



## ATYPICAL MENINGIOMAS: THE ARCHETYPICAL AND INFERENCES

## Neurosurgery

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## ABSTRACT

**Impetus:** Meningiomas are the mostly reported intracranial tumors, represent one third of all primary brain neoplasms in adults.

**Objectives:** In this analysis, we investigated outcomes of atypical meningioma diagnosed at a single institution. Special emphasis has been devoted to demographic features, predictive radiological signs, the concomitant factors predictive of tumor atypia with focus on clinical consequences, histological alterations, and risk factors related to the tumor treatment itself.

**Patients and Methods:** This retrospective study was conducted by reviewing histopathologic reports of all atypical meningiomas diagnosed and treated at King Hussein Medical Center, between January 2004 and January 2015. Demographic features; sex, age, tumor location, size of tumor, resection extent, and post-operative history of radiation therapy, and recurrence were documented.

Preoperative radiology reports were used to confirm tumor location and size based on largest single dimension. Extent of resection was based on surgical operative notes and post-operative imaging.

**Results:** Ninety-two patients showed atypical meningioma grade II. No gender predominance, young age at presentation, same topographical localization with grade one. All patients received adjuvant radiotherapy, recurrence noted in 19-patients.

**Conclusion:** Although the vast majority of meningiomas are benign, higher histological grade still reported with high frequency. The archetypical demographics of these tumors; no gender predominance, young age group, gross total resection is crucial for recurrence, adjuvant radiotherapy is still controversial.

## KEYWORDS

Atypical meningioma; Grade II meningioma; Radiosurgery; Extent of resection; Radiation; Meningioma

## Introduction

Meningiomas are the most frequently reported intracranial tumours, represent 36% of all primary brain neoplasms in adults. However, the tumor may also occur in children. The incidence peaks between the age of 60 and 70 years, the female: male ratio is 3:2. The most common locations are parasagittal, lateral convexity, the sphenoid wings, anterior fossa close to the olfactory nerve, the sellar region, and the posterior fossa in the environs of foramen magnum, respectively [1,2].

Histologically most meningiomas are benign. Meningiomas are categorized based on the World Health Organization (WHO) classification system into three histological grades (1-2-3) and 15 subtypes [3,4]. Atypical meningiomas are rare, accounting for less than 5% of all meningiomas [5]. Histologic grade has a noteworthy influence on prognosis, risk of recurrence, and the need for adjuvant radiation or chemotherapy. [6]

In the current analysis, we analyzed outcomes of atypical meningiomas diagnosed at a single institute. Special emphasis has been devoted to demographic features, predictive signs detectable by imaging techniques. We assessed the concomitant factors predictive of tumor atypia with focus on clinical consequences, histological alterations, and risk factors related to the tumor treatment itself.

## Patients and Methods:

This study was conducted by reviewing retrospectively the medical records, were clinical information documented. Six hundreds sixty-five patients with meningioma were treated at King Hussein Medical Center, between January 2004 and January 2015. Ninety-two patients showed atypical meningioma grade II. Demographic features; sex, age of diagnosis, tumor location, size of tumor, resection extent, and post-operative treatment received were documented.

Preoperative radiology reports were used to confirm tumor location and size based on largest single dimension. Extent of resection was based on surgical operative notes and post-operative imaging. Gross

total resection (GTR) was defined as Simpson 1-2 and subtotal resection (STR) as Simpson 3-4.

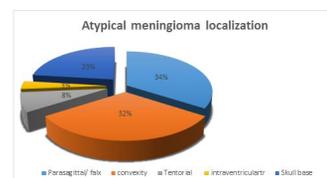
## Surgical details

After induction and general anesthesia, the patient is positioned supine with the head positioned according to the planned approach. Brain relaxation and control of intracranial pressure maintained using dehydrating agents and moderate hyperventilation prior to and during surgery. One burr hole performed as initial step, then we perform circle craniotomy around the lesion. If no tumor in the bone flap, we keep it for replacement, if involved we send it for biopsy and we perform cranioplasty. The dura beneath the flap if not involved opened in flap fashion and then re-sutured. The abnormal dura around the tumor usually resected and if need a dural patch is placed.

Our strategy is always to aim for gross total resection (Simpson 1-2).

## Results:

In this cohort of 92 treated patients, female to male ratio was 1:1. Mean age was 50-years, ranging from 24-78 years. The mean follow up was 97-months (31-177 months). Tumor locations were classified as parasagittal/ falx (34%), convexity (32%), skull base (23%), tentorial (8%), intraventricular (3%) (Figure.1).



**Fig.1: Anatomical localization of atypical meningiomas.**

Tumor size was not available in 14 patients because of incomplete medical records or lost pre-operative images; these patients were excluded from analysis of size. A cut-off of 4cm was used as this was

the average greatest single dimension in our patient base. Tumor size was >4cm in 63%, <4 cm in 28.2%, and unknown in 9.8%.

Clinically, majority of patients presented with headache and fits which were the dominant complaints, other presentations; neurological deficit, hearing loss, visual disturbances.

All patients were clinically monitored with an average follow-up of 8.1 years. Contrasted MRI performed for follow up every 6-months in those with histologically verified grade II meningioma, or if any change in clinical picture developed. In this study we achieved gross total resection in 61% of cases, subtotal resection in 33.4%, and 5.6% had unknown extent of surgical resection. All evolved favorably with neurological examination, except 4-cases, that persisted with neurogenic deficit. Nineteen cases developed recurrence.

**Discussion:**

Meningioma is one of the most common central nervous system tumors. Typically they are benign in nature [2]. Nevertheless, the World Health Organization (WHO) classification system categorized meningiomas into three histological grades (1-2-3) and 15 subtypes [3,4]. Atypical meningioma considered grade II [6].

Atypical meningiomas are characterized either by: Increased mitotic activity (4-19 mitosis/10 high power microscopic fields (HPF), or: three of the following histo-morphological features: increased cellularity; small cells with high nucleus/cytoplasm ratio; prominent nucleoli, 'patternless' or sheet-like growth; foci of spontaneous or geographic necrosis [Figure.2] [4,7].

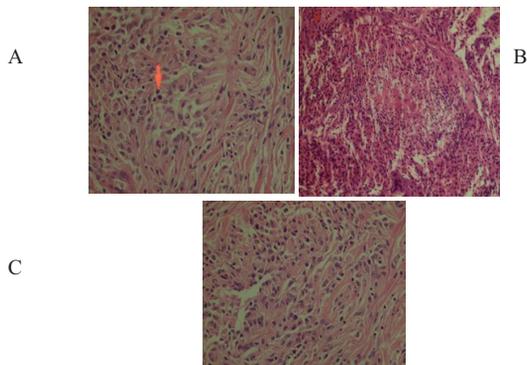


Figure.2 Histopathological slides showing: a- Meningioma with high mitotic activity ( only one HPF shown ), b- Meningioma with focus of necrosis, c- Meningioma with sheet like growth , small cells with high N/C ration and prominent nucleoli.

In immuno-histo-chemical studies the Ki-67 and p53 are the most frequently examined proteins [8]. The Ki-67 protein is expressed in mitotic cells. In the routine pathological diagnostics, the protein Ki-67 is detectable in all phases of the active cell cycle. The proliferative activity of is closely correlated with the cell amount of the protein: in the interphase it is localized in the nucleoli, whereas in the mitotic phase it is on the surface of chromosomes [Figure.3]. Therefore, the Ki-67 protein is an excellent marker for detection of the proliferation of a given cell population. Despite the large number of studies, the role of p53 in meningioma development and recurrence remains unclear [9].



Figure.3 immuno-histo-chemical stain with Ki-67 protein, showing a proliferation index of 20%

This analysis revealed some demographic features regarding this category; there was no gender predominance, mean age at presentation was 50-year, topographically the same as in grade I. The signs and symptoms found more frequently in our study were focal signs, followed by mental status alteration, seizures, and headache. Notably, a considerable part was serendipitously diagnosed [Table. 1].

Parameter	Number
<b>Gender</b>	
Male	45
female	47
<b>Age</b>	
>60	24
<60	68
<b>Clinical Presentation</b>	
Seizures	42
Headache	78
Mental status alteration	14
Focal signs	35
Nausea/vomiting/dizziness	28

Table.1: Demographic features and leading signs and symptoms of atypical meningioma diagnosed in our department

Radiological imaging is crucial in both pre-operative evaluation of tumor size and post-operative tumor resection extant and recurrence. The conventional characteristic evident on CT and MRI images of dural tail, peri-tumoral edema, and calcification are all important features [4]. Substantial connection has been found between the atypia/ higher grade tumor and the; the large tumor size (>40mm), shape, localization (base of skull), presence of brain invasion, and the severity of peritumoral edema [10-14]. The concomitant factors in this review indicating atypia were the massive peri-tumoral edema, the large tumor size and classification.

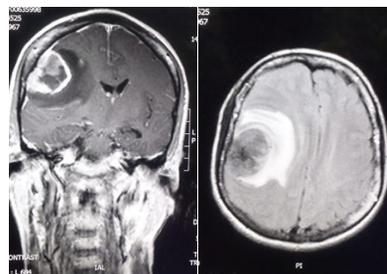


Figure.4: Coronal and axial contrasted MRI images showing the extensive peri-tumoral edema surrounding the atypical meningioma

In management of cranial meningiomas, the presence of clinical symptoms and the tumor progressive growth are the main determining factors, which lead the clinical management decision-making strategy. Surgical resection is the mainstay treatment for the majority of these cases. Complete resection of tumor is the aim of the surgical procedure (if reasonable) to achieve the best quality of life for the patient and to reduce the risk of recurrence. The extent of resection is graded according to Simpson scale [15]. There is controversy regarding the role of adjuvant radiotherapy for completely resected grade II tumors, the optimal timing and approach for radiation therapy in various clinical settings [16,17].

In our series we achieved gross total resection in 61% of cases, subtotal resection in 33.4%, and 5.6% had unknown extent of surgical resection [Figure. 5]. Although, some authors advocate that observation alone after GTR of atypical meningioma was not associated with increased risk of tumor recurrence or mortality [18].

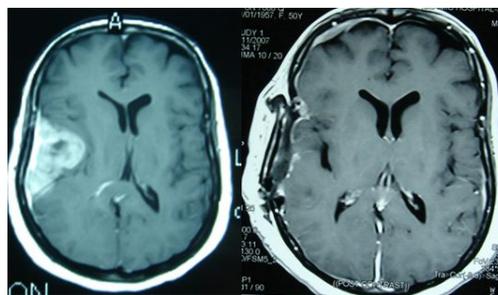


Figure.5: Post-contrast, axial cuts, pre- and post-operative MRI, showing total resection.

Recent reports supports that adjuvant radiotherapy even after Simpson Grade I, II, or III resection was found to improves local control for

atypical meningiomas [19,20]. Our strategy was till 2013, adjuvant radiotherapy based on empiric experience. Nowadays, in case we achieve GTR and on regular 6-month follow-up radiological images, there no recurrence, we observe. Otherwise, patients receive adjuvant radiotherapy. Our review revealed 19 cases developed recurrence, 13 cases had previous STR and 4 cases had GTR

Patients with atypical meningiomas have a worse prognosis than patients with benign (WHO Grade I) meningiomas. However, there is limited understanding of the pathological risk factors that affect long-term tumor control following combined treatment with surgery and radiation therapy. Brain and/or bone involvement, and a high mitotic index significantly predicted an increased risk of treatment failure despite combination therapy [21].

Conflict of interest statement: Authors state no conflict of interest.

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