

## ORIGINAL ARTICLE

# Evaluation of the Prognostic Factors Effective on Local Recurrence in Atypical Meningiomas

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## Abstract

**Introduction:** Meningiomas are the most common brain tumors and account for 13%–26% of intracranial tumors. Approximately, 5%–7% of the meningiomas are termed as atypical meningiomas. The prognosis in patients with benign meningioma (Grade I) is generally very favorable. The outcome for patients with atypical meningioma is progression that is rapid and more invasive.

**Methods:** We retrospectively analyzed 35 patients with atypical meningiomas who underwent surgery. Patients' age at diagnosis, gender, tumor location, Simpson grade, local tumor recurrence, and treatment with radiation therapy were evaluated.

**Results:** Patients were aged 29–54 (mean±standard deviation: 54.6±12.1) years; 18 were females and 17 males. The recurrence rate was 6/35 (17.1%). Recurrence was found two times more in females. The parasagittal location of the tumor was most common in 66.6% cases. One-half of the patients did not receive adjuvant radiotherapy (RT). Patients characterized with Simpson Grade I showed lower recurrence rate compared to Grade III.

**Discussion and Conclusion:** Atypical meningioma recurs more frequently than Grade I lesions. The current management of atypical meningioma is maximal safe resection of tumor followed by adjuvant RT. Adjuvant RT following surgical resection is recommended particularly for incompletely excised tumors or tumors located in the parasagittal area or posterior fossa. In our study, the resection grade was identified as one of the most important factors affecting the prognosis.

**Keywords:** Atypic meningioma; radiotherapy; surgery.

Meningiomas constitute 13%–26% of brain tumors and are the most common intracranial tumors, with an annual incidence of 6/100 per 100,000 [1]. According to the 2007 World Health Organization (WHO) classification, meningiomas are classified into 3 histopathological groups (benign, atypical, and malignant) and 15 subtypes (meningothelial, fibrous, transitional, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacytic, metaplastic, chordoid, clear cell, atypical, rhabdoid, and

anaplastic). Most of the meningiomas (90%) are benign, well-confined, slow-growing tumors and classified as WHO Grade 1 [2,3]; 5%–7% of them are considered atypical (Grade 2), and only 1%–3% of them anaplastic or malignant (Grade 3) tumors [4]. Although 20% of Grade 1 meningiomas are histopathologically benign, they are clinically aggressive, indicating that some of the meningiomas have borderline characteristics [5].

Therefore, the classification of meningiomas had to be

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renewed. Based on the revisions in the 2016 WHO classification, the presence of cerebral invasion is diagnosed as atypical meningioma, regardless of histopathological features [6]. The recurrence of atypical meningioma is associated with increased mortality and morbidity. The risk factors of recurrence in benign meningioma include age <40 years, meningiomas of the skull base, and male gender. However, the effect of these factors on the prognosis in atypical meningiomas remains controversial [7–9]. Maximal safe resection is recommended in cases with atypical meningioma for disease control, but the effect of total surgical resection on survival is unclear. Adjuvant radiotherapy (RT) is recommended in patients undergoing subtotal resection, whereas postoperative RT is controversial in patients undergoing total surgical excision [7].

The effect of RT on the long-term survival is remains unknown. There is still no consensus on the factors affecting the recurrence of atypical meningiomas and their treatment. We aimed to determine the possible risk factors for local recurrence in atypical meningioma cases.

## Materials and Methods

A total of 35 atypical meningioma cases operated through microsurgery between 2007 and 2016 were retrospectively reviewed. Patients were evaluated according to age, gender, tumor localization of tumor, Simpson grade, and postoperative adjuvant RT.

## Statistical Evaluation

Descriptive statistics were used to define continuous variables (average, standard deviation [SD], minimum, median, and maximum). The student's t-test was used for comparing two independent and normally distributed continuous variables, whereas the Mann–Whitney U test was used for comparing two independent variables with non-normal distribution. The chi-square test (or Fisher Exact test where appropriate) was used to examine the relationship between categorical variables. The statistical significance level was determined as 0.05. The analyses were performed using the MedCalc Statistical Software, version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; <http://www.medcalc.org>; 2013).

## Results

Seventeen (48.6%) patients were males and 18 (51.4%) were females. Recurrence was observed in 11.8% (2 cases) of male and in 22.2% (4/35) of female patients. Although recurrence was twice as high in female patients, no significant statistical difference was found between the two genders. The age of patients ranged between 29 and 54 years,

and the mean±SD age was 54.6±12.1 years.

There was no significant difference between the patients in terms of age distribution. In 48.6% (17/35) of the cases, the tumor was localized on convexity and in the parasagittal region in 42.8% (15/35), sphenoid wing in 5.8% (2/35), and petrous apex in 2.8% (1/35) of the cases. Recurrence was observed in 17.1% (6/35) of the cases. The tumor was located in the parasagittal location in 66.6% of the patients with recurrence, but the tumor localization did not have a significant effect on recurrence (Table 1). The postoperative resection rate in meningiomas was evaluated according to the Simpson rating system.

Grade 1 is the total removal of the tumor macroscopically, with dural, venous, and bone involvement, if any; Grade 5 refers to only simple decompression or biopsy. In Simpson Grade 1 tumors, the recurrence rate (7.4%) was significantly lower than Grade 2 (50%) and 3 (50%) tumors (Table 2). Nineteen cases (54.2%) received adjuvant RT.

**Table 1.** Relation between localization of the tumor and recurrence

	Recurrence		p
	No n (%)	Yes n (%)	
Localization			
Skull base	3 (9.7)	0 (0.0)	0.578*
Convexity	14 (45.2)	2 (28.6)	
Parasagittal	12 (38.7)	5 (71.4)	
Cerebellar convexity	2 (6.5)	0 (0.0)	
Localization			
Frontal	7 (22.6)	1 (14.3)	0.759*
Frontoparietal	2 (6.5)	2 (28.6)	
Frontotemporal	2 (6.5)	0 (0.0)	
Occipital	3 (9.7)	0 (0.0)	
Parietal	8 (25.8)	4 (57.1)	
Petrous	1 (3.2)	0 (0.0)	
Cerebellar	2 (6.5)	0 (0.0)	
Sphenoid Wing	2 (6.5)	0 (0.0)	
Temporal	2 (6.5)	0 (0.0)	
Temporoparietal	2 (6.5)	0 (0.0)	

\*Fisher's Exact p.

**Table 2.** Relation between Simpson grade and recurrence

	Recurrence		p
	No (%)	Yes (%)	
Simpson			
1	27 (77.2)	2 (7.4)	<0.05*
2	6 (17.1)	3 (50)	
3	2 (5.7)	1 (50)	

## Discussion

Atypical meningiomas constitute 5%–7% of all intracranial meningiomas (Grade 2). However, the incidence of atypical meningioma increased with the addition of the “presence of single brain invasion” criterion in the WHO 2016 classification [6]. In a case series of Perry et al, atypical meningiomas were identified in 24.3% of 643 cases [10]. The 5-year survival rate of atypical meningiomas was 67.5%–75%, and the mean survival time was 10–14 years [11].

Atypical meningiomas can be asymptomatic. However, varying symptoms, such as headache, vertigo, cranial nerve findings, and hydrocephalus, are also observed depending on the tumor location, size, mass effect, and growth rate [12].

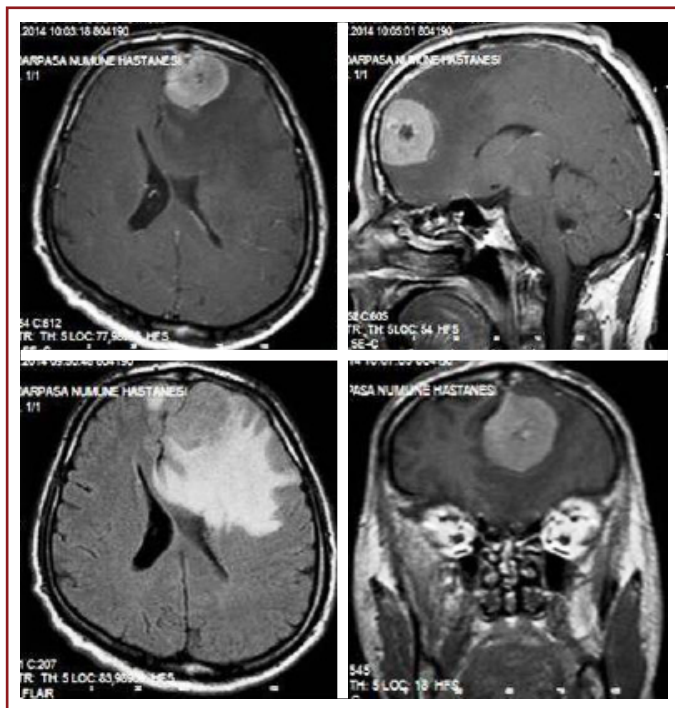
A magnetic resonance imaging scan is the most useful diagnostic procedure. The presence of peritumoral edema and heterogeneous enhancement in T2 sequences and hyperintensity in a diffusion-weighted imaging sequence suggests atypical meningioma (Fig. 1). In some Grade 1 large meningiomas, calcification is heterogeneous if there is cystic degeneration [12–15]. The shape of the tumor may not always give information about its nature.

Although irregularly shaped tumors are thought to be aggressive, histopathologically benign meningiomas with impaired focal feeding or venous drainage may also have irregular contours [2,12,16]. Therefore, histopathologically,

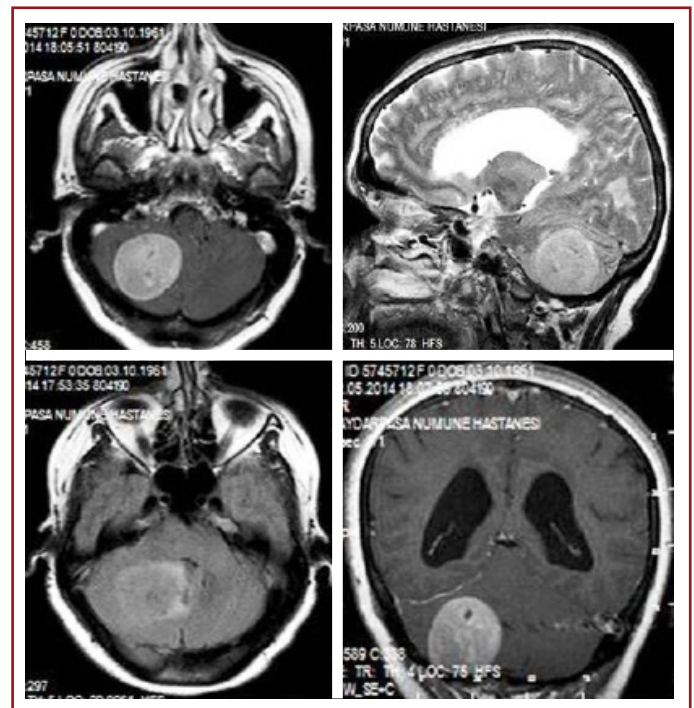
30% of Grade 1 tumors were classified as atypical, and survival rates in patients with Grade 1 tumors are similar to Grade 2 tumors [17].

In atypical meningiomas, many factors that affect the prognosis and survival have been studied, and there is still no consensus. In the current series, female gender had worse prognosis, whereas in some series, gender had no effect on the total survival [9,18]. In our study, although a 2-fold increased recurrence rate was observed in female patients, no statistically significant difference was found between both genders. Pasquier et al. [18] found that age above 60 years is a worse prognostic factor, and Milosevic et al. [19] showed that age <40 years was a good prognostic factor. There was no significant difference in terms of age distribution in our patients.

The preoperative Karnofsky performance value is effective on the survival, and overall survival is low in patients with a poor general condition [9]. The location of atypical meningiomas is also effective on the prognosis of the disease. The recurrence rates were higher in meningiomas localized in the parasagittal region, falx cerebri, and posterior fossa, with lower overall survival (Fig. 2). The reason for this is that total resection of the tumors localized on this region is challenging due to their proximity to the sinus [9,20,21]. Further, 66.6% of our cases had parasagittal tumors. However, tumor localization did not have a statistically significant ef-



**Figure 1.** A case of atypical meningioma located in the falx. Heterogeneous enhancement and peritumoral edema are observed.



**Figure 2.** Magnetic resonance imaging of atypical meningioma located in the posterior fossa. In T1 iso-hypointense and T2 hyperintense heterogeneous contrast enhancement.

fect on recurrence.

The most important step in the treatment of atypical meningiomas is local control of the disease, and maximal safe resection is recommended [7,22]. The probability of local progressive disease is quite high in patients who underwent subtotal resection. In a study, recurrence was seen 7–8 times more frequently in atypical meningiomas during a follow-up period of 3–5 years compared to Grade 1 meningiomas, and the mortality rate was also twice as high [10]. The 5-year survival rate was 67.5%–97.5% [23]. The Simpson rating is an important prognostic marker. In the present study, the Simpson grade was found to be associated with recurrence. In patients with Simpson Grade 3 resection, a recurrence rate of 50% was observed. The recurrence rate was significantly lower in the Simpson Grade 1 group.

No standard approach has yet been followed in the treatment of these tumors. Postoperative RT is controversial [7,9,24]. In recent studies, adjuvant RT has been recommended in patients who had undergone subtotal resection, but there is still no consensus in cases that had undergone maximal tumor resection. Wang et al. [9] reported that adjuvant RT did not contribute additionally to the decrease in the local recurrence of tumors in patients with maximal resection, whereas local disease control with adjuvant RT was highly effective in subtotal resection cases. Because of the challenges in the total resection of atypical meningiomas located in the posterior fossa and parasagittal regions, routine adjuvant RT is recommended for such cases [9]. However, it is noted that in recurrent tumors of atypical meningioma, patients who underwent adjuvant RT, Grade 3 pathology may be detected, and adjuvant RT may increase tumor aggressiveness [7,24]. Adjuvant RT is not recommended in patients with maximal tumor resection, considering the short-term (nausea, vomiting, weakness, edema, hair loss, etc.) and long-term (radiation necrosis, focal neurological deficit, secondary malignancies) side effects of RT [7]. Therefore, Aizer et al. [7] did not perform RT in 76% of patients with atypical meningioma who had undergone subtotal resection. In our study, 54.2% of the patients underwent postoperative adjuvant RT.

In conclusion, many factors that affect the prognosis and recurrence of atypical meningiomas have been investigated. The most important step in the treatment is local control of the disease. En bloc surgery to the maximum extent is recommended for prolonging the overall survival and ensuring recurrence-free survival. In patients with subtotal resection, the incidence rate of local progressive disease is high and adjuvant RT is usually required during

the postoperative period. The present study showed that the degree of resection is an effective factor on local recurrence in parallel with literature data.

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