
Gross total	0.79	0.27–2.33	0.682	0.82	0.22–3.08	0.762
Tumor configuration						
Anterior	1			1		
Lateral	0.45	0.17–1.21	0.118	0.35	0.10–1.24	0.097
Posterior	0.93	0.27–3.12	0.911	0.55	0.12–2.42	0.450
Pathology						
Meningioma	1			1		
Schwannoma/neurofibroma	0.94	0.42–2.07	0.878	1.66	0.56–5.02	0.348
Arachnoid cyst and others	3.95	0.84–18.57	0.081*	18.86	2.16–164.49	0.007*
Presence of pain	0.60	0.28–1.29	0.197	0.93	0.33–2.61	0.934
Presence of numbness	2.12	0.97–4.63	0.059*	2.05	0.76–5.51	0.140
Presence of weakness	1.45	0.56–3.76	0.439	0.50	0.13–1.89	0.304
Bowel/bladder involvement	1.80	0.82–3.96	0.141	3.47	1.15–10.39	0.027*
Operation						
Laminectomy	1			1		
Laminoplasty	1.00	0.37–2.67	0.997	0.94	0.29–3.09	0.941
Laminectomy with fixation	2.29	0.30–17.00	0.418	5.59	0.54–57.12	0.149
Involvement of junction	0.60	0.23–1.56	0.331	0.58	0.15–2.14	0.355

*Statistically significant. OR - Odds ratio; CI - Confidence interval; DM - Diabetes mellitus

a 96.2% improved or unchanged neurological status.[14] Even though the specific definitions of the outcomes vary between studies, most of the previous studies use functional scores.

The results of our study suggested that the presence of numbness is associated with a poor outcome. Since numbness is neither a life-threatening nor functionally compromising symptom, patients with numbness as a presenting symptom may forego a visit to the hospital.[15]

The duration between the first onset of symptoms and surgery in this study being mostly >90 days may indicate a general delay in workup and surgery appointment at our institute, but it may also indicate the behavior of our demographic patients who prefer not to go to the hospital upon the onset of a neurological symptom as long as it is tolerable. This may contribute to the tumor being considerably large and relatively more difficult to resect at the time of diagnosis. Other studies in the literature have mentioned sensory symptoms but did not find them to be associated with poor outcomes.[10,11,13] An implication for future studies might be the volumetric evaluation of the tumor size and its relation to the outcome.

Our study found no correlation between the time from initial symptom onset to operation, as the majority of symptoms appeared after 90 days. Previous studies that report the effect of time between symptom onset and operation have demonstrated mixed results.[12,16,17]

The removal of 3–6 vertebral levels and pathologies other than meningiomas, schwannomas, and neurofibromas was not statistically significant in univariate analysis but was statistically significant in multivariate analysis. This suggests that while each of these factors may not directly indicate a worse prognosis, they may have a contributing effect toward a bad prognosis in combination with other factors analyzed. A larger sample size should be able to clarify these results.

The removal of more than two levels of posterior elements to access the tumor could imply that due to a larger tumor size, it is necessary to remove more bone for exposure. Removal of a larger tumor would require more disturbance of the normal neural tissue, risk for more damage, and naturally cause more neurological deficits. A more direct measurement would be the evaluation of the tumor volume.

A review of the literature did not find any studies that report the correlation between IDEM tumor volume and outcome. Ahn *et al*. measured the percentage of tumor occupancy in the intradural space in a single axial MRI cut using the formula "([the transverse diameter of the tumor mass + the longitudinal diameter of the tumor mass]/[the transverse diameter of the intradural space + the longitudinal diameter of the intradural space]) ×100."[16] They found that the percentage of tumor occupancy is correlated with the severity of preoperative symptoms, but since all patients' symptoms improved in their series, they did not find a correlation with postoperative outcomes. Patel *et al*. used the same formula in their study and found that percent tumor occupancy was correlated with a lower KPS and worse Visual Analog Scale score for patients at discharge and 1-year follow-up.[11]

A larger bony resection might cause more instability. Even though wide laminectomies are commonly used for the treatment of IDEM tumors, they have been demonstrated to cause spinal instabilities that could present as deformities, pain, and additional neurological deficits and are directly proportional to the number of vertebral levels involved.[18-20] Recent studies also suggest that laminectomy significantly increases instability, leading to more subsequent fusions compared to laminoplasty, but we did not find a statistical difference between the two methods in this study.[21,22] The hemilaminectomy is suggested by several authors as another operation that can achieve good rates of tumor removal, achieve good outcomes, as well as preserve spinal stability for IDEM tumor resection.[23-25]

Nontraumatic spinal cord injury due to tumor compression can affect bowel and bladder function due to the compromising of neural pathways below the pontine micturition center.[3,26] Neurogenic bowel is caused by the dysfunction of peristalsis and secretions due to the disturbance of the sympathetic and parasympathetic system which can manifest in various degrees of constipation. Neurogenic bladder can cause detrusor overactivity, detrusor-sphincter dyssynergia, and decreased or absent bladder tone based on the lesion site and presents with many forms of urinary incontinence.[3,22,27] The presence of bowel and bladder symptoms associated with a poor IDEM tumor surgical outcome, to the author's knowledge, has not been reported elsewhere.

Meningiomas, schwannomas, and neurofibromas are benign entities with favorable prognoses and are the three most common types of IDEM tumors. Due to the rarity of other types of tumors, the number of samples in this study is quite limited. IDEM arachnoid cysts are rare entities that are treated surgically if symptomatic with either cyst fenestration or cyst resection. Two arachnoid cyst cases in this study were multiloculated, and the procedure performed was laminectomy with complete cyst wall resection. Both were modified McCormick Grade 5 preoperatively and did not experience clinical improvement despite postoperative MRI showing complete cyst removal. A 72-patient case series by Schmutzer *et al*. showed overall improvement following surgery in IDEM arachnoid cyst.[28] However, it should be noted that none of the patients in the series had an initial modified McCormick score of lower than 3. Other case reports seem to suggest a good prognosis but do not go into detail about the extent of preoperative neurological deficit.[29-31]

Regarding tumor location, one study reported that 3 of 66 patients who deteriorated had upper thoracic tumors and suggested this to be associated with poor outcome.[12] Similarly, Ishida *et al*. and Mehta *et al*. also reported thoracic location to be a risk factor associated with new neurological deficits after surgery.[10,32] A higher cord-to-canal ratio explains why lesions in the thoracic area have a more detrimental impact. In addition, the location of the tumor being anterior seems to produce a worse outcome in certain studies due to the fact that it is not readily resectable through the commonly performed posterior approach. Spinal cord traction also contributes to more neurological deficits.[4,10,17] However, other studies did not find a tumor's configuration in the spinal cord to have statistical significance.[16] Kobayashi *et al*. did not find any significant association in the tumor's axial or sagittal locations.[9] Our study did not demonstrate the association of tumor location on the outcome. As such, we think that the significance of a tumor's location on the outcome is unclear and warrants further investigation.

The most important limitation of this study is due to its retrospective nature. A future prospective study with a large sample size is suggested.

CONCLUSION

We found that the factors for poor outcomes included bowel/bladder involvement, number of vertebral levels removed

for tumor access, and pathology other than meningioma, schwannoma, and neurofibroma.

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Conflicts of interest

There are no conflicts of interest.

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