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Personal experience in intramedullary lesions, in adults

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Keywords
intramedullary spinal cord lesions (IMSCL), radical excision, neurofibromatosis (NF), radiotherapy, stereotactic spine radiosurgery (SSR), chemotherapy, functional outcome

ABSTRACT

Background: Intramedullary spinal cord lesions (IMSCL) although they are rare, it generates invasion and destruction of the spinal cord. Such lesions must be diagnosed as early as possible, some have histological and genetic aggressiveness, generating severe functional neurological damage.

Objective: To identify the optimal strategy for diagnosis and treatment in IMSC, to improve prognosis.

Methods: A retrospective clinical study from 2001 to 2021, was performed on 33 adult patients (18 women, 15 men), diagnosed with magnetic resonance imaging with IMSCT. The most common topography was: thoracic 27 cases disposed between T_2-T_{12}, cervical 6 cases disposed between C_2-C_6, lumbar 2 cases at L_1-L_2. The most frequent symptoms in my cases were: unilateral radicular pain related to the tumour topography or bilateral diffuse burning pain, especially during the night; back and neck stiffness; paresthesia, motor disturbances with an ASIA score of 2-4, and severe atrophy especially in cervical topography, ataxia, initial retention, impotence and later loss of bowel and bladder function with incontinence. All patients were operated by the same senior neurosurgeon with at least 6 months of follow-up postoperatively. For functional outcome, the most important predictors are the preoperative neurological grade, and the high-grade IMSCT generating recurrence and reoperations.

Results: The patients addressed the clinic for pain and neurological deficits; the topography of the intramedullary lesion was confirmed by MRI native / with contrast, ultrasonography, and spinal arteriography. Several histologic entities were recorded: ependymomas - 12 cases, astrocytomas - 8 cases, hemangioblastomas - 3 cases, cavernomas - 6 cases, metastases - 2 cases, germ cell tumour - 1 case, malignant peripheral nerve sheath tumour - 1 case. Gross total excision was performed in 25 cases, with no mortality. In eight cases recurrences were recorded requiring the resumption of surgical treatment. In all cases physiotherapy-rehabilitation approach was used, and the outcome was correlated with pre-operatory motor deficits severity, 3 patients with thoracic high-grade astrocytoma underwent stereotactic spine radiosurgery (SSR) with Cyberknife abroad, stopping tumour growth one year after.

Conclusions: Intramedullary spinal cord lesions (IMSCL) are rare conditions, and MRI development allows an early diagnosis of these tumours. To adequately counselled patients, with minor preoperative deficits, real expectations concerning the functional outcomes, in benign tumours, and even anatomical healing should be based still on refinements of radical surgical excision. Actual radiotherapy techniques should be used in aggressive tumours.

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Introduction

Intramedullary spinal cord lesions (IMSCL) are rare neoplasms, with various etiology (1-15). Spinal cord compression with mass effect in benign lesions or destruction and invasion of the gray and white matter in aggressive tumors may lead to a variable degree of neurological dysfunction, different symptomatology (2)(3). Spinal MRI is essential for early diagnosis due to its sensitivity, is the preferred modality to characterize IMSCL for preoperative planning and early detection of recurrent lesions, even if it does not allow for histological diagnosis (1)(2). The management of IMSCL is mainly surgical (3-10), despite surgical morbidity; provides the best outcome; adjuvant radiotherapy may be an available alternative in aggressive tumors subtotal excised with ill-defined margins; the role of chemotherapy is still questionable. I present my strategy, during 20 years, for diagnosis and treatment in IMSCL, to improve prognosis.

Materials and methods

A retrospective clinical study from 2001 to 2021, was performed on 33 adults patients (18 woman, 15 men), diagnosed on magnetic resonance imaging with IMSCL. The most common topography was: thoracic 27 cases disposed between T2-T12, cervical 6 cases disposed between C2-C6, lumbar 2 cases at L1-L2. Most frequent symptoms in my cases were: unilateral radicular pain related to the tumor topography or bilateral diffuse burning pain, especially during night; back and neck stiffness; paresthesia, motor disturbances with ASIA score of 2-4, severe atrophy especially in cervical topography, ataxia, initial retention, impotence and later loss of bowel and bladder function with incontinence. All patients where operated by the same senior neurosurgeon with at least 6 months follow up postoperatively. For functional outcome the most important predictor are the preoperative neurological grade, and the high grade IMSCT generating recurrence and reoperations.

Results

The patients addressed the clinic for pain and neurological deficits; the topography of the intramedullary lesion being confirmed by MRI native with contrast, ultrasonography, spinal arteriography. Several histologic entities were recorded: ependymomas 12 cases, astrocytomas 8 cases, hemangioblastomas 3 cases, cavernomas 6 cases, metastases 2 cases, germ cell tumor 1 case, malignant peripheral nerve sheath tumor 1 case. Gross total excision was performed in 25 cases, with no mortality. In eight cases recurrence were recorded requiring the resumption of surgical treatment. In all cases physiotherapy-rehabilitation approach was used, outcome was correlated with pre-operatory motor deficits severity, 3 patients with high-grade thoracic astrocytoma underwent stereotactic spine radiosurgery (SSR) with Cyber-knife abroad, stopping tumor growth one year after.

Discussion

Intramedullary spinal cord lesions (IMSCL) are rare tumors, located within the spinal cord, occur in both adult and pediatric population, predominantly in the middle decades of life (1-3). Their incidence is evaluated at: 4 cases per million inhabitants and per year (9), 2-6 % of all central nervous system tumors, found most frequently in the thoracic cord (1-3).

Most important historical data in intramedullary lesions (2)(3):

-first successful removal of an intramedullary tumor was realized by Elsberg in 1907
-Greenwald in 1963 has large series of successfully removed tumors published
-Kurze in 1964 has introduced operating microscope

IMSCL can be linked to genetic diseases (1-9) - more common in patients with neurofibromatosis: ependymomas occur more often in patients with an average of 40 years with NF_2, hemangioblastomas (associated with von Hippel Lindau syndrome); astrocytomas occur more often in young adults with an average age of 30 years with NF_1

Most common IMSCL (1-15) are:

- *glial neoplasms* - 90-95%
- *spinal ependymoma*: 60% of all glial spinal cord tumors, are found in adults in the third to sixth decades prevalence for the fourth-decade, with a slight male predominance, arise from the cells of the ependymal canal, are soft and encapsulated, grow slowly, their plane of cleavage from the surrounding medullary tissue is clear, are located centrally within the spinal cord leading to symmetric expansion, occupy the whole width of the cord. Histologically, ependymomas can be classified into 4

types: myxopapillary ependymoma (WHO Grade I), subependymoma (WHO Grade I), ependymoma (WHO Grade II), and anaplastic ependymoma (WHO Grade III). Myxopapillary ependymomas account for up to 50% of ependymoma cases, typically arise from the filum terminale, and are usually located in the cauda equina while the other 3 subtypes follow the normal distribution of IMSCTs and are most often found in the cervical or thoracic spinal cord (90%) extending on average in length across 3 to 5 medullary segments, but also lower cord, in the conus medullaris, and filum, where an exophytic component may be present, rarely metastasize. Lesions are characteristically hypo vascular, well circumscribed, and non-infiltrative of the surrounding cord. Intramedullary ependymomas are generally low-grade, symptoms are due to compression of the surrounding cord rather than infiltration, complete resection often results in prolonged survival; malignant variants having been reported only very exceptionally, also with intratumoral hemorrhage. In my series I have had 12 ependymomas, 4 cervical and 8 thoracic, from which in only 3 cases I identify aggressive malignant ependymomas, who should be reopererated. In one case of thoracic malignant IMSCT ependymoma the patient developed a secondary active hydrocephalus and shunt was placed

- *spinal astrocytoma*: 33% of all glial spinal cord tumors, are common in the third to fifth decades, are infiltrative, glossy, associated with microcysts or syrinxes. The pilocytic varieties are well differentiated and tend to be indolent, with a definable surgical plane. Spinal astrocytoma predominate at the cervical-thoracic level (80%) extending on average over 6 medullary segments, positioned more eccentrically, with a poorly defined surgical resection plane. Different histologic aspect could be seen: *low-grade astrocytomas* - papillary type, can degenerate into a malignant subtype and *high-grade astrocytomas* - more polymorphic, aggressive with nuclear abnormalities, areas of necrosis, new vessels, intra tumoral hemorrhage. (7%– 30% of astrocytomas are considered malignant). Grade III and IV astrocytomas carried a poor prognosis - the most aggressive and infiltrative, with a mean survival of 15.5 months In my series there were 8 cases in the thoracic level, 5 cases relapsed after 2 years, requiring reoperation.

- *spinal primary glioblastoma multiforme*: 7.5% of all intramedullary gliomas and only 1.5% of all spinal cord tumors, locally invasive, rapid growth, may seed the CSF, with very poorly defined surgical resection plane

- *spinal oligodendroglioma* (3%) unproved responses to chemotherapy as in intracranial type

- *spinal ganglioglioma*: 1% of all glial spinal cord tumors, they are very rare tumors from both neuronal and glial origins that are composed of glial and ganglion cells, usually located within the cervical level, larger than other types of IMSCTs and difficult to distinguish on MRI. They tend to mostly affect older children and young teenagers, are typically benign, slow-growing tumors (WHO Grade I or II), although malignant transformation has been shown and is presumed to involve the glial component of the tumor.

- *spinal hemangioblastoma*: are the third most common IMSCL, account for 2 to 15%, are rare, benign tumors of mesenchymal origin that originate from the vascular system within the spinal cord, more common in men, tend to develop in the dorsal portion of the spinal cord and thus present with progressive sensory deficits, particularly proprioceptive deficits; highly vascularized, with risk of hemorrhage: subarachnoid hemorrhage (73%) or intramedullary hemorrhage (27%). Tumor consist of small mural nodules with cysts, associated with syringomyelia (occurs in approximately 50% of all intramedullary tumors, but is most frequently associated with hemangioblastomas) rarely extend beyond one or two vertebral bodies. Some tumors have a tendency to occur in multiple areas, and imaging the entire neuroaxis may be indicated. Removal of the lesion is considered curative. Approximately 10%–30% of patients diagnosed with spinal cord hemangioblastoma is strongly associated with von Hippel-Lindau disease: multiple spinal tumors with abnormalities such as renal cell carcinoma, pheochromocytoma, pancreatic cysts; gene mutation results in the enhanced transcription of several genes, including vascular endothelial growth factor (VEGF). I have had 3 hemangioblastomas in thoracic area.

- *spinal cavernomas*, are unusual: solitary or multiple vascular malformation with abnormally dilated blood vessels, surrounded by gliotic tissue, often stained with hemosiderin, expression of previous hemorrhage. Account to woman in two thirds of cases, during the fourth decade of life, could

be concomitant discovered both in the brain and spinal cord, also skin, retina, associated with café au lait skin lesions. I have had only spinal cavernoma, disposed 2 cervical and 4 in thoracic areas.

- *developmental tumors* (3%) are slow-growing neoplasms with a thoraco-lumbar predominance: *teratoma, germ cell tumors* of the CNS are made up of cells similar to the germinal cells that develop in the gonads. There are 2 types of germ cell tumors: nongerminomatous and germinoma. Patients with primary intramedullary germinomas typically present with sensory and motor deficits of the lower extremities that can progress to include gait disturbance and urological dysfunction.

- *intramedullary spinal cord lymphoma* is a rare form of primary lymphoma and can occur anywhere in the CNS. It can originate in the spinal cord, accompany tumors in other locations throughout the CNS, or occur as a part of systemic lymphoma. It is usually an aggressive nonHodgkin lymphoma of B-cell origin.

- *spinal paraganglioma*

- *intramedullary metastasis* from a primary malignancy found in the lung (49%), breast (15%), and lymphoma (9%), are rare, they affect 0.4% of all patients with cancer and represent 1%–3% of intramedullary tumors, only two cases in my series from lung cancer

- *spinal primitive neuroectodermal tumor*

- *solitary fibrous tumor*

- *intramedullary schwannoma*, *neurofibroma*,

- *malignant peripheral nerve sheath tumor* 1 case in my series

- *primary intramedullary melanoma* are very rare, account for about 1% of all melanomas, develop with progression of symptoms more rapidly.

- *lipoma* (2%) may be associated with cutaneous abnormalities, difficult to perform complete excision due to fibrous adhesions to the spinal cord

- *spinal cysts* in 70% of intramedullary tumors:

lesional (*intratumoral*) *cysts*, contained within the tumor itself, may result from necrosis, fluid secretion, or degeneration of the neoplasm; with peripheral enhancement; need to be resected along with the solid portion of the tumor because there is a high likelihood of neoplastic cells within the cyst wall. Such cysts were described in: ganglioglioma - 46%, spinal ependymoma - 22%, spinal astrocytoma - 21%, spinal hemangioblastoma 2-4%

non-tumoral (*reactive*) *cysts* occur rostral or caudal to the solid portion of the tumor, due to dilatation of the central canal, do not enhance, present in 60% of all intramedullary spinal tumors, may resolve once the neoplasm is resected.

Clinical signs in IMSCT lesions (2-16) depends on lesion size and topography, evolve in general slowly; diagnosis is often made late - on average after 4 years of evolution. Symptoms are in general not specific to spinal cord lesions, may be present in any myelopathic process; vulnerable vascular areas for vascular insult are cervical, T_1-T_4 and L_1 areas. More rapid evolution it is found in intramedullary metastasis (12-14), which are diagnosed within one month of symptom, onset in up to 75% of cases.

-pain - more than 50% of cases, may be local or radiating; often is the earliest symptom, characteristically occurring at night when the patient is supine. Pain could be: *spinal type* - occurring at rest, increasing with exercise, typically dull, deep, tenacious, with stiffness, *radicular type* - cervical, brachial, thoracic, sciatic and *posterior cord pains* - with numbness, paresthesia, sensation of burning, stricture.

-cervical stiffness, weakness of an upper limb in particular clumsiness of one hand progressive weakness may occur in the arms or legs. Intramedullary thoracic tumors associate pain, motor deficit of the lower limbs with variable limitation of walking, spasticity, abolition of osteo-tendinous reflexes, paresthesia and localized suspended hypoesthesia, accompanied by sub-lesional signs - Brown-Sequard syndrome

-limping, instability, weakness in walking, poor or loss of balance

-sphincter disorders (dysuria, constipation, genital problems even impotence) – see conus medullary involvement.

In cavernomas there are 4 clinical patterns (10):

-acute headache due to subarachnoid hemorrhage, also complete paralysis due to hemorrhage extension into the spinal cord

-mild neurological symptoms with acute onset of gradual decline during weeks to months, events related to small hemorrhage or thrombosis within the lesion, with changes in the microcirculation surrounding the lesions

-chronic mild neurological deterioration from months to years with acute episodes lasting for

hours to days with possible neurological recovery between episodes during weeks to months

-gradual slow neurological deterioration over months to years, caused by small hemorrhages, changes in the blood flow surrounding the lesion or to changes in the size of the malformation.

IMSCL diagnosis is difficult, with discreet not specific neurological signs; it is sustained on MRI (1-9)(16-18):

-T1 weighted images sequences: spinal cord is increased in volume on one or more levels; hypo- or isointense signal for both ependymomas and astrocytomas span multiple vertebral segments, also cavities secondary to trauma, arachnoiditis, anomaly of the cranio-cervical hinge, rostral and caudal cysts, malformative syringomyelia. Hypointensity at the tumor margin (17) was found to be a relatively firm pseudocapsule and hypointensity within the tumor corresponded to intratumoral hematoma. When MR imaging shows an intramedullary tumor with hypointensity at the tumor margin, it is suggestive, but not pathognomonic, of an ependymoma (17)

-T2 weighted images sequences: hyper signal of the fleshy portion of the tumor both ependymomas and astrocytomas, by the cysts; hyposignals linked sometimes to chronic bleeding (deposits of hemosiderin, etc)

-after Gadolinium intravenous injection MRI exams highlights, a contrast enhancement in the majority of cases, in contrast to intracranial neoplasms, even low-grade intramedullary tumors enhance to some degree; however, the absence of enhancement does not exclude an intramedullary neoplasm in the presence of cord expansion

Ependymomas often are located centrally within the spinal cord leading to symmetric expansion, occupy the whole width of the cord, and enhance diffusely with a well-defined border.

Astrocytomas tend to be positioned more eccentrically, can be non-enhancing or have an enhancing nodule or large satellite cysts, usually do not have a well-defined border. Intratumoral hemorrhage can be seen in both types but are more common in ependymomas (17).

Hemangioblastomas have homogeneous contrast enhancement compared to the more heterogeneous pattern found in astrocytomas or ependymomas. They also have mural nodules, are associated with syringomyelia, and can have significant surrounding edema, also several topographies.

In cavernomas: MRI is the current study of choice both for diagnosis and for surgical planning, with high sensitivity blood oxygenation level. The typical manifestation is that of a webbed core, composed of blood and blood products in various states of evolution "popcorn appearance", of mixed spinal intensity on both T_1 and T_2-weighted images, with a moderate occasionally strong absorption of contrast medium after Gadolinium. For previous hemorrhage a proof is a black ring of low signal intensity around the cavernoma consistent with hemosiderin deposits both in T_1 and T_2 indicating disturbances of susceptibility caused by the iron in hemosiderin. If edema is present, the signal outside the hemosiderin rim is increased on the T_2-weighted images. Small cavernous malformations may appear only as petechial areas of decreased signal density "black dots". Depending the age of a hemorrhage blood products are isointense to slighty hypointense on T_1-weighted images and hypointense on T_2-weighted images – susceptibility effect. Few days later in the subacute hemorrhage stade, the lesion that contains methemoglobine are hyperintense on T_1-weighted images and hypointense on T_2-weighted images. After several weeks on the hemosiderin chronic stade old blood products are hypointense on both T_1 and T_2 weighted images. In cavernomas edema is usually absent in smaller cavernous malformations, different from hemorrhagic neoplasms, even when small, with characteristic surrounding edema.

In germinomas: MRI typically shows an expanding mass - often at the lower thoracic level, contrast enhancement with T_1 - and T_2 - weighted MRI can vary and focal spinal cord atrophy may be an important sign (one case in my series). These may have a dense capsule, precluding complete removal; although, this may be compatible with prolonged symptom-free survival. When complete removal is unobtainable, debris produced by the tumor may cause an early recurrence of symptoms

In lymphomas: T_1 - weighted MRI shows homogeneous contrast enhancement in an enlarged area of the spinal cord, while diffusion-weighted and T_2 - weighted MRI demonstrate hyperintensity

Melanomas typically display hyperintensity on T_1 - weighted images due to the presence of melanin, while T_2 - weighted images are generally hypo- or isointense.

Spinal arteriography is useful in hemangioblastoma (8), to characterize feeding

vessels and associated dilated pial veins, for pre-operative embolization.

The study of somatosensory evoked potentials (P.E.S.) and motor evoked potentials (P.E.M.) makes it possible to quantify the neurological impairment, to specify its topography at the medullary level and to monitor postoperative progress. Intraoperatively, it is possible to record the P.E.S. but this exploration is complicated and ultimately not very useful because it does not modify the surgical technique (19).

Surgery is the treatment of choice, It should be performed as soon as possible, observation can lead to further neurologic deficits, some of which are irreversible; outcome it correlate with the preoperative neurologic conditions (2-15) (20-21). In the perioperative period or in a rapid decline in neurologic function occurs, steroids are used. The goals of surgical treatment are:

1. to maximize tumor resection – good predictor of outcome, looking for a clear dissection plane, with preservation of neurologic function, in one stage operation, to avoid adhesions, using operating microscope, micro neurosurgical instrumentation, CUSA, electrophysiological monitoring to reduce the incidence of iatrogenic damage: intraoperative somatosensory, motor evoked potentials
2. to obtain a tissue diagnosis, after analysis of the surgical sample
3. to improve neurologic functions minimizing further neurologic deficits, avoiding pain
4. in case of clinical and/or radiological progression, especially in benign lesions
5. adjuvant therapy for those cases where the lesion cannot be completely excised
6. to be suited by physiotherapy-rehabilitation approach to provide better outcomes (21)(22)

Surgical technique (2-6). After general anesthesia induction, opioids, propofol and low levels of muscle relaxants are used to minimize spontaneous muscle activity, to enable EMG, motor evoked potentials. Halogenated volatile anesthetics are avoided because these interfere with sensory evoked potentials (SSEP). An arterial line is needed to ensure that dips in blood pressure are detected and corrected as quickly as possible because the spinal cord is sensitive to decreased perfusion. The patient is positioned prone on bolsters or a Wilson frame, freeing the abdomen and thorax from pressure and taking care to pad all pressure points. For cervical and high thoracic lesions, the head is immobilized using a Mayfield head holder or equivalent. The level is confirmed by with C- arm, O-arm, navigation. A standard dorsal midline approach is used, subperiosteal dissection of the paraspinal musculature expose the lamina and spinous processes A wide laminectomy or laminoplasty next to the fleshy portion of the tumour is performed. Meticulous hemostasis is obtained. A closed dura mater ultrasound is performed to confirm the correct exposure of the tumor, the satellite cysts being empty of echo. The dura is wide, bloodless exposed for 2 cm rostral and caudal to the upper and lower lesion margins. The dura is sharply incised on the midline, reflected to expose the lesion, the dural edges, without tension, are tacked to the soft tissues laterally using No. 4-0 silk sutures exposing the arachnoid overlying the swollen spinal cord. The tumor is localized visually with intraoperative ultrasound. Under operating microscope, the arachnoid is opened and tacked laterally to the dural edges, a midline longitudinal myelotomy between the dorsal columns, at the thinnest area between the tumor and spinal cord are performed, exposing the entire posterior face of the tumour, cysts adjacent to the tumor poles are open, the fine vascular network on the posterior face of the tumour is preserved also the white matter tracts; for eccentric lesions, incision through the dorsal root entry zone can be performed. The pia is sharply incised, the dorsal columns are dissected apart, traversing blood vessels are cauterized and divided, the tumor is encountered. The spinal cord parenchyma is dissected circumferentially off of the tumor capsule, looking for a clear plane between cord and tumor, sectioning and cauterizing thin vessels. the initial area of approach could be changed if the tumor has an exophytic component. A tumor specimen should be sent for frozen section early on in the dissection.

Intramedullary benign lesions (10) should optimally be removed en bloc, releasing the lesion poles and the anterior part of the lesion, disconnecting from its major blood supply off of the anterior spinal artery. If lesion are located more ventrally the margins of the myelotomy may be retracted with pial sutures. For very large lesions, for lesions with poor internal integrity and lesions with

an unclear surgical plane: a micro dissector, Cavitron ultrasonic surgical aspirator (CUSA) is often useful either to debulk internally to facilitate capsule dissection or to perform an inside-out resection, facilitating complete removal (20)

Intraoperative electrophysiology, such as somatosensory-evoked potentials and motor-evoked potentials may lead to improved outcomes, had a high sensitivity and specificity to prevent neurologic damage, but limited the extent of tumor resection (19) .

Dura is closed primary using a running stitch, or in case of subtotal resection dural grafting and sealants may be necessary to aid closure water-tight. Hemostasis should be careful performed, then the musculo-aponeurotic and cutaneous planes are closed, without drainage.

The outcomes of surgery (3)(4)(9)(10)(21-22) are related to:

-*early intervention*

-*younger age* (advancing age > 60 y is a negative prognostic factor)

-*the extent of preoperative neurologic deficit*: mild-to-moderate deficits often improve significantly following surgical removal, while those with advanced neurologic compromise generally have no worthwhile improvement

-*lesion topography*: patients with cervical tumors should be considered for continued mechanical ventilation in the immediate postoperative period with corticosteroid usage, upper thoracic and conus lesions induce higher morbidity, tumors spanning several levels requires extensive dissection of the spinal cord in order to expose the tumor.

-*extent of resection* - MRI the day after surgery gives the best estimate of completeness of resection, quality of surgery

-tumor histology:

-*for grade II WHO ependymomas* - gross total resection is reported in more than 90% of cases, with a distinct tumor and normal spinal cord interface. The rate of recurrence is dependent on the extent of tumor resection, avoiding scarring and cord atrophy

-*for low-grade astrocytoma*, if a plane can be developed between the non-encapsulated tumors tumor and spinal cord, gross total resection is an option

-*for low-grade astrocytoma with no definable plane of resection, high-grade astrocytoma*, biopsy plus limited resection or subtotal resection can be attempted, despite recurrence in 47.6% of patients (4). Postoperative radiotherapy can be used for *high-grade astrocytomas*, but with longer-term consequences - several adverse effects, including radiation myelopathy, radiation necrosis, vasculopathy, changes to the normal spine parenchyma and a 25% risk of secondary tumors in 30 years (6). For high-grade lesions, such as anaplastic astrocytoma and glioblastoma (15), the prognosis is clearly poor, aggressive surgical resection having a debatable role in prolonging survival.

- in *hemangioblastomas* preoperative embolization can attenuate their rich vascular supply, such tumors exhibit a clear dissection plane, a complete resection is expected in 83% to 92% of patients with clinical improvements, especially for those disposed in the posterior half of the spinal cord. The presence of a syrinx suggests a noninfiltrative lesion and carries a better prognosis. Patients with von Hippel Lindau disease (8) are at risk of developing new lesions and must have their entire neuroaxis imaged periodically.

- in *spinal gangliogliomas*, resection is the primary treatment of choice, achieved at a much higher rate (83.3%) even in cervical spinal cord; spinal gangliogliomas have a higher relative risk of recurrence than both cerebral and brainstem topography and have a 10-year survival rate of 83%.

- In *aggressive intramedullary tumors* removal of tumor has not been shown to be of value, with survival of less than 2 years see anaplastic astrocytoma, a radical surgical removal can lead to severe neurologic impairment Recent studies, however, have shown that surgical intervention for the management of high-grade astrocytoma is associated with higher rates of long-term neurological complications with no derived benefit for patients (4). When a plane of dissection is absent (15), resection is often associated with poor outcomes (despite advances in microsurgical techniques, electrophysiological monitoring during the procedure). Fluorescence-guided resection of malignant cerebral gliomas utilizing 5-aminolevulinic acid (5-ALA) and protoporphyrin IX (PpIX) accumulation in tumors has not been determined in spinal intramedullary tumors (4)

- in *intramedullary lipomas* limits between lipoma and medullary tissue are imprecise, limiting surgical technique

- for *metastases, neuromas, teratomas, germ cell tumor, malignant peripheral nerve sheath tumor* the surgical technique remains unchanged, type of excision depending on the infiltrative nature of the lesion.

- in *cavernomas* surgical indication should be reserved to those with symptomatic lesion, causing objective neurological deficit, especially to those lesions that extend to the dorsal surface of the spinal cord with an exophytic component, subtotal removal can generate future hemorrhages.

- for *residual tumor growth or recurrence*, imaging the entire neuraxis is warranted to detect seeding. Therapeutic alternatives are: observation, repeat resection (reoperation is possible even in high grade lesions, but with high functional results), radiation therapy. For astrocytomas and ependymomas with no clear surgical resection planes, initial irradiation (20) improves neurological deficits.

- *closed follow-up*: increasing symptoms or new neurological deficits should lead to a search for tumor growth; *in general there is a transiently neurological worsening after surgery* - deep sensitivity disorders, balance, motor deficits; new-onset urinary retention may require prolonged bladder catheterization, either continual or intermittent, also a bowel stimulation regimen.

- *possible postoperatory complications*: spinal hematoma, deep vein thrombosis, pulmonary embolism, atelectasis, arachnoiditis, tumor dissemination, bedsores, infectious or chemical meningitis particularly from epidermoid and dermoid tumors, CSF fistula and meningocele, wound infection, sepsis, hydrocephalus.

- physical therapy, occupational therapy, rehabilitation should be instituted early in the postoperative course.

Radiotherapy in the management of IMSCL remains controversial (23-25):

- no lesion should undergo radiotherapy without a tissue diagnosis

- in spinal myxopapillary ependymomas more recent studies suggest that radiotherapy is not associated with lower overall recurrence regardless of the extent of resection (24)

- in radiosensitive germinomas 5-year survival rates of 65%–95% with irradiation alone is possible; for multiple spinal cord germinomas chemotherapy with cisplatin and etoposide might provide an alternate option in the treatment of intramedullary germinomas that could avoid the negative side effects associated with radiation treatment

- radiotherapy may be primary treatment for local control and survival in case of inoperable tumors and aggressive tumors such as: high grade ependymomas, anaplastic astrocytomas and glioblastomas with modestly improvement. Modern treatment planning and imaging allow more accurate target definition and respect for related normal tissue tolerances (23)

- in cases of residual or recurrent tumor viable options are watchful waiting, reoperation, radiation

- radiotherapy is responsible for acute and delayed myelopathy, increased difficulty with subsequent surgical tumor removal, diminished skeletal growth in young people.

- stereotactic spine radiosurgery (SSR)(25) is an alternative treatment option to conventional radiotherapy, effective and safe, using externally generated ionizing radiation to inactivate or eradicate defined targets in the spine, to reach local control by delivering large cumulative doses of RT in fewer fractions (less than 5). The most commonly utilized SSR machines include Elekta Synergy S, Novalis (Brainlab) and CyberKnife; all systems have excellent accuracy, targeting areas remain accurate to within 1mm. Prior reports of stereotactic spine radiosurgery for intramedullary metastases, arteriovenous malformations, ependymomas, and hemangioblastomas demonstrated favorable outcomes (25).

Chemotherapy (2-15) is considered experimental in the treatment of spinal cord tumors; is knowed the inability of large molecules to bypass the blood–spinal cord barrier (BSCB); unlike cerebral topography, intramedullary tumors do not respond to chemotherapy, also the rarity of these types of tumors make it very difficult to evaluate therapeutic options and potential at a statistically significant level

- *the topoisomerase-2 inhibitor, etoposide, temozolomide* had modest benefit and had a partial response in 2 of 10 treated patients (20%)(6) also with constipation, fatigue, neutropenia, lymphopenia and thrombocytopenia in several patients; 27% progression-free survival at 2 years with a median survival of 23 months

- *antiangiogenic therapy using the VEGF receptor-2 inhibitor SU5416* in patients with hemangioblastomas

and von Hippel Lindau disease (4)(8) shown to be somewhat effective; in contrast, the use of the monoclonal antibody bevacizumab to inhibit the VEGF receptor was shown to be ineffective, resulting in increased tumor invasiveness following antiangiogenic therapy, in conclusion some hemangioblastomas might show responsiveness to angiogenesis inhibitors, while others may not, depending on the level of upregulation of the VEGF gene

- *bevacizumab* may be beneficial for patients with significant tumor burden that is not amenable to resection - spinal cord ependymomas in neurofibromatosis type NF_2 (2)(3)(9)

- *epidermal growth factor receptor (EGFR) inhibitor gefitinib* following radiotherapy and other chemotherapeutic agents in intramedullary metastases from lung adenocarcinoma with mixed results of efficacy: 2 weeks improvements, even complete response; such response warrants continued investigation (13)

- *high-dose methotrexate-based therapy combined with alkylating agents such as temozolomide* has been shown to be effective in elderly patients suffering from primary CNS intramedullary lymphomas

- *in spinal melanomas* intrathecal injections of interferon-b, chemotherapy with dacarbazine following the resection of a primary spinal melanoma

While resection is the primary treatment option for intramedullary melanoma, gross total resection is difficult and most patients will require (20) postoperative radiotherapy (a combination of whole-brain and local radiation therapy), intrathecal injections of interferon-b and chemotherapy with dacarbazine following the resection of a primary spinal melanoma and demonstrated the control of progression and prolonged survival.

Therapeutic perspectives (22)(25) in intramedullary tumors are:

-development of neuroprotective agents to be use during surgery

-the development of drug delivery systems that allow the precise localization of chemotherapeutic drugs

Conclusions

Intramedullary spinal cord lesions (IMSCL) are rare condition. MRI even if it does not allow for histological diagnosis, still is the preferred method of diagnosis due to its sensitivity de detect lesion for preoperative planning: size, location, length, extent of surrounding edema, focal or diffuse spinal cord expansion, the cord - lesion interface, associated cysts, also to early detect recurrent lesions. To adequately counseled patients, with minor preoperative deficits, in benign lesion, real anatomical healing should be based on refinements of radical surgical excision. Actual radiotherapy techniques should be used in aggressive tumors anaplastic astrocytomas and high-grade ependymomas who are associated with a higher rate of recurrence, where radical excision is not achieved or in inoperable cases.

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