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SURGICAL TREATMENT OF PRIMARY INTRAMEDULLARY SPINAL CORD TUMORS IN ADULT PATIENTS

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Abstract – Background: Primary spinal cord intramedullary tumors are rare and present with insidious symptoms. Previous treatment protocols emphasized biopsy and radiation/chemotherapy but more aggressive protocols have emerged. **Objective:** To report our experience. **Method:** Forty-eight patients were diagnosed with primary intramedullary tumors. The cervical cord was involved in 27% and thoracic in 42% of patients. Complete microsurgical removal was attempted whenever possible without added neurological morbidity. **Results:** Complete resection was obtained in 33 (71%) patients. Neurological function remained stable or improved in 32 patients (66.7%). Ependymoma was the most frequent tumor (66.7%). **Conclusion:** Neurological outcome is superior in patients with subtle findings; aggressive microsurgical resection should be pursued with acceptable neurological outcomes.

KEY WORDS: spinal cord, spastic paraparesis, spinal cord neoplasms, ependymoma; microsurgery.

Tratamento cirúrgico de tumores intramedulares primários em adultos

Resumo – Introdução: Tumores intramedulares primários são raros e apresentam-se com sintomas insidiosos. Protocolos de tratamento anteriores enfatizavam biópsia e radio/quimioterapia, mas protocolos mais agressivos têm surgido. **Objetivo:** Relatar nossa experiência. **Método:** Tumores intramedulares foram diagnosticados em 48 pacientes. O segmento cervical estava envolvido em 27% e torácico em 42% dos pacientes. Remoção completa foi tentada quando possível sem aumento da morbidade neurológica. **Resultados:** Ressecção total foi obtida em 33 (71%) pacientes. Função neurológica: permaneceu inalterada/melhorou em 32 (66,7%) pacientes. O tumor mais freqüente foi ependimoma (66,7%). **Conclusão:** O prognóstico é melhor em pacientes oligossintomáticos; ressecção microcirúrgica agressiva deve ser tentada sempre, com resultados clínicos aceitáveis.

PALAVRAS-CHAVE: medula espinhal, paraparesia espástica, neoplasias da medula espinhal, microcirurgia.

Spinal cord primary intramedullary tumors are relatively rare and account for approximately 2% of all central nervous system tumors and one third of primary spinal tumors. The diverse cell types which may be typically found in the spinal cord are responsible for the similar variety of histological subtypes of intramedullary tumors. Astrocytes, oligodendrocytes, neurons, ependymal lining and blood vessels may all give rise to intramedullary tumors. The most frequent of these tumors are of glial origin, astrocytomas and ependymomas comprising the majority of them. These are slow-growing lesions that may involve several cord levels without exuberant symptoms arising. This behavior often leads to considering these tumors as "benign" when compared to intramedullary metastases which are usually aggressive and quickly induce severe neurological signs[1-4].

These growth characteristics are the main determinants of the usual clinical presentation of primary intramedullary tumors. These patients most frequently present with insidious, non-specific symptoms that often elude primary care physicians, neurologists and patients themselves into ignoring these complaints or attributing them to other factors. By the time evident neurological signs are present, neurological compromise is irreversible and these tumors have often grown to an extent that makes surgical resection morbid or impossible[5]. Since the first report of successful resection of a primary intramedullary tumor in 1907 by Van Eiselberg, only a few surgeons initially reported good outcomes[6]. Several treatment protocols involving biopsies, decompressive laminectomies and adjuvant treatments such as radiation therapy became the norm up to as far as the 1960s[3,6], when technological ad-

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vances significantly decreased surgical morbidity. The first few successful series pointed toward increased aggressiveness when dealing with these tumors[3,4]. Greenwood was one of these pioneering neurosurgeons and since his 1954 paper was an advocate of total resection of these tumors[7]. He was later joined by other accomplished surgeons such as Yasargil, Malis, Stein and De Sousa[8-10]. Even though they had shown improved results with the help of the surgical microscope and bipolar coagulation, diagnosis was frequently established late in the clinical course of this condition, a situation that would only improve in the mid-1980s with the advent of magnetic resonance imaging (MRI). The number of patient series in the 1990s subsequently increased but treatment protocols still varied significantly between neurosurgical centers. Even though the concept of total aggressive resection was increasingly becoming popular as shown by the good results of Brotchi, Nadkarni and Rekate and Jallo et al. among others[11-13], some centers still emphasized the role of adjuvant therapies and limited surgical intervention, arguing that neurological function should be preserved at all costs considering a clinical course that is frequently lenient[1,14-18]. Although considering the general trend toward a more aggressive surgical stance, a 'consensus' surgical orientation is far from being elaborated. The question of whether patients with only subtle clinical findings should be subjected to aggressive surgical procedures in particular is still open to debate.

The objective of this study is to present the clinical aspects and surgical results of a series of forty-eight patients treated in the city of São Paulo, Brazil according to the principles of aggressive total resection, especially trying to correlate preoperative neurological condition, the surgeons´ intraoperative impression concerning resection extent and functional recovery.

METHOD

Forty-eight adult patients were operated on at the Hospital das Clinicas da Faculdade de Medicina de São Paulo (39 patients) and the Hospital Alemão Oswaldo Cruz (9 patients), both located in São Paulo, Brazil, in the period between July 1992 and November 2005. Patient data are listed in Table 1; all subjects underwent full clinical investigation and MRI of the spinal cord segment in question before every surgical procedure. The most common presenting symptom was pain usually related to the affected cord segment (Table 1). All patients were grouped into the McCormick clinical classification for patients with spinal cord tumors[19]. Seven patients had already been submitted to some form of surgical procedure at another institution, usually biopsies and thus already had their histological diagnosis established but due to worsening clinical conditions were referred to our group.

All patients were operated on in the prone position following general anesthesia and antibiotic (first-generation cephalosporin) and 10 mg dexamethasone IV bolus. Patients with upper thoracic or cervical cord tumors had their heads immobilized in a three-point Mayfield-Kees device. Surgical technique emphasized a longitudinal skin incision, large enough to allow the exposure of normal cord above and below the level of the neoplastic lesion. Laminectomies were performed when one or two levels were operated; when three or more laminae had to be removed, a laminotomy was performed instead, in order to prevent future deformities. The dura was opened longitudinally and a median longitudinal myelotomy was usually employed; only in those cases with a distinctive lateral cord topography was a paramedian myelotomy performed. Our initial surgical goal was always aggressive, complete tumor removal. The tumor was resected in the caudal direction, en bloc whenever possible without added morbidity (Fig 1). When severe morbidity was anticipated based on intraoperative findings, a subtotal or partial tumor resection was conducted. Patients were usually discharged on the fourth postoperative day and followed indefinitely, including a new evaluation utilizing the McCormick scale at 6 months postoperatively.

Statistical analysis was performed with SPSS software (SPSS Inc., Chicago, IL, USA) with a significance level (p) of 0.05.

RESULTS

The most common presenting symptom was pain located to the dorsum in half (24) of our patients (Table 1). This complaint varied immensely in nature and intensity but was correctly related to the affected cord segment in most patients. Other subjective neurological complains such as paresthesia were the initial symptom in 35% (17 patients) while objective neurological signs including motor weakness were the first symptom in only a minority of our patients (7 patients – 15%). The 48 cases in our series included 20 (42%) thoracic, 13 (27%) cervical and 15 (31%) cervico-thoracic cord tumors. Ependymoma was the most frequent histological diagnosis obtained (32 patients – 66.7%), followed by cavernous angioma (7 patients – 14.6%), three astrocytomas (6.3%), two lipomas and one ganglioglioma and hemangioblastoma each (Table 2).

Complete microsurgical resection was possible in 34 patients (71%) while in the remaining 14 cases resection was deemed partial with evident tumor remains on the operative field due to concerns about added morbidity. Postoperative complications were present in 8 (16.7%) patients, as shown in Table 2. There were no intraoperative or immediate postoperative deaths. However, four patients died during follow-up (Fig 1) due to deep venous thrombosis and pulmonary embolism (2 patients), ventilator-associated pneumonia and respiratory failure following anaplastic astrocytoma progression after 4 years follow-up (one each). Both motor strength and sensation worsened in the first 24 hours following surgery in all patients, gradually improving in the first few days. All surviv-

Table 1. Patient's data.

Mean age	35.0
Age distribution	<25 y: 11 (23%) 25–40 y: 25 (52%) >40 y: 12 (25%)
Gender	Male: 29 (60%) Female: 19 (40%)
Presenting symptom	Back pain: 24 (50%) Paresthesias: 17 (35%) Motor weakness: 7 (15%)
Tumor location	Cervical: 13 (27%) Cervico-thoracic: 15 (31%) Thoracic: 20 (42%)
Preoperative McCormick grade	I: 14 (24%) II: 9 (19%) III: 10 (21%) IV: 15 (31%)

Table 2. Postoperative results and complications.

Histological subtype	Ependymoma 32 (66.7%) Cavernous angioma 7 (14.6%) Astrocytoma 3 (6.3%) Anaplastic astrocytoma 2 (4.2%) Lypoma 2 (4.2%) Hemangioblastoma 1 (2.1%) Ganglioglioma 1 (2.1%)
Extent of resection	Aggressive 34 (71%) Subtotal 14 (29%)
Complications	Death 4 (8.3%) Pneumonia 3 (6.3%) CSF fistula 2 (4.2%) UTI 2 (4.2%) Respiratory failure 1 (2.1%) Facial burn 1 (2.1%)

ing patients have been followed for at least six months, including four patients for more than 13 years. Late postoperative evaluation (>6 months) of the surviving patients has shown that 19 of them had improved McCormick scores compared to their preoperative status (39.6%) and another 13 (27.1%) had maintained the same score while the remaining 12 patients (25%) were clinically worse than before the surgical procedure. When stratified according to preoperative neurological function, a statistically significant trend of clinical improvement after surgery was evident in patients with McCormick I and II scores (Fig 2). Eighteen out of 23 patients with McCormick scores I and II were neurologically stable or better postoperatively; even patients with only discrete symptoms (Group I) clearly benefited from the surgical procedure. On the other hand, clinical worsening could be expected from grade III patients; none of them improved while only 2 out of 10 maintained preoperative function. Those patients with severe lifestyle restrictions preoperatively (grade IV) remained largely stable but a small subset of them (five patients) exhibited some degree of improvement. Deaths were present only in class III and IV patients.

It is also noteworthy that only 5 of the 13 patients which underwent partial resection eventually worsened and exhibited a decreasing McCormick score during the first two years of follow-up. These five patients were thus submitted to a second-stage procedure and in three of these patients total aggressive resection was obtained this time. Another three patients died but the surviving five patients maintained stable neurological conditions and thus chose not to undergo another resection. All surviving 44 patients underwent postoperative imaging control with MR in the first six months. Out of the 33 surviving patients that underwent complete resection, MRI demonstrated remaining neoplastic tissue in only three (9.1%).

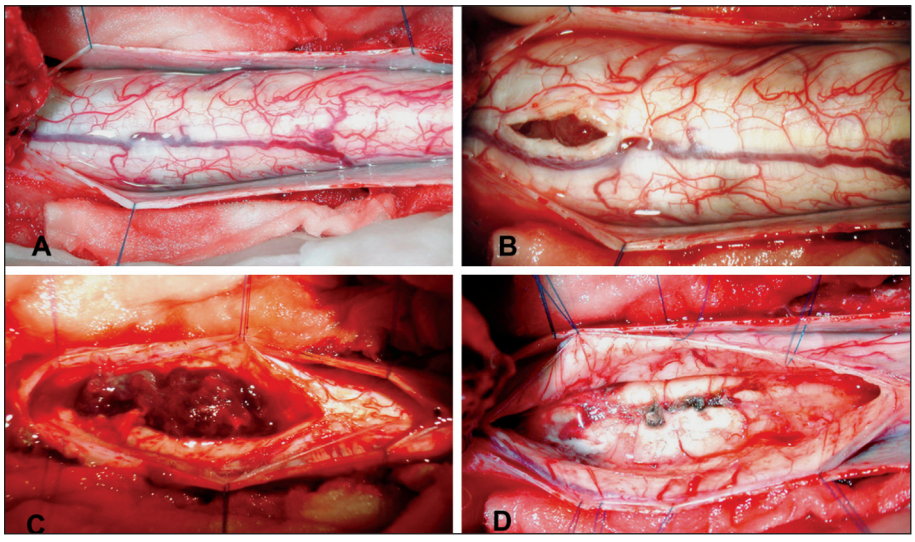

Fig 1. Intraoperative view on the surgical microscope. (A) Enlarged cervical cord segment without any signs of neoplastic tissue on the surface. (B) Beginning of the myelotomy, neoplastic tissue now evident. (C) Aiming at en bloc resection, the entire tumor has been exposed. (D) Surgical result. After initial deterioration, late postoperative McCormick score improved from II to I. Histological diagnosis was ependymoma.

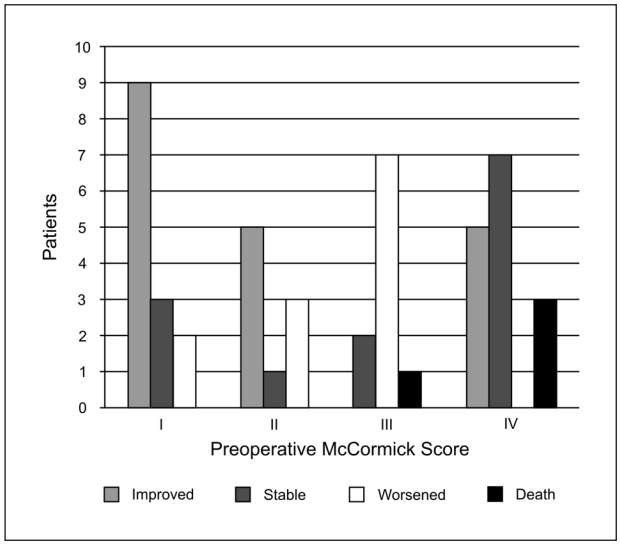

Fig 2. Postoperative neurological evolution according to preoperative McCormick score. Pearson chi-square p=0.001 for I, II and IV scores versus III score.

Comparatively, 2 of the 11 surviving patients of the partial resection group did not exhibit any signs on MRI of remaining neoplastic tissue, thus largely confirming the surgeon´s impression on the operative microscope (chi-square test, $p<0.001$).

DISCUSSION

Our series comprises 48 patients with spinal cord primary intramedullary tumors. Demographic data of our series are compatible with those of other authors: predominantly young patients (75% under 40 years of age) with slightly male preponderance but differences start when analyzing presenting symptoms. Similarly to most recent patient series, the most common presenting feature was pain usually but not always related to the affected segment. On the other hand, only a minority of our patients exhibited evident clinical signs of motor compromise at presentation. This is considered logical due to the slowly progressing nature of primary intramedullary tumors, in contrast to the rapidly advancing clinical picture of intramedullary metastases[5,13,20,21]. This non-specific clinical picture emphasizes the need for aggressive imaging investigation, further stressed by the improved prognosis if the patient still possesses a good preoperative McCormick score. Earlier authors of the pre-MRI era were thus frequently in an uncomfortable situation. The most useful investigation tool at the time was myelography, an invasive and uncomfortable procedure, often yielding insatisfactory results and almost always incapable of distinguishing intramedullary from extramedullary tumors. Their patients were frequently diagnosed with cord tumors late in their clinical course and this fact should be at least partially responsible for many of the poor results of early treatment protocols for intramedullary tumors. Furthermore these authors insisted on relatively lenient surgical actions, often limiting themselves to biopsies or partial resections, sometimes including adjuvant radiotherapy. Poppen, for instance, relied on decompressive laminectomy and radiation therapy only while Woods and Pimenta advocated partial resections and demonstrated prolonged survival for an interesting portion of their patients[3,6].

Apart from improved diagnostic tools, another two important technological advances must be held responsible for these improved surgical results, namely the operating microscope and accurate bipolar coagulation. From the 1960s onward, the first patient series with complete microsurgical removal of intramedullary tumors while maintaining satisfactory postoperative function appeared. Important literature contributions such as those by Garrido and Stein, Malis and Stein gradually led to complete tumor removal becoming standard practice and later even eliminating the need for adjuvant therapies[9,10,22]. The modern surgical technique is still based on the principles laid by those pioneering neurosurgeons with few variations. Our group employs a wide laminoplasty reaching at least one level above and below the tumor, even though this procedure was originally intended to be employed in young patients to avoid future deformities. It is our firm belief that it is not more time consuming than a standard laminectomy and greatly facilitates surgical exposure should the patient need to be reoperated on. Aggressive total resection is the surgical aim but this should not be pursued at all costs. In this series, neither ultrasonic aspiration nor physiological monitoring were available. Some surgeons have shown these instruments to be helpful but not indispensable for a successful outcome. Our results show that aggressive total resection goal may be safely reached in the absolute majority of our cases.

This series also included an unusually important number of cavernous angiomas, which was more frequent than astrocytomas, in contrast to what is usually found in the literature[10,23]. Apart from this fact, the surgeons´ impression regarding complete resection correlated favorably with postoperative MRI. In only five of the 44 patients who underwent postoperative investigation these two criteria did not exactly correlate, which is the first time that the concept of aggressive resection of these tumors is corroborated by objective imaging findings and further statistical analysis. Immediate postoperative neurological deterioration was observed in all cases but those patients who seek treatment early in their clinical course frequently reach their preoperative activity level or even improve beyond that. The immense value of rehabilitation cannot be overestimated in this situation; only the group

with severe but not complete neurological compromise exhibited a worse functional outcome. Finally, adjuvant chemo- and radiotherapy are reserved for the few patients whose tumor histology was shown on examination to be particularly aggressive, in this series being indicated only for the two patients with anaplastic astrocytomas.

Our results largely corroborate those previously found in the literature but provide new evidences to finally engrave the concept of aggressive resection of primary intramedullary tumors especially in patients with subtle neurological complaints. In fact, this subgroup may be the most benefited by early surgical intervention. The treatment of this complex problem has certainly come a long way; the results of this study demonstrate the validity of the modifications gradually introduced while the correlation of intraoperative surgical impression with postoperative imaging and the demonstration of significant functional recovery after surgery are the two main new arguments supplied by this study to help support this concept. Several points still need to be reassessed and there certainly is room for improvement. Even more aggressive imaging investigation of subtle clinical findings, enhanced intraoperative electrophysiological monitoring and increased understanding of the molecular biology of these tumors will certainly spearhead research on this subject into this century and ultimately lead to improved treatment of these patients.

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