Case report

A case of an anaplastic meningioma metastasizing to the mediastinal lymph nodes

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Context: Grade II and III (World Health Organization classification) meningiomas rarely develop in the spinal cord. However, we experienced a case with an anaplastic meningioma that developed in the spinal cord at the cervicothoracic junction and metastasized to the mediastinal lymph nodes. No such cases have previously been reported.

Findings: The patient was a 68-year-old man who developed back pain that did not affect his daily living. He developed left lower limb paralysis, and was admitted after magnetic resonance imaging (MRI) revealed an intramedullary tumor at the level of cervical vertebra 7 and thoracic vertebra 1. Positron emission tomography revealed tracer uptake in the intramedullary tumor and the mediastinal lymph nodes, suggesting a metastatic spinal cord tumor or malignant lymphoma. A lymph node biopsy was then performed. Although the tumor was highly malignant, its primary site was not identified. Detailed examinations by several other departments revealed no abnormalities. On hospital day 30, his left lower limb paralysis deteriorated, and MRI revealed that the tumor had grown. Thus, laminoplasty, laminectomy, and tumor resection were performed. The tumor was an anaplastic meningioma that resembled mediastinal lymph node tissue, and other tumor lesions were not found. These findings suggested that an anaplastic meningioma had metastasized to the mediastinal lymph nodes. The patient did not respond to radiotherapy, and he was transferred to another hospital.

Conclusion: In cases of intramedullary spinal tumors with metastasis without other potential primary tumor lesions, early diagnosis and treatment should be performed while considering anaplastic meningioma.

Keywords: Anaplastic meningioma, Malignant meningioma, Lymph nodes, Metastasis, World Health Organization classification

Introduction

Tumors that originate from arachnoid cap cells which form the outer layer of the arachnoid mater and arachnoid villi are usually benign and are known as meningiomas. They are classified as Grade I by the World Health Organization (WHO) classification system and include meningothelial, fibrous, transitional, and psammomatous tumors.^{1,2} Spinal meningiomas account for 25% to 46% of all spinal cord tumors and approximately 12% of all meningiomas. These often develop in the thoracic spine, arising most commonly in middle-aged women, and are likely to develop in the thoracic spine.^{3,4} Although spinal meningiomas usually develop in the intradural extramedullary space, they also occasionally develop in the intramedullary space.^{5,6}

Meningiomas of WHO Grade-II (clear cell, chordoid, atypical meningiomas) or Grade-III (papillary, rhabdoid, anaplastic meningiomas) usually do not develop in the spinal cord.⁷

We describe a case of anaplastic meningioma at the cervicothoracic junction of the spinal cord that metastasized to mediastinal lymph nodes. To the best of our knowledge, this is the first report of such a case.

Case report

The patient was a 68-year-old man who developed back pain without any known trigger 4 months earlier. Because he also had bradycardia and other symptoms, he visited a cardiovascular clinic. A detailed examination was performed, but no abnormalities requiring treatment were found and he was subsequently monitored as an outpatient. Four months later, he noted sudden muscle weakness in his left lower limb. He

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visited an orthopedic clinic with a referral and underwent cervical magnetic resonance imaging (MRI). The MRI revealed an intramedullary tumor that extended from cervical vertebra 7 (C7) to thoracic vertebra 2 (T2). He was then referred and admitted to our hospital.

Upon admission, his tactile and pain perceptions were hypersensitive at or below the papilla, and his position sense was impaired in both lower limbs. All tendon reflexes were normal, and no pathologic reflexes were found. Manual muscle test (MMT) results were Grade N for all the upper limbs. For the lower limbs, results were Grade P for left iliopsoas muscle, Grade G for left hamstring, and Grade N for other muscles.

Radiography did not reveal instability or scalloping. T2-weighted MRI revealed a high-intensity area that was suggestive of edema in the marrow from C3/4 to T5 and an intramedullary lesion with relatively homogeneous enhancement on the left side of the spinal cord at the C7-T1/2 level. In addition, an intradural extramedullary lesion that was not contiguous with the other lesions was observed on the left side of the spinal cord at the T2/3 level. Contrast-enhanced imaging revealed continuous enhancement in the area from the intradural extramedullary tumor to the radicle (Fig. 1). Positron emission tomography (PET) revealed tracer uptake with a standardized uptake value (SUV) of 9.8 in the tumors in the thoracic spine and uptake in the lymph nodes on the lateral side of the thoracic aortic arch. No uptake was observed anywhere else (Fig. 2). Although contrast-enhanced head-to-pelvis computed tomography (CT) revealed bullae and bilateral renal cysts, no apparent tumor lesions, inclusive of intracranial tumors, were observed. The exception was lymphadenopathy on the lateral side of the thoracic aortic arch, which exhibited uptake on PET.

A blood test did not reveal anything of note in the biochemistry, blood counts and coagulation factors. The levels of tumor markers including soluble interleukin (IL)-2 receptor, carcinoembryonic antigen, squamous cell carcinoma antigen, and prostate-specific antigen were all within normal ranges. An upper and lower gastrointestinal endoscopy (echo imaging) performed in the Department of Otorhinolaryngology and examination in the Department of Dental Surgery found no abnormalities. Referral to the Department of Dermatology revealed no apparent lesions on the body surface. Cerebrospinal fluid examination revealed albuminocytologic dissociation with a protein level of 157 mg/dL, glucose level of 53 mg/dL, and normal levels of the angiotensin-converting enzyme and soluble IL-2 receptor.

Cytology revealed a large number of lymphocytes and macrophages; however, these results were graded as Class II and no apparent tumor cells were found. Contrast-enhanced MRI of the head did not yield any abnormal findings. However, contrast-enhanced spinal CT revealed swelling of the spinal cord at the T1-2 level. At the level of the T2/3 intervertebral foramen, a space-occupying lesion lacking enhancement was observed on the left side of the dura mater. An extramedullary lesion was also observed on the dorsal side of the spinal cord at the T1-2 level (Fig. 3). No bone destruction was observed. Because no other lesions were observed, differentiation based only on imaging studies was difficult to achieve. On hospital day 14, a biopsy was performed on the mediastinal lymph node in the left thorax. In the tissue biopsy specimen, large polymorphic spindle cells with prominent nucleoli were diffusely distributed on a background of fibrous stroma (Fig. 4). These findings raised the suspicion of metastasis of a malignant tumor. However, immunostaining was positive for cytokeratin (anion exchanger 1/3 and myocyte nuclear factor 116) and negative for the cluster of differentiation (CD) markers 79a, CD20, CD3, CD30, CD15, S-100, melanoma antigen, and human melanocyte black 45, thus indicating that presence of hematopoietic tumors was unlikely. Immunostaining for thyroid transcription factor-1 and surfactant protein suggestive of lung cancer, was also negative.

On hospital day 30, all muscles in the left lower limb were graded as Grades Z to T, and numbness of the left lower limb was observed. Contrast-enhanced MRI was again performed on the cervicothoracic junction, the T2-weighted images revealed enlargement of the intramedullary edematous lesion to the cranial side and continuity between the tumor and the extramedullary lesion from C7 to T2. At the T1/2 level, the spinal cord was occupied by the tumor except for an area on the right side that appeared normal (Fig. 5). Whole-body CT was performed again, however no new lesions were detected compared with the previous CT scans. Five days later, a C6-7 laminoplasty, T1-3 laminectomy, and tumor resection were performed for decompression and biopsy of the thoracic tumors.

Surgical findings

With the patient under general anesthesia, a C6-7 laminoplasty and T1-3 laminectomy were performed with a Mayfield three-point fixation device. At the T2 level, the dura mater was tense and bluish in color. Because the tumor arose from C7 and extended up to the T2/3 level, a median incision of the dura mater at the C7 level was performed with a sharp-pointed scalpel and

Figure 1 Magnetic resonance imaging (MRI) that was performed at the initial examination. A T1-weighted image revealed swelling of the spinal cord from C3/4 to T5 (A). T2-weighted images revealed a high-signal intensity area that was suggestive of edema in the spinal cord (B and C) and an intramedullary lesion with relatively homogeneous enhancement on the left side of the spinal cord at the C7-T1/2 level (D, E and F). Moreover, an intradural extramedullary lesion that was not contiguous with the intramedullary lesion was observed on the left side of the spinal cord at the T2/3 level. Contrast-enhanced imaging revealed enhancement in the area from the intradural extramedullary tumor to the radicle (G, H and I).

the dura mater deployed. In addition, the arachnoid mater was incised. The thickened arachnoid mater was strongly adhered to the spinal cord. On the left side of the spinal cord at the T2/3 level, a red-brown soft

tumor that adhered to the white dura mater was detected. Along the root of T2, a similar tumor was observed on the dorsal root, and another tumor was observed on the dura mater. These tumors were resected

Figure 2 Positron emission tomography revealed tracer uptake with a standardized uptake value of 9.8 in the tumor in the thoracic spine as well as uptake in the lymph nodes on the lateral side of the thoracic aortic arch. However, no uptake was observed in any other part.

piece by piece. In addition, the root of T2 was resected. When the spinal cord was examined after resection of the tumor on the dura mater, a tumor with a similar color that had invaded from the left lateral side into the spinal cord was observed. The spinal cord was decompressed on the lateral side and became slightly more movable. However, the impression remained on the spinal cord. The posterior median sulcus was closely examined but no clear line was evident. A small incision was made on the lateral side and the tumor detached while identifying normal spinal cord. A soft white tumor resembling fatty tissue was observed in the spinal cord. The tumor was resected from the left lateral side of the spinal cord up to the T1 level as completely as possible. It was impossible to excise the portion that adhered tightly to the spinal cord and had an unclear border with the normal spinal cord. The border between the ventral side of the spinal cord and the dura mater was also unclear, hence the portion of dura mater that was apparently involved with the tumor at the T2/3 level was resected. The proximal margin of the resection was placed directly above the root of T1. Artificial dura mater was applied to the defective area of the dura mater (Fig. 6).

Postoperative course

The final pathological diagnosis of the intramedullary tumor was anaplastic meningioma. The pathological

findings revealed scattered psammoma bodies in less atypical areas, suggestive of meningioma. The adjacent area contained tumor cells that had proliferated as a fibrous, sarcomatoid, or adenoepithelial cellular mass characterized by marked cellular atypism. The latter area was positive for cytokeratin anion exchanger 1/3, cytokeratin 18, and epithelial membrane antigen. In addition, direct invasion into the spinal cord tumor was observed (Fig. 7). These findings resembled the histopathological findings of the biopsied mediastinal lymph node. Lymph node metastasis of a malignant meningioma has been described previously in a case report.⁸ However this is the first report of mediastinal lymph node metastasis of an anaplastic meningioma. On postoperative day 2, right lower limb paralysis and dyskinesia in the hands and fingers occurred. The MRI results showed that hematoma and other problems were unlikely and that the spinal cord was swollen. Thus, the condition was thought to be attributable to spinal cord edema. The patient did not respond to steroid pulse therapy. Hyperbaric oxygen therapy was not performed because of the presence of pulmonary emphysema. Difficulty in expectoration due to the spinal cord injury resulted in methicillin-resistant *Staphylococcus aureus* pneumonia, and a pulmonary infarction occurred. Because spontaneous breathing was maintained, the cricothyroid membrane was incised, a mini-trach cannula inserted and antibiotics

Figure 3 Contrast-enhanced spinal computed tomography revealed swelling of the spinal cord at the C6-7 level (A). At the level of the T2/3 intervertebral foramen, a space-occupying lesion without enhancement was observed on the left side of the dura mater (B, C and D).

administered while sputum was suctioned. The pneumonia was gradually resolved. Around that time, however, all the muscles in the lower limbs were rated as Grade Z, and hypoesthesia from the groin down and bladder and rectal disorders were noted. Although a dexterous movement disorder was noted in the fingers, the MMT results of the deltoids, biceps and triceps brachii, and wrist palmar and dorsal flexion were Normal (N). Once the patient's general condition had improved, radiotherapy

with opposing portal irradiation was applied to the area from C5 to T2 on postoperative day 21. Although the radiation dose was increased to 46 Gy, MRI revealed growth of the tumor in the irradiated area (C5 to T3 level) and the analgesic effect was inadequate (Fig. 8). Neurologically, the MMT results of the biceps and triceps brachii and wrist palmar and dorsal flexion were Fair (F), and the patient was unable to eat by himself. Hypoesthesia from the forearms down and

Figure 4 Tissue biopsy of the mediastinal lymph node. Large polymorphic spindle cells with prominent nucleoli were diffusely proliferated on a background of fibrous stroma (hematoxylin-eosin [HE] staining).

sensory loss from the groin down were noted. For activities of daily living, the patient was able to move to a wheel chair with full assistance. The patient and his family requested transfer to another hospital nearer their home 3 months after surgery.

Discussion

Intramedullary tumors are reported to account for 2–4% of all tumors arising from the central nervous system.^{8–10} One study reported the proportion of

intramedullary tumors amongst spinal cord tumors was 18%, but no patients with intramedullary tumors were diagnosed with meningioma.¹¹

The types of tumors that display contrast enhancement on MRI and are accompanied by extensive edema and outward progress from the medulla include hemangioblastoma,^{12,13} intramedullary metastatic tumor,^{14–16} intramedullary malignant lymphoma,¹⁸ ependymoma¹⁹ and intramedullary neurinoma.²⁰ The most common primary tumors that cause intramedullary metastasis are lung cancer, malignant melanoma and malignant lymphoma.^{21,22}

Our case was diagnosed as lymph node metastasis of anaplastic meningioma based on the following: mediastinal lymphoma is highly malignant, meningioma is also highly malignant, and no other lesion was found that could be the primary site. Malignant meningiomas include meningiomas that are rated as Grade II or III based on the WHO Classification of Tumors Affecting the Central Nervous System. Approximately 1% to 2.8% are considered to be anaplastic meningiomas.⁶ These develop more commonly in men, grow rapidly,

Figure 5 When contrast-enhanced MRI was performed again on the cervicothoracic junction, T2-weighted images revealed enlargement of the intramedullary edematous lesion to the cranial side (A). Compared with the MRI images obtained soon after admission, the tumor had grown and showed continuity with the extramedullary lesion at the level from C7 to T2. At the T1/2 level, the spinal cord was occupied by the tumor except for an area that appeared to be normal spinal cord on the right side (B–F).

Figure 6 Intraoperative pictures. Cranial is towards the top of the image, and caudal is towards the bottom. A laminoplasty was performed at the level of C6-7, and a rachiotomy was performed at the level of T1, 2, and 3. An enlargement is seen on the left side of the dura mater at the level of T2/3 (A). Micrographs taken after the dural incision (B–E) show infiltration of the tumor from the left side of the spinal cord (B). A soft white tumor resembling fatty tissue was observed in the spinal cord (C). The tumor had ill-defined borders, and was resected as much as possible (D, E).

recur within a short period after resection and metastasize distally even to sites other than the nervous system.^{23–25} The median survival time for anaplastic meningioma is 1.4 years, demonstrating the extremely life threatening nature of this tumor.²⁶

For the treatment of meningioma, it is important to attempt complete resection regardless of the degree of malignancy. Below we describe the treatment of anaplastic meningioma by partial resection.

Although meningiomas are less sensitive to radiation, the application of radiotherapy has been reported to be

useful against residual tumor.^{25,27–29} However, another report presented negative therapeutic outcomes from the use of stereotactic radiosurgery for anaplastic meningioma.³⁰

Intensity-modulated radiotherapy is performed at a limited number of institutions and has been reported to be effective.^{31,32}

However, the above studies describe cases of anaplastic meningioma arising from the brain, with no reports to date of cases arising from the spinal cord. In general, the tolerance dose for the spinal cord is considered to be 45 to

Figure 7 Psammoma bodies (arrow) were scattered in less atypical areas, which had the appearance of a meningioma (A and B, HE staining, 100× and 400× magnification, respectively). B. The adjacent area that had tumor cells that proliferated as a fibrous, sarcomatoid, or adenoepithelial cellular mass and that was characterized by marked cellular atypism (C and D, HE staining, 100× and 400× magnification, respectively). C. Direct invasion into the spinal cord tumor was observed (E and F, HE staining, 100× and 400× magnification, respectively).

Figure 8 MRI that was performed after radiotherapy: On T2-weighted images, the signal intensity in the spinal cord deteriorated on the cranial side, and the tumor was observed to be growing in the irradiated area.

50 Gy (single dose: 1.8–2 Gy) and hence radiotherapy is commonly administered so as not to exceed this dose.^{33,34} Because of this uncertainty, further studies are required to determine the appropriate radiation dose for anaplastic meningioma arising in the spinal cord.

The combination of cyclophosphamide, adriamycin and vincristine treatment was reported to be effective chemotherapy for a malignant meningioma that arose within the cranium.³⁵ Moreover, hydroxyurea has been reported to suppress the growth of meningioma cells.^{36–38} However, no effective chemotherapy has so far been reported for anaplastic meningioma.

As described above, treatments for anaplastic intracerebral meningioma have been reported but there is no established treatment protocol, especially for cases with anaplastic meningiomas arising in the spinal cord. Further studies are required to address this.

Conclusion

We experienced an extremely rare case in which detailed examinations revealed the patient had an intramedullary tumor accompanied by mediastinal lymph node metastasis. The primary tumor was found to be anaplastic meningioma. The tumor grew rapidly and it was difficult to establish the diagnosis. For cases involving intramedullary tumors in the spinal cord and metastasis but no other tumor lesions that could be the primary site, it is important to obtain early diagnosis and treatment. In such case, consideration should be given to the diagnosis of anaplastic meningioma.

Disclaimer statements

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Conflicts of interest None.

Ethics approval We reported this case to the Institutional Review Board and obtained approval for its publication (Control No. 20141224-6-1).

References

- Sandalcioglu IE, Hunold A, Müller O, Bassiouni H, Stolke D, Asgari S. Spinal meningiomas: critical review of 131 surgically treated patients. *Eur Spine J* 2008;17(8):1035–41.
- Setzer M, Vatter H, Marquardt G, Seifert V, Vronis FD. Management of spinal meningiomas: surgical results and a review of the literature. *Neurosurg Focus* 2007;23(4):E14.
- Vranic A, Peyre M, Kalamarides M. New insights into meningioma: from genetics to trials. *Curr Opin Oncol* 2012;24(6):660–65.
- Barresi V, Alafaci C, Caffo M, Barresi G, Tuccari G. Clinicopathological characteristics, hormone receptor status and matrix metallo-proteinase-9 (MMP-9) immunohistochemical expression in spinal meningiomas. *Pathol Res Pract* 2012;208(6):350–5.
- Salvati M, Artico M, Lunardi P, Gagliardi FM. Intramedullary meningioma: case report and review of the literature. *Surg Neurol* 1992;37(1):42–5.
- Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol* 2007;114(2):97–109.
- Sade B, Chahlav A, Krishnaney A, Nagel S, Choi E, Lee JH. World Health Organization Grades II and III meningiomas are rare in the cranial base and spine. *Neurosurgery* 2007;61(6):1194–8.
- Brothi J. Intrinsic spinal cord tumor resection. *Neurosurgery* 2002;50(5):1059–63.
- Constantini S, Miller DC, Allen JC, Rorke LB, Freed D, Epstein FJ. Radical excision of intramedullary spinal cord tumors: surgical morbidity and long-term follow-up evaluation in 164 children and young adults. *J Neurosurg* 2000;93(2 Suppl):183–93.
- Hanbali F, Fourney DR, Marmor E, Suki D, Rhines LD, Weinberg JS, et al. Spinal cord ependymoma: radical surgical resection and outcome. *Neurosurgery* 2002;51(5):1162–72.
- Hirano K, Imagama S, Sato K, Kato F, Yukawa Y, Yoshihara H, et al. Primary spinal cord tumors: review of 678 surgically treated patients in Japan. A multicenter study. *Eur Spine J* 2012;21(10):2019–26.
- Chu BC, Terae S, Hida K, Furukawa M, Abe S, Miyasaka K. MR findings in spinal hemangioblastoma: correlation with symptoms and with angiographic and surgical findings. *Am J Neuroradiol* 2001;22(1):206–17.
- Sawyer B, Heng R, Ferris N. Typical magnetic resonance features of a haemangioblastoma, an uncommon nerve root lesion: case report and literature review. *Australas Radiol* 2007;51:B28–30.
- Kalayci M, Çağvi F, Gül S, Yenidünya S, Açıkgöz B. Intramedullary spinal cord metastases: diagnosis and treatment – an illustrated review. *Acta Neurochir* 2004;146(12):1347–54.
- Schiff D, O'Neill BP. Intramedullary spinal cord metastases: clinical features and treatment outcome. *Neurology* 1996;47(4):906–12.
- Schijns OE, Kurt E, Wessels P, Luijckx GJ, Beuls EA. Intramedullary spinal cord metastasis as a first manifestation of a renal cell carcinoma: report of a case and review of the literature. *Clin Neurol Neurosurg* 2000;102(4):249–54.
- Koeller KK, Rosenblum RS, Morrison AL. Neoplasms of the spinal cord and filum terminale: radiologic-pathologic correlation. *Radiographics* 2000;20(6):1721–49.
- Nakamizo T, Inoue H, Uda K, Oda M, Kawai M, Uemura K, et al. Magnetic resonance imaging of primary spinal intramedullary lymphoma. *J Neuroimaging* 2002;12(2):183–6.
- White JB, Miller GM, Layton KF, Krauss WE. Nonenhancing tumors of the spinal cord. *J Neurosurg Spine* 2007;7(4):403–7.
- Kodama Y, Terae S, Hida K, Chu BC, Kaneko K, Miyasaka K. Intramedullary schwannoma of the spinal cord: report of two cases. *Neuroradiology* 2001;43(7):567–71.
- Costigan DA, Winkelman MD. Intramedullary spinal cord metastasis. A clinicopathological study of 13 cases. *J Neurosurg* 1985;62(2):227–33.
- Okamoto H, Shinkai T, Matsuno Y, Saijo N. Intradural parenchymal involvement in the spinal subarachnoid space associated with primary lung cancer. *Cancer* 1993;72(9):2583–8.
- Mawrin C, Perry A. Pathological classification and molecular genetics of meningiomas. *J Neurooncol* 2010;99(3):379–91.
- Hug EB, Devries A, Thornton AF, Munzenrider JE, Pardo FS, Hedley-Whyte ET, et al. Management of atypical and malignant meningiomas: role of high-dose, 3D-conformal radiation therapy. *J Neurooncol* 2000;48(2):151–60.
- Milosevic MF, Frost PJ, Laperriere NJ, Wong CS, Simpson WJ. Radiotherapy for atypical or malignant intracranial meningioma. *Int J Radiat Oncol Biol Phys* 1996;34(4):817–22.
- Modha A, Gutin PH. Diagnosis and treatment of atypical and anaplastic meningiomas: a review. *Neurosurgery* 2005;57(3):538–50.
- Horowitz A, Orentlicher G, Goldsmith D. Computerized implantology for the irradiated patient. *J Oral Maxillofac Surg* 2009;67(3):619–23.
- Dziuk TW, Woo S, Butler EB, Thornby J, Grossman R, Dennis WS, et al. Malignant meningioma: an indication for initial aggressive surgery and adjuvant radiotherapy. *J Neurooncol* 1998;37(2):177–88.
- Hakim R, Alexander E, 3rd, Loeffler JS, Shrieve DC, Wen P, Fallon MP, et al. Results of linear accelerator-based radiosurgery for intracranial meningiomas. *Neurosurgery* 1998;42(3):446–53.
- Stafford SL, Pollock BE, Foote RL, Link MJ, Gorman DA, Schomberg PJ, et al. Meningioma radiosurgery: tumor control, outcomes, and complications among 190 consecutive patients. *Neurosurgery* 2001;49(5):1029–37.
- Zabel-du Bois A, Nikoghosyan A, Schwahof A, Huber P, Schlegel W, Debus J, et al. Intensity modulated radiotherapy in the management of sacral chordoma in primary versus recurrent disease. *Radiother Oncol* 2010;97(3):408–12.
- Moubayed SP, Guertin L, Lambert C, Desrochers P, Nehmé J, Coulombe G. Successful treatment of anaplastic meningioma metastatic to cervical lymph nodes. *Head Neck* 2013;35(4):E115–8.
- Waldron JN, Laperriere NJ, Jaakkimainen L, Simpson WJ, Payne D, Milosevic M, et al. Spinal cord ependymomas: a retrospective analysis of 59 cases. *Int J Radiat Oncol Biol Phys* 1993;27(2):223–9.
- Marcus RB, Jr, Million RR. The incidence of myelitis after irradiation of the cervical spinal cord. *Int J Radiat Oncol Biol Phys* 1990;19(1):3–8.
- Chamberlain MC. Adjuvant combined modality therapy for malignant meningiomas. *J Neurosurg* 1996;84(5):733–6.
- Schrell UM, Rittig MG, Anders M, Kiesewetter F, Marschalek R, Koch UH, et al. Hydroxyurea for treatment of unresectable and recurrent meningiomas. I-Inhibition of primary human meningioma cells in culture and in meningioma transplants by induction of the apoptotic pathway. *J Neurosurg* 1997;86(5):845–52.
- Schrell UM, Rittig MG, Anders M, Koch UH, Marschalek R, Kiesewetter F, et al. Hydroxyurea for treatment of unresectable and recurrent meningiomas. II. Decrease in the size of meningiomas in patients treated with hydroxyurea. *J Neurosurg* 1997;86(5):840–4.
- Mason WP, Gentili F, Macdonald DR, Hariharan S, Cruz CR, Abrey LE. Stabilization of disease progression by hydroxyurea in patients with recurrent or unresectable meningioma. *J Neurosurg* 2002;97(2):341–6.