ANAPLASTIC MENINGIOMA

Case report

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ABSTRACT - Intracranial meningiomas continue to challenge our best clinical efforts to eliminate them once discovered and deemed appropriate for treatment. Malignant meningiomas constitute 10% to 15% of all meningiomas and limited information exists regarding adjuvant treatment. The external whole brain irradiation is recommended. Traditional chemotherapy has proven ineffective; thus, new chemotherapeutic agents and new methods of delivery should be developed. Immunotherapy may be considered for patients with malignant meningiomas when all others previous treatment have failed. We report a case of anaplastic papillary meningioma. A 67-year-old man presented with partial complex seizures, headache and aggressiveness. A computerized tomography and magnetic resonance image demonstrated a large left temporo-occipital mass with diffuse contrast enhancement and extensive surrounding edema. A left temporo-occipital flap was performed. The tumor and the infiltrated dura were radically removed. Postoperatively, the patient remained neurologically intact. The treatment was complemented by external whole brain radiation.

KEY WORDS: papillary meningioma, pathology, radiotherapy, chemotherapy.

Meningioma anaplásico: relato de caso

RESUMO – O tratamento adequado para os pacientes com meningiomas intracranianos continua sendo um desafio, principalmente o de sua variante maligna, a qual tem incidência de 10% a 15%, sem uma certeza do melhor tratamento adjuvante. O uso da radioterapia externa holocrâniana. O uso da quimioterapia tradicional se mostra eficaz, havendo necessidade de estudos para desenvolver outros agentes quimioterápicos e novos métodos de administração desses agentes no tumor cerebral. A imunoterapia pode ser considerada para os casos de refratariedade aos outros tratamentos adjuvantes. Relatamos o caso de um paciente de 67 anos, com história progressiva de cefaléia, crises convulsivas parciais complexas e agressividade. A investigação radiológica com tomografia computadorizada e ressonância magnética evidenciaram um processo expansivo na região temporoparietal esquerda com contrastação difusa e edema peritumoral importante. Foi realizada craniotomia frontoparietal com remoção radical da dura-máter infiltrada e do tumor. O paciente evoluiu sem déficit neurológico no pós-operatório. O exame anatomopatológico foi compatível com meningioma maligno do tipo papilar. Foi instituído tratamento complementar com radioterapia externa holocraniana.

PALAVRAS-CHAVE: meningeoma papilar, patologia, radioterapia, quimioterapia.

Meningioma, one of the most common types of brain tumors in adults, remains a clinical problem yet to be solved by neurologist, neurosurgeons and oncologists. Meningiomas constitute 15% to 20% of all primary brain tumor and 10% to 15% of all meningioma are considered malignant¹². These tumors will recur after standard therapies of surgical excision, radiation therapy, radiosurgical techniques, and chemotherapy¹³⁶.

We report a case of papillary meningioma, considered be analastic, and the literature is reviewed.

CASE

This 67-year-old man presented with strong headache, behavior disorder, vomiting and two episodes of partial complex seizures in the last three months. The neurological examination revealed a mild mental confusion and bilateral papilledema. There was no motor or sensitive signs...
or symptoms. A computerized tomography (CT) scan of head with contrast demonstrated a large left temporo-occipital mass, diffuse contrast enhancement and some small hypodense areas located at anteromesial portion. A magnetic resonance image (MRI) obtained with and without contrast showed an enhancing lesion in the left temporal and occipital lobe with extensive surrounding edema and a transtentorial herniation (Fig 1). The left tentorium and the dura adjacent to the lesion were strongly enhancing. A left temporo-occipital flap was performed. There were some areas of clear cut between the normal brain tissue and the tumor. But on other areas these limits could not be so evident. The tumor was strongly vascularized. The dura infiltrated by the tumor was removed. The tumor was removed radically and it can see at the postoperative MRI scans (Fig 2). Postoperatively, the patient remained neurologically intact. He stayed at ICU for 48 hours with intracranial pressure monitoring within normal values at all. There were no complications and the patient was discharged at one week. The patient was referred to radio-
therapy unit to receive complementary treatment with external whole brain radiation. The histopathologic exam showed malignant meningioma with vascular channels surrounded by neoplastic meningothelial cells with a papilliferous aspect and highly cellular areas with mitoses (Fig 3).

**DISCUSSION**

Malignant meningiomas represent 10% to 15% of all meningiomas. The peak incidence of atypical and malignant meningioma was in the seventh and sixth decades, respectively. These malignant meningiomas are defined by several criteria including: 1) invasion of adjacent brain parenchyma or skull; 2) numerous mitoses (>5/high-powered field); 3) elevated proliferative index (>3%) as assessed by either 5-bromodeoxyuridine or Ki-67 staining; 4) necrosis; 5) increased cellularity; 6) nuclear pleomorphism; and 7) metastasis.

The cell origin of the meningiomas is the arachnoid cap cell, which has a slow rate of cell division. Although tumors originating from the meninges are typically benign, they occasionally behave in an aggressive fashion and carry a much poorer prognosis than do benign meningiomas. Tumorigenesis must be the result of exogenous or endogenous factors acting alone or together. Exogenous factors include trauma, viral infection, and prior brain irradiation. Endogenous stimulation can occur through the action of hormones or growth factors.

There was a clear tendency toward a progressively higher frequency of malignant meningiomas among recurrent tumors. Malignant meningiomas were tumors that had undergone reoperation and had originally been either benign or aggressive meningioma. This suggests a likelihood that any benign tumor that recurs will be malignant. Whereas benign meningiomas tend to show preponderance in females, atypical and malignant meningiomas have a male preponderance.

Pathology

Cushing coined the term “meningioma” to describe this tumor attached to the meninges. Since that time, a number of histopathologic schemes have been presented. Currently the WHO-II classifications of meningiomas are the most used. This histological classification system divides tumors of meningothelial cells into four groups: classic, atypical, papillary and anaplastic. These classifications can be complemented with the Helsinki grading system. This grading system assigns points from 0-3 for six pathological features: loss of architecture, increased cellularity, nuclear pleomorphism, mitotic figures, focal necrosis, and brain infiltration. The sum of these points is then used to describe the benign, atypical, anaplastic and sarcomatous forms of meningiomas. The proliferative potential of tumors can be quantitated, using bromodeoxyuridine, Ki-67, MIB-1 and proliferating cell nuclear antigen (PCNA) labeling index, and this information helps in predicting the clinical behavior of tumors and the need for treatment.

Palma et al. defined the differences between atypical (42 cases) and malignant (29 cases) meningiomas by the World Health Organization and studied the influence on prognostic: survival at 5 and 10 years was obtained in 95% and 79%, respectively, of patients with atypical meningioma and in 64.3% and 34.5% of patients with malignant meningioma; recurrence-free survival was 11.9 years in patients with atypical meningioma and 2 years with malignant meningioma; the authors concluded that radical extirpation and histological findings were significantly related to prolonged survival.

**Radiological Features**

Servo et al. and Younis et al. determined that CT cannot reliably distinguish malignant meningiomas from benign ones. There are, however, some CT or MRI trends that point in favor of malignant meningioma: 1) the absence of visible calcium aggregates; 2) “mushrooming” or the presence of a prominent pannus of tumor extending well away from the globoid mass; 3) nonhomogeneous enhancement; 4) necrosis; and 5) presence of indistinct tumor margins. If angiography is performed, arteriovenous shunting is a feature that suggests malignancy.

Marked peritumoral edema, osteolysis, intrinsic cystlike areas and tumor density have a controversial radiological feature in relation to malignancy. Elster et al. could not detect any significant difference on either T1-weighted or T2-weighted studies which allowed differentiation of malignant from benign meningiomas.

**Surgery**

Surgery remains an important part of treatment of malignant meningiomas. Over the past several years, advances in surgical technique and a revisiting of surgical anatomy have prompted more agres-
sive approaches to brain tumors. Despite the gross-total tumor resection, the survival of malignant meningiomas without adjuvant therapy is less than 2 years. In patients with malignant meningiomas treated with surgery and adjuvant therapy (either radiation alone or radiation plus chemotherapy), median survival time was 5 years and the degree of tumor resection did not predict recurrence.

Chen & Liu reported that a recurrence rate with a median follow-up of 3 years after surgery was 44% for atypical or anaplastic meningioma and 6% for benign meningiomas. Younis et al. reported that recurrence and survival time was shorter in patients with malignant meningiomas who had received partial resection on first presentation of tumor than in those who underwent total resection; in their series the patient’s prognosis did not improve as a result of either chemotherapy or radiotherapy.

Dziuk et al. reported a disease free/progression free survival at 5 years was 39% following total resection versus 0% after subtotal resection (p = 0.001) in patients with malignant meningioma; they stated that complete surgical resection is crucial for long-term control.

Malignant meningiomas located at the parasellar region and the posterior fossa a conservative removal of tumor followed by irradiation is advocated in preference to a radical operation that may cause neurological injury without being curative.

Radiation Therapy

The value of fractionated external beam radiation therapy or stereotactic radiosurgery in improving tumor control and survival for patients with subtotally resected, recurrent and malignant meningiomas is confirmed.

Goldsmith et al. showed that the 5-year progression-free survival rate after subtotal resection and radiation therapy was 89% for benign meningiomas and only 48% for malignant meningiomas; an improved progression-free survival rate was related with a younger age and treatment after 1980 with innovative technologies, none of these variables affected the progression-free survival rate in the patients with malignant meningioma.

Milosevic et al. reported 59 patients with atypical or malignant meningiomas treated during the period of 1966 and 1990; the 5-year overall and cause-specific survivals after surgery and radiotherapy were 28 and 34%, respectively; age less than 58 years, treatment after the year 1975 and a radiation dose greater than or equal to 50 GY were associated with improved cause-specific survival; the authors recommended that all patients with atypical or malignant meningiomas receive radiation therapy immediately after surgery.

Rodriguez et al. analyzed 35 patients with malignant meningioma, of whom 15 (43%) were treated with surgery alone, 12 (34%) with surgery plus radiotherapy, six (17%) with surgery plus radiotherapy and chemotherapy, and two (6%) with no further treatment: the 3-year recurrence probability was 27% for patients who received adjuvant radiotherapy versus 69% for patients treated solely with surgical resection; the 5-year survival rate was estimated at 64%. Sixty-seven patients experienced recurrence at 5 years.

According Dziuk et al. adjuvant irradiation following initial resection increased the 5-years disease free survival rates from 15% to 80% (p = 0.002); when administered for recurrent lesions, adjuvant radiotherapy improved the 2-years disease free survival from 50% to 89% (p = 0.015), but had no impact on 5-years disease free survival; the authors concluded that extent of resection, adjuvant radiotherapy, and recurrence status are independent prognostic factors.

Kondziolka et al. treated 50 patients with meningiomas using the 201-source cobalt-60 gamma knife with a follow-up of 30-month; the authors concluded that radiosurgery was an effective primary treatment alternative for patients with advanced age, medical condition, or high-risk tumor location.

Interstitial brachytherapy has been used to the treatment of malignant meningiomas after standard therapies have failed. Rogano et al. reported their experience with iodine-125 sources placed at open operation for 22 patients with recurrent or malignant meningiomas obtained a 96 weeks of the median time to tumor progression and a 124 weeks of the median survival from the time of implantation; 38% of their patients had complications related to therapy; the authors conclude that interstitial brachytherapy remains an option for tumor volumes, shapes, and locations not amenable to stereotactic techniques.

Chemotherapy

The role of cytotoxic chemotherapy in the management of recurrent or malignant meningiomas has not fully investigated. The value of adjuvant chemo-
therapy is not clear giving the confounding and probably more beneficial effects of adjuvant radiotherapy also administered to these patients.  

Wilson reported 11 cases with recurrent malignant meningiomas treated with surgery, radiotherapy and chemotherapy using cyclophosphamide, doxorubicin and vincristine with 73% progressed at 1 year and 100% at 2 years.

Stewart et al. used intra-arterial cis-platinum and intravenous doxorubicin for inoperable recurrent meningiomas with a response in one case and tumor control in the other case.

Chamberlain reported the use of cyclophosphamide, Adriamycin and vincristine after external beam radiation therapy for up to six cycles of treatment for 14 cases of malignant meningiomas. Patients who had gross total resection only received three cycles of chemotherapy; the median time to tumor progression was 4.6 years and the median survival was 5.3 years; the author concluded that these combined modality therapies is associated with acceptable toxicity and a modest improvement in survival when compared to patients treated with surgery alone.

Younis et al. reported 10 patients with aggressive meningeal tumors who received intra-arterial or intravenous cis-platinum, intravenous dacarbazine and intravenous doxorubicin; clinical improvement or radiologic tumor response related to chemotherapy could not be observed.

Rodriguez et al. treated six patients with malignant meningioma with surgery plus radiotherapy and chemotherapy with free of recurrence at a median follow-up period of 4 years. The initial encouraging results on long-term oral therapy of 14 cases of unresectable meningiomas with the antiprogestational agent mifepristone (RU486) remain to be proven in a larger cohort of patients.

Immunoimmunotherapy

Immunoimmunotherapy may be considered for malignant meningiomas when all others previous treatment have failed. The most effective immunoimmunotherapy appears to be administration of interferon-alpha, which is relatively non-toxic and easily tolerated. More studies are needed to better define the roles of these agents in the treatment of malignant meningiomas.

In conclusion, an aggressive treatment approach with radical surgery and postoperative radiotherapy is warranted in patients with these tumors. Traditional chemotherapy has proved ineffective and the role of adjuvant immunotherapy, brachytherapy or radiosurgery are unknown. Because malignant meningiomas are uncommon tumors, a cooperative group study would be required to assess covariants.

REFERENCES