Regression of Multiple Meningiomas After Discontinuation of Chronic Hormone Therapy

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Background

Meningioma is the most common primary central nervous system tumor and is known to express both estrogen and progesterone receptors. There is a female preponderance, with female to male ratio reported as high as 3:1.1 During reproductive age,2,3 together these characteristics led to the theory that sex hormones may play a role in the etiology and pathogenesis of meningiomas. While a correlation between meningioma and pregnancy is well established4–5, the association between meningioma and other sources of potential hormone exposure, such as gender reassignment surgery or fertility treatment, has recently gained attention.6–9 Endometriosis is a chronic disease characterized by endometrial tissue outside of the uterus, potentially requiring lifelong treatment with hormone-based therapy. Treatment strategies include: estrogens, progestins, androgens, gonadotropin releasing hormone agonists or antagonists and aromatase inhibitors. Here we describe the case of a middle-aged woman with endometriosis and over twenty years of progesterone therapy who was found to have multiple, symptomatic meningiomas that shrank after cessation of hormone supplementation.

Case Description

A 40-year-old female with a history of cervical cancer and endometriosis managed with at least 20 years of progesterone therapy (Megestrol) presented with 4–5 months of worsening visual acuity in her right eye found to have temporal visual field cut prompting brain imaging. Her neurologic exam was significant for an inability to count fingers in the temporal and superior nasal field. Magnetic resonance imaging (MRI) brain demonstrated multiple dural based masses (at least five), the largest of which was along the planum sphenoidale with extension into the sella and displacement of the optic nerves (Figure 1). Other lesions include right anterior falx, left parietal and a frontal calvarial based lesion (Figure 3). She underwent expanded endoscopic endonasal approach for resection of the planum sphenoidale lesion. Histological examination revealed a WHO grade I meningothelial meningioma, which stained diffusely positive for progesterone receptor (PR) and somatostatin 2 receptor (SSTR2A), with estrogen receptor (ER) positivity in a subset of cells (Figure 2). Postoperatively her visual fields improved to full to confrontation. Megestrol was discontinued 5 months post operatively with interval decrease in size of multiple meningiomas 4 months after cessation of megestrol.

Discussion

We present, to our knowledge, the first report of multiple meningiomas in the setting of chronic progesterone therapy (megestrol) for treatment of endometriosis with subsequent regression upon cessation of exogenous hormone.

Recently, several series have called attention to scenarios where increased hormonal levels, either endogenous or exogenous, correlate with meningioma growth and progression, such as pregnancy, oral contraception, fertility treatment, and gender reassignment.10–11,12 Using progesterone-only contraception is associated with increased recurrence of WHO grade I meningiomas (33.3 vs 19.6%) as well as decreased time to recurrence (18 vs. 32 months). Peyre, et al., compared 40 female meningioma patients with a history of long-term progesteron therapy to a control group of female meningioma patients and similarly found significant differences in patient and tumor characteristics. Patients exposed to progesterin therapy were younger at tumor onset (mean 48 years vs 58 years) and more often had multiple/multi-focal meningiomas (48% vs 5%). Furthermore, meningiomas in the progesterin therapy cohort had a shift in their mutational landscape, which may suggest progesterin-selects for specific molecular profiles.12

Conclusion

The potential role of progesterone in meningioma pathogenesis should be taken into account when considering initiation of lifelong progesterone therapy in a patient. While this patient’s multiple meningiomas are not definitively connected to chronic progesterone use, her young age, finding of multiple meningiomas, and especially their subsequent regression upon cessation of exogenous hormone use do support this notion.12,13

References


Fig. 1 Preoperative imaging. A and B Axial T1-weighted MRI showing multiple dural based masses at the convexity, parasagittal data, and dural base. C and D Axial and coronal T2-weighted MRI. E and F Coronal and axial T1-weighted MRI slices 10 month post-surgery demonstrating interval decrease in size of multiple meningiomas, including: right anterior falx (A) 11 mm, now (B) 5 x 4 x 8 mm, left parietal (C) 8 x 11 mm, now (D) 7 x 4 mm, and lateral frontal parafalcine based lesion (E) 12 x 13 mm, now (F) 7 x 6 mm.

Fig. 2 Histological sections demonstrating (A) Hematoxylin and eosin (H&E) staining as well as immunohistochemistry for (B) progesterone receptor (PR), (C) estrogen receptor (ER) and (D) somatostatin 2 receptor (SSTR2A) in a 66 year old patient with a history of chronic progesterone treatment for endometriosis and a WHO grade I meningioma.

Fig. 3 Postoperative imaging. A and B Axial T1-weighted MRI showing 10 month post-operative and 6 month post-megestrol cessation demonstrating interval decrease in size of multiple meningiomas, including: right anterior falx (A) 11 mm, now (B) 6 x 8 x 4 mm, left parietal (C) 8 x 6 mm, now (D) 5 x 3 mm, and lateral frontal parafalcine based lesion (E) 12 x 13 mm, now (F) 7 x 6 mm.