Atypical meningioma case series

The medical records of all patients who underwent surgery (2007-2017 in 4 neurosurgical departments) for a histologically diagnosed primary atypical meningioma were reviewed to assess progression-free survival (PFS) and prognostic factors.

This analysis included 258 patients with a median age of 60 years (54.7% female). The predominant tumor locations were convexity and falx (60.9%) followed by the skull base (37.2%). Simpson grade I-II resection was achieved in 194 (75.2%) patients, Simpson grade III-IV in 53 patients (20.5%). Tumor progressed in 54 cases (20.9%). Postoperative RT was performed in 46 cases (17.8%). RT was more often applied after incomplete resection (37.7% vs. 13.4% Simpson III-IV vs. I-II). A multivariate analysis showed a significantly shorter PFS associated with Simpson III-IV [HR 1.19, (95% CI) 1.09-1.29, p < 0.001] and age > 65 years [HR 2.89, (95% CI) 1.56-5.33, p = 0.001]. A subgroup analysis with a minimal follow-up of 36 months revealed that Simpson III-IV [HR 3.01, 95% CI 1.31-6.931.03-1.24, p = 0.009] and age > 65 years [HR 2.48, 95% CI 1.20-5.13, p = 0.014] reduced PFS. The impact of postoperative RT on PFS remained statistically insignificant, even in a propensity-score matched survival analysis [n = 46; p = 0.438; OR 0.710 (0.299-1.687)].

In the present study, postoperative RT did not improve PFS. The most important prognostic factors remain the extent of resection and age [1)].

2019

Clinical, histopathological, and radiological variables from 138 patients, including 64 females and 74 males (46% and 54%, median age 62 years), who underwent surgery for intracranial atypical meningioma were retrospectively analyzed. Associations between variables and recurrence and mortality were investigated using uni- and multivariate analyses.

Gross total (GTR) and subtotal resection (STR) was achieved in 81% and 19% of cases, respectively. Within a median follow-up of 62 months, recurrence occurred in 52 (38%) and mortality in 22 (16%) cases. In patients who did not receive adjuvant irradiation, recurrence rates were higher after STR than after GTR (32% vs 63%, p = 0.025). In univariate analyses, only intratumoral calcifications on preoperative MRI (p = 0.012) and the presence of brain invasion in the absence of other histological grading criteria (p = 0.010) were correlated with longer progression-free intervals (PFI). In multivariate analyses, patient age was positively (HR 1.03, 95%CI 1.04-1.05; p = 0.018) and the presence of brain invasion as the only grading criterion (HR 0.37, 95%CI 0.19-0.74; p = 0.005) was negatively related with progression, while rising age at the time of surgery (HR 1.07, 95%CI 1.03-1.12; p = 0.001) was prognostic for mortality.

PFI was longer in brain invasive but otherwise histological benign meningiomas and in tumors displaying calcifications on preoperative MRI. Advancing patient age and lower Karnofsky Performance Score were associated with higher overall mortality [2)].

2017

Wang et al. retrospectively analyzed 102 patients with atypical or malignant meningiomas. Seizures occurring before and after the operation were reviewed. They compared demographic data and clinical characteristics including anti-epileptic drug (AED) treatment to extract potential risk factors for seizures.

Preoperative and postoperative early seizures occurred in 15 (14.7%) and 13 (12.7%) patients, respectively. All preoperative seizures occurred with tumors located at the convexity or parasagittal area (P = .001) and were influenced by peritumor edema (P = .027). Preoperative seizures were predictive of early seizures occurrence postoperatively (P = .016). Twenty-one patients (20.6%) had late seizures postoperatively. SFS was influenced by preoperative seizures, tumor location, AED use, and tumor relapse (P = .003, .001, .013, and .046, respectively). Among 15 patients with preoperative seizures, malignant meningiomas were associated with shorter SFS than atypical meningiomas (P = .001). Fifty one of 87 patients without preoperative seizures had prophylactic AEDs, and none had early seizures (P = .001). Gross total resection (GTR) of tumors induced more new-onset seizure than subtotal resection (P = .045).

Convexity and parasagittal area tumors as well as peritumor edema induce seizures. Preoperative seizures and tumor relapse predict seizures postoperatively. AEDs treatment improves SFS, and prophylactic AEDs eliminate early seizures after surgery. GTR has negative impact to seizure control [3].

The National Cancer Database was used to identify 2515 patients who were diagnosed with AM between 2009 and 2012 and underwent STR or GTR with or without adjuvant RT. Propensity score matching was first applied to balance covariates including age, year of diagnosis, sex, race, histology, and tumor size in STR or GTR cohorts stratified by adjuvant RT status. Multivariate regression according to the Cox proportional hazards model and Kaplan-Meier survival plots with log-rank test were then used to evaluate OS difference associated with adjuvant RT.

GTR is associated with improved OS compared with STR. In the subgroup analysis, adjuvant RT in patients who underwent STR demonstrated significant association with improved OS compared with no adjuvant RT (adjusted hazard ratio [AHR] 0.590, P = .045); however, adjuvant RT is not associated with improved OS in patients who underwent GTR (AHR 1.093, P = .737).

Despite the lack of consensus on whether adjuvant RT reduces recurrence after surgical resection of AM, our study observed significantly improved OS with adjuvant RT compared with no adjuvant RT after STR [4].

2016

Real-Peña et al published 27 patients with pathological diagnosis of atypical meningioma, and who had a minimum follow-up time of 6 months after diagnosis. Later prognostic factors (age <50years, male gender, bone involvement, peri-lesional swelling, tumour volume, location, Ki67/MIB-1) were evaluated after the stratification of patients undergoing complete resection in recurrencies and non-recurrencies. Univariate analysis was performed using Mann-Whitney test, $\chi(2)$ homogeneity test/Fisher exact test. Finally, multivariate analysis was performed using binary logistic regression to obtain the values for $R(2)$ Nagelkerke and the Hosmer-Lemeshow to evaluate the goodness of fit.

The uni- and multivariate analysis showed no statistically significant differences between recurrent and non-recurrent subgroups of patients undergoing complete resection. It is noted in the results that for each year of age above 50 years, the risk of recurrence is decreased by 5.8%.

Although current prognostic factors may show an increased risk of recurrence once patients are stratified by the two most important factors (pathology and extent of resection), those factors are insufficient to predict the ultimate outcome of patients affected by this pathology [5)]

Endo et al., reviewed 45 patients with atypical meningioma who underwent surgical intervention between January 2000 and December 2013. The mean age of the patients and mean follow-up period was 58.7 years and 81.0 months, respectively. Analyses included factors such as patient age, gender, location and size of tumor, extent of surgical resection (Simpson Grading System), and MIB-1 index (LI). Univariate analysis was used to detect prognostic factors associated with recurrence and survival.

The 5-year recurrence-free rate for all 45 patients was 58.4 %; 5- and 10-year survival rates were 83.2 % and 79.9 %, respectively. In univariate analyses, age >60 years, and MIB-1 LI correlated with disease recurrence, whereas age >60 years, subtotal surgical resection, MIB-1 LI, and indication for radiotherapy correlated with death. MIB-1 LI levels higher than 12.8 % and 19.7 % predicted recurrence and death, respectively. In our cohort, 26 patients received postoperative radiotherapy including conventional radiation (n = 21) or gamma knife radiosurgery (n = 5). Postoperative radiotherapy did not decrease recurrence rates in our cohort (p = 0.63). Six and two patients who died during the study period underwent conventional radiation and radiosurgery, respectively.

Age, male gender, extent of surgical resection, and higher MIB-1 LI influenced the outcome of atypical meningioma. In our cohort, postoperative radiotherapy failed to provide long-term tumor control. Following incomplete surgical resection of atypical meningioma in elderly patients, adjuvant postoperative radiotherapy may not be an ideal treatment option, particularly when MIB-1 LI is higher than 19.7 % [6)].

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44 WHO Grade II and 9 WHO Grade III meningiomas treated by CyberKnife for adjuvant or salvage therapy. Patient demographics, treatment parameters, local control, regional control, locoregional control, overall survival, radiation history, and complications were documented.

For WHO Grade II patients, recurrence occurred in 41%, with local, regional, and locoregional failure at 60 months recorded as 49%, 58% and 36%, respectively. For WHO Grade III patients, recurrence occurred in 66%, with local, regional, and locoregional failure at 12 months recorded as 57%, 100%, and 43%. The 60-month locoregional control rates for radiation naïve and experienced patients were 48% and 0% (p = 0.14), respectively. Overall, 7 of 44 Grade II patients and 8 of 9 Grade III patients had died at last follow-up. The 60-month and 12-month overall survival rates for Grade II and III meningioma were 87% and 50%, respectively. Serious complications occurred in 7.5% of patients.

SRS for adjuvant and salvage treatment of WHO Grade II meningioma by a hypofractionated plan is a viable treatment strategy with acceptable long-term tumor control, overall survival, and complication rates. Future work should contribute additional study toward the radiation naïve and the local management of malignant meningioma [7)].

A triple center case-note review of adults with newly-diagnosed atypical meningiomas between 2001 and 2010 was performed. Pathology diagnosis was made according to the World Health Organization classification in use at the time of surgery. Patients with multiple meningiomas, neurofibromatosis type 2 and radiation-induced meningiomas were excluded. Extent of resection was defined as gross total resection (GTR; Simpson Grade I-III) or subtotal resection (STR; Simpson Grade IV-V). Survival analysis was performed using the Kaplan-Meier method. One hundred thirty-three patients were identified with a median age of 62years (range 22-86years) and median follow-up of 57.4months (range 0.1-152.2months). Tumors were mostly located in the convexity (50.4%) or falcine/parasagittal regions (27.1%). GTR (achieved in 85%) was associated with longer progression free survival (PFS) (5year PFS 81.2% versus 40.08%, log-rank=11.117, p=0.001) but not overall survival (OS) (5year OS 76.6% versus 39.7%, log-rank=3.652, p=0.056). Following GTR, early adjuvant radiotherapy was administered to 28.3% of patients and did not influence OS (5year OS 77.0% versus 75.7%, log-rank=0.075, p=0.784) or PFS (5year PFS 82.0% versus 79.3%, log-rank=0.059, p=0.808). Although extent of resection emerged as an important prognostic variable, early adjuvant radiotherapy did not influence outcome following GTR of atypical meningiomas. Prospective randomized controlled trials are planned [8].

2015

Twenty-eight patients with skull base atypical meningiomas underwent microsurgical resection between June 2001 and November 2009. The clinical characteristics of the patients and meningiomas, the extent of surgical resection, and complications after treatment were retrospectively analyzed.

Thirteen patients (46.4%) had disease recurrence or progression during follow up time. The median time to disease progression was 64 months. The extent of the surgical resection significantly impacted prognosis. Gross total resection (GTR) of the tumor improved progression free survival (PFS) compared to subtotal resection (STR, p = 0.011). An older patient age at diagnosis also resulted in a worse outcome (p = 0.024). An MIB-1 index <8% also contributed to improved PFS (p = 0.031). None of the patients that underwent GTR and received adjuvant radiotherapy had tumors recur during follow up. STR with adjuvant radiotherapy tended to result in better local tumor control than STR alone (p = 0.074). Three of 28 patients (10.7%) developed complications after microsurgery. The GTR group had a higher rate of complications than those with STR. There were no late adverse effects after adjuvant radiotherapy during follow up.

For patients with skull base atypical meningiomas, GTR is desirable for longer PFS, unless radical excision is expected to lead to severe complications. Adjuvant radiation therapy is advisable to reduce tumor recurrence regardless of the extent of surgical resection. Age of disease onset and the MIB-1 index of the tumor were both independent prognostic factors of clinical outcome [9].

A retrospective analysis of the patients operated at the Clinic of Neurosurgery, Clinical Center of Serbia, Belgrade, between January 1st 1995 and December 31th 2006 was performed. In that period 88 lesions met the histological criteria for atypical (75) and anaplastic (13) meningioma. Postoperative radiotherapy was conducted in 63.6% of patients.

At a median follow-up of 67.4 months in all patients the overall survival was 68 months and five-year survival was about 54.5%. The median survival was 76 months with surgery and adjuvant radiotherapy and 40 months with surgery alone (Log rank=7.4; p=0.006). Recurrent disease occurred in 58 patients (65.9%). Median time between first surgery and tumor recurrence in patients undergoing radiotherapy was 51 months, while in non-irradiated group 24 months (Log rank=17.7;

p˂0.001). Multivariate analysis identified as recurrence-predicting factors anaplastic histotype (hazard ratio=2,9; p=0,003) and postoperative radiotherapy (hazard ratio=4,5; p<0,001).

The addition of adjuvant radiotherapy to surgery for atypical and anaplastic meningiomas resulted in a clinically meaningful and statistically significant survival benefit [10].

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