SURGICAL MANAGEMENT OF INTRAMEDULLARY SPINAL CORD EPENDYMOMA

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ABSTRACT

Background: The intramedullary spinal cord tumors are relatively uncommon disease that can leave the patients neurologically and functionally devastated. **Aim and Objectives:** Identifying the operative strategies for completing resection of intramedullary spinal cord ependymomas as well as assessing the functional results of patients over the postoperative follow-up period. **Patients and methods:** This prospective and retrospective study was conducted on twenty-five consecutive patients, harboring intradural intramedullary spinal cord ependymomas, all were operated on at Al Azhar University hospitals starting from June 2012 till June 2021. **Results:** There was not a statistically significant distinction among the groups that were evaluated concerning the pathological subtypes of spinal ependymoma with the degree of surgical excision and outcome. There was a statistically significant relation between pre-operative clinical state and the clinical outcome postoperatively as if the patient had no or mild motor affection preoperatively, the clinical results were much better p-value 0.000. **Conclusion:** early diagnosis, and early treatment guarantee the best clinical outcome for those patients.

Keywords: Surgical Management; Intramedullary; Spinal Cord; Ependymoma.

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INTRODUCTION

Intramedullary tumors of the spinal cord represent 3 to 6 % of central nervous system tumors.[1] ependymoma accounts for 30 to 45% of all intramedullary spinal cord tumors.[2] They are typically slowly growing tumors that originate from ependymal cells of the central canal of the spinal cord. Ependymomas are more common in adults than in pediatrics with peak incidence in the middle age. Axial pain is the major presenting symptom. The clinical picture of the tumor depends on its location in the spinal cord. A strong index of suspicion is based mainly on clinical symptoms as well as clinical signs, in addition to spine-directed MRI, which is required for the diagnosis of a primary tumor of the spinal cord. [1, 3]

The primary method of treatment is surgical resection. Although ependymomas are non-capsulated tumors the surrounding compressed glial tissue between the tumor and spinal cord forms a false capsule and the cleavage plane enables safe near total removal of the tumor. [4] The preoperative functional status, use of intraoperative neuromonitoring, and the degree of surgical resection all are factors that predict the patient's fate and outcome.[1, 4, 5-7]

PATIENTS AND METHODS

A prospective and retrospective study was conducted on twenty-five consecutive patients, harboring intradural intramedullary spinal cord ependymoma operated in Al Azhar University hospitals. The initial study was conducted on 32 patients with intramedullary spinal cord

tumors. 25 cases were proven histopathologically as ependymomas. 15 patients were retrospective; the oldest patient was operated on in 2012 and the remaining 10 prospective cases were operated on from June 2019 till June 2021.

Inclusion criteria: All patients of intramedullary spinal cord ependymoma, individuals who were fit for surgery, Patients were selected for surgery based on their magnetic resonant imaging (MRI) disclosure of an intradural intramedullary spinal ependymoma. the patients were either operated upon for the first time or reoperated for recurrent lesions. The inclusion criteria based on histopathological analysis

Exclusion criteria: Patients with other intramedullary lesions rather than ependymoma such as astrocytoma and hemangioblastoma, and patients with filum terminal ependymoma. Intradural extramedullary tumors such as meningioma and schwannoma, Patients who had intradural tumors associated with extradural extension, and Patients who were not fit for surgery.

Each person went through the standard protocol of having their medical history taken, comprehensive clinical examination, and regular laboratory tests were performed. In every patient, a contrasted magnetic resonance imaging (MRI) examination of the spinal cord was carried out.

All patients were evaluated clinically by the Modified McCormick scale which consists of five grades as follows: I Intact neurologically, normal ambulation, minimal dysesthesia, II Mild motor or sensory deficit, functional independence, III Moderate deficit, limitation of function, independent with external aid, IV Severe motor or sensory deficit, limited function, dependent and V Paraplegia or quadriplegia, even with flickering movement.[8] This scale was applied both preoperatively and postoperatively for all patients to compare the pre-and postoperative functional outcomes. All patients had been counseled and consented before surgery as regards complications that might occur and surgical steps.

An endotracheal intubation and general anesthesia were both utilized for every one of the twenty-five patients. With the patient in the prone position, a posterior midline surgical incision, and laminectomy were done. The operating surgical microscope was utilized for all cases, in addition, intraoperative somatosensory evoked potential monitoring was accessible and utilized in only 6 cases. In cases where motor evoked potential (MEP) and somatosensory evoked potential (SSEP) were utilized, surgical removal was stopped when there was a drop in the amplitude of MEP, SSEP greater than 50% of the baseline intraoperatively. dexamethasone administration and saline irrigation if the record of neuromonitoring improved, the tumor debulking could be returned if no changes occurred, we ought to stop the removal of the tumor.

The postoperative follow-up period ranged from 6 months up to 3 years with mean a follow-up period of 18 months. Follow-up was done clinically by clinical neurological examination, by evaluation of MAC Cormick score, and by MRI spine post-contrast.

RESULTS

Table (1): Age, sex & spinal level distribution in 25 cases with intramedullary spinal cord tumors.

		Total no. = 25
Age (years)	Median (IQR) Range	39 (32 – 42) 6 – 65
Sex	Female Male	11 (44.0%) 14 (56.0%)
Spinal level	conus Cervical Dorsal Dorsolumber	10 (40.0%) 6 (24.0%) 5 (20.0%) 4 (16.0%)

The mean age was 39 years old. The youngest participant was a 6-years-old female with ependymoma grade 2 papillary type at the level of the dorsal spine. The oldest participant was a 65-year-old male with Ependymoma Grade 2 at the level of the cervical spine was of cellular type.

Table (2): spinal level of the lesion, clinical picture and functional presentation.

	Axial pain	**sensory**	**motor**	**sphincter**	**McCormick score**
Cervical 6cases	6 cases	2 cases (minimal sensory deficit). 4 cases(tingling ,numbness in both hands)	2 cases (intact motor) 4 quadriparesis	2 cases (precipitancy of micturition)	2 cases grade 1 4cases grade 3
Dorsal 5 cases	5 cases	5 cases Sensory level hypothesia	3 cases paraparesis 2 cases paraplegia	3cases (precipitancy of micturition)	3 cases grade 3 2 cases grade 4
Dorsolumber 4 cases	3 cases	3 cases (Sensory level hypothesia), 1case parethesia	3cases paraparesis	2 cases precipitancy	3 cases grade 2 1cases grade 1
Conus 10 cases	3 cases	6cases (minimal sensory deficit)	2 cases (Intact motor) 8 cases (motor deficit).	2cases precipitancy	1 cases grade 1 9 cases grade 2

Table (3): MRI finding T1, T2 and T1 with contrast in our study

Investigations		**Total no. = 25**
T1	Isointense	12 (48.0%)
	Hypo intense	13 (52.0%)
T2	Hyper intense	20 (80.0%)
	Hypo intense	2 (8.0%)
	Hetero intense	3 (12.0%)
T1 (post-contrast)	Heterogeneous	6 (24.0%)
	Homogenous	19 (76.0%)
Others	No	17 (68.0%)
	Cervical syrinx	6 (24.0%)
	Lithiasis L5 S1	2 (8.0%)

There were four patients with associated syrinx at the cervical cord region, and two were cervicodorsal. There were 2 patients with spondylolisthesis L5 S 1 as coincident association.

Table (4): Relation among different pathological subtypes of spinal ependymoma with surgical excision and outcome.

		Pathology subtype				**Test value**	**P-value**	**Sig.**
		Cellular	**Maxopapillary**	**Papillary**	**Tanycytic**			
		No. = 9	**No. = 7**	**No. = 4**	**No. = 4**			
Total complications	Not complicated	4 (44.4%)	3 (42.9%)	1 (25.0%)	2 (50.0%)	0.604*	0.895	NS
	Complicated	5 (55.6%)	4 (57.1%)	3 (75.0%)	2 (50.0%)			
Extent of Surgical Removal	Total	6 (66.7%)	6 (85.7%)	1 (25.0%)	3 (75.0%)	4.393*	0.222	NS
	Subtotal	3 (33.3%)	1 (14.3%)	3 (75.0%)	1 (25.0%)			
Outcome groups	Poor + Fair	5 (55.6%)	1 (14.3%)	0 (0.0%)	1 (25.0%)	12.436*	0.053	NS
	Good	2 (22.2%)	1 (14.3%)	3 (75.0%)	0 (0.0%)			
	Excellent	2 (22.2%)	5 (71.4%)	1 (25.0%)	3 (75.0%)			

P-value > 0.05: Non-significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant

*: Chi-square test

There was not a significant relationship between different pathological subtypes of spinal ependymoma and the extent of surgical excision and outcome.

Table 5: Different complications after surgical management of spinal ependymoma.

Complications		Total no. = 25
Worsening of neurological deficit	Reversible	15 (60.0%)
	Irreversible	10 (40.0%)
Infection	No	23 (92.0%)
	Yes	2 (8.0%)
CSF leak	No	17 (68.0%)
	Yes	8 (32.0%)
Recurrence	No	21 (84.0%)
	Yes	4 (16.0%)
Spinal deformity	No	20 (80.0%)
	Kyphosis	3 (12.0%)
	Scolosis	2 (8.0%)
Total complications	Not complicated	10 (40.0%)
	Complicated	15 (60.0%)
Extent of Surgical Removal	Total	16 (64.0%)
	Subtotal	9 (36.0%)

CSF leakage occurred in eight patients (32%), five cases had intramedullary Ependymoma of Grade 2 two cases with ependymoma of Grade 1, and in the last case the tumor was of Grade 3. All patients with CSF leakage were treated conservatively except for one who needed surgical repair 3 weeks later. Wound infection occurred in 2/25 patients (8%). The 1st case was a male patient 16 years old with dorsolumber ependymoma grade 2 and 2nd case was 40 years old male with conus ependymoma grade 2 the two cases were managed by antibiotics and daily dressing of their wounds improved and complete healing occurred within one-month duration.

Early post-operative collection of epidural hematomata occurred in one patient (5%) (This happened with 18 years old male patient who had GII cervicodorsal Ependymoma. Pre-operatively, this patient was categorized as McCormick (GII). 24 hours following surgery the patient started to experience gradual deterioration of the motor power in both lower limbs. Cervicodorsal (MRI and CT) were done and revealed epidural hematoma and immediate surgical evacuation was done. No complications occurred in 10/25 of intramedullary spinal cord tumor patients (40%). We had 5patients with delayed complications in the form of scoliosis and kyphosis, all those patients were operated on earlier in 2012 to 2014 and submitted to wide and long segments laminectomies without fixation. All were treated conservatively as the degree of deformity was mild.

Table (5): postoperative follow-up according to the modified McCormick scale for group 1 with subtotal resection.

McCormick Scale	Pre op.	Immediate Post-op.	After 3months	After 1 year
Grade I	2 cases	2 cases	6 cases	6 cases
Grade II	6 cases	6 cases	3 cases	3 cases
Grade III	1 case	1 case	-	-
Grade IV	-	-	-	-
Grade V	-	-	-	-

One-year post-operative follow-up according to Modified McCormick Scale for those patients was the same as after 3 months follow-up.

Table (6): postoperative follow-up according to the modified McCormick scale for group 2 with total excision.

McCormick Classification	Pre-op.	Immediate Post-op.	After 3 months	After 1 year
Grade I	2 cases	1	5 cases	8 cases
Grade II	6 cases	4 cases	8 cases	5 cases
Grade III	6 cases	6 cases	1 case	2 cases
Grade IV	2 cases	4 cases	1 case	1 case
Grade V	-	1 case	1 case	0 case

This group of patients had a narrow neurological functional reserve preoperatively as most of them were mac Cormick grade 2 and 3, so it was a must to meticulously handle the neurological tissues to preserve the remaining function as much as possible. we used MEP and SSEP intraoperatively in some patients, and it seemed that it was beneficial in those patients and allowed us to do total resection without further neurological deficit even if in some patients with the immediate post-operative new deficit it was transient likewise cases were evoked potential was not employed. Unfortunately, neuromonitoring was available intraoperatively in only 6 cases.

Table (7): Relation between postoperative clinical outcome and preoperative clinical presentation.

		Poor + Fair	Good	Excellent	Test value	P-value	Sig.
		No. = 8	No. = 6	No. = 11			
Sensory	Negative	6 (75.0%)	6 (100.0%)	11 (100.0%)	4.620*	0.099	NS
	Positive	2 (25.0%)	0 (0.0%)	0 (0.0%)			
Motor	Negative	0 (0.0%)	4 (66.7%)	11 (100.0%)	19.444*	0.000	HS
	Positive	8 (100.0%)	2 (33.3%)	0 (0.0%)			
Sphincteric	Negative	3 (37.5%)	3 (50.0%)	10 (90.9%)	6.406*	0.041	S
	Positive	5 (62.5%)	3 (50.0%)	1 (9.1%)			
Follow up period	Median (IQR)	14 (8 – 18)	12.5 (10 – 20)	12 (12 – 12)	0.408≠	0.815	NS
	Range	6 S– 24	7 – 24	6 – 24			

≠: Mann-Whitney

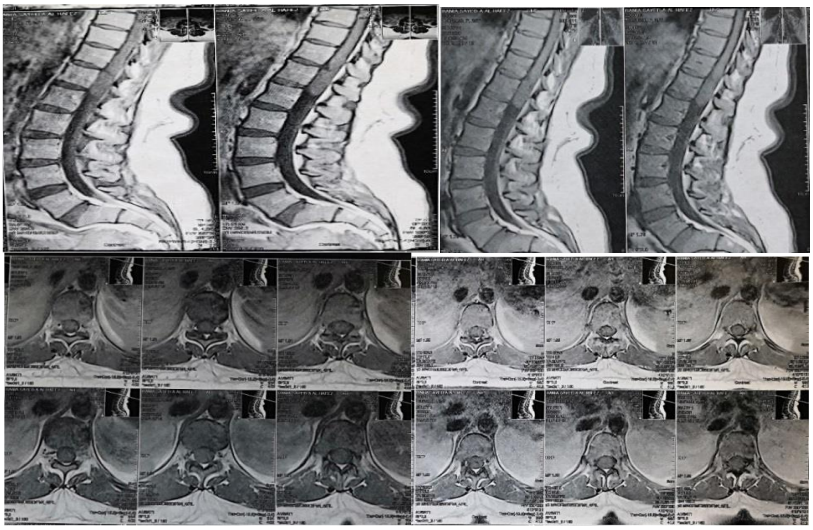
There is a significant statistical relation between pre-operative clinical state (motor power and sphinctric function) and outcome post-operative if the patient has no or mild motor affection, the best results are obtained.

ILLUSTRATED CASES

Case (1)

46-year-old female patient, housewife, diabetic presented with mild dorsal back pain and paresthesia of both lower limbs of 6-months duration. Modified Mc Cormick grade 1 also Precipitancy of micturition of one-month duration. on examination: intact motor power and normoreflexia. pre-operative: MRI dorsolumber spine with and without contrast was done.

Preoperative imaging study



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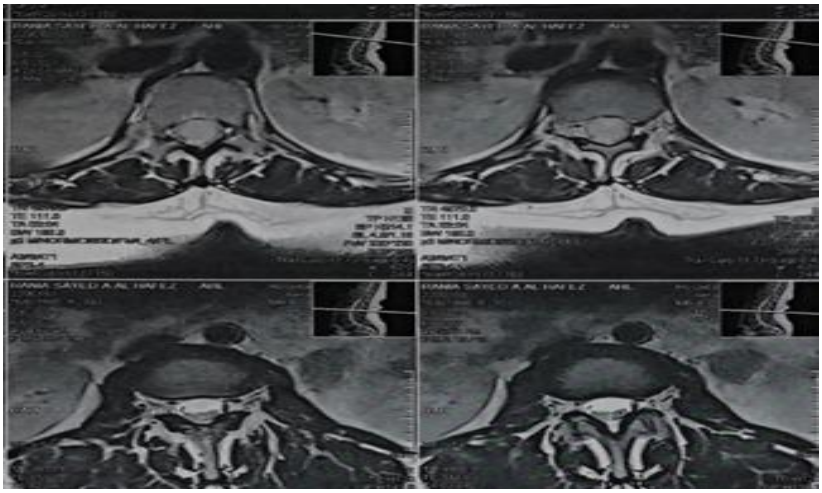


B

Figure (1): (A) Pre-operative MRI study T1axial and sagittal views with and without contrast and T2WI axial cuts showed intramedullary lesion in dorsolumber spine opposite D 12 up to D 8) and **(B)** Post-operative imaging after near total tumor excision and histopathological result and patient still Mc Cormick grade 1.

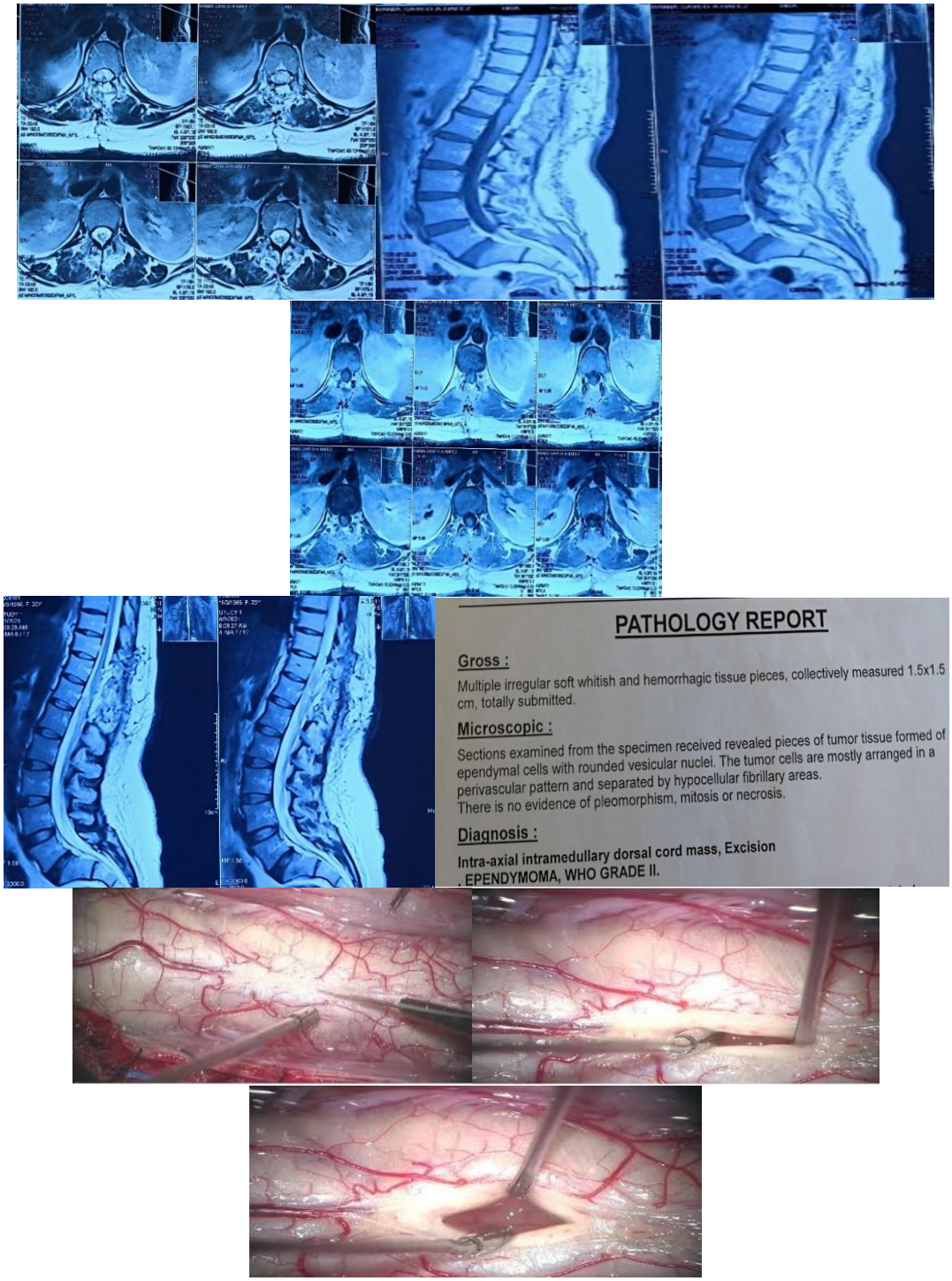
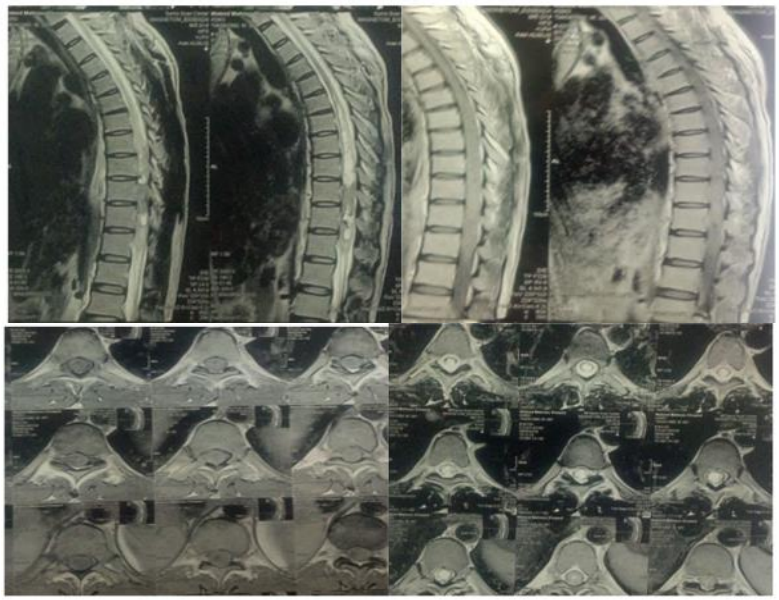


Figure (2): MRI post T1 with contrast axial and sagittal views and T2 WI axial and sagittal study revealed subtotal excision of intramedullary spinal ependymoma WHO grade 1 also intraoperative cord enlargement and mylotomy.

Case (2)

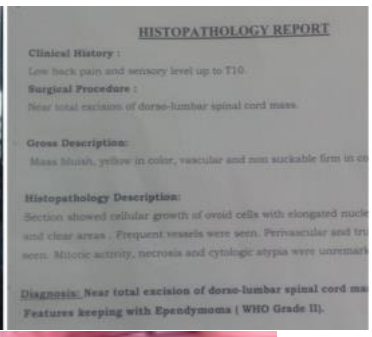
Male patient 50 years old, presented with dorsal back pain that increased by the night, inability to walk freely MC cormick grade 3, and urinary precipitancy. On examination, Para paresis GII, MRI dorsal spine was done and showed intra-axial lesion associated with 2ry syringohydromeylia. subtotal tumor resection was done, with a histopathological report revealing ependymoma GII.



MRI Dorsal Spine (PRE)

Figure (3): Pre-operative sagittal and axial enhanced T1WI and T2WI MRI showing dorsal spinal intramedullary ependymoma associated with 2ry syringomyelia.

MRI Dorsal Spine (POST)



HISTOPATHOLOGY REPORT

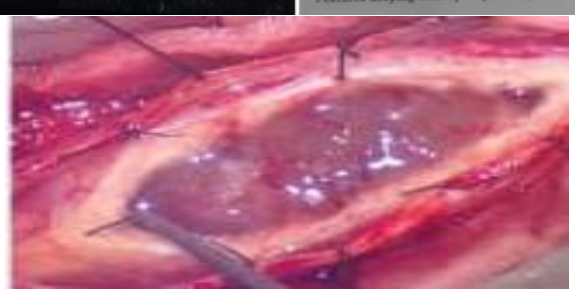
Clinical History :
Low back pain and sensory level up to T10.

Surgical Procedure :
Near total excision of dorso-lumbar spinal cord mass.

Gross Description:
Mass bluish, yellow in color, vascular and non suckable firm in

Histopathology Description:
Section showed cellular growth of ovoid cells with elongated nucle
and clear areas . Frequent vessels were seen. Perivascular and tr
seen. Mitotic activity, necrosis and cytologic atypia were unremar

Diagnosis: Near total excision of dorso-lumbar spinal cord ma
Features keeping with Ependymoma (WHO Grade II).



Histopathology

Figure (4): Post-operative sagittal MRI dorsal spine showed subtotal excision of ependymoma also intraoperative finding as tumor slightly has a clear line of demarcation which is WHO grade 2 as the histopathological study revealed it.

DISCUSSION

In this study, 25 consecutive patients. The mean age was 32 years to 42 years old. The youngest participant was a 6-year-old female with intramedullary spinal cord ependymoma of Grade 2 papillary type at the level of the dorsal spine. The oldest study participant was a 65-year-old male with intramedullary spinal Ependymoma Grade 2 at the level of the cervical spine of cellular type.
In this study when considering sex distribution, the majority of intramedullary ependymomas were widely observed in males 56%, while 44% of the intramedullary ependymoma occurred in females.

As regards histopathological types; nine patients were of cellular type 36%, five were males and four were females. Myxopapillary type was noticed in 7 patients 28%three females and four males, whereas intramedullary Ependymomas papillary type was found in four patients 16% of all of them were females. Tany cystic type was found in 4 patients 16%, all of them were males.

Liigant et al. found in their studies in young adults that according to the proportion of sex, 61.8% of myxopapillary ependymomas were in males and 38.8% of myxopapillary ependymomas were in females.[9] Constantini et al. stated that cellular type was the most frequent intradural intramedullary ependymoma in children and following it were the myxopapillary cases, also he stated that ependymomas were observed in adults more frequently than pediatrics. [10] Syed I.et al found that ependymomas with high grades histological types had worse prognosis than low grades types.[1] In the present study there was no significant difference.

In our study as regards the spinal level of ependymoma ten patients were conus at 40%; six patients had cervical ependymoma 24%, five patients had dorsal ependymoma at 20%, and four patients had dorsolumber ependymoma level 16%. In the study of Sandalcioglu et al., it was observed that most intramedullary tumors were (55%) located in the cervical and cervicothoracic region. 32% were in the thoracic region, and 13% were in the lumbar region.[11] In Taricco et al. study of primary intramedullary tumors in adolescence, out of 48 patients 20 (42%) were thoracic, 13 (27%) cervical and 15 (31%) were cervicothoracic cord tumors. [12] Shrivastava et al. pointed out in their study on young adults with intramedullary tumors that; 63% of their cases were ependymomas and in 55% of cases, the tumors were located in the thoracic region.[13]

In the present study, Six out of 25 patients with intramedullary spinal cord ependymoma had associated syrinx 24 %. In five patients the syrinx was at the cervical cord region, and in one patient it was cervicodorsal. Pre-operative functional outcome according to the Modified McCormick scale, was compared with one-year post-operative functional grades in 6 patients with a tumor-associated syrinx, which facilitated tumor resection during surgery, but there was no statistical importance between the presence of syrinx and postoperative clinical outcome. Total surgical resection was achieved for 16/25 patients (64%) of the whole patients. Subtotal resection was achieved for 9/25 patients (36%). Traul et al. stated that: it is generally agreed that preservation of neurological function is more important than complete excision by force. [14,15]

In this study, recurrence happened in four cases with subtotal excision. Spinal deformity occurred in five cases, 2 patients had scoliosis and three patients had kyphosis after surgery, those patients had large-sized tumors that needed multiple levels of laminectomies to enable complete exposure of the tumors, unfortunately, those patients were not submitted to intraoperative spinal fusion.

The need for postoperative radiotherapy and/or chemotherapy was assessed according to the individual needs of each patient. The policy was not to use routine radiotherapy as an adjunct to treatment when total macroscopic removal of Ependymomas had been achieved. In two patients (the 45 years old female patient with cervical Ependymoma GII with subtotal resection, and a 39-year-old male patient with

cervicodorsal Ependymoma GII with subtotal surgical resection) radiation therapy was used as adjuvant therapy for those two patients.

Gepp et al. It has been claimed that the restrictions placed on the use of radiotherapy and chemotherapy, in addition to the lack of clear evidence suggesting that these therapies may enhance outcomes in children, have made surgery the best option for treating spinal cord malignancies.[16]

Early postoperative follow-up of our patients showed transient deterioration of the clinical condition according to Modified McCormick grades. Fifteen out of twenty-five patients (60%) had reversible worsening of their early postoperative deficits, while ten of twenty-five patients (40%) had a permanently irreversible deficit. No surgical mortality has been recorded in this study.

Fischer et al. pointed out in their study that, postoperative dysesthesia and pain were a well-known phenomenon and were often difficult to manage. Postoperative hyperesthesia and allodynia may be caused by disturbances of the dorsal columns, as tumor removal is usually performed by midline spreading and retraction of posterior columns. Postoperative position-sense disturbance causing gait disturbance is usually transient and improves within 3 months. [17]

Manzano et al. got no noticeable difference in McCormick grades before and after surgery. but, 43.6% of patients suffered postoperative sensory ataxia due to dorsal columen dysfunction.[8]

Regarding functional outcomes at one-year follow-up in the current study compared to the extent of surgical resection, 16 out of 25 patients 60%% with total resection were categorized as GI in eight patients, five patients grade 2, two patients grade 3, and only one patient grade one. According to the Modified MacCormick scale after one year of follow-up,9 out of 25 patients with subtotal resection functional outcomes were as follows; six patients (24%) were categorized as GI, three patients as GII according to the Modified McCormick scale after one year follow up.

Constantini et al. stated that whether the resection was a gross total resection or a subtotal resection, it did not significantly affect the postoperative functional state in the long run and for the first 3 years. [10]

Taricco et al. reported that 5 of 13 patients who underwent partial tumor resection eventually worsened and exhibited a decreasing McCormick score during the first two years of follow-up. [12]

Furthermore, in the present study we found it was beneficial; to use evoked potential, especially in cases with preoperative neurological deficit to protect neural tissues, it was obvious in the second group with gross total excision without further neurological deficit because 6 of them were operated with aid of evoked potential but unfortunately, it was utilized in only six patients as in the future we need to use it in a large sample size to give more reliable results and to be applicable in statistical methods.

CONCLUSION

For individuals harboring intramedullary spinal cord tumors, we need further attention to early diagnosis and surgical interference. It became possible with the aid of intraoperative neuromonitoring to excise the tumor to achieve the best prognosis without further neurological deficit.

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