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Review

Clinical Aspects of Spinal Meningiomas: a Review

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Abstract

Spinal meningiomas are found in all age groups, predominantly in women aged over 50 years. The clinical symptoms of this condition may range from mild to significant neurological deficit, varying widely depending on the location, position in relation to the spinal cord, size and histological type of the tumor. Magnetic resonance imaging is the diagnostic tool of choice because it shows the location, size, the axial position of the tumor, and the presence of concomitant conditions such as spinal malformations, edema or syringomyelia. According to the degree of malignancy, the World Health Organization divides meningiomas into three grades: grade I - benign; grade II – atypical, and grade III - malignant. The goal of the surgery is total resection which is achievable in 82%–98% of cases. Advances in radiosurgery have led to its increased use as primary or adjunct therapy. The current paper aims to review the fundamental clinical aspects of spinal meningiomas such as their epidemiology, clinical presentation, histological characteristics, diagnostics, and management.

Keywords

management, outcome, radiosurgery, spinal meningioma, surgery

INTRODUCTION

Spinal meningiomas (SM) are benign, slow-growing, well-delineated, extramedullary tumors with tendency for lateral spread in the subarachnoid space.[1] They are one of the most common spinal intradural extramedullary tumors (SIET) and are observed along the entire length of the spine axis, but predominantly in the thoracic region.[2] Timely diagnosis and treatment of SM continue to be a challenge, depending on their histological nature, localization in the various segments of the spine and their position in relation to the spinal cord.

The current paper aims to review the fundamental clinical aspects of SMs such as their epidemiology, clinical presentation, histological characteristics, diagnostics and management.

Epidemiology

The incidence of primary intraspinal neoplasms is about 5 per 1,000,000 for females and 3 per 1,000,000 for males.[3] SIETs account for two-thirds of the primary spinal tumors in adults and about 50% in children.[4] SMs represent 25% –50% of all intradural extramedullary tumors with a frequency of 0.5 to 2 per 100,000 people per year.[5,6] In 64%–84% of cases, SMs are located in the thoracic region with dorsal, dorsal-lateral or lateral location; in 14%–27%, they are located in the cervical area and have predominantly ventral location and only in 2%–14% they are located in the lumbar region.[7,8] According to Subačiūtė[9], the localization of CM depends mostly on gender. In men, they are 21.4% in the cervical region, 21.4% in the lumbar and 57.1% in the thoracic, while in women, they are only

5.9% in the cervical, 12.8% in the lumbar, and 81.4% in the thoracic region.[9]

Meningiomas are the most common benign tumors localized at the level of foramen magnum, while they are found much less frequently in the lower cervical area.[10] In people under 50, the incidence of cervical localization is more common, with most of them located in the upper cervical region.[7,10] Unlike thoracic meningiomas, those in the upper cervical spine and foramen magnum are ventrally or ventro-laterally positioned and sometimes are closely adherent to the vertebral artery.[11]

Spinal meningiomas with intradural and extradural spread are observed in 5% to 6% **(Fig. 1)**.[12] Atypical localization, such as intramedullary, purely epidural or extraforaminal is very rare.[13-15]

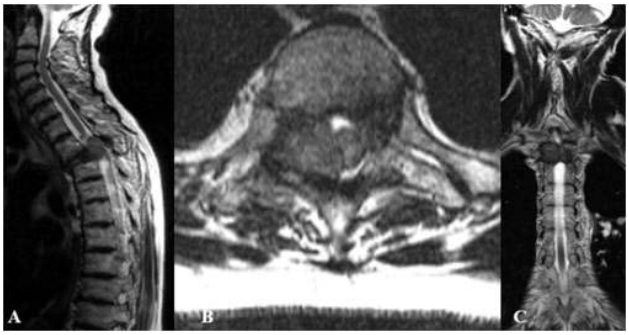

Figure 1. T2-weighted MRI (A-C) in a patient with extradural and intradural atypical thoracic meningioma at T2–T3 level infiltrating the right pedicle of Th2 vertebra.

SMs are found in all age groups, but much more often between the 5th and 7th decades of life.[16] 75%–85% of the meningiomas are observed in women, and according to Pereira et al., the ratio of women to men ranges from 4:1 to 8:1.[4,12] Prevalence in females is explained by the presence of sex hormones and other receptor types (steroids, peptidergic hormones, growth factor, etc.) that can initiate tumor formation.[17] According to Pradenkova et al., progesterone and estrogen have opposing prognostic indications for meningiomas.[18] They found that the expression of progesterone receptors in meningiomas resulted in a more favourable outcome, whereas the presence of estrogen receptors correlated with more aggressive clinical behavior and relapses.

From an epidemiological point of view, SMs are more common in post-menopausal women, especially those diagnosed with osteoporosis.[2] According to some authors, traumatic injury to the spinal meninges from direct contact with fragments of osteoporotic fractures may trigger a reparative proliferative process leading to the onset of a tumor process.[19]

Clinical presentation

The clinical symptoms of SM range from mild to significant neurological deficit, varying widely depending on the location, position in relation to the spinal cord, size and histological nature of the tumor.[20] SMs are manifested clinically by symptoms of progressive radiculalgia, radiculopathy and myelopathy.[21] Pain is the most common symptom at the onset of the disease, and it can be radicular, funicular or local. Sensory impairment (paresthesia, hypesthesia or anesthesia) and pronounced motor weakness (paresis or paralysis) are the next most common symptoms that are falsely attributed to multiple sclerosis, syringomyelia, pernicious anemia and disc herniation.[22] Sphincter disorder is late symptom seen in 15% to 40% of patients.[23]

The time span from the debut of complaints to diagnosis ranges from 12 to 24 months.[24,25] Delayed diagnosis is more commonly observed in the elderly, as complaints are attributed to comorbid conditions such as cerebral atherosclerosis, parkinsonism, diabetic neuropathy, spondylosis, osteoporosis, etc.[12]

Diagnostics

Magnetic resonance imaging (MRI) is the diagnostic tool of choice because it shows the location, size, and axial position of the lesion and the possible presence of existing spinal malformations, edema or syringomyelic cavities within the spinal cord.[5,26] On MRI, the tumor usually presents as iso- or hypointense on T1 and slightly hyperintense on T2. Gadolinium enhancement may result in accumulation of contrast media in the lesion itself, and in the adjacent part of the dura, known as "dural tail sign" **(Fig. 2)**.[26,27]

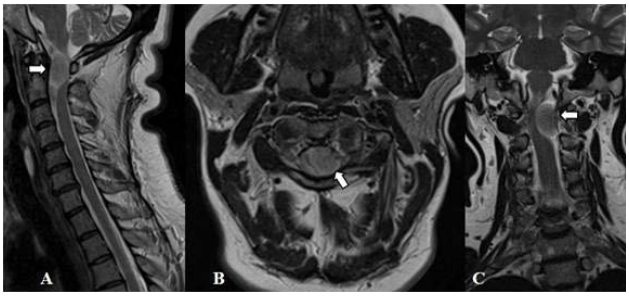

Figure 2. T2-weighted MRI in a patient with left ventro-lateral foramen magnum meningioma extending to C1-C2 level in sagittal, axial and coronal views (A-C).

The presence of calcifications in the tumor elicits a strong signal in the T2 sequence, but those are better visualized by CT.[28] CT-assisted myelography is considered to be complementary to MRI, especially for the identification of intradural tumors in the lumbosacral region or in cases of intradurally and extradurally located tumors and is still used in cases where MRI is contraindicated **(Fig. 3)**.[29]

Spondylography is of low informative value in the diagnosis of SMs, but sometimes the visualisation of a pronounced calcified tumor is possible.[30]

The en-plaque types of meningiomas are very rare and fixed to dura mater on a broad base. The presence of peripheral calcifications on the dura should cast suspicion

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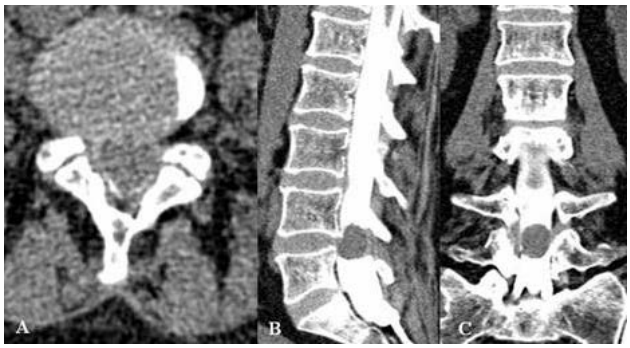

Figure 3. CT-assisted myelography with axial, sagittal and coronal reconstruction, demonstrating lumbar meningioma at L4-L5 level (A-C).

for such type of tumor.[31] Generally, SMs are smooth and fibrous with crumbly content. The epidural space is well defined, which is why the involvement of bone structures is rarely observed in SM.

Unlike intracranial meningiomas, spinal meningiomas do not penetrate the pia mater, which can be explained by the earlier detection of myelopathic signs and the presence of intact arachnoid layer.[32]

Spinal angiography is often used preoperatively in cases of SMs in the thoraco-lumbar region to identify the Adamkiewicz artery and its relationship to the tumor.[2] In some cases, spinal angiography is used to perform preoperative embolization of tumor-feeding vessels to reduce neoplasm volume and intraoperative hemorrhage.[2]

Histological characteristics of meningiomas

CNS meningiomas are thought to originate from arachnoid cap cells of the neural crest or mesodermal cells. While arachnoid cap cells of the telencephalon meninges originate from neural crest cells, meningiomas of the rest of the CNS arise from mesodermal fibroblasts, which determines the rare ventral and dorsal location of the SM.[33] The typical lateral localization of the SMs is attributed to arachnoid cap cells located in the leptomeningeal sheaths near the outlet areas of the spinal nerve roots or to the entry points of the arteries in the spinal canal.[4] Because SMs originate from the leptomeninges, most of them have a wide attachment area and their blood supply originates from dural vessels.[4]

According to the World Health Organization classification, there are 15 histological subtypes of meningiomas. Despite their morphological diversity, the prognosis is generally favourable, owing mainly to their benign nature and slow growth which makes them amenable to radical surgical resection.[34] The extent of resection on the Simpson scale is an important prognostic factor for tumor recurrence.[34] On the other hand, a study by Jääskeläinen found that in 20% of benign meningiomas with total resection, recurrences still occur within 20 years.[35] According to Harter et al., there are subgroups of meningiomas that are prone to recur or even undergo malignant transformation despite total excision.[36]

The WHO classification of CNS tumors subdivides meningiomas into three main grades, reflecting the degrees of malignancy, based on histo- and cytomorphological criteria: grade I (benign), grade II (atypical) and grade III (malignant).[37] The meningiomas are subdivided into 15 histo- and cytomorphological types, nine of which correspond to WHO grade I, three correspond to WHO grade II, and the other three correspond to WHO grade III.[37] WHO grade I meningiomas have a frequency of 3.68/100,000 in males and 8.56/100,000 in females.[38] The incidence rate of grade II meningiomas is 0.26/100,000 in men and 0.30/100,000 in women, and of grade III - 0.08/100,000 in males and 0.09/100,000 in females.[38]

The most common histomorphologic subtypes of WHO grade I meningiomas are meningothelial, fibrous, transitional and psammomatous variants.[37] A criterion for determining atypical meningiomas (grade II) is the presence of increased mitotic activity (4-9 mitoses/10 high-power fields) or at least 3 of 5 histo- and cytomorphological criteria.[36] As anaplastic (grade III) meningiomas are considered those with >20 mitoses/10 high-power fields or loss of meningothelial differentiation which leads to the occurrence of tumor-like sarcomas, carcinomas or melanomas.[39]

WHO accepts the degree of SM resection as the most important prognostic factor affecting recurrence rate. Nevertheless, approximately 20% of grade I tumors tend to recur and adjuvant radiation therapy is not required in all grade II tumors.[40-42]

Treatment

SM treatment is mainly surgical. The most commonly used surgical approach is posterior or posterolateral by single-level laminectomy, or single- or two-level hemilaminectomy that can extend laterally if needed to reach ventral or ventral-lateral tumors. This standard access is used in about 100% of cases.[6] According to the literature, the rate of total resection of SM approximates 95% with low morbidity and mortality.[24,43] These results render the general opinion that the purpose of surgical treatment is total resection, with the greatest difficulty arising from the localization of the tumor in relation to the spinal cord.[12] In ventrally located tumors, extensive bone resection may require additional instrumentation to augment spinal stability.[44] The selection of appropriate surgical approach and technique should depend on the site of SM origin. In neoplasms localized dorsally, complete resection of the attachment zone followed by plastic dural closure is feasible, whereas in those located ventrally, this is technically demanding and many surgeons use electrocoagulation only. Studies with follow-up exceeding 10 years found recurrence rates between 6% and 9.7%, despite total resection (Simpson grade I or II).[45] The recurrence rate is significantly higher with subtotal resection (Simpson grade ≥ 3).[45,46] There is conflicting evidence regarding the benefit of radical resection of spinal meningiomas, in particular Simpson grade I versus grade

II. According to Heald et al., there is no significant difference between grade I and II resections.[46] Nakamura et al. established the presence of residual tumor cells on histological examination in the adjacent dura after Simpson grade I resection and negative postoperative MRI.[45] In patients with subtotal resection (Simpson grade IV), the inability to remove the attachment zone is significantly associated with shorter recurrence period, depending on the extent of tumor excision.[47] Further studies are needed to determine the optimal treatment strategy in cases where radical resection is impossible or hazardous. Although the literature data discussing surgical outcome of recurrent meningiomas is based on small series, it still reports favourable results, which suggests that tumor recurrence does not necessarily preclude good postoperative outcome.[48]

Recently, radiosurgery has also been used to treat SMs with results that are promising and comparable to those of intracranial meningiomas.[2] Although most studies do not have long-term follow-up, adequate disease control and reduction of tumor size are reported, but further MRI based research is required for definitive evaluation of this treatment modality.[49]

In addition to the degree of surgical resection, a number of other factors are associated with poor prognosis in the treatment of SMs. According to Bruner et al., the psammomatous histological subtype is associated with poorer results after neoplasm resection compared to other subtypes.[50] This indicates that the degree of cellular aplasia can serve to predict long-term outcome in patients harbouring these tumors.

In the past, immunohistochemical quantification of proliferative potential by examination of the Ki-67 marker was used as an indicator to predict the probability for recurrence and malignant transformation of resected meningiomas.[51,52] Although the trend of exploring this marker is increasing, more research is needed to determine its significance. When comparing SMs with their intracranial counterpart, Ki-67 indexes are significantly higher in intracranial meningiomas, although there is no difference in the observed rates of recurrence.[53] Further study on the molecular basis for recurrence and malignant transformation is needed to determine the exact impact of these markers on the prognosis of SM.

There is insufficient evidence regarding the outcome of surgical treatment of anaplastic meningiomas due to the extreme rarity of these tumors. The total surgical excision of these lesions is a major factor that plays a role in the 5-year survival rate of such patients.[54,55]

CONCLUSIONS

SMs represent a significant proportion of spinal tumors. Nowadays, these lesions are easily diagnosed through modern neuroimaging that allows early diagnosis. The main goal of surgery should be total tumor removal. The main factor determining the prognosis of the disease is the early diagnosis in order to avoid the development of irreversible neurological deficit. Despite delayed diagnosis and difficult localizations, these tumors can be successfully removed with minimal complications. In cases where subtotal resection is performed, radiosurgery may be used as an adjunct therapy. Extensive bone resections during surgical approach may necessitate the use of instrumentation to guarantee spinal stability.

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Клинические аспекты менингиом позвоночника: обзор

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Резюме

Менингиомы позвоночника встречаются во всех возрастных группах, но преобладают у женщин старше 50 лет. Клинические симптомы этого состояния могут варьироваться от лёгких до значительных неврологических нарушений, широко варьируя в зависимости от локализации, положения по отношению к позвоночнику, размера и гистологического типа опухоли. Магнитно-резонансная томография является предпочтительным диагностическим инструментом, поскольку она определяет местоположение, размер, осевое положение опухоли, наличие сопутствующих состояний, таких как пороки развития позвоночника, отек или сирингомиелия. По степени злокачественности Всемирная организация здравоохранения делит менингиомы на три степени: 1 степень – доброкачественная; 2 степень – атипичная и 3 степень – злокачественная. Целью операции является тотальная резекция, которая достижима в 82–98% случаев. Достижения в радиохирургии привели к её частому использованию в качестве основной или адъювантной терапии. Эта статья направлена на обзор основных клинических аспектов гемангиом позвоночника, таких как эпидемиология, клинические проявления, гистологические особенности, диагностика и лечение.

Ключевые слова

лечение, исход, радиохирургия, менингиома позвоночника, хирургия