GLIAL INTRAMEDULLARY TUMORS - AN INSTITUTIONAL EXPERIENCE OF 16 YEARS

Submitted for MCh Neurosurgery

By

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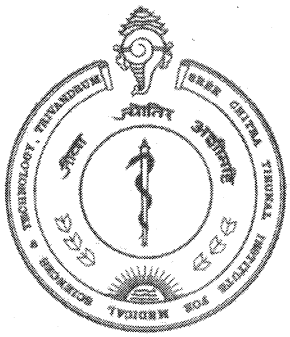

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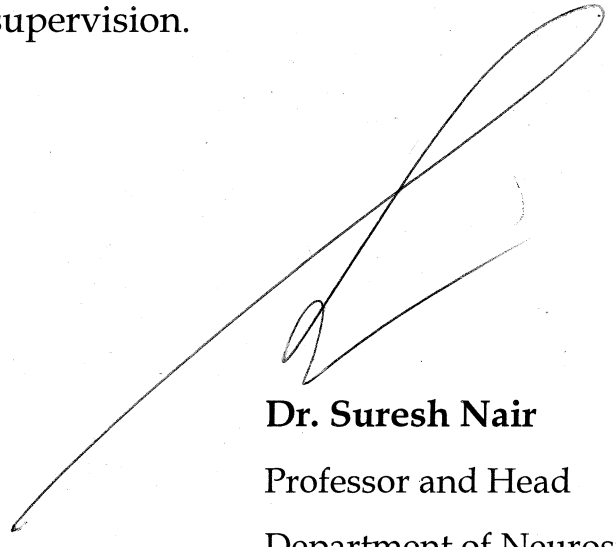
CERTIFICATE

This is to certify that the thesis entitled "**Glial Intramedullary Tumors - An Institutional Experience Of 16 Years**" is a bonafide work of Dr. Nilesh Jain and was conducted in the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram under my guidance and supervision.



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DECLARATION

This thesis titled "**Glial Intramedullary Tumors - An Institutional Experience Of 16 Years**" is a consolidated report based on a bonafide study done by me during January 2007 to September 2009 under the Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences & Technology, Thiruvananthapuram.

This thesis is submitted to SCTIMST in partial fulfillment of rules and regulations of MCh Neurosurgery examination.

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Dr. Nilesh Jain

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INTRODUCTION

Intramedullary spinal cord tumours are rare. Intramedullary spinal cord tumors (IMSCTs) comprise 5% to 6%% of all central nervous system (CNS) tumors and one third of primary spinal tumors[9].

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 . 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 [30,46,59].

Although similar tumor types exist in the brain, patients with spinal cord tumors tend to be younger and the spinal cord tumors do not seem to occur in connection with primary brain tumors. Spinal astrocytoma seems to occur in childhood or young adulthood , whereas ependymoma can occur throughout life but most commonly in the early to middle adult years.

Much less attention seem to be paid to spinal cord tumors because of their overall rarity. The long-term results depend on their varying natural histories

and the surgical approach. Historically, treatment of these tumors consisted of biopsy, bone decompression, and/or radiation therapy. This approach resulted in only moderate improvements in slowing disease progression. Modern advances in microsurgical technology have allowed for increasingly aggressive resection of these tumors , often permitting radical resection and resulting in increased long-term survival and improved quality of life [72].

The present study was undertaken to retrospectively analyze our institutional experience in the surgical management of glial intramedullary tumours. It was our aim to study the clinical & radiological features, the histological subtypes, operative findings including resectability, postoperative complications & procedure or disease related morbidity and mortality. The functional outcome of these patients was determined in relation to the tumour subtypes & the extent of resection.

REVIEW OF LITERATURE

Historical aspect:

Surgery for tumors within the spinal cord began nearly a century ago [3,19,20,]. In 1905, Cushing [3] undertook the first surgical decompression of an intramedullary tumor, and in 1907, Von Eiselberg and Ranzi [70] successfully removed an intramedullary neoplasm. Elsberg published extensively on spinal pathology & brought out three authoritive books on spinal cord surgery in 1916,1925, & 1941.These have stood the test of time & guided future development in the field[4]. However ,early attempts at removal of intramedullary spinal cord tumours were associated with prohibitive operative morbidity and mortality.[45] Surgery was primarily employed for diagnosis (frequently by visual inspection alone), cyst aspiration & duroplasty[45].For the next several decades , radiation therapy evolved as the major treatment modality for these tumours.

In 1954,Greenwoods utilization of bipolar cautery & loupe magnification enabled complete removal of nine intramedullary ependymomas.[26] Since then, advances in technology, pharmacology, and neurosurgical anesthesia have remarkably improved the prognosis, especially the functional outcome of surgery [25]. The two most innovative surgical techniques developed were the operating microscope and the Cavitron ultrasonic surgical aspirator (CUSA).

In 1970s & 1980s Epstein & colleagues at new York University challenged the previously conservative approach to spinal cord lesions by performing radical surgical resections of spinal cord lesion by using operating microscope,CUSA and intra operative ultrasound with acceptable morbidity[21].With better imaging with MRI and further refinement of microsurgical techniques,& the continued use of surgical adjuvants like CUSA, intra operative ultrasound & other image guidance techniques, electrophysiological monitoring & radical resection of well defined spinal neoplasms like ependymomas, hemangioblastomas , epidermoids & dermoid cyst have become possible with less complications.[45]. Howerever, the surgical treatment of intramedullary astrocytomas remains a much more controversial issue [5,21,22,]. Some authors reported that a radical resection of astrocytic tumors, because of their infiltrative nature, bore in general a higher morbidity; they thought that neuronal elements found in their histological specimens could possibly represent viable spinal cord tissue [6,]. There have been other reports of radically resected astrocytomas without increased morbidity despite registering neuronal inclusions in the resected material [21,72].

Epidemiology

Intramedullary tumors are rare tumors. Among intradural spinal tumors, intramedullary neoplasms account for only 8% to 10%. [53] The most common intramedullary lesions are spinal ependymoma (60%) and spinal astrocytoma (10%–20%), but others include hemangioblastoma (3%–8%), cavernous malformation, metastases, and lipoma [53].

As a rule, intramedullary tumors are more common in children and extramedullary tumors are more common in adults. Tumors of the spinal cord are much less frequent than intracranial tumors, with the overall prevalence approximating four intracranial lesions for every spinal tumor, which varies based on tumor type . For example , the intracranial/ spinal ratio of astrocytomas is approximately 10:1, whereas the intracranial/spinal ratio of ependymomas can range from 3:1 to 20:1 depending on the specific histologic variant.

Spinal tumors occur predominantly in young or middle-aged adults and are less common in childhood and old age. Although spinal tumors are more common in the thoracic region, when the actual length of the various portions of the spinal cord is taken into consideration, the distribution is relatively equal.

The histologic characteristics of different types of primary and secondary spinal tumors are, to a large extent, similar to those of intracranial

tumors. The leading primary tumors are gliomas, including astrocytomas and ependymomas. More than 80% of these tumors are glial in origin ,constituted by astrocytomas and ependymomas. Other rare tumours of glial lineage include are gangliogliomas, oligodendrogliomas & subependymomas. [6,21,22,41]. Vascular tumours like hemangioblastomas & cavernomas constitute 3% to 8 % of tumors while intradural metastasis comprises less than 5 % of the lesions.

Gliomas of the spinal cord have historically been one of the most challenging lesions of the central nervous system to treat. Surgery was once reserved exclusively for diagnosis, but it is now emerging as one of the most effective treatments for most of these tumors. Primary glial tumors of the spinal cord include astrocytomas , ependymomas, and gangliogliomas, which together comprise greater than 85% of all intramedullary tumors in pediatric and adult patients [46]. Astrocytomas of the spinal cord have a reported incidence of 0.8 to 2.5 per 100,000 per year [1]. These tumors can affect individuals of all ages, although rarely presenting before 2 years of age or after 60 years of age. Astrocytomas are the most common spinal cord tumors in children, and they are second only to ependymomas in adults. They are the most frequent histologic type of intramedullary spinal cord tumor encountered in the pediatric population, representing 59% of the lesions reported in a survey of the literature [46]. In adult series, the proportion of astrocytomas vary but is generally slightly less than that of ependymomas [24]. There is a slight male predominance in the occurrence of astrocytomas[24].

Genetics and molecular biology.

Much less attention seems to be paid to spinal cord tumors because of their overall rarity. Certain genetic syndromes are associated with IMSCTs and provide a special opportunity to study their genetics and molecular biology.

Historically, ependymoma and astrocytoma of the spinal cord have been little distinguished from their cerebral counterparts. More and more evidence suggests that distinct differences in genetics and molecular biology exist between primary tumors in the brain and spinal cord with similar histology .

Neurofibromatosis 1 & 2 are well known phakomatoses which are associated with protean CNS manifestations including intramedullary tumours in upto 19% of patients.Based on reports by Lee et al[43] & Yagi et al [75],it can be reasonably presumed that an intramedullary tumour occurring in a patient with NF-1 in most probably an astrocytoma, whereas that in NF-2 is an ependymoma.

Genetic mutations associated with spinal ependymoma:

Ependymomas are neuroectodermal tumors that occur in the brain and spinal cord. They are thought to arise from the ependymal lining of the ventricles and spinal canal. Most ependymomas are sporadic, but they are also associated with patients with neurofibromatosis.

Myxopapillary ependymoma has been shown to exhibit a much higher propensity for aneuploidy or polyploidy, especially of chromosome 7, compared with other ependymomas based on chromogenic in situ hybridization (CISH) . This unique genetic trait may explain its unique localization within the spinal cord. Monosomy of chromosome 22 is present approximately 30% of ependymomas with aberration and / or alteration of 22q involving both NF-2 & non NF2 genes in upto 40% of them. Overall ,75% of all ependymomas display chromosomal aberrations or rearrangements over several different chromosomes, with most frequent LOHs(Loss of Heterozygosity) being found on long arm of chromosomes 6,9,17,10, & 11.

Genetic mutations associated with spinal astrocytomas:

Spinal astrocytomas are glial neoplasms that are thought to arise from similar glial predecessors as primary brain gliomas. Astrocytoma of the spinal cord is usually always sporadic, and no associations with other genetic syndromes are currently recognized. There are few published studies specifically examining the genetic mutations in intramedullary astrocytomas.

Three general transitions have been studied as a paradigm for glioma progression: (1) astrocyte to astrocytoma, (2) astrocytoma to anaplastic astrocytoma, and (3) anaplastic astrocytoma to glioblastoma. In the first transition, mutations in p53 and losses of chromosome 17p and 22q have been implicated. Recently, Rubio and colleagues [47] have shown that the NF2 gene

was not mutated in 30 astrocytomas examined, making it an unlikely candidate for the 22q locus lost during this transition. In the progression from astrocytoma to anaplastic astrocytoma, genetic defects include retinoblastoma gene mutations, chromosome 13q loss, p16 gene deletions, chromosome 9p loss, and chromosome 19q loss [74]. The transition from anaplastic astrocytoma to glioblastoma has been shown to involve chromosome 10 loss and epidermal growth factor (EGF) receptor gene amplification [41].

Pathology

Understanding the significance of the histologic type and grade is critical in the diagnosis and treatment of spinal cord tumors. The histologic characteristics of different types of primary and secondary spinal tumors are, to a large extent, similar to those of intracranial tumors. The leading primary tumors are gliomas, including astrocytomas and ependymomas.

Astrocytomas:

Astrocytomas are a heterogeneous group of tumors that include two essentially distinct categories: the circumscribed astrocytomas, such as the pilocytic astrocytoma, and the infiltrating astrocytomas, such as the low-grade fibrillary astrocytoma. These tumors occur at any age but are most prevalent in the first three decades of life. The major tumor type in the circumscribed category is the pilocytic astrocytoma, whereas another tumor in the category, the pleomorphic xanthoastrocytoma, is extremely rare. The infiltrating

astrocytomas range from World Health Organization (WHO) grade II fibrillary astrocytoma to WHO grade III anaplastic astrocytoma and, finally, to the most malignant WHO grade IV glioblastoma multiforme. Unusual types of astrocytomas that are not readily classifiable can also occur in the spinal cord .

Approximately 3% of central nervous system (CNS) astrocytomas arise within the spinal cord[47]. Nearly 60% of spinal astrocytomas occur in the cervical and cervicothoracic segments. Astrocytic tumors are the most common pediatric intramedullary spinal cord neoplasms, comprising approximately 90% of such tumors in patients less than 10 years of age and approximately 60% of adolescent intramedullary neoplasms [37]. By approximately 30 years of age, ependymomas become slightly more common than astrocytomas and predominate in the latter decades of life [37,45]. After the sixth decade, the overall incidence of both intramedullary glial tumors drops significantly and both neoplasms are encountered with approximately equal frequency [51]. Pilocytic astrocytomas constitute most spinal astrocytic tumors in children and are associated with a particularly indolent natural history . The next most common lesion is the low-grade infiltrating astrocytoma, otherwise referred to as WHO grade II fibrillary astrocytoma .High-grade astrocytomas, anaplastic astrocytoma (WHO grade III), and glioblastoma multiforme (WHO grade IV) account for approximately 10% of intramedullary astrocytomas. These lesions are characterized by a rapidly progressing clinical course, high incidence of cerebrospinal fluid spread, and poor survival [51,60]. Infiltrating

astrocytomas of all grades are more common than pilocytic astrocytomas in adults. Other low grade lesions like pleomorpic xanthoastroctomas, ganglioglioma, and oligodendrogliomas are relatively rare[5,21,]

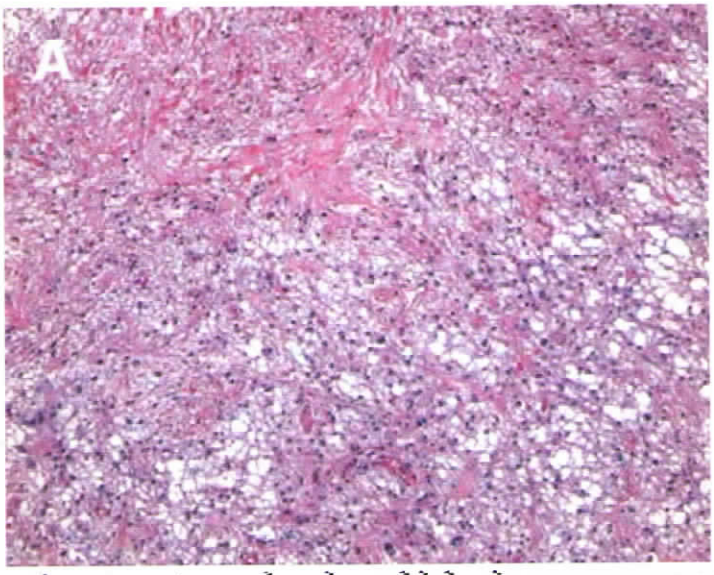


Fig 1: Pilocytic astrocytoma showing a biphasic appearance and scattered Rosenthal fibers .

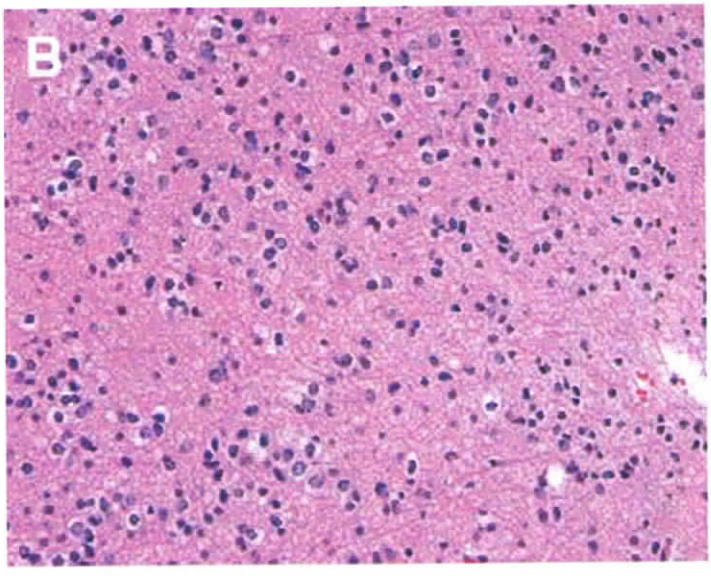


Fig 2 : Low grade (WHO grade II) infiltrating astrocytoma with moderate nuclear pleomorphism. More aggressive histologic features, such as mitotic figures, vascular proliferation, or necrosis, are absent .

Ependymomas

Ependymomas are the most common intramedullary tumor in adults. They occur throughout life but are most common in the middle adult years. Although the spinal cord and filum terminale account for only 3% of the CNS by weight, nearly half of all adult CNS ependymomas originate within the spinal canal. The cervical region is the most common level of true intramedullary occurrence; however, 40% of intradural ependymomas arise from the filum[37].

Most of the ependymal tumors arising in the filum are myxopapillary ependymomas. For anatomic and surgical reasons, these lesions are generally considered to be extramedullary tumors.

Ependymomas are thought to arise from ependymal lining of central canal & thus enlarge the spinal cord symmetrically from within,first causing symptoms referable to spinothalamic tract dysfunction[45,].

A variety of histologic ependymoma subtypes may be encountered. The classic cellular ependymoma is the most common and is considered a WHO grade II neoplasm . Most spinal cord ependymomas have a more indolent course compared with those in the posterior fossa or supratentorial region. The critical histologic features associated with a more aggressive clinical course are increased rate of mitotic figures and bona fide vascular proliferation within the tumor. Similar to their intracranial counterparts, ependymomas harboring these

two features are considered as anaplastic neoplasms (WHO grade III ependymoma). The presence of necrosis and intratumoral hemorrhage is frequent and is often related to factors unrelated to biologic aggressiveness [57]. Most ependymomas are rather well circumscribed and may present a relatively clear surgical plane for resection[8]. In a significant percentage, however, the tumor appears at least focally infiltrative and presents a surgical challenge.

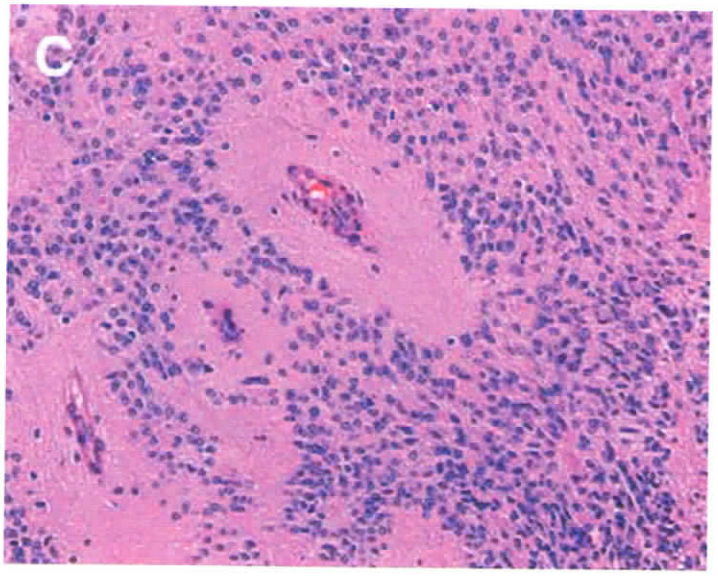


Fig 3: Typical perivascular pseudorosettes of classic (WHO grade II) ependymoma from spinal cord

Subependymoma:

Intramedullary subependymomas are extremely rare entities, with approximately 40 cases reported in the literature [64]. A review of reported cases revealed a mean age of diagnosis in the fifth decade, a 2:1 male/female preference, and fairly equal distribution along the spinal axis. Because

intramedullary subependymomas lack imaging features distinctive from the more common glial neoplasms, diagnosis is based on pathologic findings.

Subependymomas have a paucicellular appearance with striking glial differentiation and abundant cellular processes that make up the nodular architecture. Subependymomas typically do not exhibit perivascular pseudorosettes or true ependymal rosettes, which helps to distinguish them from ependymomas.

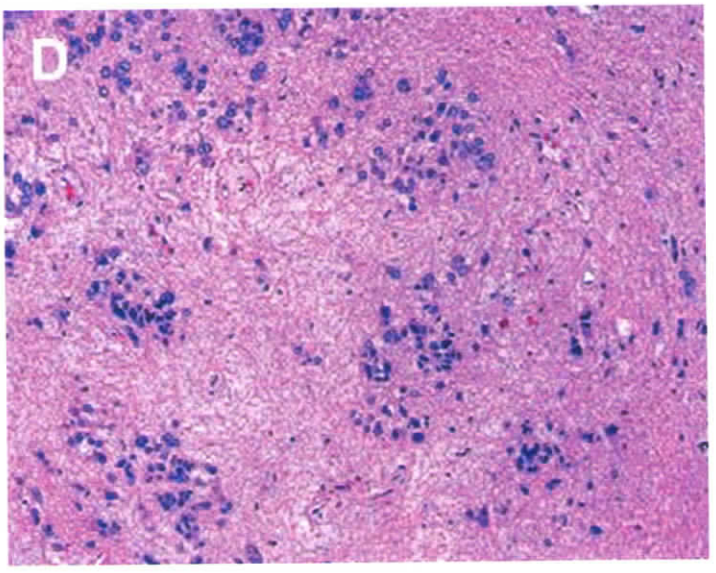


Fig 4 : Paucicellular appearance of a subependymoma with markedly fibrillary background .

Ganglioglioma :

Intramedullary gangliogliomas are extremely rare entities, with a reported occurrence of approximately 1% of all spinal cord tumors [32,48,54]. They occur predominantly in children and young adults, with a mean age of 12 years [55]. In a review of 27 reported cases by Patel and colleagues [55],

gangliogliomas were found to extend over more vertebral segments than astrocytomas or ependymomas (8 to 4 segments). 40% of lesions were localized to the cervical cord, 22% to the thoracic cord, 15% to the conus and/or filum, and holocord involvement was found in 15%.

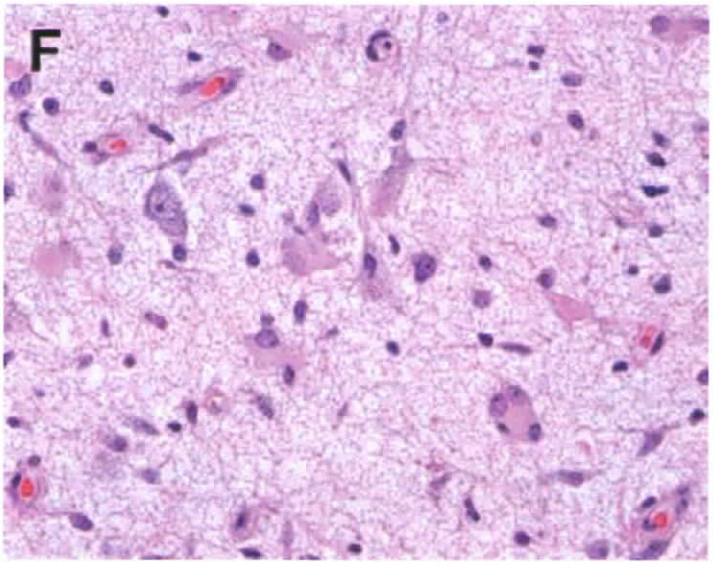


Fig 5 : Atypical binucleated neuronal cells and scattered abnormal glial cells in a typical ganglioglioma

Radiology:

The advent of MRI revolutionized the characterization of intramedullary spinal cord lesions. By providing detailed resolution of the spinal cord in multiple planes, MRI has become a key tool for the differentiation of operative tumors from nonoperative lesions, such as multiple sclerosis (MS) plaques, transverse myelitis, or cord infarction.Within the tumor subpopulation, MRI has allowed for detailed preoperative planning through understanding the

precise limits of the tumor and surrounding edema, the presence of cysts, or evidence of preexisting hemorrhage.

Ependymoma

Intramedullary ependymomas are almost always centrally located [23]. MRI typically reveals enlargement of the cord centered around the lesion on T1-weighted images. Approximately 65% of lesions are associated with syringomyelia, because most arise in the cervicothoracic region [61]. Rostrally and caudally located cysts are present with great frequency, although they are not specific. Most lesions span multiple vertebral segments [42]. The central location results from the believed origin of ependymomas from the ependymal cells that line the central canal [63]. Ependymomas are frequently associated with hemorrhage, revealed as hemosiderin on T2 and gradient-recalled echo (GRE) sequences [42].

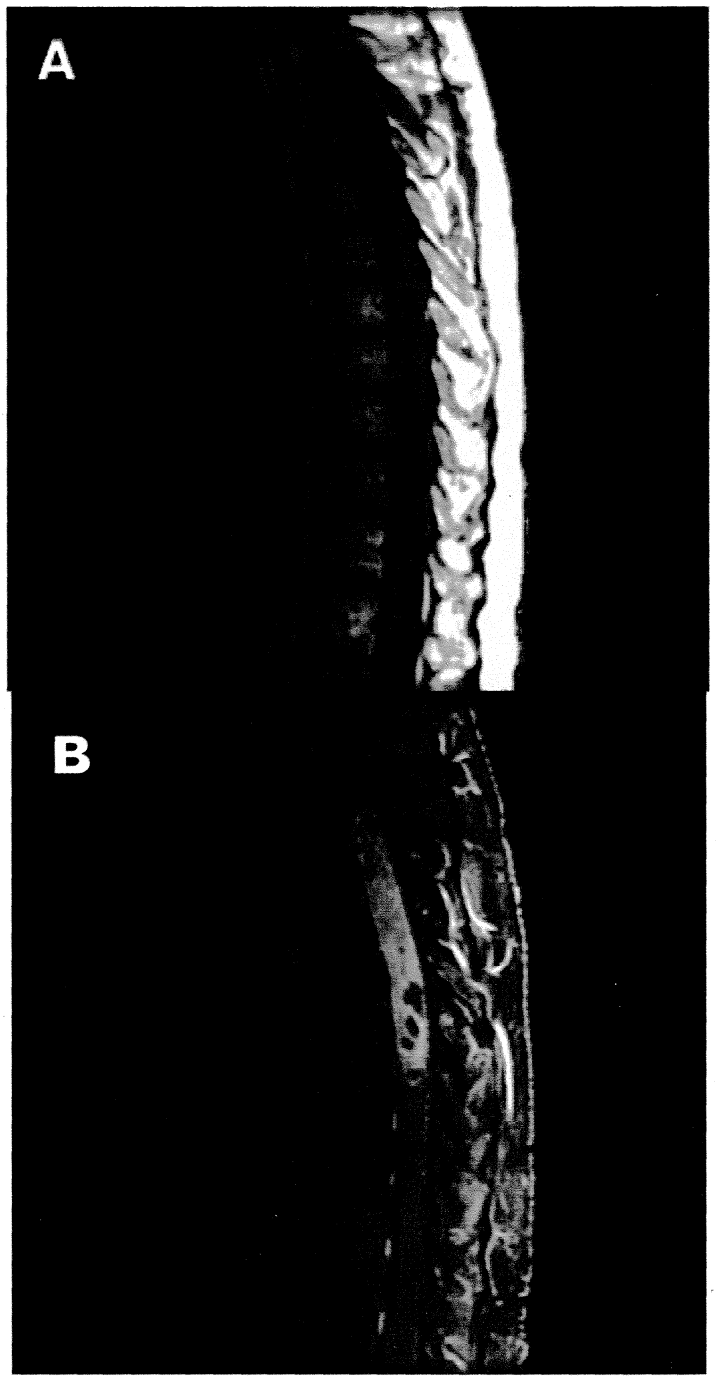


Fig. 6 Ependymoma. Precontrast sagittal T1-weighted (A), and post contrast sagittal T1- weighted (B) images of the thoracic spine demonstrate a large, expansile, heterogeneous intramedullary mass involving multiple vertebral body levels. (B) The mass shows avid enhancement after the intravenous administration of gadolinium contrast agent, with a few areas of cystic degeneration.

Astrocytoma

Several imaging characteristics may suggest the presence of an astrocytoma over an ependymoma. In most cases, astrocytomas are eccentric in location and, unlike ependymomas, are frequently infiltrative, presenting with ill-defined borders. Most lesions present with a cervical location; a series of 17 astrocytomas revealed 11 cervical, 2 cervicothoracic, and 4 thoracic lesions [39]. Rostral and/or caudal cysts are less frequently associated with astrocytomas than with ependymomas, although this is not significant enough to assist with diagnosis [9]. Consistent with most intramedullary spinal cord tumors, astrocytomas are hypointense to isointense on T1-weighted images and hyperintense on T2-weighted images .

Astrocytoma borders are less distinct than ependymomas, reflecting their invasive nature. Correspondingly, T1 postgadolinium sequences reveal less well-defined patchy borders [31].

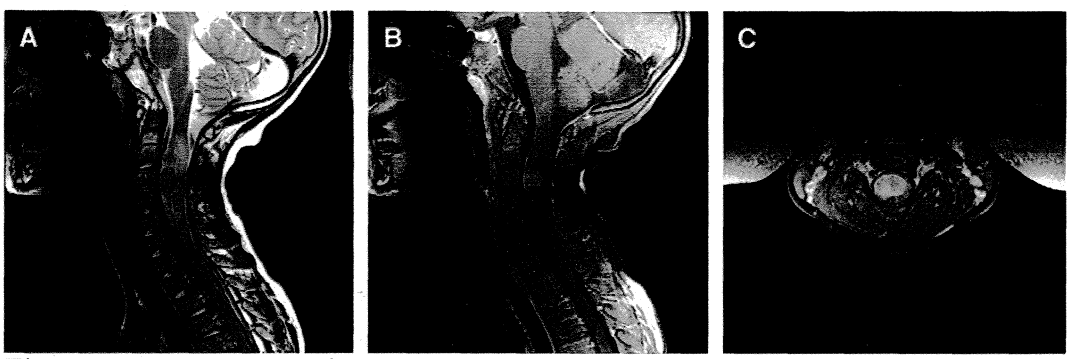


Fig. 7. Astrocytoma. Sagittal T2-weighted (A), post contrast sagittal T2- weighted (B), and post contrast saggital T1-weighted images (C) images of the cervical spine demonstrate a ventral intramedullary mass centered at the C3 vertebral body level. There is a moderate amount of tumor-related edema, which extends superiorly to the level of the medulla and inferiorly to the C6 level as seen on sagittal T2-weighted images. The mass demonstrates homogeneous enhancement.

Given the enhancement of most intramedullary astrocytomas, unlike the case with intracranial lesions, tumor grade is not evident on imaging. Less than 2% are pathologically diagnosed as oligodendroglioma [46].

Ganglioglioma

Patel et al reported these tumors are mostly eccentrically located. Tumoral and polar reactive cysts were common. Forty-six percent of intramedullary gangliogliomas demonstrated tumoral cysts, a result the authors found to be statistically significant when compared with ependymomas and astrocytomas [55]. T1- weighted images of gangliogliomas revealed a mixed pattern of hyperintensity and hypointensity in 82% of cases .

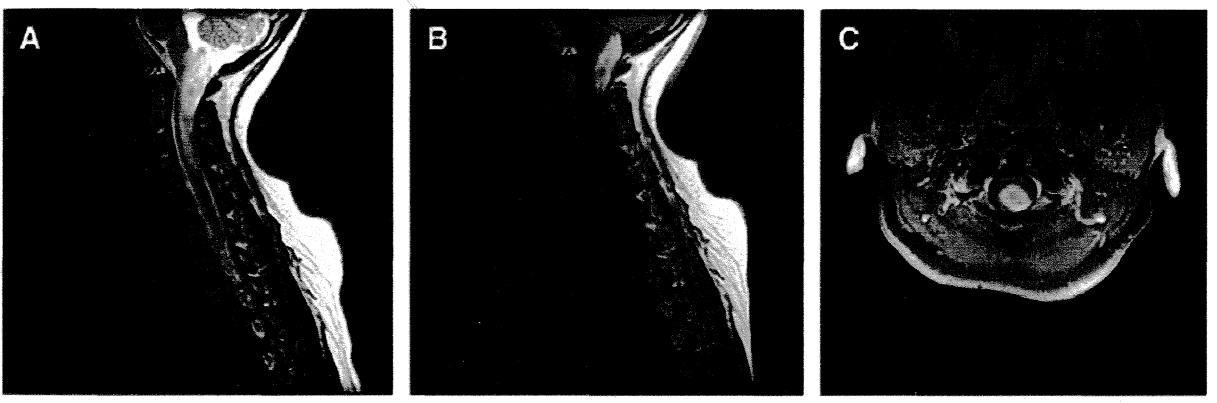


Fig. 8. Ganglioglioma. Sagittal T2-weighted (A), post contrast sagittal T2-weighted (B), and post contrast saggital T1-weighted images (C) images of the cervical spine demonstrate a dorsal intramedullary mass centered at the level of the cervicomedullary junction. The mass enhances avidly but heterogeneously. There is tumor-related edema that extends inferiorly to the C4 level as seen on T2-weighted imaging.

This pattern of mixed signal intensity is distinct from the pattern noted for astrocytomas or ependymomas. T2-weighted images revealed hyperintense signal in all cases; however, gangliogliomas were significantly distinct in the absence of peritumoral edema. Contrast-enhanced T1-weighted images revealed patchy enhancement in 65% of cases and none in 15%.

Subependymoma

Intramedullary subependymomas are extremely rare entities, with approximately 40 cases reported in the literature [64]. MRI findings of subependymoma are hypointensity on T1-weighted images, hyperintensity on T2-weighted images, and contrast enhancement in a homogeneous or nodular pattern [64,65]. Because intramedullary subependymomas lack imaging features distinctive from the more common glial neoplasms, diagnosis is based on pathologic findings.

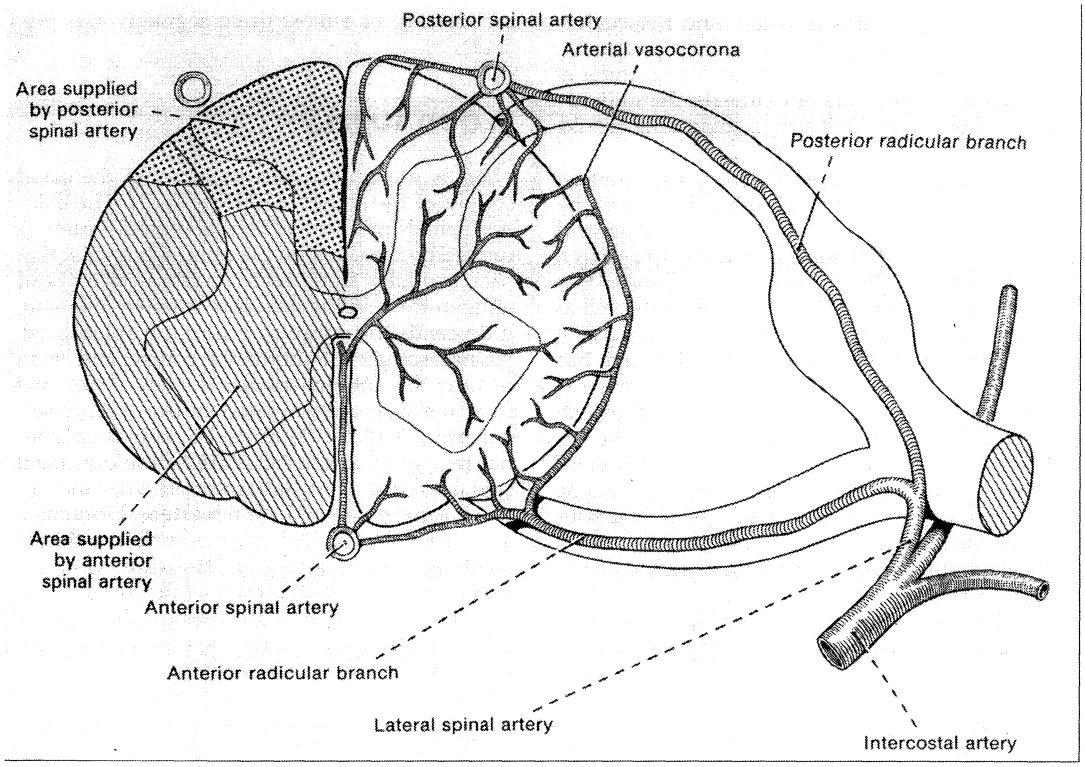
Spinal Cord Anatomy

The spinal cord averages 47cm in length and 32g in weight accounting for about 3% of central nervous system. Spinal cord generally occupies less than one-half of the cross sectional area of the spinal canal. It is divided almost into two halves by the anterior median fissure and the posterior median septum. This fissure contains the anterior spinal artery and vein and their penetrating branches and is rarely encountered during surgery. The posterior median

septum is composed of fused pia matter from the medial surface of each posterior column. It is the route of entry for removal of most intramedullary pathology and can be identified by a longitudinal array of penetrating vessels.

The blood supply to the spinal cord is by way of a single anterior and paired posterior spinal arteries. These vessels are supplemented throughout their course by a variable number of medullary vessels which are well protected on the ventral surface of their respective nerve roots. The intra dural spinal vascular system is well protected and not threatened during intradural surgery.

The spinal dura extends as an oval tube from the foramen magnum to the S2 level. It is a tough fibrous membrane composed of longitudinal bundles of collagen and lined one either side by a single layer of flattened fibroblasts. It demonstrates negligible resistance to compression, but has considerable tensile strength. It is under resting tension and possesses elastic properties that allow for folding and unfolding in response to changes in canal length. Spinal dura is an effective barrier and is rarely transgressed by inflammatory or neoplastic pathology.



The pia and arachnoid (leptomeninges) are probably neural crest and mesodermal in origin. Arachnoid is a thin transparent membrane which is closely applied to the dura allowing only a potential subdural space. Fenestrated reflections of arachnoid occur through out the subarachnoid space to become continuous with the outer pia. The spinal vasculature is loosely held to the surface of the spinal cord within this layer. The arachnoid reflections also sheath the individual nerve roots. Spinal pia is a well defined collagenous membrane and is thicker than the intracranial pia and it accounts for the white colour and firm consistency of the spinal cord. Lateral reflections of the pia form the dentate ligaments. The pia matter is tightly applied to the outer glial limiting membrane of the spinal cord and completely encircles the cord except at the root entry zones where it is briefly reflected over the exiting nerve roots. It is here that the pia may be transgressed by benign pathology. Benign

intramedullary tumours such as ependymoma or astrocytoma may rarely present with an exophytic tumour component which exits the spinal cord through the root entry zone. Centripetal growth of a benign nerve sheath tumour may elevate the pia to become partially subpial in location. In these cases, excision of a segment of pia will be required to affect complete removal.

Clinical Features :

The clinical features of intramedullary lesions are variable . Most tumors are benign and slow growing. This often results in prolonged symptom duration before establishment of the diagnosis (2–3 years). Malignant lesions present with a much shorter course. Intratumoral hemorrhage in this latter group produces an ictal event and a precipitous presentation. The examination may reveal a combination of upper and lower motor neuron signs. The lower motor signs may be at the level of the lesion and may aid in localization .[66]

In the adult population, pain is the most common presenting symptom. It occurs in 60% to 70% of patients[45]. Pain is less common as a presenting symptom in the pediatric population. Motor and gait disturbances predominate in this age group. The pain is usually funicular type ,poorly described, of variable intensity, localized to the general level of the lesion, rarely radicular, infrequently affected by activity or Valsalva maneuvers, and often described as a localized ache or muscle spasm. It may worsen at night or with recumbency [45].

In the case of an intramedullary tumor, a so-called ''dissociated'' sensory loss is common. In these cases, there is loss of sensitivity to pain and temperature below the segmental spinal level of the tumor but preserved sensitivity to light touch. Sensory or motor complaints are the initial symptom in approximately one third of patients. Unilateral or asymmetric involvement is typical. Numbness is a common complaint and typically begins distally in the legs, with proximal progression. Urinary frequency is usual complaint, and gait difficulties are common and related to spasticity as well as to sensory dysfunction. Children can present with some motor deficits. These deficits can initially be seen as clumsiness, weakness, or frequent falls. In young infants, this may manifest as motor regression, such as a refusal to stand or crawl after having learned to walk. Complaints of sensory dysfunction are quite uncommon in children[40]. Tumors of the middle and lower cervical regions produce a suspended cape-like sensory loss with pain involving the upper extremities, most often the shoulders or fingers.

A Horner syndrome may be unilateral or bilateral, depending on the degree of involvement of the sympathetic system. Involvement of the upper thoracic region produces pain in a girdle-type distribution. This is occasionally mistaken for angina pectoris, myocardial infarction, or pleurisy. Lesions in the middle and lower thoracic regions may evoke pain that may erroneously suggest an abdominal lesion.

Patients with tumors of the lumbar enlargement and conus medullaris often present with a history of back pain and leg pain, which may be radicular in origin. Urogenital and anorectal dysfunction are common. These symptoms may be mistakenly attributed to herniated nucleus pulposus or spondylosis. (45,67)

Intramedullary tumors in children may be associated with orthopedic deformities (kyphoscoliosis) and extremity weakness. Gait abnormalities or deformities of the feet, such as talipes equinovarus or pes cavus, may be observed in the young child. Enuresis in the previously toilet-trained child is another symptom of caudal tumor involvement. A sinus tract or a hairy or pigmented cutaneous lesion suggests the diagnosis of teratoma, epidermoid lesion, or dermoid lesion. (16)

Spinal Cord Ependymoma: Presentation, Management, and Outcome

Clinical features.

Usually these patients typically complain of dysesthesia correlating to the level of the tumor for months to years before diagnosis. Other presenting symptoms include paresthesia, radicular pain, bowel and bladder dysfunction, and other sensory disturbances (10,11,33). Decline in neurologic symptoms may occur after intratumoral hemorrhage (45). Motor impairment usually only occurs late in the disease progression as the expanding tumor thins the surrounding spinal cord to a few millimeters (18). This differs from intramedullary

astrocytomas, which tend to present with neuraxis pain and progressive motor dysfunction over a shorter time course [18].

Surgical objectives

The goals of surgery for intramedullary ependymoma are gross total resection and preservation of neurologic function [10,18,45,47,6,7,69]. Gross total resection is usually sufficient to achieve long-term tumor control or cure in these low-grade lesions [10]. The most important factor in achieving the surgical objective is the plane between the tumor and the spinal cord. This interface can only be accurately assessed through an adequate myelotomy that extends over the entire rostral caudal extent of the tumor . Although the presence of a syrinx may improve the chances of a gross total resection by facilitating surgical manipulation of the tumor, it cannot be used as an independent predictor of outcome [10,56,61,].

Ependymomas, although unencapsulated, are non infiltrative lesions that typically cause compression of the adjacent cord parenchyma and display a distinct plane . Gross total removal is the treatment of choice in these cases for optimum disease control [6,7,10,18,45,,47,69].

An intraoperative biopsy can be useful in certain circumstances but should not be used as the sole criterion dictating the surgical objective.

(1) Interpretation of tiny biopsy fragments often is inaccurate or nondiagnostic and may consist of only peritumoral gliosis, which may be erroneously interpreted as an infiltrating astrocytoma [33].

(2) It is difficult if not impossible to assess the nature of the tumor/spinal cord interface accurately through a tiny myelotomy [33].

(3) Biopsy results, however, may be particularly helpful in some circumstances; for example, identification of a histologically malignant tumor independently signals an end to the procedure, because surgery is of no benefit for malignant intramedullary neoplasms [5,6,68,]. In other cases in which the tumor/ spinal cord interface may not be apparent, confident histologic identification of an ependymoma reassures the surgeon that a plane must exist and that surgical removal should continue.

Adjuvant therapy

For intramedullary ependymomas, long-term outcome and risk of recurrence are dependent primarily on the extent of initial tumor resection. Gross total resection of benign intramedullary ependymomas provides better long-term tumor control or cure compared with subtotal resection and radiation therapy [7,18,34,35,45].

Most authors agree that radiation therapy is unnecessary after gross total resection [6,12,18,45,61]. Although many authors report a 100% recurrence- free survival after gross total resection [27,45], other authors report a 5% to 10% recurrence rate [6,10,27,35]. Ependymomas are slow growing tumors, and late recurrence can occur, even up to 12 years after surgery [27]. Subtotal resection, conversely, has a high recurrence rate [10].

Even 99% removal can lead to tumor recurrence in up to 30% of patients in spite of postoperative radiation therapy, whereas subtotal resection can lead to significant recurrence in up to 50% to 70% of patients [6,44].

In the event of tumor recurrence, reoperation and another attempt at gross total resection should be considered [6,13,33]. Reports of 5- and 10-year recurrence- free survival, however, vary widely from 60% to 100% with fractionated external beam doses of greater than 40 Gy (83,85). Craniospinal radiation is only indicated for the rare patient who presents with multifocal disease [29,35,44]. Although the outcome is worse for this subgroup, good control rates have been reported [28,44]. Patients who present with focal disease usually have local recurrence and do not manifest late dissemination [13,14].

Salvage chemotherapy in patients who fail surgery and radiotherapy is largely unexplored. A pilot study using etoposide, a topoisomerase II inhibitor, to treat recurrent intramedullary ependymomas resulted in 3 patients with progressive disease, 2 patients with a partial response, and 5 patients with

stable disease. Overall, the median disease-free progression was 15 months and the overall median survival was 17.5 months. This drug seemed to be well tolerated, with modest toxicity [13,14]. Further trials are needed to determine the efficacy of this potential therapy for recurrent and refractory intramedullary ependymomas.

Functional outcome(ependymoma)

Most surgical series indicate that the strongest predictor of postoperative functional outcome is preoperative functional ability [6,7,10,34,45,61]. Significant improvement of a severe or long-standing preoperative neurologic deficit rarely occurs, even after technically successful surgical excision [10]. Surgical morbidity is also greater in patients with more significant preoperative deficits. The ratio of the tumor width to the largest cord width at the tumor site is also associated with pre- and postoperative neurologic grade [56].

In general, most patients note sensory loss in the early postoperative period, most likely as a result of the midline myelotomy, transient edema, or vascular compromise [18,47]. These complaints are more subjective than objective in nature and can be significant even with little or no objective deficit. These deficits usually resolve within 3 months [34,56], although they may not return to their preoperative baseline [47].

Additional surgical morbidity is directly related to the patient's preoperative status, the location of the tumor, and the presence of spinal cord

atrophy and arachnoid scarring [34,61]. Patients with significant or long-standing deficit rarely demonstrate any significant recovery and are more likely to worsen after surgery. A shorter duration of preoperative symptoms, however, may favor improvement even in patients with a significant preoperative deficit [34]. Thoracic location has also been correlated with a decline in postoperative function [33,34], perhaps because of a more tenuous blood supply in this region. Appreciation of spinal cord atrophy and arachnoid scarring may indicate chronic spinal cord compression and predict poor functional outcome [34,61]. Preservation rather than restoration of neurologic function is the reasonable expectation for intramedullary tumor surgery. The greatest benefit and most minimal risk of surgery for intramedullary tumors are therefore derived in those patients who are only minimally symptomatic [6,18,33,45,47].

Spinal Cord Astrocytomas: Presentation, Management, and Outcome .

Gliomas of the spinal cord have historically been one of the most challenging lesions of the central nervous system to treat. The predominance of benign histopathologic subtypes translates into a usual indolent prodromal course. Patients generally report symptoms that have been present for months to years. As would be anticipated, the rarer high-grade astrocytomas demonstrate a more rapid symptom progression. The lack of a characteristic pattern of symptoms often leads to a delay in diagnosis. With the prevalence of MRI, these tumors are now being diagnosed earlier.

Paravertebral pain is the most common symptom, although radicular pain may be experienced in some cases [24]. The ways in which an intramedullary spinal cord tumor can cause back pain are diverse and not entirely understood. Back pain may be the result of direct pressure on the surrounding dura, an innervated structure, by the expanded spinal cord. Musculoskeletal pain may be caused by derangement of the paraspinal muscle innervation. Impingement on or involvement of a nerve root may result in radicular pain. Other frequent presenting complaints relate to impingement on the motor neurons or white matter tracts of the spinal cord. These symptoms include extremity weakness or clumsiness, gait difficulty, and abnormal sensory perception. Bowel, bladder, or sexual dysfunction is typically a feature of more advanced disease; however, in tumors of the conus medullaris, such dysfunction may be part of the initial symptomatology.

Sensory disturbances other than pain may consist of dysesthesias, loss of pain and temperature sense, and loss of proprioception. Centrally situated intramedullary tumors destroy the crossing segmental fibers from the spinothalamic tract, resulting in impaired pain and temperature sensation. Sacral sparing may occur, given the outermost location of the lumbosacral spinothalamic fibers. Motor deficits are a common presenting complaint. In malignant tumors presenting with symptoms of pain, rapid deterioration of motor function follows, resulting in significant disability in 3 to 5 months [21,9].

Hydrocephalus may be present in patients with intramedullary spinal cord tumors and is most often seen in the pediatric population [6,7]. The cause of hydrocephalus may be increased protein in the cerebrospinal fluid (CSF) or from dissemination of tumor cells in the subarachnoid space. Tumors near the cervicomedullary junction may produce thickening of the leptomeninges, which results in outflow obstruction from the fourth ventricle.

Lumbar puncture rarely provides a diagnosis. Typically, CSF analysis is nonspecific, usually revealing increased protein. CSF cytology rarely yields malignant cells, even in instances in which there has been frank leptomeningeal dissemination [15].

Surgical goals and preoperative patient selection

Surgery is the primary diagnostic and treatment modality because it allows for procurement of tissue for histopathologic staging and debulking or full resection of the tumor. The goals of intramedullary spinal cord tumor surgery are to obtain a tissue diagnosis and to maintain or improve neurologic function. Unlike other intramedullary tumors, astrocytomas are infiltrative and may not demonstrate a clear plane of demarcation from the normal spinal cord. This may not be readily apparent on preoperative MRI. As a result, the risk of subtotal resection must be balanced against the risk of neurologic impairment. Patient selection and intraoperative technique are of paramount importance.

The best surgical candidates are those for whom functional independence may be prolonged by forestalling the development of severe motor deficit. Some patients with significant deficit may still benefit from surgery if sphincter function or the ability to position in bed is preserved[31]. Patients with few medical comorbidities generally have a better postoperative course with fewer complications. Those with complete neurologic deficits or extensive tumor dissemination are not appropriate surgical candidates [62]. The decision to proceed to surgery in patients with a slowly progressive minor motor or sensory deficit is difficult, particularly if imaging studies suggest the presence of an infiltrating astrocytoma, which may not be removed without significant risk of neurologic deficit. One rational strategy in such cases is to follow the patient with serial neurologic assessments and MRI scans until there is tumor progression with functional deterioration. There is now evidence suggesting that the better the patient's preoperative clinical status is, the better is the postoperative outcome [58,68].

Adjuvant therapy

For low- to intermediate-grade spinal astrocytomas, there have been minimal improvements in the long-term survival of patients directly attributed to adjuvant therapy. In fact, the spinal cord has a lower tolerance for irradiation. Some studies have shown that postoperative radiation therapy improves survival and recurrence rates [49,52]. There is disagreement, however, on whether it should be used if gross total resection is achieved because it may

complicate reoperation for recurrence [21]. Given the significant advances in surgery of intramedullary tumors, second surgery has become a viable option.

Indications for second surgery have included (1) delayed recurrent growth in the solid or cystic component of the tumor, resulting in new symptoms, and (2) early re-exploration after the original subtotal resection was halted prematurely because of transient intraoperative injury confirmed by monitoring. The goal of these reoperations is identical to that of the first operation (ie, sufficient debulking of the tumor so as to lessen symptoms without causing progression in neurologic deficits). It has not been established whether there is any role for chemotherapy in the treatment of spinal cord astrocytomas [17].

High-grade spinal astrocytomas cannot be fully resected. As a result, adjuvant therapies, such as spinal irradiation [38] and chemotherapy [2], for high-grade tumors have been attempted without significant clinical improvement.

In his review of literature, Isaacson proposes these specific guidelines [38]:

1. Low grade astrocytoma and residual low grade ependymomas should be prescribed a total dose of 5040cGy in 180cGy fractions over 28 days using EBRT

2. High grade astrocytomas whatever be the extent of resection, same dose as above is recommended

3. Malignant ependymomas and benign multifocal ependymomas are treated with a locally delivered dose of 5040 to 5400cGy in 28 to 30 fractions with occasional consideration of radiation to neuraxis.

Outcome

The outcome for intramedullary spinal cord astrocytoma is significantly worse than that for ependymoma and is predicted by pathologic grade. Low-grade tumors (WHO grades I and II) may recur and result in death. Sandler and colleagues [69] report a 5-year survival of 57% in a series of 21 patients, of whom 18 had a pathologic grade of I or II, and Cooper [6] presented a series of 11 patients with grade I or II astrocytomas, of whom 4 of 11 died within the follow-up period and only 4 were not neurologically worse in functional grade. In addition, it was found that tumors initially found on pathologic examination as lowgrade astrocytomas that have progressed to higher grade tumors.

Younger age is a positive prognostic factor; Sandler and colleagues [69] found that younger patients had a substantially increased length of time to recurrence. This observation may be related to the fact that low-grade tumors in pediatric patients are usually the pilocytic histologic subtype, which has a more favorable prognosis [49].

Although numerous studies have attempted to assess the likelihood of recurrence with respect to extent of tumor resection, a convincing relation has yet to be demonstrated [36,37,49,61,69]. Postoperative MRI is necessary to

determine objectively any residual tumor. The absence of an enhancing tumor does not always ensure complete resection, especially with regard to high-grade lesions.

Preoperative neurologic function is the best prognostic indicator for functional outcome [7,37]. In the immediate postoperative period, transient neurologic deterioration from the preoperative baseline is typically seen [21,61]. Recovery generally occurs over a period of days to months, with improvement in sensory loss earlier than improvement in motor deficits. Those with severe long-standing neurologic deficits, however, are unlikely to have any improvement.

The prognosis of high-grade astrocytomas is extremely poor, with disease progression, widespread leptomeningeal dissemination, and hydrocephalus frequently seen [10]. Improvement of neurologic function as a result of surgery is unlikely [21]. Previous reports of survival after surgery averaged 6 months in adults and 13 months in children [10,50]. The immediate cause of death is typically pulmonary embolus and pneumonia or respiratory failure from direct tumor extension into the cervicomedullary region.

Surgical Technique and Adjuncts:

The goals of surgery for intramedullary lesions are to obtain a tissue diagnosis, excise the lesion wherever feasible, and delay or prevent recurrence of the lesion thus maintaining or improving neurological function.

Adjuncts

Operating microscope, intra-operative ultrasound, neuronavigation and other technical advances have made surgical resection safe and achievable. Intraoperative elecrophysiological monitoring techniques like somatosensory evoked potentials, transcranial epidural motor evoked potentials (MEP), transcranial muscle MEPs and extremity electromyography with direct spinal cord stimulation have become essential monitoring tools while operating on intramedullary tumors. The analysis of the waveforms elicited on stimulation of intact neural connections signal that normal neural tissue has been reached and further resection will jeopardize the surrounding spinal cord parenchyma. Thus, electrophysiological monitoring helps differentiate tumor tissue from normal cord and prevents and forewarns against postoperative neurological deterioration.

SSEP remains the benchmark technique for intraoperative monitoring. Responses are obtained at peripheral, subcortical and cortical locations with stimulation of a peripheral nerve. The criteria for warning signs in SSEP

monitoring are a 10% or greater increase in latency or a 50 to 60% decrease in amplitude compared with the baseline.

SSEP is a measure of the sensory function and hence development of purely motor deficits is not detected intraoperatively. Presence of neuromuscular scoliosis is also considered an "unmonitorable" condition and the development of a cerebrovascular event predisposes to the loss of all SSEP data if only the cortical responses are monitored. SSEP waveforms may be hardly recordable in patients with profound sensory loss. The waveforms are also known to become unrecordable after a midline myelotomy. These shortcomings of SSEP monitoring are well documented in literature and hence motor evoked potential monitoring has assumed greater importance. Transcranial magnetic stimulation with MEPs has become the standard method of monitoring motor function in many centers doing intramedullry surgeries routinely[112]. Calancie et al[113] have developed the threshold level technique in which the primary outcome measure is the minimum stimulus intensity needed to elicit a barely perceptible muscle contraction. An increase of J00V above threshold is considered a warning sign to the surgeon. Alternately, a decrease to 60 to 80% of the baseline amplitude of the response is also taken as a warning sign. The documented sensitivity and specificity of these values utilizing this method in this series was 100%.

Surgical Technique

Laminectomy is the standard approach in adults; however in children, osteoplastic laminotomy is considered if a multilevel exposure is required to protect against spinal deformity. Location of the tumor is confirmed using ultrasound and an adequate midline myelotomy is made. The use of Nd:Yag laser has been advocated to prevent dorsal column injury. Pial traction sutures are applied to hold the myelotomy apart and the tumor is entered at its thickest part.Tumor-cyst, or tumor-syrinx interface, if present, can also aid in the site of entry. After internal decompression using CUSA, a definite plane of cleavage is usually found in case of ependymomas and pilocytic astrocytomas and the tumor is delivered after coagulating the underlying vessels. In case of diffuse astrocytomas, the plane is not as well developed and tumor is sequentially vaporized using C02 laser or decompressed with CUSA until normal cord is seen. If the lesion is identified as high grade, the procedure is can be limited to a biopsy as an extensive resection has not been shown to influence the overall outcome or further progression of the disease. Hemostasis is achieved is by packing and use of hemostatic agents. Dura is closed primarily or with a patch duraplasty.

Post operative care :

Early mobilization and deep venous thrombosis prophylaxis with subcutaneous heparin is begun along with use of physical and occupational therapy to optimize functional recovery.

Transient or permanent worsening of neurologic status including sensory, motor or sphincter functions may occur which may respond to steroids and physiotherapy. Several authors have noted immediate postoperative paresthesiae and proprioceptive dysfunction related to dorsal myelotomy[45]. These dysesthesiae pose the greatest problem in the neurologically well-preserved patients. These disappear gradually over time in most of the patients, but can be permanent in few others. The extent of myelotomy, transient edema or vascular compromise during cord dissection directly correlates with the postoperative deterioration . Deterioration may also be related to poor plane of cleavage of the tumor and the cord.

Orthostatic hypotension may occur especially following surgery for upper thoracic or cervical intramedullary lesions. This is usually self-limiting and responds to fluids and gradual mobilization.

Complications related to wound dehiscence, CSF leak and infection are more common in previously irradiated patients. They may need to be managed aggressively, if necessary with re-exploration, use of tissue glue for dural closure, and use of rotation flaps and other plastic surgical procedures for skin closure .

AIM OF STUDY

To study the clinico-radiological profile , surgical intervention and outcome in correlation with the histological diagnoses of all glial intramedullary lesions operated in the study period .

1) To evaluate and quantify the preoperative, postoperative and last follow up status of the patients in terms of a functional scale.
2) To assess the surgical outcome in relation to
    a. the lesion subtype
    b. the extent of resection
    c. pre-operative functional grade .
    d. location of lesion .

MATERIALS & METHODS

A retrospective study of consecutive series of **68** patients who underwent surgery for intramedullary glial tumors at the department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, India between January 1991 and December 2006. (15 years)

Patients were contacted by letters and requested to come for evaluation of their clinical condition.

Patients unable to come for follow up were sent a questionnaire to assess their clinical status.

All patients underwent preoperative and postoperative functional assessment using Modified Mc- Cormick scale .

Table : Modified Mc- Cormick scale

Grade I: Normal Ambulation

Grade II: Mild motor, sensory deficit, Independent without external aid

Grade III: Independent with external aid

Grade IV: Care required

Grade V: Bedridden

The scale was used to assess the functional status of the patient preoperatively, at the time of discharge and at last follow up.

The outcome was interpreted as

(a) Improved - if there was improvement in modified Mc Cormick grade when compared to pre-operative status.

(b) Static - if modified Mc Cormick grade is same as preoperative grade

(c) Worsened - if modified Mc Cormick grade is more than pre-operative grade.

Patients treated early in the series underwent diagnostic imaging with myelography or computed tomographic myelography or both procedures and those treated from 1994 onwards underwent gadolinium-enhanced spinal magnetic resonance imaging (MRI) .

Surgical Technique: [71]

The principles of surgical techniques employed to treat these lesions are summarised as follows:

(1) Full extent of tumour to be exposed with laminectomy one level above and below the level of the lesion

(2) Dural opening sparing the arachnoid layer.

(3) Spinal cord opened after securing pial stitches through a midline myleotomy or through the most enlarged avascular part of the cord.

(4) Initially 1–2cm myelotomy done over the maximum enlarged part of cord and to be extended over the entire rostrocaudal limit of the tumour.

(5) Myelotomy deepened gently by spreading microforceps in longitudinal axis and tumour surface identified.

(6) Both tumour poles identified and polar cysts entered.

(7) Apply pial traction sutures for better visualisation and to provide counter traction for development of dorsal and dorsolateral tumour plane.

(8) Retraction of the tumour done rather than the cord.

(9) Biopsy obtained for histological confirmation.

(10) Dissection done from one end. Internal decompression if tumour is bulky and hinders dissection plane.

(11) Dissection of the ventral plane done last and supply from anterior spinal vessels are cauterises and divided.

(12) Dura closed primarily or using a dural patch graft.

(13) Useful intraoperative adjuncts include SSEP, intraoperative ultrasonography, CUSA, LASER.

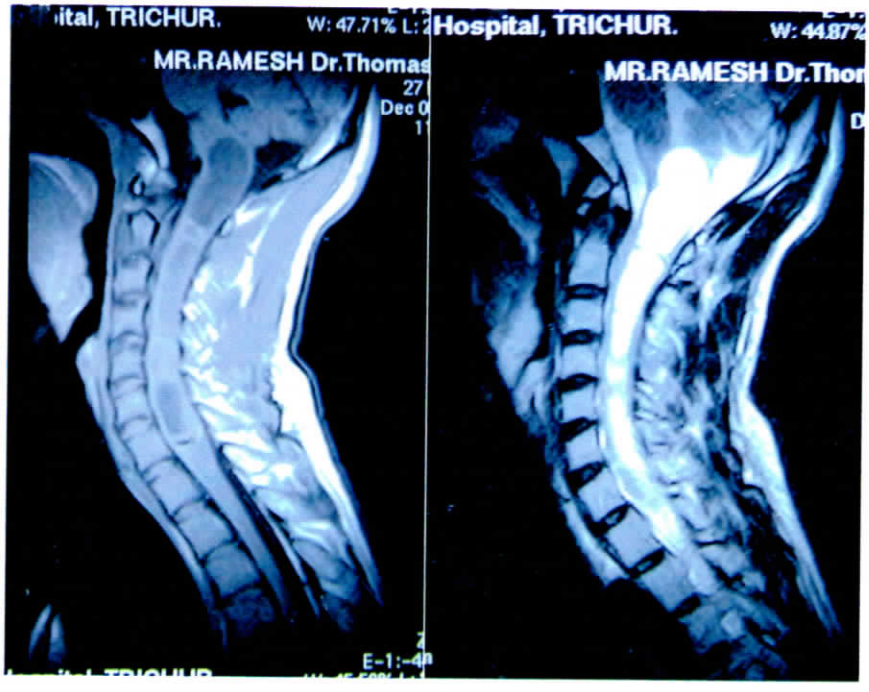
The plane of cleavage from the normal looking cord was the basis of decompression of lesion – so lesions were either biopsied, sub total, near total or totally removed depending on the plane of cleavage ; frozen section report was also a determinant for deciding the extent of resection. Resections were classified total, near total , subtotal, partial or biopsy based on the surgeon's operative impression.

All patients with histopathology proven malignant astrocytoma or incompletely removed low grade astrocytoma/ependymoma were advised adjuvant therapy. Ependymoma with total or near total excision were kept on regular follow up with serial imaging.

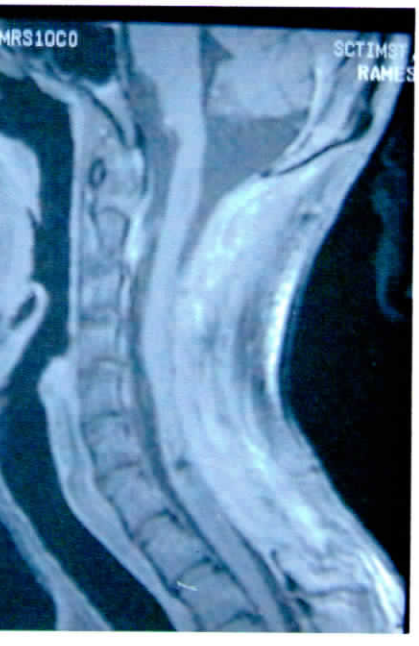
The data were analysed using SPSS software.

EPENDYMOMA

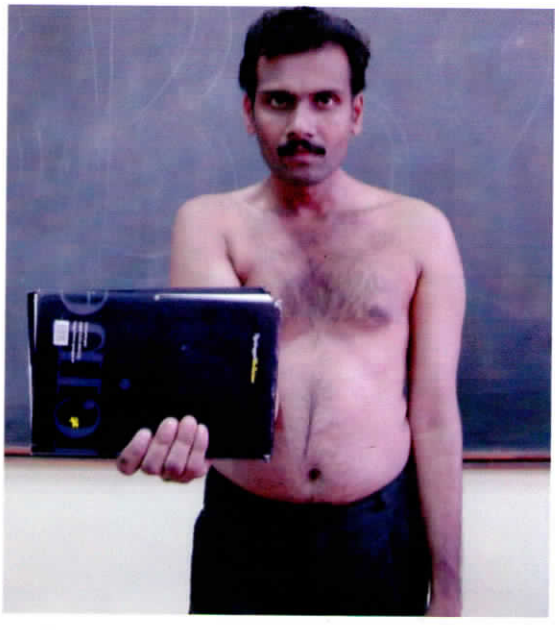
Pre Operative MRI



Post Operative MRI

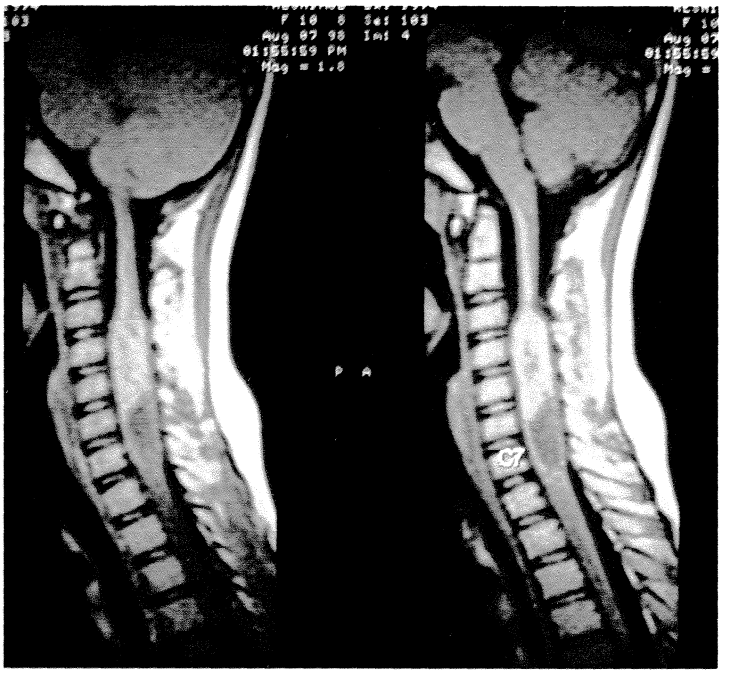


Patient on follow up

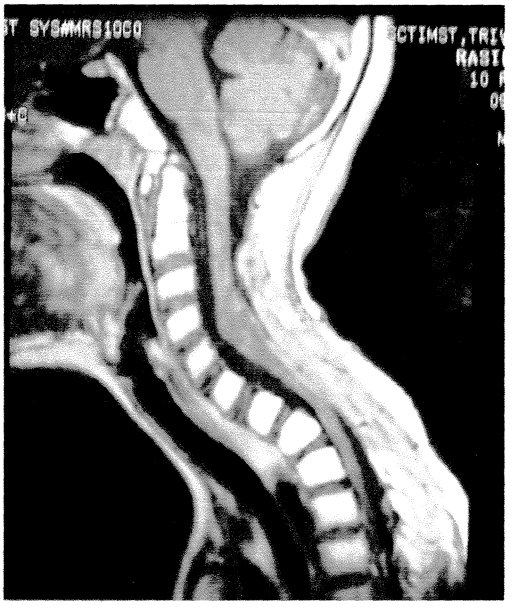


ASTROCYTOMA

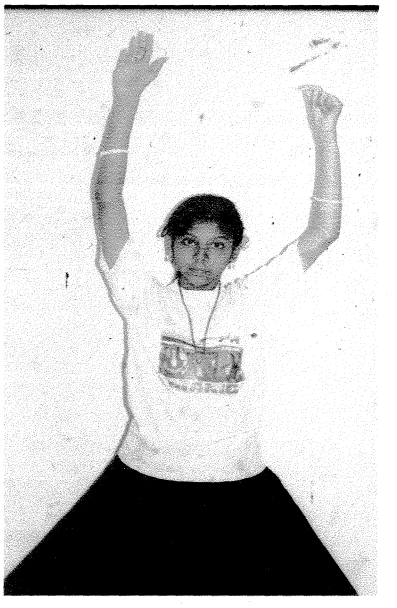
Pre Operative MRI



Post Operative MRI

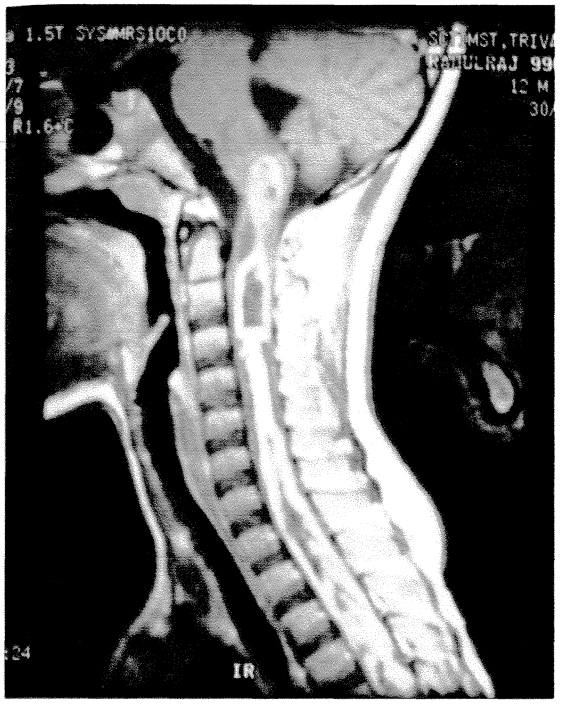


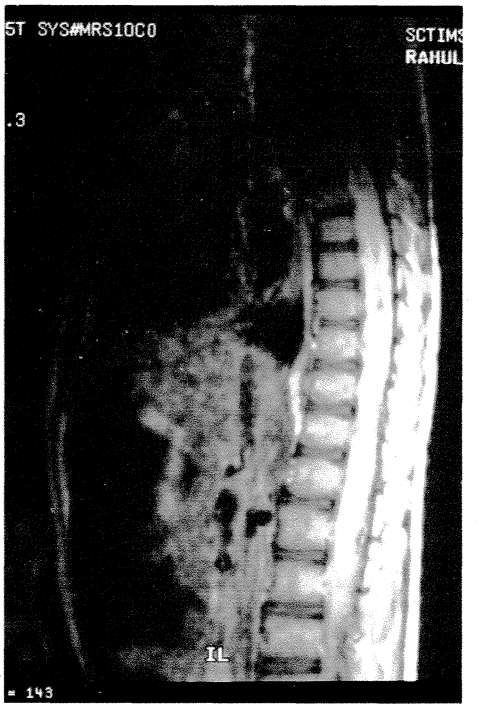
Patient on follow up



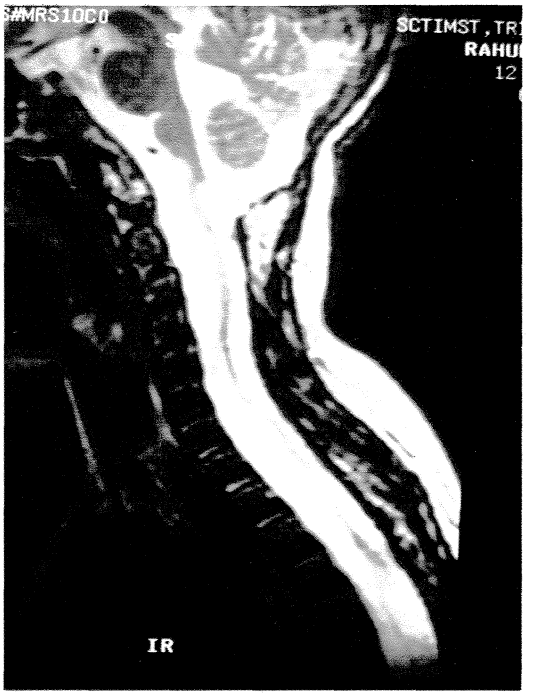
HOLOCORD ASTROCYTOMA

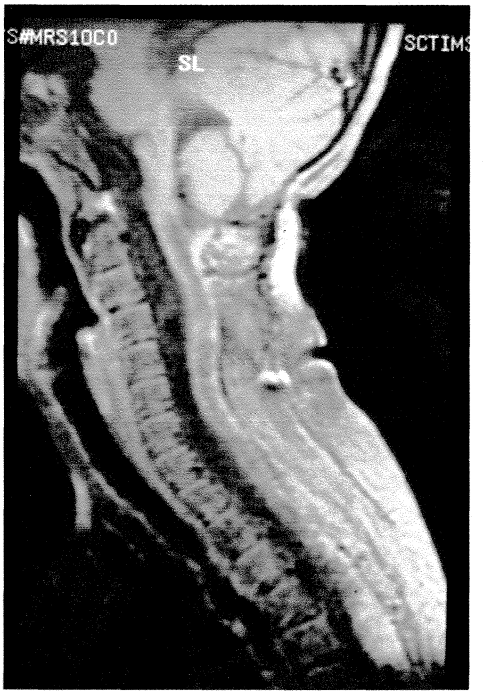
Pre Operative MRI





Post Operative MRI





RESULTS AND ANALYSIS

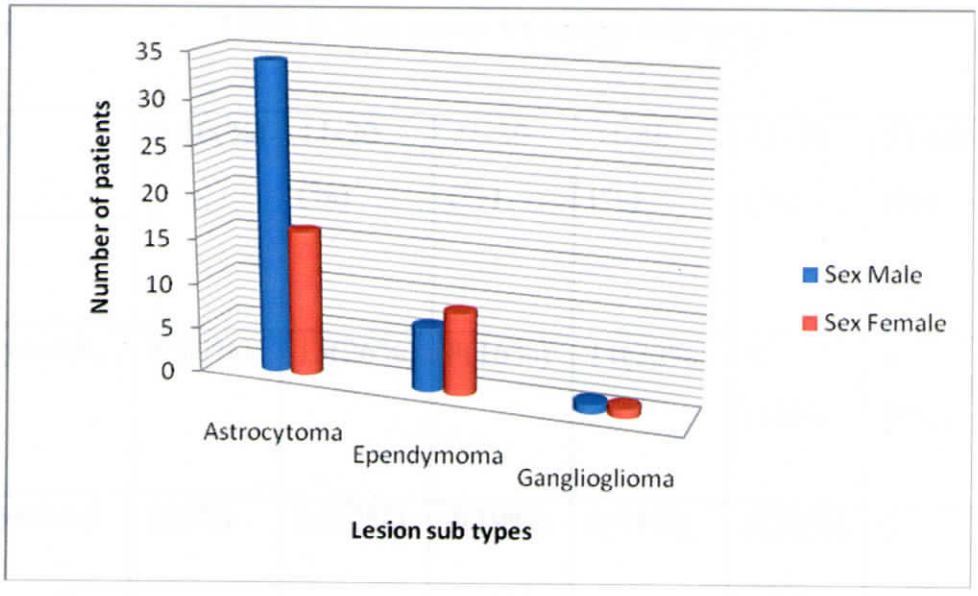
Patient characteristics:

The population of 68 patients comprised 42 male patients (62%) and 26 female patients (38%), whose ages ranged from 1.5 to 56 years (mean,29.6 yr).

The proportion of males and females among various histological subtypes are as shown below :

Table 1: Gender distribution in lesion sub types

Histopathology	Sex		Total
	Male	Female	
Astrocytoma	34	16	50
Ependymoma	7	9	16
Ganglioglioma	1	1	2
Total	42	26	68



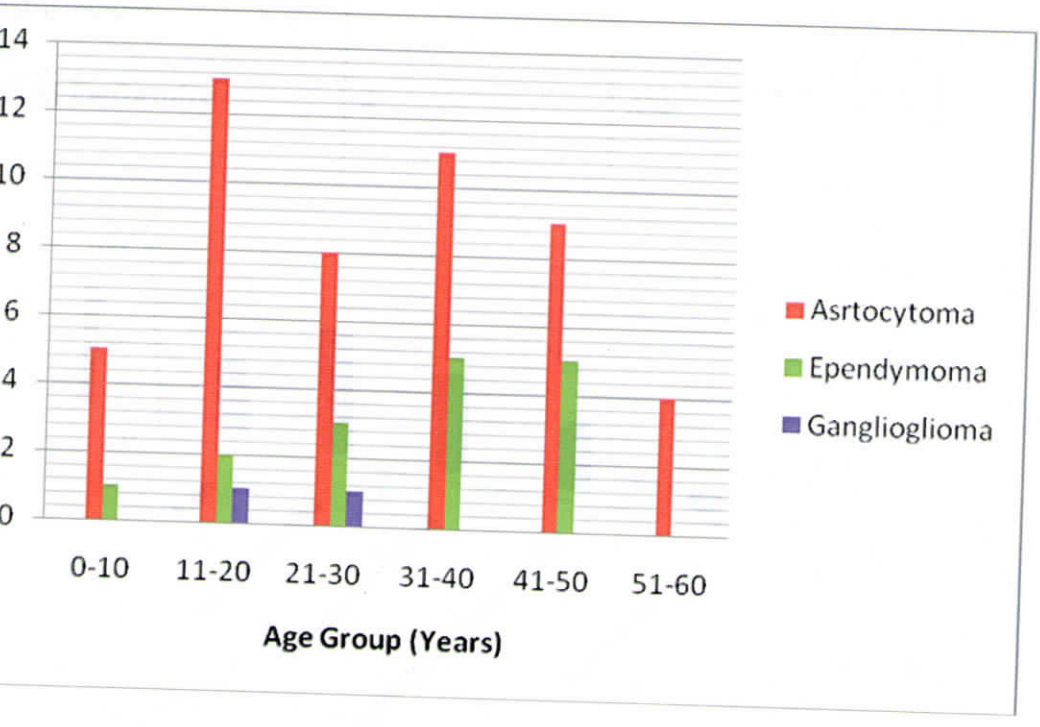
The most common age group for astrocytoma is 2nd decade while for ependymoma it is 4th and 5th decades.

Table 2 : Age Distribution

Age group (Years)	N=68	Percentage
0-10	6	9%
11-20	16	24%
21-30	12	19%
31-40	16	19%
41-50	14	22%
51-60	4	6%
Total	68	

Table 3: Age group Vs lesion subtypes:

	0-10(%)	11-20 (%)	21-30 (%)	31-40 (%)	41-50 (%)	51-60 (%)	Total
toma	5(10%)	13(26%)	8(16%)	11(22%)	9 (18%)	4 (8%)	50
noma	1(6%)	2 (12%)	3(19%)	5(31%)	5(31%)	0	16
glioma	0	1(50%)	1 (50%)	0	0	0	2

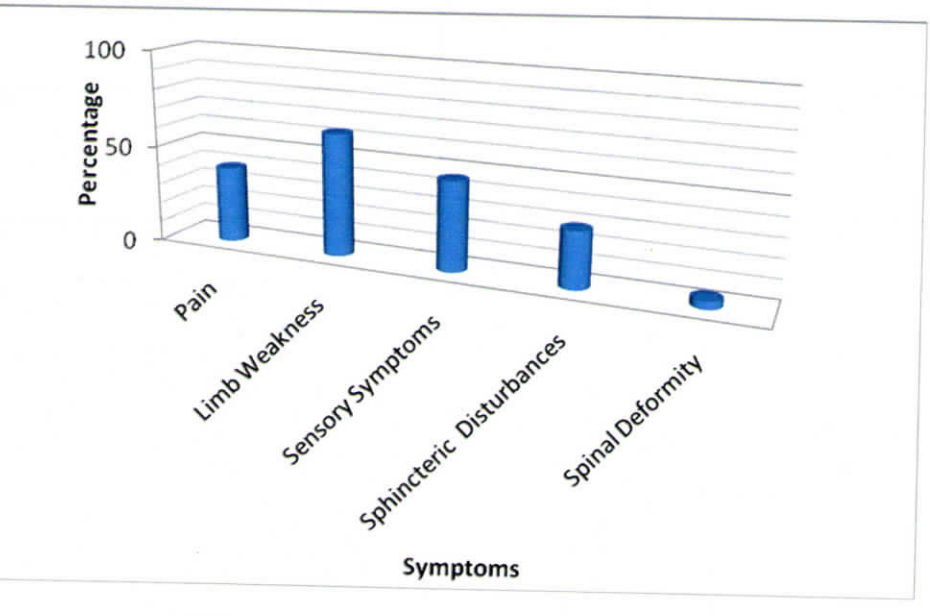


al Features:

The duration of clinical symptoms ranged from1 months to 15 years. esenting symptoms and signs were limb weakness in 63 patients (93%) y disturbances in 46 patients (68%), pain in 39 patients(57%) , teric dysfunction in 29 patients (43%) and spine deformity in 4 s(6%).

Table 4: Clinical Features

Clinical Features	N=68	Percentage
ain	39	57%
imb Weakness	63	93%
ensory Symptoms	46	68%
phincteric isturbances	29	43%
pinal Deformity	4	6%



The pre operative Functional Grade 1 and 2 constituted 63% of patient population and Grade 3 to 5 was 37% .

Table 4 Pre Operative Functional Grade

Grade (Mod. Mc Cormik)	N=68	Percentage
1	18	26%
2	25	37%
3	12	18%
4	7	10%
5	6	9%
Total	68	

The functional grade in lesion subtypes were given below in tabular form.

Table 5 : Pre operative functional grade in lesion subtypes :

HPR Mc Cormick grade	Astrocytoma	Ependymoma	Ganglioglioma
Grade 1	14	5	2
Grade 2	16	6	O
Grade 3	10	4	0
Grade 4	6	0	0
Grade 5	4	1	0
Total	50	16	2

Radiological characteristics:

Cervical spinal cord was the commonest site for occurrence of Intramedullary glial neoplasms. (35%), 22 patients (32%) had lesion at cervicodorsal region, at a dorsal site in 13 patients (19%), at dorsolumbar in 5 patients (7%),at cervico-medullary junction in 3 (4%) , and holocord in 1 patients (1%). The vertical extension ranged from 1 to 13 vertebral segments (apart from one holocord tumor).

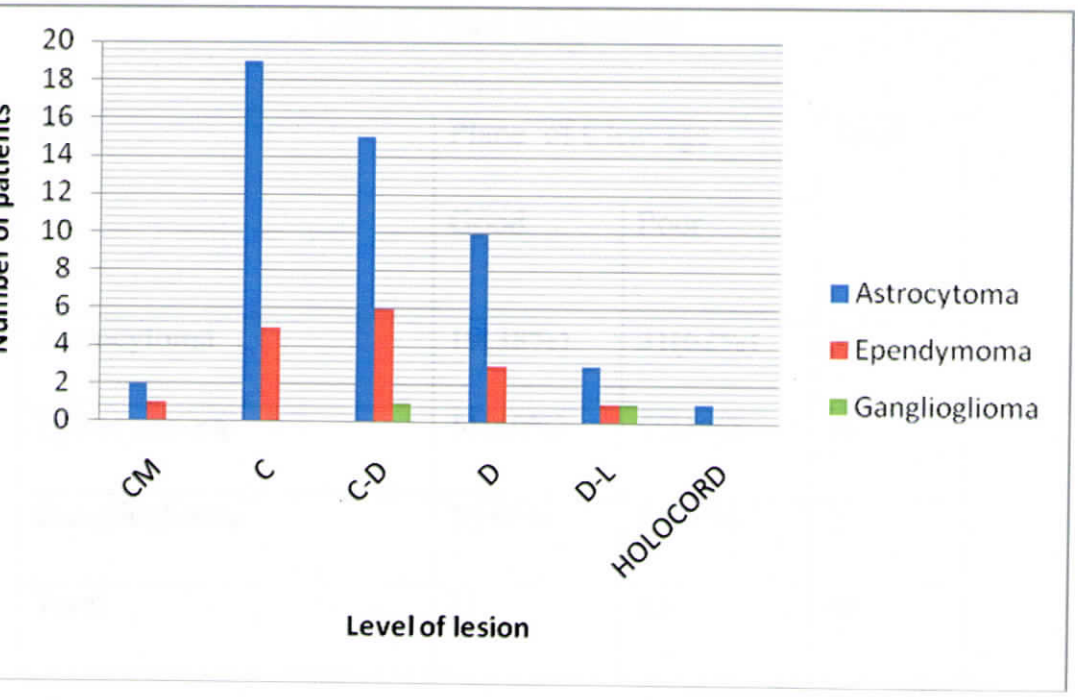
Table 6 : Level of lesion

Location	N=68	Percentage
Cervicomedullary	3	4%
Cervical	24	35%
Cervicodorsal	22	32%
Dorsal	13	19%
Dorsolumbar	5	7%
Holocord	1	1%
Total	68	

The distribution of various levels with regard to tumour histology is given in the table below. The cervical or cervico dorsal level is most common level in both astrocytoma and ependymoma.

Table 7: Level of lesion Vs Subtypes

HPR	CM	C	C-D	D	D-L	HOLOCORD	Total
Astrocytoma	2	19	15	10	3	1	50
Ependymoma	1	5	6	3	1	0	16
Ganglioglioma	0	0	1	0	1	0	2
Total	3	24	22	13	5	1	68



The average number of vertebral levels involved is more for dymoma than for astrocytoma.

Table 8 : Number of vertebral levels involved

PE	Average no of levels
strocytoma	5.96
pendymoma	6.73
anglioglioma	6.5

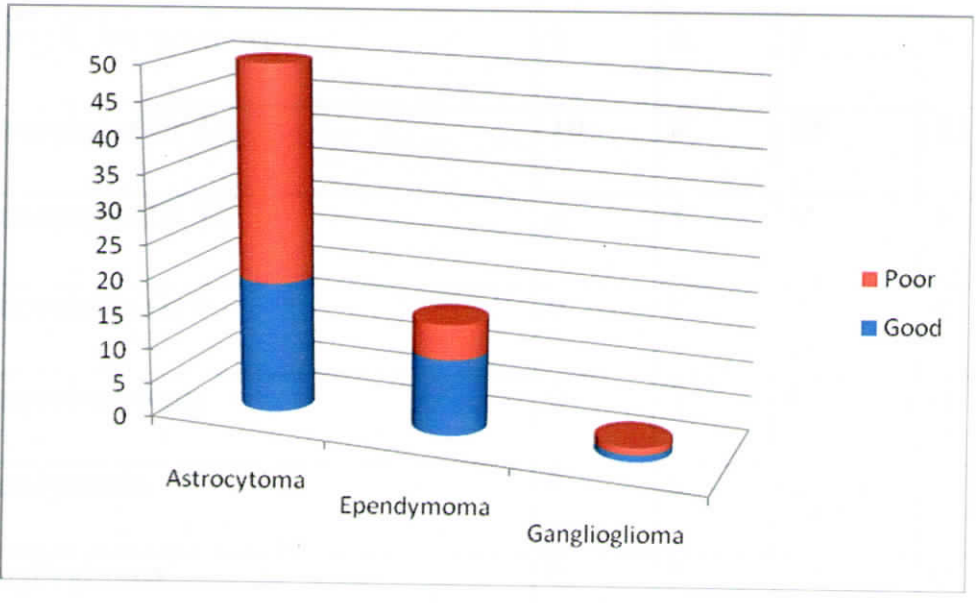
ical Aspects

In all 68 patients with glial intramedullary tumors who underwent ry, the tumors were removed through a posterior- median approach with a ectomy, or a laminotomy in children, and a median continuous otomy .

A good plane of cleavage was found in 11 patients (69%) of ymoma and 19 patients (38%) of astrocytoma .

Table 9: Plane of Cleavage

HPR	Plane of Cleavage		Total
	Good	Poor	
Astrocytoma	19(38%)	31(62%)	50
Ependymoma	11(69%)	5(31%)	16
Ganglioglioma	1(50%)	1(50%)	2
Total	31	37	68



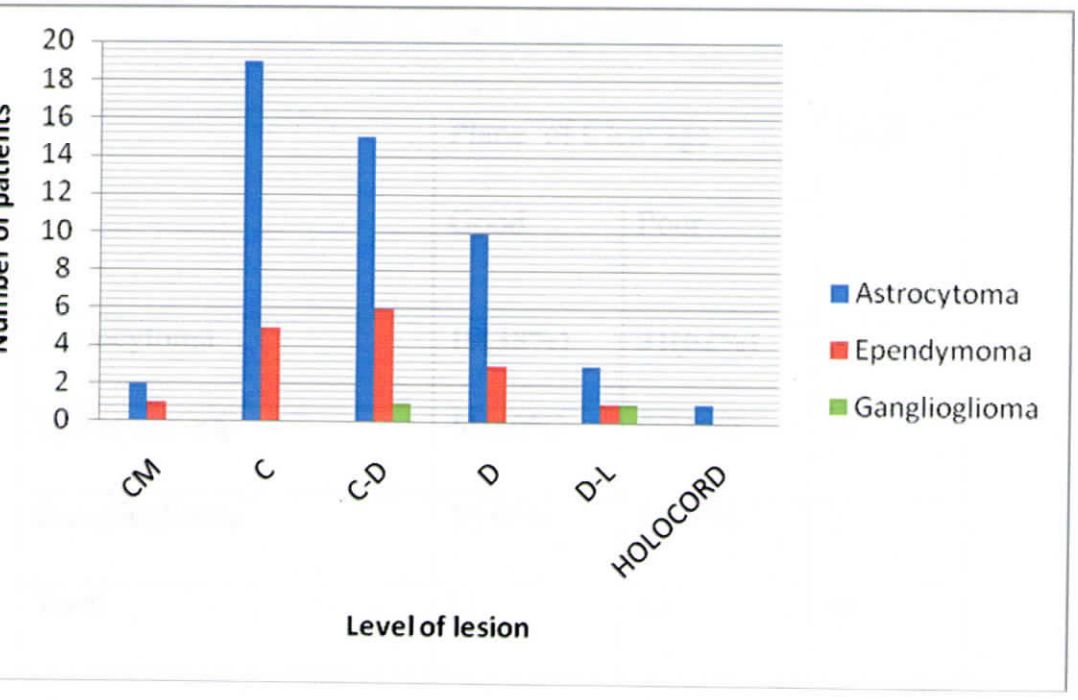
Total resection could be achieved in 10 out of 48 patient with grade II cytoma ; 9 patients underwent near total resection, 18 patients underwent tal resection and biopsy alone was obtained in 11 patients. There were 2 nts with grade III astrocytoma of which one underwent near total resection one patient underwent biopsy of the lesion.

Out of 16 patients with ependymoma , total excision was possible in 8 patients ; 6 patient underwent near total and 2 patient subtotal resection .

In the 2 patients with ganglioglioma one underwent near total resection while one patient underwent subtotal resection of the lesion.

Table 10 : Extent of Resection Vs Lesion subtypes

Type	Extent of Resection			
	Total	Near total	Subtotal	Biopsy
Pilocytic Astrocytoma	0	0	0	0
Astrocytoma Gr 2	10	9	18	11
Astrocytoma Gr 3	0	1	0	1
Astrocytoma Gr 4	0	0	0	0
Oligoastrocytoma	0	0	0	0
Ependymoma	8	6	2	0
Ganglioglioma	0	1	1	0
Total	18	17	21	12



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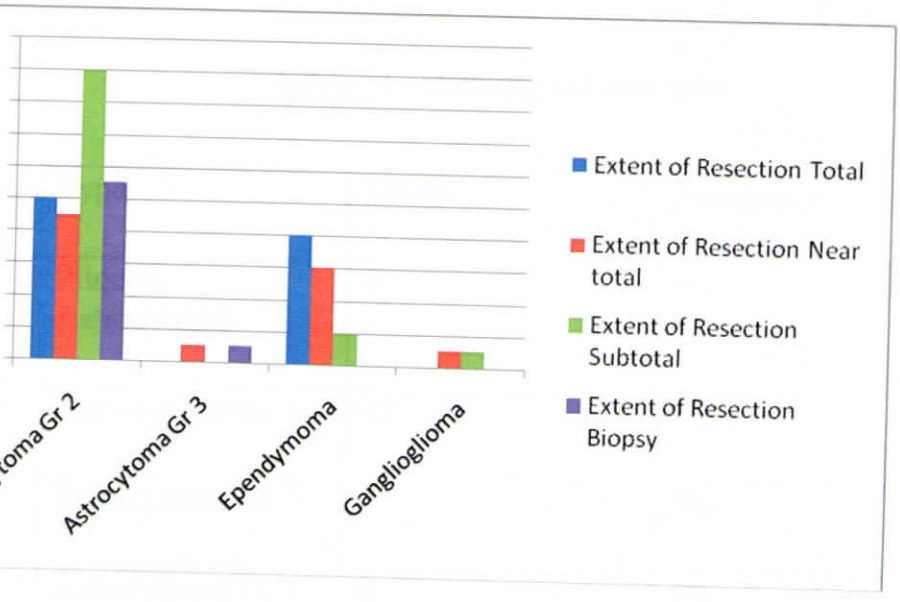


The most frequent histological tumour type was astrocytoma (50 ts, 71%). Ependymomas, constituted 16 patients, (24%), followed by oglioma (2 patients). 48 patients were in Grade II,(71%) and 2 patients in Grade III as per histological classification of the astrocytic edullary tumors according to the World Health Organization (WHO)

Table 11 : Histological Subtypes.

Type	N= 68	Percentage
Pilocytic Astrocytoma	0	0%
Astrocytoma Gr 2	48	71%
Astrocytoma Gr 3	2	3%
Astrocytoma Gr 4	0	0%
Oligoastrocytoma	0	0%
Ependymoma	16	24%
Ganglioglioma	2	3%
Total	68	

Post Operative course and complications :

Out of the 68 patients who underwent surgery for Intramedullary glial neoplasms, 6 patients showed improvement in neurological status in the late post-operative period before discharge from hospital ; 18 patients were static in their neurological status while 43 patient showed some worsening in pre-operative neurological deficits .

Table 12 : Outcome at discharge Vs Extent of resection

Extent of resection	N=67			Total
	Improved	Static	Worsened	
Total resection	2	3	12	17
Near total	1	4	13	18
Subtotal	2	6	13	21
Biopsy	1	5	5	11
Total	6	18	43	67

One patient developed wound infection , 3 patients developed wound CSF leak out of which 2 patients had to undergo wound re-suturing. One patient with cervicomedullary astrocytoma died in post operative period due to intra- operative autonomic disturbances (severe hypotension and bradycardia).

Table 13 : Post op complication - immediate

Complication	N=68	%
Wound Infection	1	1%
CSF leak	3	5%
Sec. Resuturing	2	3%
Mortality	1	1%

Five patient had to undergo re exploratory surgery .Out of 2 patients previously had a diagnosis of astrocytoma Grade II and had undergone biopsy of the lesion previously one patient was reoperated after 6 month while other patient after 26 months.

3 patients with ependymoma recurred who had previously undergone near total excision (one patient received post operative radiotherapy) were re explored with average duration of 30.6 months(9-47 months).

Adjuvant therapy:

Of the 68 patients, 57 patients were available for "late" follow-up review. (2month – 217 month).

Twenty four patients (out of 48) with grade II astrocytoma, all patients with grade III astrocytoma and 3 out of 16 patient with ependymoma received adjuvant radiotherapy.

Ten patients lost the follow up in which one patient was of ependymoma and rest were astrocytoma .

Long term Follow up

The mean follow up period was 68.7 months (5.7 yr). Range 2 months – 217 months. Follow up was available for 57 patient s (84%) out of 68 who underwent surgery for intramedullary spinal cord glial neoplasms. CE MRI was performed in 31 patients who came for follow-up.

11 patients among them showed no residual lesion ; these included 7 patients who underwent resection of astrocytoma ,3 patient of ependymoma and 1 patient of ganglioglioma .

Table 14: Post op MRI in lesion subtypes showing recurrent / residual lesion

EOR	Total	Near total	Subtotal	Biopsy	Total
Lesion					
Astrocytoma gr II	1	2	6	6	15
Astrocytoma gr III	0	1	0	0	1
Ependymoma	0	2	1	0	3
Ganglioglioma	0	0	1	0	1
Total	1	5	8	6	20

The mean functional grade at follow up was 2.11, a significant improvement (p=<0.003) over preoperative grade as shown in the below table

Table 15 : Mean Functional Grade

Grade	1	2	3	4	5	Mean
Pre op (n=68)	18	25	12	7	6	2.29
At discharge (n=67)	6	14	19	20	8	3.13
At last Follow up (n=57)	21	20	5	8	3	2.11

The above table shows that there are more number of patients in grade 1 and 2 at follow up as compared to preoperative grade where they were predominantly in grades 2 and 3 .

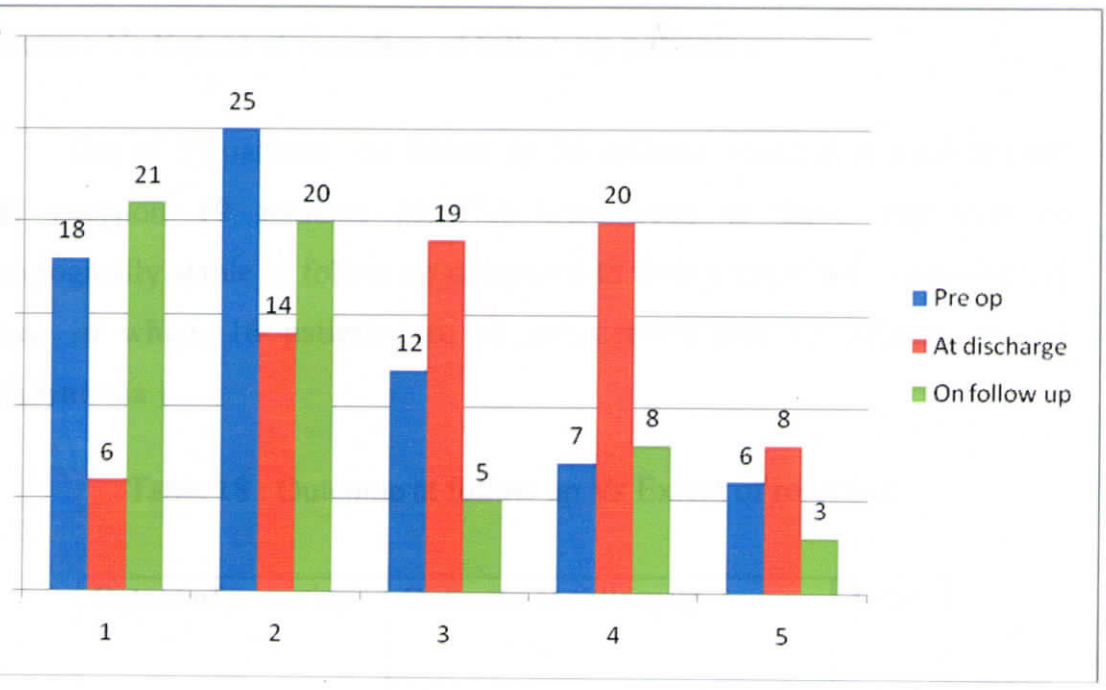
Table 16: Mean Functional Grade in lesion sub types

Grade	Pre op	At discharge	On follow up
Astrocytoma II	2.42	3.13	2.18
Astrocytoma III	2.00	3.50	4.00
Ependymoma	2.13	3.12	1.79
Ganglioglioma	1.00	3.00	1.00

Above table shows that astrocytoma II and ependymoma showed improvement in mean functional grade at follow up .

Outcome Vs preoperative grade :

The graph below depicts the number of patients in each grade – preoperatively, at discharge and at follow up . This shows that most patients tend to either remain in the same preoperative grade or improve to one grade higher . This means that ,better pre operative grade correlated with better outcome .



come at discharge Vs extent of resection :

At discharge patients who underwent total or near total resection only (10/35) showed either improvement or unchanged neurological status and showed worsening .

Table 17 : Outcome at discharge Vs Extent of resection

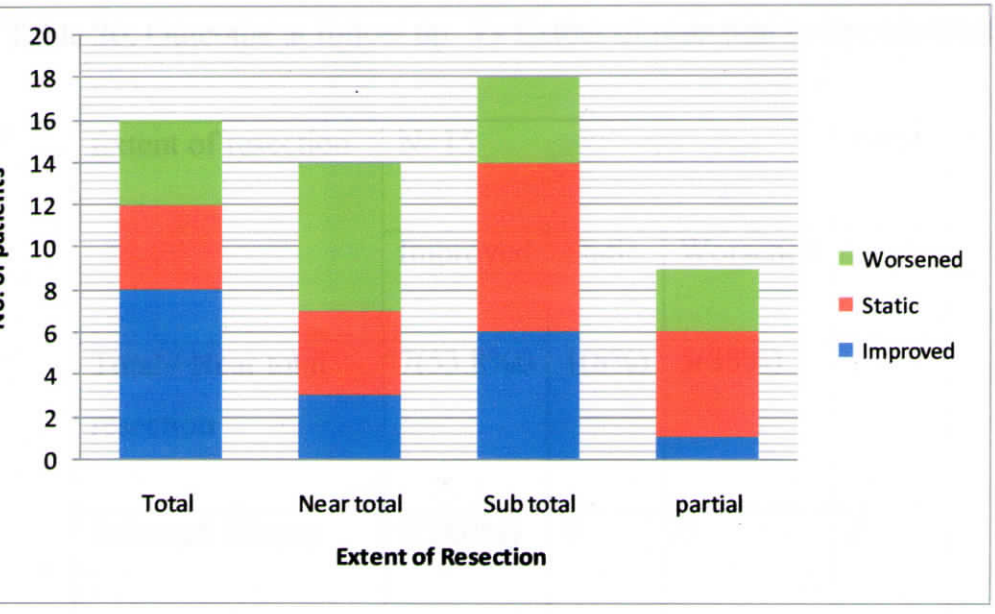
Extent of resection	N=67			Total
	Improved	Static	Worsened	
Total resection	2	3	12	17
Near total	1	4	13	18
Subtotal	2	6	13	21
Biopsy	1	5	5	11
Total	6	18	43	67

Outcome Vs Extent of resection of follow up patients :

Out of 57 patients on follow up 30 patients underwent total or near total excision 19 patients (63.3%) were seen to have improved or neurologically stable at follow up compared to their preoperative neurological status(in which 16 patients are of astrocytoma and 13 patients are of ependymoma) .

Table 18 : Outcome at follow up Vs Extent of resection

Extent of resection	Outcome at follow up			Total
	Improved	Static	Worsened	
Total resection	8	4	4	16
Near total	3	4	7	14
Subtotal	6	8	4	18
Biopsy	1	5	3	9
Total	18	21	18	57



The outcome Vs extent of resection in lesion subtypes is given in ar form below .

Table 19: Outcome at follow up Vs Extent of resection in astrocytoma

Extent of resection	N=40			Total
	Improved	Static	Worsened	
Total / Near total resection	5(31%)	6(37%)	5(31%)	16
Subtotal/Biopsy	6(25%)	10(42%)	8(33%)	24
Total	11(27.5%)	16(40%)	13(32.5%)	40

Table 20: Outcome at follow up Vs Extent of resection in Ependymoma

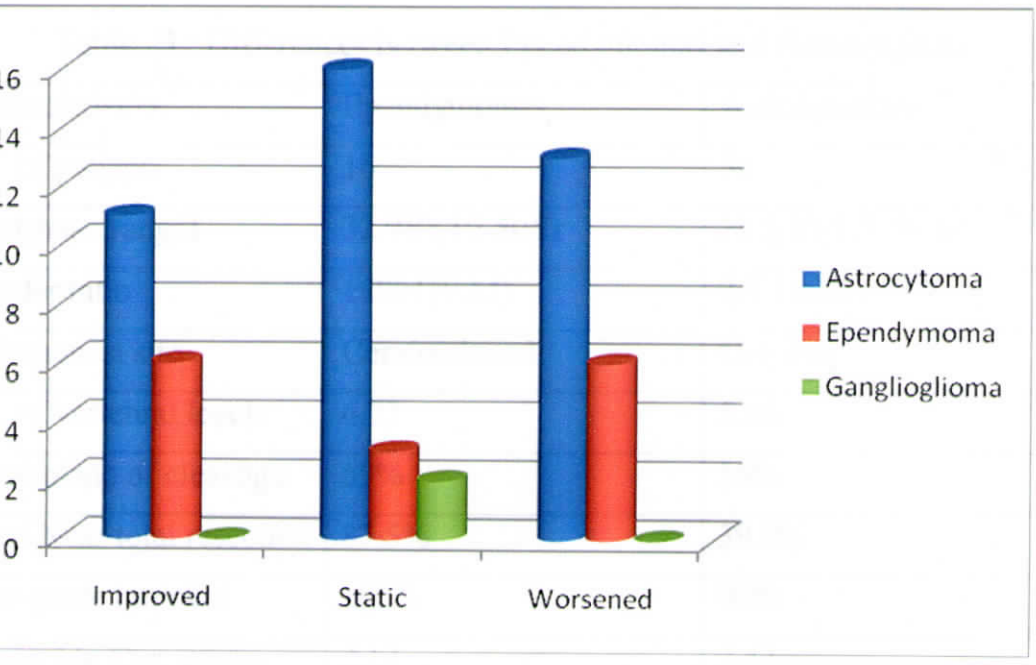
Extent of resection	N=15			Total
	Improved	Static	Worsened	
Total / Near total resection	7(53.8%0	1(8%)	5(38%)	13
Subtotal/ Biopsy	2(100%)	0	0	2
Total	9(60%)	1(7%)	5(33%)	15

Outcome Vs lesion subtypes of follow up patients :

Patients who were operated for astrocytoma 67.5%(27/40) were either improved or neurologically stable while 32.5%(13/40) showed worsening in neurological status while in ependymomas 60%(9/15) patients showed improvement neurologically static and 40% (6/15)showed worsening in neurological status.

Table 21: Outcome Vs lesion subtypes of follow up patients.

HPE	Improved	Static	Worsened	Total
Astrocytoma	11(27.5%)	16(40%)	13(32.5%)	40
Ependymoma	6(40%)	3(20%)	6(40%)	15
Ganglioglioma	0	2(100%)	0	2
Total	17(31%)	21(37%)	19(33%)	57



ome Vs level of lesion :

The patients with cervical or dorsal lesions 89% (33/37) showed ovement or static neurological status while patients with other level lesion (15/20) showed improvement or static neurological status.

Table 22 : Thoracic Vs Non thoracic Outcome

Follow up status	Level of lesion	
	Cervico-dorsal & dorsal	Other level
Improved	14(38%)	4(20%)
Static	19(51%)	13(65%)
Worsened	4(11%)	3(15%)
Total	37	20

Out of 19 patients whose post op x -ray were done 3 new patients ed spinal deformity inform of scoliosis or kyphoscoliosis but they were otomatic for the same.

Table 23 : Differences between Ependymomas and Astrocytomas

Characteristics	Ependymomas	Astrocytomas
No. of patients	16	50
Age(mean,range)	32.9Yr,10-50Yr	28.8 Yr,1.5-56 Yr
Gender ratio	1.28:1(F:M)	2.1:1(M:F)
Commonest site	Cervicodorsal	Cervical
No. of vertebral levels	6.73	5.96
Good plane of cleavage	69%	38%
Total/Near total resection	87.5%	39.5%
Low grade tumours	100%	96%
Pre op Mc Cor. grade	2.13	2.42
At discharge Mc Cor. grade	3.12	3.13
Follow up Mc Cor. grade	1.79	2.18
Outcome-Improved	6(40%)	11(27.5%)
Outcome-Static	3(20%)	16(40%)
Outcome-Worsened	6(40%)	13(32.5%)
Outcome-Dead	0	1

DISCUSSION

The advent of modern microsurgical techniques has led to a significant change in the approach to IMSCTs. The pioneering work of Epstein and colleagues [21,22], and the legacy of detailed neurosurgical studies over the last 24 years have dramatically improved the outcome in patients harboring these tumors. In cases of IMSCTs one should not wait for the onset of clinical deterioration but rather institute treatment as soon as possible. The earlier the diagnosis and the more radical the resection of an IMSCT, the greater the likelihood of preserving the patient's neurological function[62].

The present study was undertaken to analyze our institutional experience in the surgical management of glial intramedullary tumours. It was our aim to evaluate the clinical & radiological features, the histological subtypes, operative findings including resectability, postoperative complications & procedure or disease related morbidity and mortality. The functional outcome of these patients was determined in relation to the tumour subtypes & the extent of resection and preoperative functional grade .

The differences between astrocytomas and ependymomas in terms of age, incidence, clinical presentation, radiological characteristics, surgical aspects and outcome have all been described in the literature[6,8,47]. The present study also noted similar differences and was tabulated in the earlier section. The above features confirm the fact that ependymomas are mostly low grade

neoplasms, have a good tumor-cord interface, seen more commonly in the 3rd to 4th decades , are amenable to total excision in most cases and have a good functional outcome. In contrast, astrocytomas are seen to be more heterogenous as far as the histological grade is concerned with low and high grade lesions. They tend to occur in a slightly younger population, many lesions have a poor plane of cleavage from the surrounding cord, less amenable to radical resection and have a less favorable outcome.

Epstein et al[18] in 1993 in their series of 38 patients with ependymomas have noted the male preponderance and a mean age of occurrence of 37 years. In our study slight female preponderance was seen and a mean age is 32.9 years . They reported a gross total excision rate of 97% while our study this was found to be 87.5% . Cooper[6] reports a total excision rate of 49%, while "99%" removal was accomplished in another 25%. The decision regarding post-operative radiotherapy is usually taken in those patients who have undergone a less than radical resection of ependymomas and is advocated in these instances by Cooper[6], Chandy et al[8]and Sandalcioglu et al[68]. Epstein[18] on the contrary, believes that adjuvant radiation is unnecessary and surgery is curative in these lesions, reserving radiation only for future recurrences. Most of the studies so far report a good outcome in ependymomas following radical surgery [6,68].

Astrocytomas in the present study were mostly of low grade variants and the same has been validated in other series[5,69]. Epstein[21] reported gross

total excision of astrocytomas (n=25) and did not advise radiotherapy for any patient. On the contrary, in a study by Sandler et al[69] (n=21), 15 patients received adjuvant radiation following surgery. The present study records a total excision rate of 21% and near total excision in 18.8% only and adjuvant therapy was advised in 24(out of 48 patients) of grade II astrocytoma & all patients with grade III astrocytoma .

Outcome analysis

Outcome in the present study was correlated with various prognostic factors elucidated in the literature and includes preoperative functional grade, histological subtype, histological grade, and extent of resection.

Our analysis of the functional grade of the patients preoperatively, at discharge and at follow up reveals that better the preoperative functional grade, better is the outcome. There were forty three (63%) out of 68 patients in grade 1 and 2 preoperatively (mean grade= 2.29) . This number rose to 39 out of 57 patients (72%) at follow up. This indicates that the benefits of surgery for intramedullary tumors are more "prophylactic" as propounded by Cristante[7] and yields better results in a patient with minimal neurological deficits[45,8,21,6,7,61].

An argument has been made for radical excision of intramedullary lesions by various authors[5,6,8,68]. Chandy et al advocated radical excision of all intramedullary lesions, provided there is a good plane of cleavage [8]. Cohen et

al advise radical surgery even for a high grade lesion, citing that the sampling error of the tissue to determine true histology is better with larger volume of tissue. They also advocate radical resection for cytoreductive debulking and pain control[5]. Extent of resection has shown to affect outcome in ependymomas in other series as well[7,8,18,45]. S Nair et al [70] in 1997 advocated although total resection of ependymomas have become a procedure with good functional results in most hands, a radical resection can be achieved with long term stabilisation of neurological deficits in majority of astrocytomas.

The present study substantiates this, based on our observation that patients who underwent either a total or near total resection improved in the majority or remained the same in the postoperative period. In our study, out of 57 patients on follow up, 30 patients underwent total or near total excision. 19 patients (63.3%) improved or were neurologically stable at follow up compared to their preoperative status (16 patients were astrocytoma and 13 patients were ependymoma histologically) .

Among the factors influencing outcome, apart from the extent of resection as previously mentioned, the histology was also found to be important, as seen by other studies[6,7,8,61].

In 1994 Cristante and Herrmann[7] reported that the outcome was aggravated, unchanged, and improved in 31, 55, and 17% of 69 patients with intramedullary tumors respectively. Constantini et al.[9] reported the outcomes of

aggravated, unchanged, and improved in 23.8, 60.4, and 15.8% of 164 cases of pediatric intramedullary tumor respectively, and Sandalcioglu et al [68] reported that the outcome was aggravated in 27 (34.6%) and unchanged in 51 (65%) of 78 cases of intramedullary tumor. In our study 30% patients showed improvement in their functional grades when compared to pre-operative status; in 33% outcome was not better while 27% were unchanged. In patients with a histological diagnosis of astrocytoma, 27.5% improved, 40% were neurologically stable while 32.5% showed worsening in their functional grade. 40% of patients with ependymomas showed improvement when compared to their pre-operative status while remained 20% static and 40% showed worsening in neurological status.

Intramedullary lesions arising in the thoracic cord have been found to have a less favourable outcome by various authors[7,21,34]. Hoshimaru et al have postulated that the tenuous blood supply of the thoracic cord may explain its higher susceptibility to operative injury during tumor removal[34]. Another reason is that thoracic lesions cause minor and vague symptoms and their long standing nature causes cord atrophy and arachnoid scarring which that particular segment of the cord tolerates poorly[34].

In the present study out of 68 patients there were 13(19%) patients harbouring tumors in the thoracic cord and 22 (32%) were in the cervico-dorsal region . Out of the 37 patients whose follow up is known , 33 patients out of 37 patients (89%) showed improvement in the late post operative period

/ follow up period when tumor was located in thoracic cord while in other level 17 out of 20 patients (85%) showed improvement .

Though thoracic location of tumor has been found to have a poorer outcome in most series in literature, our study did not show such a trend .

Adjuvant therapy in case of high grade astrocytomas is a well established standard of care though outcome is guarded[5,21]. The issue of external beam radiation therapy in astrocytomas and incompletely resected ependymomas is still debated. Cooper et al in his series of 51 patients, advised radiotherapy for all patients with astrocytomas irrespective of grading or extent of removal and for all incompletely resected ependymomas[6]. However. Constantini et al[9] advocate radiotherapy in those patients who have a short interval between recurrences, high grade tumors or significant residual disease in the conus here second surgery is unlikely to be contemplated. Sandalcioglu et al[68] have opined that a favorable outcome is more a result of radical tumor excision than adjuvant therapy and radiation should be reserved for malignant or non-resectable low-grade tumors with clinical and radiological evidence of progression [68]. Issacson[38] in his literature review also recommends conservative management for totally resected low grade tumors, while he advises radiotherapy for high grade lesions and for multifocal disease.

The role of adjuvant chemotherapy is still not established as a standard of care for spinal intramedullary astrocytomas. Various authors have used various drug regimen including cisplatin, carboplatin, irinotecan, vincristine and temozolamide either alone or in combinations [9] . The main utility of chemotherapy is in the setting of paediatric intramedullary tumors where the outcome is shown not to be influenced by radiotherapy, whereas radiation effects on the immature developing nervous and systems is well known[9]. Irradiation in this setting may also induce second malignancy in the spinal cord or brain in upto 20% over 30 years . A longer follow up with serial clinical and radiological documentation will probably help us in forming future guidelines regarding the regimen, the feasibility and safety of such therapies.

There have been various advances in diagnosis, surgical adjuncts like electrophysiological monitoring and advanced microsurgical techniques which help us evaluate, plan and execute better treatment for patients with spinal cord intramedullary tumors. Recent advances in adjuvant therapies including Cyberknife stereotactic frameless radiosurgery, improved drug delivery systems and gene-based therapies have also revolutionized the approach to these difficult tumors and their long term management. A healthy trend towards aggressive surgery followed by equally aggressive rehabilitation programs along with appropriate adjuvant therapy will probably aid in preserving and improving the neurological status of patients with this functionally devastating disease.

CONCLUSIONS

Intramedullary glial tumours occur commonly among males in the 2nd to 4th decades .

Among the glial tumours astrocytoma grade II form the commonest lesion subtypes .

Most common location is cervical cord segment .

Ependymomas have a good plane of cleavage and are thus amenable to radical excision.

Patients with good Mc Cormicks grade in pre operative stage are more amenable for total or near total excision.

Prognostic factors affecting outcome are the preoperative neurological status, the plane of cleavage, the extent of resection, the nature and grade of the lesion .

Surgery for intramedullary lesions can be carried out with acceptable morbidity and mortality .

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