

Introduction

Meningiomas are more common in females and 70-80% express the progesterone receptor. They have been reported in gender reassignment therapy, suggesting that high-dose exogenous estrogen/progesterone exposure, such as occurs during fertility treatments, may increase the risk of developing a meningioma. The goal of this study was to report the incidence of prior fertility treatment in a consecutive series of female patients presenting with meningioma.

Methods

A retrospective review of patients presenting with meningioma from 2015-2018 was conducted. Female patients with prior fertility treatments were compared to those who did not receive fertility treatment using standard statistical methods.

Table 1: Demographics Fertility Group	
Patients Fertility (#)	26
Age at Diagnosis	
Median (yrs, range)	48.6 (33.5-69.4)
Mean (yrs, std dev)	51.8 (10.5)
Median follow up post diagnosis (yrs, range)	1.8 (0-18.6)
Ethnicity	
White (Non-Hispanic)	23 (88.5%)
Hispanic	3 (11.5%)
Time to Diagnosis after Fertility Treat.	
Median time (yrs, range)	15.8 (1.8-31.7)
Table 2: Pharmacological Treatments	
Fertility Treatment	n (%)
Clomiphene +/- IUI	9 (34.6)
In Vitro Fertilization	13 (50.0)
Unspecified/Unknown	5 (19.2)
Other	
Progesterone	1 (3.8)

Results

Of 206 female patients with meningioma, 26 (12.6%) had a history of fertility treatments. Patients underwent various forms of assisted reproductive technology including: in vitro fertilization (50.0%), clomiphene +/- intrauterine insemination (34.6%), and unspecified (19.2%). One patient (3.8%) received supplemental progesterone during her fertility treatment. The most common presenting symptoms were incidental (57.7%) and headache (26.9%). Median follow up was 1.8 years. Tumors were WHO grade I (78.6%) or grade II (21.4%). Patients who underwent fertility treatments presented at significantly younger mean age compared to those who had not (51.8 vs 57.3 yrs, $p = 0.0135$, 2-tailed T-test) and were more likely to have multiple (OR: 4.5, 95% CI: 1.4-14.8, $p = 0.0196$) and convexity/falx meningiomas (OR: 3.5, 95% CI: 1.5-8.0, $p = 0.0018$).

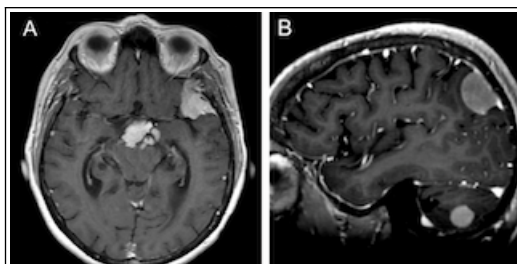


Fig 1. Case examples of multiple meningiomas in patients with a history of fertility treatment. Post-contrast T1-weighted MRI two different patients in the series. Axial (A) shows a patient with a left lateral sphenoid wing and large clival meningioma extending above the dorsum, and sagittal (B) shows a patient with a parietal convexity and cerebellar convexity.

Table 3: Histology			
WHO Grade	n (%)		
I	11 (78.6)		
II	3 (21.4)		
Histological Subtype			
Transitional	8 (61.5%)		
Fibrous	3 (23.1%)		
Meningothelial	1 (7.7%)		
Meningothelial with focal rhabdoid features	1 (7.7%)		
Progesterone Receptor Positive (n, %)			
WHO Grade 1	9, 90%		
WHO Grade 2	1, 100%		
Estrogen Receptor Positive (n, %)			
WHO Grade 1	1, 10%		
WHO Grade 2	0, 0%		
Table 4: Univariate Fertility vs. Non-fertility Group			
	Fertility n (%)		P-Value
	Yes	No	
Sex			
Female	26 (100)	180 (100)	
Mean Age at Diagnosis	51.8	57.3	0.0135 (T test)
WHO Grade			
I	11 (78.6)	133 (84.7)	0.6979 (Pearson)
II	3 (21.4)	22 (14.0)	
III	0 (0.0)	2 (1.3)	
Tumor Location			
Skull Base	9 (29.0)	112 (59.0)	0.0019 (Pearson)
Convexity/Falx	22 (71.0)	78 (41.0)	
Multiple Meningiomas			
Single	21 (80.8)	171 (95.0)	0.0070 (Pearson)
Multiple	5 (19.2)	9 (5.0)	

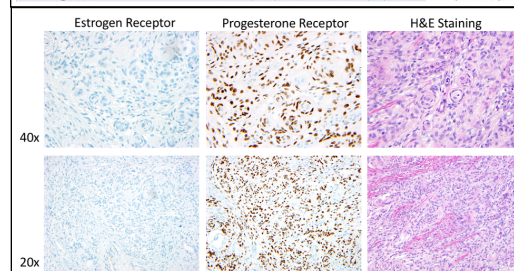


Fig 2. Examples of immunohistological staining for estrogen receptor, progesterone receptor and H&E in meningioma patients with a history of fertility treatment.

Conclusions

A history of fertility treatment is common in female patients presenting with meningioma. Furthermore, patients with meningioma and a history of fertility treatment were more likely to present at a younger age and have multiple and convexity/falx tumors. These findings stress the need for assessment of prior estrogen/progesterone exposure in patients presenting with meningioma. Future prospective series and laboratory investigations are needed to determine the impact of fertility treatment on meningioma development.

Learning Objectives

By the conclusion of this session, participants should be able to:

- 1) Describe the incidence of prior fertility treatment among female patients presenting with meningioma.
- 2) Discuss the meningioma locations most commonly found in patients with a history of fertility treatment.
- 3) Incorporate history of estrogen/progesterone exposure when working up patients with a new diagnosis of meningioma.

References

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 Wengel P V., Martin E, Gooren L, Den Heijer M, Peerdeman SM. Meningiomas in three male-to-female transgender subjects using oestrogens/progestogens and review of the literature. *Andrologia*. 2016;48(10):1130-1137. doi:10.1111/and.12550.