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Outcome Analyses after Microsurgical Resection of Intra Medullary Spinal Cord Tumors: Our Institutional Experience

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Abstract: Intramedullary spinal cord tumors are rare entity accounting for 5-6% of all central nervous system tumors. Surgery, once used for the diagnosis of intramedullary spinal cord tumors, now represents the most effective treatment of benign well-circumscribed tumors. Long-term tumor control or cure, with preservation of neurologic function, can be achieved in most patients with microsurgical removal alone. We analyzed the clinical profile and outcome of microsurgical resection, and histological diagnosis of all intramedullary lesions. Post-operative status of functional outcome in relation to extent of resection was also analyzed. Among the intramedullary tumors ependymoma is the commonest lesion with good plane of cleavage, amenable to complete microsurgical resection. Prognosis depends on preoperative neurological status, plane of cleavage, extent of resection, nature and subtype of the lesion.
Keywords: Intramedullary spinal cord tumors, ependymomas, astrocytomas, microsurgical resection.

INTRODUCTION

Intramedullary spinal cord tumors are rare entity accounting for 5-6% of all central nervous system tumors and one third of primary spinal tumors. Ependymomas and astrocytomas comprising the majority of them. Surgery, once used for the diagnosis of intramedullary spinal cord tumors, now represents the most effective treatment of benign well-circumscribed tumors [1]. Long-term tumor control or cure, with preservation of neurologic function, can be achieved in most patients with microsurgical removal alone [2, 3].

The benign nature of most intramedullary neoplasms, advances in microsurgical techniques, early clinical diagnosis with magnetic resonance imaging (MRI), and the ineffectual or inconsistent treatment response of most intramedullary tumors to radiation therapy largely account for the expanded role of surgery in the management of these lesions. Therefore, optimization of surgical treatment is the key to successful management of patients with intramedullary masses. This includes early diagnosis and aggressive primary treatment, the avoidance of technical and judgmental errors and their associated complications, and a strict adherence to contemporary microsurgical technique [4].

The predominant benefit of surgery for an intramedullary tumor is prophylactic. Preservation, rather than restoration, of neurologic function is the most likely outcome after successful surgical treatment. In fact, significant improvement of a severe or long-standing preoperative neurologic deficit rarely occurs after a technically successful surgical excision. Surgical morbidity is also greater in patients with more significant preoperative deficits. This creates a therapeutic irony in which the risk of surgery is actually less in patients with minimal or no objective neurologic deficit. Thus, early clinical diagnosis and, if possible, definitive initial treatment are critical to the successful management of most intramedullary tumors.

The primary surgical objective for intramedullary tumors is long-term tumor control or cure with preservation of neurologic function. The most important factor influencing the surgical objective is the nature of the tumor–spinal cord interface. This interface can be assessed accurately only through an adequate

myelotomy, which extends over the entire rostro-caudal extent of the tumor. Benign tumors, such as ependymomas and hemangioblastomas, although un-encapsulated, are non-infiltrative lesions that typically exhibit a distinct tumor– spinal cord interface. Gross total removal is the treatment of choice in these cases. Astrocytomas are much more variable with respect to histology, physical characteristics, and natural history; unlike the consistently benign histology, circumscribed nature, and natural history of ependymoma and hemangioblastoma. Although some benign astrocytomas are well circumscribed and allow gross total resection, most exhibit variable infiltration into the surrounding spinal cord, which requires careful microsurgical resection. Metastatic spinal cord tumors, for example, usually appear as well-circumscribed focal masses amenable to gross total resection. Post-resection radiation therapy, as is the case with intracranial metastasis, however, may reduce the risk of local tumor recurrence.

METHODS

We have analyzed 30 cases of intra medullary spinal cord tumors (IMSCTs) and their various clinical manifestations, which underwent resection for the primary pathology at the Gandhi Medical College and Hospital, Secunderabad, Telangana between January 2010 and October 2018. Contrast MRI of spine done in all patients. Standard bilateral laminectomy, durotomy and arachnoidal opening, dorsal myelotomy done in all cases. Tumor-cord interface delineated well and microsurgical resection done. Goal of surgery was complete microsurgical resection (CMR) with preservation of neurologic function and long-term tumor control. Comparative analyses done with postoperative period and in follow up.

Data collected included demographic information and preoperative neurological status as classified by the Frankel [5] and modified McCormick [6] scales (Tables 1 and 2). Each patient underwent neurological examination in the postoperative period. Length of hospital stay was also recorded. Reports from staff neuropathologists and neuro- radiologists were used to confirm the histopathology of the tumor and describe the postoperative MRI imaging changes, respectively. Complete microsurgical resection (CMR) refers to the absence of residual tumor on initial postoperative MRI studies, while radical microsurgical resection (RMR) describes a tumor residual of < 20% on MRI. Subtotal resection (STR) was defined as an incomplete resection of the bulk tumor. Functional and neurological status at 1 year follow-up was also classified by Frankel grades and McCormick scores.

Continuous predictors were summarized using means, medians, standard deviations, and ranges. Categorical variables were described using frequencies and percentages. Survival analysis was performed to determine key predictors of tumor progression following surgery, as evidenced by postoperative MRI. Present study explored the predictive value of general demographics (age, sex, and preoperative neurological status), tumor characteristics (spinal region, extent of tumor, and histology), and surgical factors (extent of resection, number of levels). Multivariate analysis was conducted on variables that yielded a p value of < 0.2 on univariate analysis.

A secondary analysis was performed to evaluate key predictors of postoperative functional outcomes. Changes in Frankel and McCormick scores were determined by subtracting 1-year scores from preoperative scores. Logistic regression analysis was used to evaluate the association between an “optimal” outcome and several demographic, tumor-related, and surgical factors. Patients were classified as having an “optimal” outcome if 1) they had a preoperative Frankel grade of C or D or a McCormick score of II, III, or IV and improved by 1 or more point or 2) they had an initial Frankel score of E or a McCormick score of I and remained stable following surgery. A “suboptimal” outcome was defined as a decline in Frankel (e.g., from D to C) or McCormick score (e.g., from II to III), or no improvement if the preoperative Frankel and McCormick scores were C or D and II, III, or IV, respectively.

RESULTS

Present study consisted of 30 patients, of which 16 (53.33%) females and 14 (46.66%) males, whose mean age was 41.92 ± 14.36 years (range 17.60–75.40 years). On initial presentation, the majority of patients presented with symptoms consistent with Frankel Grade D (73.02%) (Table 1) and mild to moderate motor or sensory deficit, as classified using the modified McCormick Scale (Grades II–III; 71.43%) (Table 2). Weakness seen in 20 patients, funicular pain in 14, dysaesthesias in 12, dissociative sensory loss in 4, gait disturbances in 2, and bladder involvement in 1. Classic ependymomas (WHO Grade II) were the most frequent tumor subtype 10 (33.33%) followed by myxopapillary ependymomas 8 (26.66%), WHO Grade I/II astrocytomas 5 (16.66%) and hemangioblastomas 2 (6.66%). Of the patients with hemangioblastomas, 1 of 2 had known von Hippel-Lindau (VHL) syndrome. Other pathological types included Ganglioglioma (1), epidermoid (1), Mucinous cyst (1), Meningioma (1), and Metastasis (1). Tumors spanned an average of 4.65 ± 1.67 spinal levels (range 2–9). Two patients (6.66%) had a lesion located in the cervicomedullary region, 9 (30%) in cervical region, 3 (10%) in the cervicothoracic segments, 4 (13.33%) in the thoracic segments, 1 (3.33%) in dorsolumbar segment, and 11 (36.66%) in the conus.

Table-1: Frankel grading scale*

Grade	Description
A	Absent motor & sensory function
B	Sensation present; motor function absent
C	Sensation present; motor function present but not useful (Grade 2–3/5)
D	Sensation present, motor function present & useful (Grade 4/5)
E	Normal motor & sensory function

* Based on the description in Frankel *et al.* The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. I. *Paraplegia 7:*179–192, 1969.

Table-2: Modified McCormick grading scale*

Score	Description
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
V	Paraplegia or quadriplegia, even with flickering movement

*Reproduced with permission from Constantini *et al*. intramedullary spinal cord tumors in children under the age of 3 years. *J Neurosurg 85:*1036–1043, 1996

Complete microsurgical resection (CMR) was achieved in 14 (46.66%) cases, radical microsurgical resection (RMR) in 9 (30%), and Subtotal resection (STR) in 7 (23.33%). CMR was achieved in the majority of patients with WHO Grade II ependymomas, myxopapillary ependymomas, and hemangioblastomas. The median length of hospital stay following surgery was 8 days.

Predictors of progression-free survival

Univariate Analysis

In this series, 12 patients (40%) experienced clinical and/or radiological progression of disease. There was no significant difference in age or sex between patients who did (38.35 ± 12.99 years, 57.89%) and did not (43.50 ± 14.79, 45.45%) experience tumor progression ($p = 0.24$ and $p = 0.71$ for age and sex, respectively). On univariate analysis, the most significant predictor of progression-free survival was tumor histology ($p = 0.0027$). Patients with Grade I/II astrocytomas were more likely to have tumor progression than patients with WHO Grade II ependymomas ($p = 0.0026$) and myxopapillary ependymomas ($p = 0.017$). Preoperative Frankel or McCormick scores were not significant predictors of progression-free survival ($p = 0.11$, $p = 0.82$, respectively). Patients who underwent radical or subtotal resection were more likely to have tumor progression than those who had a complete resection ($p = 0.018$). Extent of tumor resection ($p = 0.33$), number of operated segments ($p = 0.49$), and region of the spine where tumor was located ($p = 0.32$) were not important predictors of tumor progression.

Multivariate Analysis

Following multivariate analysis, the only significant predictor of tumor progression was tumor pathology. Although the extent of residual disease was no longer significant, tumor pathology likely encompasses this variable. In particular, surgical management of infiltrative lesions such as astrocytomas involves subtotal resection. Most importantly, patients with Grade I/II astrocytomas were at a significantly higher risk of progression than those with classic ependymomas.

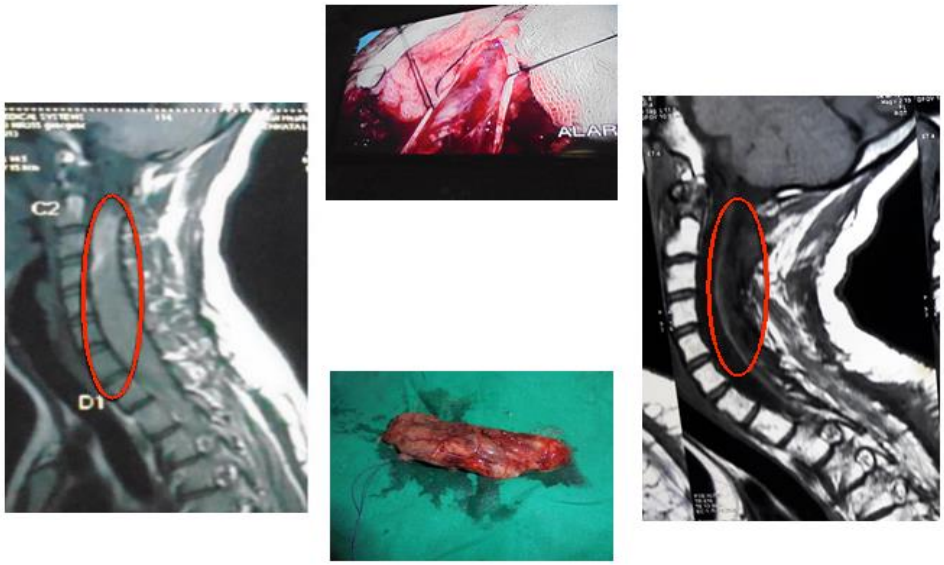

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Fig-1: *A*. Gadolinium-enhanced sagittal MRI shows an upper cervical intramedullary enhancing mass. Significant spinal cord enlargement is present over several spinal cord segments, although the solid tumor extends only from C2 to C5. *B*. Intraoperative picture demonstrates distinct tissue margins. *C*. At surgery, a benign ependymoma was totally removed. *D*. Postoperative image demonstrating a CMR

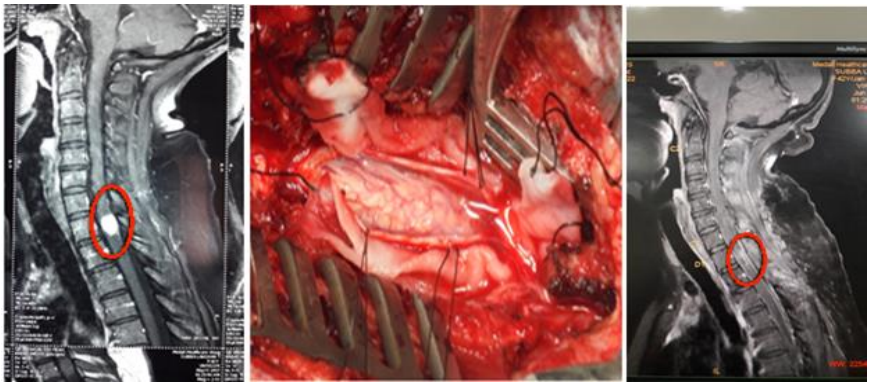

Fig-2: *A*. An enhancing ISCT representing a low-grade astrocytoma centered behind the D-1 body. *B*. Demonstrates indistinct infiltrating tissue margins. *C*. Postoperative parasagittal image demonstrating a small area of enhancement that represents an RMR

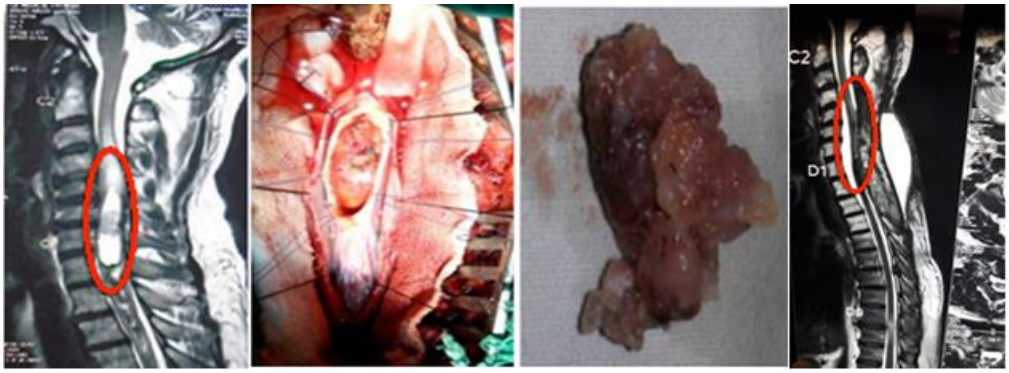

Fig-3: *A*. A faintly enhancing cervical IMSCT representing an ependymoma. *B*. An intraoperative photograph after gross total resection of an intramedullary ependymoma shows clean tumor margins without evidence of residual tumor. *C*. A lobulated, glistening reddish or brownish mass consistent with ependymoma. *D*. Postoperative image demonstrating a CMR.

Predictors of Functional outcomes at 1-year Follow-Up

Functional outcomes were determined based on change in Frankel and McCormick scores at 1 year follow-up. Thirty patients were evaluated using the Frankel and McCormick scales at 1-year follow-up. One patient (3.33%) improved by two Frankel grades and 11 (36.66%) by one grade. Scores were stable in 12 patients (40%) following surgery, while in 6 (20%) there was a decline in functional status. Based on McCormick scores, one (3.33%) patient improved by 3 points and 12 (40%) by 1 point. Twelve patients (40%) did not exhibit improvement, while 5 (16.66%) demonstrated a decrease in function. Twelve patients (40%) achieved an "optimal" outcome at 1-year on the Frankel scale and 13 (43.33%) achieved this on the McCormick scale.

On univariate analysis, the most significant predictors of an "optimal" outcome on the Frankel scale were age ($p = 0.0062$) and preoperative Frankel ($p = 0.017$) and McCormick ($p = 0.0018$) scores. Patients who achieved an "optimal" outcome had a greater number of decompressed levels (5.30 ± 2.28) than those who did not (4.18 ± 1.10), although this relationship did not reach statistical significance ($p = 0.053$). Patients with a tumor in the cervical ($p = 0.0023$) and thoracic ($p = 0.0013$) regions were less likely to achieve an "optimal" outcome than patients with a tumor in the conus medullaris.

Furthermore, patients who underwent a CMR were more likely to achieve an "optimal" outcome than patients who had a subtotal or radical resection ($p = 0.081$); however, this association did not reach statistical significance. Sex ($p = 0.44$) was not an important predictor of postoperative Frankel outcomes. Compared with myxopapillary ependymomas, patients with WHO Grade II ependymomas ($p = 0.0060$) and Grade I/II astrocytomas ($p = 0.013$) were less likely to achieve an "optimal" outcome on the Frankel scale. Additionally, as surgical techniques continue to advance, it is expected that patient outcomes will improve and that risks associated with resection will decrease [7].

Using the McCormick classification, age was a significant predictor of an "optimal" outcome ($p = 0.0045$). Tumor pathology was also significantly associated with outcomes: patients with myxopapillary ependymomas (WHO Grade I) were more likely to achieve an "optimal" outcome than patients with WHO Grade I/II astrocytomas ($p = 0.013$) and WHO Grade II classic ependymomas ($p = 0.027$). Patients with a tumor in the cervical ($p = 0.0079$) and thoracic ($p = 0.0013$) regions were less likely to achieve an "optimal" outcome than patients with a tumor in the conus medullaris. Sex ($p = 0.68$), number of levels decompressed ($p = 0.83$), extent of tumor resection ($p = 0.49$), and type of resection ($p = 0.22$) were not important predictors of McCormick scores. Furthermore, preoperative McCormick score ($p = 0.32$) and Frankel grade ($p = 0.44$) were not significantly associated with outcome. Wound infection, wound dehiscence, and CSF leaks were observed in some patients post-operatively.

Table-3: Post-operative outcome (Frankel/McCormick) of IMSCTs in relation to extent of resection

Extent of resection/ post op status	Improved		Static		Deteriorated	
	Frankel	McCormick	Frankel	McCormick	Frankel	McCormick
Complete (n=14)	6	6	7	7	1	1
Radical (n=9)	4	4	3	3	2	2
Subtotal (n=7)	2	3	2	2	3	2
Total	12	13	12	12	6	5

Table-4: Post-operative outcome of IMSCTs in relation to tumor histology

Histologic type of tumor	Improved		Static		Deteriorated	
	Frankel	McCormick	Frankel	McCormick	Frankel	McCormick
Ependymoma (n=10)	6	6	2	3	2	1
Mixopapillary ependymoma (n=8)	3	3	4	4	1	1
Astrocytoma (n=5)	1	2	2	1	2	2
Hemangioblastoma (n=2)	1	1	1	1	0	0
Ganglioglioma (n=1)	0	0	1	1	0	0
Epidermoid (n=1)	0	0	1	1	0	0
Mucinous cyst (n=1)	0	0	1	1	0	0
Meningioma (n=1)	1	1	0	0	0	0
Metastasis (n=1)	0	0	0	0	1	1
Total (n=30)	12	13	12	12	6	5

DISCUSSION

Resection of IMSCTs is the favored first-line approach for patients presenting with neurological impairment. Additionally, as surgical techniques continue to advance, it is expected that patient outcomes will improve and that risks associated with

resection will decrease [7]. The findings from this study provide strong support that tumor histology is the most important predictor of tumor progression. On univariate analysis, residual tumor was associated with a lower rate of progression-free survival; however, all patients who underwent RMR or STR had astrocytic tumors or tumors of malignant histology. By contrast, CMR and RMR were achieved in the majority of patients with WHO Grade II ependymomas, myxopapillary ependymomas, and hemangioblastomas. This finding suggests that the relationship between extent of tumor resection and progression is likely reflective of the underlying tumor pathology. This is consistent with a published single-center case series of 102 patients surgically treated for IMSCTs, which reported that histopathology predicts extent of resection as well as tumor recurrence [8]. Most ependymomas have a more defined surgical plane in contrast to astrocytomas, which have no surgical plane. The presence of a tumor resection plane alone has been shown to improve progression free survival, irrespective of tumor histology [9,10]. However, although postoperative residual tumor is an important predictor of progression, the aggressiveness of resection should be cautiously weighed against the risk of new postoperative neurological deficit [11]. Collectively, favorable histology combined with complete or radical resection favors long-term survival in patients with IMSCTs. Chandy et al in their study demonstrated a good outcome with radical excision, provided there is a good plane of cleavage [12]. Nair et al in their study demonstrated that, complete microsurgical resection of ependymomas shows good functional results in most hands, and a radical microsurgical resection can be achieved with long term stabilization of neurological deficits in majority of astrocytomas [13]. Sreedharala SS et al. in their study of 60 spinal cord tumors, demonstrated improved functional outcome (56%) in patients with infiltrative astrocytomas after safe margin microsurgical resection [14].

Regarding functional outcomes, results of present study demonstrates that preoperative functional status, tumor histology and age are the most important predictors of stable or improved outcomes as evaluated by Frankel and McCormick scores. Patients with WHO Grade II ependymomas and myxopapillary ependymomas largely have stable immediate postsurgical outcomes and stable or improved neurological status at 1 year follow-up. Results from a targeted case series of spinal cord ependymomas corroborate these findings [15]. The majority of patients with astrocytic tumors presented with no change or a decline in neurological status at 1 year follow-up. Previous studies of malignant IMSCTs have demonstrated that aggressive resection may preserve neurological function, particularly in astrocytomas; however, this may be associated with a significant risk of decline in postoperative motor function [10]. Additionally, 1 patient with hemangioblastomas in present study were previously diagnosed with a genetic predisposition syndrome such as VHL syndrome. The authors of a large case series involving neurosurgical resection of hemangioblastomas in patients with VHL syndrome reported that 78% of their patients remained functionally stable during a 15-year follow-up [16]. Long-term decline was usually associated with disease progression secondary to other associated lesions. Numerous studies in the literature have demonstrated significant benefits, in terms of survival and quality of life, when hemangioblastomas were resected in VHL patients [17,18].

Consistent with findings of present study, the importance of preoperative functional status in predicting postoperative functional outcomes, a clinical systematic review of the treatment of IMSCTs concluded that a patient's preoperative neurological status is the most important factor in determining long-term postoperative neurological and functional outcomes [19]. In particular, improved postoperative ambulatory ability is more likely in patients with good preoperative neurological status, classified as either normal ambulation or mild motor sensory deficit with independent ambulation not requiring external aid [20]. Short and long-term post-operative functional outcomes in patients with IMSCTs are likely multifactorial and additional systematic analyses are needed to further delineate the most clinically relevant and measureable predictors.

While most of these tumors are amenable to some extent of resection, the majority of them will require some form of adjuvant therapy, either radiation therapy or chemotherapy. Unfortunately, the efficacy and safety of radiation therapy and chemotherapy are not well agreed upon and are often not beneficial for these patients. Consequently, it is imperative that novel treatments be developed to help manage these devastating tumors. One interesting area of ongoing research in developing new treatments is nanomedicine and the ability to develop localizable, targeted therapies for these tumors. While there is a significant amount of work left to be done in this field, the early results achieved with cell targeting and the magnetic guidance of nanoparticles seem promising for the future applications of this technology. Electrophysiological monitoring, advanced microsurgical techniques; adjuvant therapies like Cyber knife, stereotactic frameless radiosurgery, improved drug delivery systems, and gene-based therapies improves overall outcome.

CONCLUSION

This study demonstrates that tumor pathology is the most important predictor of progression-free survival in patients treated surgically for IMSCTs. Long-term functional outcomes are expected to be most favorable in patients with ependymomas, and myxopapillary ependymomas; younger age, and good

preoperative functional status. Surgery represents the only established effective treatment modality for benign intramedullary neoplasms. Optimization of surgical outcome, therefore, is the most important treatment consideration. Aggressive initial management, appropriate judgment and technique, and adherence to strict microsurgical techniques are the most effective methods of avoiding complications and ensuring an optimal treatment outcome. Nearly all patients exhibit some degree of posterior column dysfunction following midline myelotomy for intramedullary glial tumor resection. Although this proprioceptive deficit may improve, it rarely fully recovers. With few exceptions, preoperative deficits do not improve following tumor resection. Thus, preservation of existing function is the primary surgical goal.

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