Progression of Low-Grade Glioma During Pregnancy With Subsequent Regression Postpartum Without Treatment—A Case Report

BACKGROUND AND IMPORTANCE: This report illustrates a case of a low-grade glioma that showed significant disease progression during pregnancy, and then subsequent regression spontaneously in the postpartum period without treatment. This is a rare case of spontaneous glioma regression in the postpartum period, and may suggest underlying mechanisms of hormonal influences upon glioma progression.

CLINICAL PRESENTATION: The patient is a 27-yr-old female who underwent placement of a right-sided ventriculoperitoneal shunt for aqueductal stenosis at 8 wk of age. At the age of 24 yr, she was evaluated for chronic headaches and was found on magnetic resonance imaging (MRI) for the first time to have a small nonenhancing tectal glioma that remained stable on follow-up MRI. At the age of 25 yr, she returned for annual follow-up after giving birth and reported a significant increase in headache frequency and severity during the pregnancy. Repeat imaging now showed a larger, contrast-enhancing lesion. A decision was made to pursue radiosurgery, but during the pretreatment planning phase, the lesion and symptoms regressed spontaneously, and the lesion has remained stable on repeat MRI studies over a 30-mo period since delivery of her child.

CONCLUSION: A young woman with a tectal glioma developed symptomatic disease progression during pregnancy, and subsequently had regression of the lesion and symptoms in the postpartum period without treatment. This case supports watchful waiting in select cases and suggests a potential role of hormones in glioma progression.

KEYWORDS: Disease Progression, Glioma, Headache, Pregnancy, Regression, Watchful Waiting

During pregnancy, various factors including hormonal changes,1,2 alterations in blood flow, and other physiological mechanisms have been hypothesized to lead to growth and/or hemorrhage in select cases of various intracranial tumors including pituitary adenomas,3,4 gliomas, and meningiomas.5,6 Several studies have pointed to a potential role of estrogen and progesterone receptors in glioma growth.7,8 Pregnancy is characterized by high levels of progesterone along with alterations in the hypothalamus-pituitary axis. Placental growth hormones may induce release of growth factors that upregulate glioma proliferation and migration. Regression of intracranial tumors postpartum has not been previously described in the literature.9 A case is presented of a suspected low-grade glioma that demonstrated evidence of growth and imaging features concerning for malignant transformation to a higher grade during pregnancy with subsequent spontaneous tumor regression in the postpartum period without treatment of the lesion. The case is summarized and possible mechanisms discussed.10

CLINICAL PRESENTATION

Informed consent was obtained from the patient. The patient is a 27-yr-old Caucasian female. At 8 wk of age, she had a right parieto-occipital ventriculoperitoneal shunt placement

ABBREVIATIONS: MR, Magnetic resonance; MRI, magnetic resonance imaging

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at another institution for hydrocephalus due to apparent aqueductal stenosis (Figure 1). No apparent tumor was identified at that time. She was followed by neurosurgeons periodically over the years and generally was in good health with no significant issues except chronic headaches. At 20 yr of age, she was evaluated at another institution for headache associated with nausea and vomiting. Computed tomography of the head was performed, and a subsequent radio-isotope “shuntogram” did not identify any evidence of shunt malfunction (Figure, Supplemental Digital Content 1). A diagnosis of migraine headaches was made, and she was started on prophylactic medications. She did not require any neurosurgical intervention over the years including no revisions of the shunt. She generally functioned well, completed a college education, and maintained a full-time job.

At 24 yr of age, the patient presented for neurosurgical evaluation for assessment of an exacerbation of her chronic headaches and to establish adult neurosurgical evaluation. Given her previous history of shunted hydrocephalus, magnetic resonance imaging (MRI) of the brain was completed (Figure 2). The MRI demonstrated small ventricles, and it was concluded that her shunt was functioning well. In addition, a 6-mm nonenhancing lesion was identified in the midbrain tectal region with MRI characteristics consistent with a low-grade glioma. The headaches were managed medically with a plan for interval imaging. After 6 additional months, a follow-up MRI was stable, and plans were made for patient to return in 1 yr with a repeat MRI.

In the interim, the patient noted a dramatic increase in headache frequency after becoming pregnant. The pregnancy itself was uncomplicated except for a subjective increase in migraine headaches. Her physicians pursued close monitoring of her headaches and neurological condition without imaging during pregnancy. Subsequent MRI studies during the postpartum period revealed a significant increase in the size of the apparent tectal glioma (Figure, Supplemental Digital Content 1). She was evaluated by a neurosurgeon, and an MRI 4 months post-partum with mild interval decrease in lesion size (Supp. figure 3).

At 25.5 yr of age, she was evaluated at another institution for headaches with small ventricles (figure 2). Computed tomography of the head was performed, and a subsequent radio-isotope “shuntogram” did not identify any evidence of shunt malfunction (Figure, Supplemental Digital Content 1). A diagnosis of migraine headaches was made, and she was started on prophylactic medications. She did not require any neurosurgical intervention over the years including no revisions of the shunt. She generally functioned well, completed a college education, and maintained a full-time job.

At 26 yr of age, the patient presented for neurosurgical evaluation for assessment of an exacerbation of her chronic headaches and to establish adult neurosurgical evaluation. Given her previous history of shunted hydrocephalus, magnetic resonance imaging (MRI) of the brain was completed (Figure 2). The MRI demonstrated small ventricles, and it was concluded that her shunt was functioning well. In addition, a 6-mm nonenhancing lesion was identified in the midbrain tectal region with MRI characteristics consistent with a low-grade glioma. The headaches were managed medically with a plan for interval imaging. After 6 additional months, a follow-up MRI was stable, and plans were made for patient to return in 1 yr with a repeat MRI.

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At 28 yr of age, the patient presented for neurosurgical evaluation for assessment of an exacerbation of her chronic headaches and to establish adult neurosurgical evaluation. Given her previous history of shunted hydrocephalus, magnetic resonance imaging (MRI) of the brain was completed (Figure 2). The MRI demonstrated small ventricles, and it was concluded that her shunt was functioning well. In addition, a 6-mm nonenhancing lesion was identified in the midbrain tectal region with MRI characteristics consistent with a low-grade glioma. The headaches were managed medically with a plan for interval imaging. After 6 additional months, a follow-up MRI was stable, and plans were made for patient to return in 1 yr with a repeat MRI.

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Figure 2. A brain MRI at age 24 revealed a non-enhancing T1 hypointense, T2/FLAIR hyperintense lesion eccentrically located in the dorsal midbrain measuring 7 mm (transverse) × 5.7 mm anterior-posterior consistent with a tectal glioma. This lesion had not been identified on imaging at the time of diagnosis of hydrocephalus and aqueductal stenosis at 8 wk of age, or on subsequent imaging during her childhood. A. Axial T1 contrast-enhanced scan. B. Axial T2-contrast enhanced scan. C. Sagittal T1 scan.

DISCUSSION

Intracranial tumors including meningiomas, pituitary adenomas, and gliomas have been demonstrated in select patients to grow and/or hemorrhage during pregnancy.11,12 A number of hormonal changes, alterations of blood flow, and other physiological parameters have been identified as possibly contributing to this phenomenon. To our knowledge, this is the first reported case of spontaneous regression of a glioma in the postpartum period without treatment. It is likely that hormonal changes during pregnancy contributed to the growth of the tumor, and the subsequent normalization of these hormonal changes also played a role in the eventual spontaneous tumor regression.

While the lesion was not biopsied for tissue sampling, the proposed diagnosis of tectal glioma is highly likely in light of the MRI characteristics, spectroscopic findings, and general behavior. Additionally, when the lesion first arose cannot be
ascertained with certainty. There are case reports of pediatric patients diagnosed with hydrocephalus secondary to aqueductal stenosis that later were identified to develop an obstructive tumor, and this scenario may be the case for the patient described in this report.

There is a growing body of evidence that shows hormonal changes associated with pregnancy can stimulate glial cell growth and may confer an increased risk of tumors of the central nervous system. Clinically, there is growing evidence that pregnancy increases the growth rate and the risk of malignant transformation of low-grade gliomas. De novo tumors that arise during pregnancy are also more likely to be high-grade lesions. The management of brain tumors during pregnancy remains an active area of investigation. In many cases, radiological and surgical treatment is deferred to the immediate postpartum period unless an acute intervention is needed.

This phenomenon of tumor regression postpartum is one that clinicians should bear in mind when managing patients with brain tumors during pregnancy and the postpartum timeframe.

**FIGURE 3.** A follow-up MRI at approximately 3 mo postpartum showed further mild increase in the size of the lesion with central enhancement. A, Axial T1 contrast-enhanced scan. B, Axial T2 contrast-enhanced scan. C, Sagittal T1 contrast-enhanced scan. D, Sagittal T2 contrast-enhanced scan.
Furthermore, a clearer understanding of the hormonal and physiological factors that might lead to such tumor progression and regression during and after pregnancy might give some insight into possible mechanisms of glioma growth, and possible strategies to target for therapeutic intervention.

CONCLUSION

A case of a young woman with symptomatic growth of an apparent low-grade tectal glioma during pregnancy with subsequent spontaneous regression of the tumor and symptoms during the postpartum period is presented. While several small case series and retrospective cohort analyses of both low- and high-grade gliomas have shown increased growth and malignant transformation during pregnancy, spontaneous tumor regression in the postpartum period has not been previously described. This case supports watchful waiting in select cases and suggests a potential role for hormones in glioma progression.

Disclosures

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REFERENCES


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**Supplemental Digital Content 1. Figure.** Contrasted head CT scan obtained at age 20 for evaluation of headache with no evidence of a mass lesion. A representative axial slice from contrast-enhanced scan. A radioisotope shuntogram performed at that time showed a normally functioning shunt.

**Supplemental Digital Content 2. Figure.** Follow-up MRI at the age of 25 yr, 1 yr after the MRI study in Figure 3, and approximately 2 mo postpartum showed interval enlargement of the lesion to 1.5 cm by 1.4 cm, with avid central contrast enhancement, and increased cerebral blood volume. The findings on this MRI were interpreted by the neuroradiologists as consistent with pilocytic astrocytoma or high-grade transformation of existing low-grade glioma. A, Axial T1 contrast-enhanced scan. B, Axial T2 contrast-enhanced scan. C, Sagittal T1 contrast-enhanced scan.

**Supplemental Digital Content 3. Figure.** Repeat MRI 4 mo postpartum showed interval decrease in the size of the lesion to 1.2 cm by 1.2 cm with decreased central enhancement (0.8 cm by 0.8 cm). A, Axial T1 contrast-enhanced scan. B, Axial T2 contrast-enhanced scan. C, Sagittal T1 contrast-enhanced scan. D, Sagittal T2 contrast-enhanced scan.

**Supplemental Digital Content 4. Figure.** MRI at 6 mo postpartum demonstrated that the lesion had decreased to 0.9 cm by 0.9 cm, and no longer exhibited central enhancement. A, Axial T1 contrast-enhanced scan. B, Axial T2 contrast-enhanced scan. C, Sagittal T1 contrast-enhanced scan. D, Sagittal T2 contrast-enhanced scan.

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**COMMENT**

The authors describe a case of a patient with a low-grade glioma that progressed during pregnancy and then demonstrated regression postpartum without treatment. The case is interesting although one could make the argument that this is simply a change in the blood brain barrier permeability during pregnancy and not actual tumor growth. Nevertheless, the imaging is interesting. The lesion is quite small so it would be easy to be skeptical of the MR spectroscopy. Without more follow-up or a tissue diagnosis it is unclear what is really going on in this case report.

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