Hormone-dependent shrinkage of a sphenoid wing meningioma after pregnancy: case report

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Meningiomas are known to be associated with female sex hormones. Worsening neurological symptoms or newly diagnosed meningiomas have been described in the context of elevated levels of sex hormones, for example, in pregnancy. To the authors' knowledge, tumor shrinkage after the normalization of hormones has not been described, even if it is known that neurological deficits due to meningioma compression may improve after giving birth.

A 32-year-old female patient presented with severe headache and vision disturbances at the end of her second pregnancy. Magnetic resonance imaging revealed an extended mass at the lateral left-sided sphenoid wing that was suspected to be a meningioma. After delivery, the patient's symptoms improved, and MRI obtained 2 months postpartum showed significant shrinkage of the lesion.

Significant tumor shrinkage can occur after pregnancy. Thus, repeat imaging is indicated in these patients.

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KEY WORDS meningioma; shrinkage; pregnancy; progesterone; hormone dependent; oncology

MENINGIOMAS compose the most frequently reported intracranial tumors with an incidence rate of 10%–20% of all intracranial neoplasms,⁶ although their etiology is still unclear. Several risk factors have been described for meningiomas arising from arachnoidal cap cells. Previous radiation therapy and genetic disorders (for example, neurofibromatosis Type 2) increase the prevalence of intracranial meningiomas. Furthermore, sex hormones in general and female sex hormones especially⁷ promote meningioma development.

Pregnancy itself does not increase the incidence of intracranial neoplasms.²² However, a worsening of symptoms by the accelerated growth of meningiomas during pregnancy has been described.^{16,17,19} The underlying mechanism for this growth may consist of elevated serum estrogen and progesterone levels in pregnant patients.^{22,30,32} The diagnosis of a symptomatic intracranial meningioma during pregnancy presents a challenge for both gynecologists and neurosurgeons. If there is a need for surgical intervention,²⁵ potential risks will involve not only the patient her-

self but also the unborn child. Therefore the management and finally the treatment of meningiomas during pregnancy require close interdisciplinary cooperation among gynecologists, neurologists, and neurosurgeons.¹⁸ We present a case of significant postpartum tumor shrinkage of a sphenoid wing meningioma diagnosed during pregnancy. Immunohistochemical analysis of the tumor specimen demonstrated an overexpression of progesterone, which may explain the hormone-dependent growth and shrinkage documented by MRI.

Case Report

History and Examination

A 32-year-old female (gravida 2, para 1) presented to the Department of Obstetrics and Gynecology at the Medical University of Innsbruck at gestation week 39 +2 with prolonged and severe headache combined with vomiting, vision disturbance, and persistent tearing from her left eye. Migraines had been diagnosed in her teenage years, and

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during her first pregnancy she had experienced worsening of her migraines with attacks every 2–3 weeks. Ultrasonography studies of the fetus showed no abnormalities, and there was no evidence of HELLP syndrome in the patient's serum. The patient was also seen by neurology and ophthalmology, and migraine attack with cluster headache was diagnosed. To exclude a vascular pathology as the cause of her symptoms, standard cranial MRI (without contrast agent; T1- and T2-weighted and time-of-flight angiography) was performed. A left-sided lesion (53 × 66 mm, 53.1 cm³) with local mass effect and perifocal edema was detected and suspicious for a lateral sphenoid wing meningioma (Fig. 1). After the tentative diagnosis, an uneventful cesarean section was performed because of a term unborn (no retardation in growth or organ formation) in ultrasonography diagnostics. Delivery was followed by Gd-enhanced MRI, which showed homogeneous enhancement of contrast agent, reinforcing the suspected diagnosis.

Postpartum, the patient still demonstrated no neurological deficit and no evidence of epileptic seizures under low-dose steroid therapy; thus, the resection was postponed for elective surgery 2 months after delivery. Magnetic resonance imaging was repeated before the scheduled surgery, revealing significant mass reduction (50%) of the initial tumor (30 × 35 mm, 27.6 cm³; Fig. 1). Options were discussed with the patient.

Operation

Microsurgical resection was uneventfully performed via a left frontotemporal craniotomy without complications. A complete resection could be achieved by excising the basal dura mater and drilling the hyperostotic areas of the lateral sphenoid with a high-speed bur.

Postoperative Course

Except for a single epileptic seizure 1 day after surgery, the patient's course was uneventful. Anticonvulsive treatment was administered for 3 months, so breastfeeding had to be discontinued. Postoperative imaging showed complete resection of the tumor.

Histopathological Workup

Histopathological workup was performed using ready-to-use antibodies against the estrogen receptor and the progesterone receptor (both Ventana). It revealed the diagnosis of a microcystic meningioma (WHO Grade I) with progesterone receptor expression over 90% (Fig. 2). The tumor showed no expression of the estrogen receptor.

Discussion

In WHO Grade I meningiomas a slow growth pattern is usually observed. While there are well-known relations between proliferation and tumor grade,^{20,21} different patterns of behavior for intracranial meningiomas under the influence of elevated serum levels of sex hormones (for example, progesterone) during pregnancy have also been reported; tumor growth⁹ and neurological improvement due to possible minimal regression⁴ have both been observed. Clear volumetric tumor regression after pregnancy has not

FIG. 1. **A:** First MR image obtained during pregnancy, showing an extraaxial lesion. **B:** Axial MR image obtained the 1st day after cesarean section, showing homogeneous Gd enhancement (lesion volume 53.1 cm³). **C:** Axial MR image obtained 2 months after giving birth, revealing a significant mass reduction (lesion volume 27.6 cm³). **D:** Postoperative MR image showing complete tumor resection.

been documented. Given the meningioma's expression of different hormone receptors for progesterone, androgen, estrogen, and placenta growth factor^{2,10,11} and its response to increased serum levels of sex hormones during pregnancy, rapid tumor growth or the sudden onset of symptoms (for example, headache, double vision), as occurred in the presented case, seems plausible. This may also explain why symptoms might develop for the first time during the course of a pregnancy. After delivery significant reduction of the tumor was observed, most likely because it lacked stimulation by a decreased serum progesterone level. The high level of progesterone receptor expression of more than 90% in the specimen is particularly noteworthy given the numerous studies investigating the role of sex hormones and the over-abundance of such tumors in women.^{1,8,28,31}

A small cohort study²³ revealed a correlation between progesterone receptor status and the biological behavior of tumors; patients with progesterone-positive tumors showed decreased recurrence rates after tumor resection. Furthermore, several case reports dealing with symptomatic meningiomas during pregnancy have been published.^{3,26} In the presented case, the patient experienced minor symptoms despite the extent of the intracranial mass. The advanced pregnancy and concomitant low risk in delivering the fetus just days before reaching full term facilitated the decision-making toward cesarean delivery. Postpartum,

FIG. 2. Photomicrographs with antibody against the progesterone receptor showing strong nuclear immunoreactivity in nearly all tumor cells. H & E (upper). Figure is available in color online only.

the low-dose steroids could be tapered until the resection, resulting in elective surgery under controlled conditions for the patient, her family, and the treating physicians. Contrast-enhanced MRI was conducted just after delivery because there is a general recommendation against the use of Gd in pregnant women. A potential risk especially for the unborn includes nephrogenic systemic fibrosis because of immature renal function. Furthermore, Gd retention in the tissue with less stable agents and the lack of knowledge regarding its long-term effects are causes for concern, restricting use in neonates.²⁹ The same precaution seems reasonable in pregnant women. This compels postponement of elective surgery in patients with minor symptoms until after the first vulnerable postpartum months, which provides the opportunity for the augmented risks of thromboembolic events such as pulmonary embolism, deep vein thrombosis, or coagulopathy disorders after birth to become normal.^{12,24} Furthermore, emotional components such as postpartum depression that could be aggravated after brain surgery may stabilize, leading to a better outcome. It seems reasonable to perform interdisciplinary risk assessments in patients presenting earlier in pregnancy and with symptomatic meningiomas, taking

into account possible harm to the unborn and permanent neurological deficits.⁵ Depending on the severity of symptoms and a potential trial of steroids, surgery may often still be indicated.

In cases with minor symptoms and relief with low-dose steroids following cesarean section, this strategy of delayed elective surgery might be the right choice for women at the end of a pregnancy. Elective surgery postponed for some months if possible leads to a stabilized situation and may also facilitate resection due to a reduced tumor size in meningiomas highly sensitive to levels of sex hormones.

RU-486, a progesterone receptor antagonist, has been tested in clinical trials with mixed results. Grunberg et al. treated 14 patients, 5 of whom had an objective response and 3 of whom also experienced subjective improvement.^{13,15} In a later series, the same group of investigators described 28 patients treated with the same drug, with a minor response in only 8 patients (all premenopausal).¹⁴ Immunohistochemical testing was not performed. A recent publication showed favorable results in postmenopausal patients with multiple meningiomas with up to 10 years of follow-up.²⁷ Overall, the side effects of long-term RU-486 treatment seem to be minor, so no discontinuation of treatment was necessary in either study. Immunohistochemical progesterone receptor staining was done, although there was no proof of progesterone receptor expression; such staining seems to be mandatory when considering RU-486 treatment. Both of the latter studies showed promising results in patients with a high progesterone receptor density in tumor tissue.

Conclusions

Meningiomas can be influenced by levels of female sex hormones, leading to accelerated growth during pregnancy. If possible and in cases of only minor symptoms, resection should be conducted after delivery. To our knowledge, the presented case shows, for the first time, that delaying surgery for some months after delivery may result in easier resection given the possible shrinkage of hormone-sensitive meningiomas. In addition, a stabilized condition after pregnancy may be beneficial for those patients.

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