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Case Report

Management of intracranial pathology during pregnancy: Case example and review of management strategies

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Abstract

Background: Intracranial tumors during pregnancy are uncommon, and they present an interesting challenge to both the neurosurgeon and the obstetrician. Special considerations must be made in every aspect of care. The authors use the rare case of a 27-year-old pregnant female with suspected pineal region tumor eventually diagnosed as a thalamic region ganglioglioma to review the current literature on management of pathology in this unique patient population.

Case Description: A 27-year-old female who was 26 weeks pregnant presented to her obstetrician with complaints of headaches, blurriness of vision, and left-sided numbness and tingling. She was diagnosed with 1-cm mass in the pineal region and obstructive hydrocephalus. She initially underwent an endoscopic third ventriculostomy with biopsy of what appeared grossly to be a thalamic mass. The child was delivered via cesarean section at 39 weeks. Serial postpartum imaging demonstrated increasing tumor size and enhancement, which led the authors to proceed with subtotal resection via a supracerebellar infratentorial approach with stereotactic neuronavigation. Tissue specimens obtained for pathological analysis resulted in a revised diagnosis of World Health Organization (WHO) grade II ganglioglioma.

Conclusions: Pregnancy presents a challenge for any patient requiring neurosurgical intervention. We present an interesting case example with a rare central nervous system neoplasm and discuss the management of intracranial pathology in pregnant patients.

Key Words: Arteriovenous malformations, brain tumor, cerebral venous sinus thrombosis, ganglioglioma, gadolinium, immunoperoxidase, pregnancy

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INTRODUCTION

Pregnancy can predispose women to a higher incidence of neurological pathology including preeclampsia and eclampsia, subarachnoid hemorrhage (SAH), stroke, cortical vein or venous sinus thrombosis, pseudotumor cerebri, pituitary apoplexy, and neoplasms.[3,4,10,34,39] Anatomic and physiologic changes of pregnancy can

also place pregnant women at increased risk for certain intracranial tumors and low back pain caused by disk herniation.[27] Intracranial tumors during pregnancy are uncommon, but they present an interesting challenge to both the neurosurgeon and the obstetrician.[13] Certain tumors, such as choriocarcinomas, meningiomas, and pituitary adenomas, are specifically associated with pregnancy.[27] Other tumors carry the same prevalence in both pregnant and nonpregnant patients.[30] Pregnancy may promote the unmasking of an underlying neoplasm by factors such as immunogenic tolerance, steroid-mediated growth, and hemodynamic changes that increase the intracranial mass effect.[27] In addition, tumors with rapid growth and subsequent vasogenic edema can simultaneously contribute to increased intracranial pressure (ICP). When superimposed on the physiologic changes of pregnancy, symptoms can be amplified and quite severe in pregnant patients.[36]

Gangliоglioma is a rare primary neoplasm of the central nervous system with an incidence that ranges from 1.2% to 7.6%. Gangliоglioma typically affects older children and young adults.[26] These tumors usually present with seizures and are the most common tumors in young patients who have chronic temporal lobe epilepsy.[22] We present a case of a 27-year-old pregnant female with suspected pineal region tumor eventually diagnosed as a thalamic region gangliоglioma as the basis to review the current literature on management of intracranial pathology in this unique patient population.

CASE REPORT

History and presentation

A 27-year-old female who was 26 weeks pregnant presented to her obstetrician with complaints of headaches, blurriness of vision, and left-sided numbness and tingling. She had suffered weekly episodes of headaches for 2 months that were accompanied by blurry vision in both eyes and diffuse left-sided weakness. A computed tomography (CT) scan with contrast enhancement demonstrated ventriculomegaly and was interpreted as an ill-defined pineal thalamic mass. Magnetic resonance imaging (MRI) without gadolinium enhancement showed a 1-cm mass in the pineal region and obstructive hydrocephalus [Figure 1]. An initial neurologic examination yielded normal findings.

Initial operative intervention

To treat the patient's hydrocephalus and obtain tissue for histological diagnosis, we performed an endoscopic third ventriculostomy with biopsy of what appeared grossly to be a thalamic mass. The pathological evaluation, based on a small sample, demonstrated a World Health Organization (WHO) grade II ependymoma.

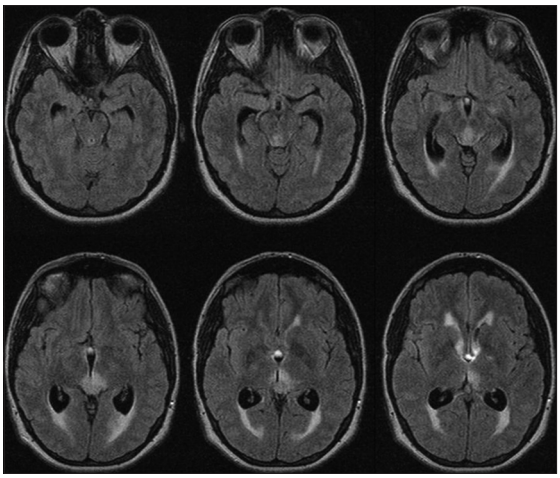

Figure 1: Axial fluid attenuation inversion recovery images obtained at presentation demonstrating a right-sided posterior thalamic mass lesion with hyperintensity and associated ventriculomegaly with periventricular hyperintensity suggestive of transependymal flow

Immunoperoxidase staining was strongly positive for glial fibrillary acidic protein (GFAP) with mild diffuse staining for synaptophysin. The Ki-67 proliferation index was below 2%. The initial biopsy report indicated that the biopsy sample was very small, and the biologic behavior of this neoplasm was difficult to ascertain.

Postoperative course

The consensus at our multidisciplinary neuro-oncology tumor board was to proceed with expectant management without immediate operative intervention and to perform an MRI with gadolinium after delivery. A follow-up noncontrast CT scan one month later showed stable to decreased ventricle size representing a functional third ventriculostomy. The patient was slowly weaned off of steroids, which had been started perioperatively. After an uncomplicated completion of the pregnancy, the child was delivered via cesarean section at 39 weeks of gestation.

A postpartum MRI showed an increase in the size of the left thalamic mass with extension into the right thalamus, quadrigeminal plate, and midbrain. There was no evidence of obstructive hydrocephalus. A subsequent MRI of the entire spinal cord showed no evidence of drop metastases. A repeat MRI brain 3 months postpartum demonstrated increasing tumor size and enhancement that was indicative of a higher-grade tumor. Because the patient had radiographic evidence of tumor progression and remained minimally symptomatic, resection for tumor debulking and confirmation of histological diagnosis was deemed necessary.

Secondary operative intervention

The patient underwent a subtotal resection via a supracerebellar infratentorial approach with stereotactic

neuronavigation. Tissue specimens obtained for pathological analysis resulted in a revised diagnosis of WHO grade II ganglioglioma. The pathologic specimen contained marked pleomorphism and gigantic nuclei. There was abundant positive staining with reticulin [Figure 2a] and rare periodic acid–Schiff (PAS)- and PAS–diastase (PAS-D)-positive droplets [Figure 2b]. Immunoperoxidase revealed strong staining for the neural markers neurofilament, neuron-specific enolase (NSE), synaptophysin, and glial markers including GFAP [Figure 2c]. The Ki-67 index was between 3% and 5% [Figure 2d].

Secondary postoperative course

A multidisciplinary decision was made to begin radiation therapy with a cumulative dose of 59.4 Gy given over 33 treatments. The patient tolerated the therapy with minimal complications, but remained steroid dependent after the resection.

One month after completion of radiation therapy, the patient developed diplopia and headache, which responded to an escalation of her steroid dose. She continued to have nausea and diplopia despite aggressive steroid use. Follow-up MRI 9 months after resection showed increased size and local mass effect of the enhancing mass centered in the midbrain and extension into the thalamus. The steroid dose had to be escalated further to address the patient's persistent blurred vision and headache. She developed significant cushingoid side effects. Imaging showed changes in the amount of necrosis and vasogenic edema surrounding the area in question. After several months of intermittent hospital admissions and emergency department visits, the patient succumbed to her disease almost 2 years after initial presentation.

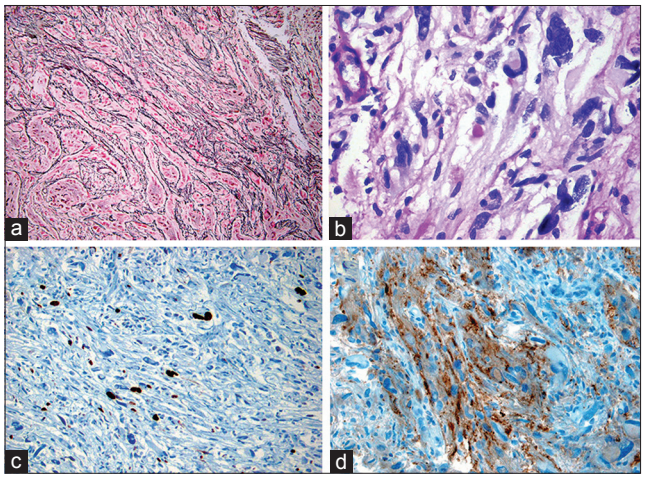

Figure 2: Histopathological staining. (a) Reticulin stain; (b) PAS staining shows marked nuclear pleomorphism and isonucleosis. Note PAS-positive droplet (pink); (c) Ki-67 staining shows 3–5% proliferation; (d) Synaptophysin and neuron-specific enolase (NSE) staining reveals pleomorphic cells of neuronal origin

DISCUSSION

Epidemiology and diagnostic concerns

Complications during pregnancy present a challenge to physicians because two individuals are affected by any intervention. In this case example, a pregnant patient was experiencing symptoms resulting from an intracranial mass. Although neurological complications are rare during pregnancy, the most common intracranial issues that arise involve ruptured arteriovenous malformations (AVMs), aneurysms, and intracranial bleeding due to preeclampsia.[6] While vascular pathology poses a more immediate challenge, typically requiring immediate treatment, intracranial tumors may usually be managed with more deliberation. Brain tumors in pregnant women tend to occur with the same relative frequency as in their age-matched, nonpregnant counterparts;[30] primary intracranial tumors are the fifth leading causes of cancer-related death in women aged 20–39 years.[7] Glioma is the most common (38%), followed closely by meningioma (28%) and acoustic neuroma (14%), with a small population of women with pilocytic astrocytoma (7%) and medulloblastoma (3%).[36]

It is of paramount importance for neurosurgeons and obstetricians to work in conjunction with one another when treating pregnant patients with intracranial pathology. The treatment algorithm shown in Figure 3 demonstrates steps and measures that should be followed when evaluating these patients. Multidisciplinary efforts are needed not only to successfully diagnose and treat the underlying pathology but also to ensure the safety of the mother and her unborn child. Table 1 summarizes six large series of intracranial tumors in pregnancy, their histological diagnosis, management, and delivery method.[8,14,21,30,40]

Generalized symptoms resulting from these tumors, such as headache, nausea, vomiting, and visual changes, are

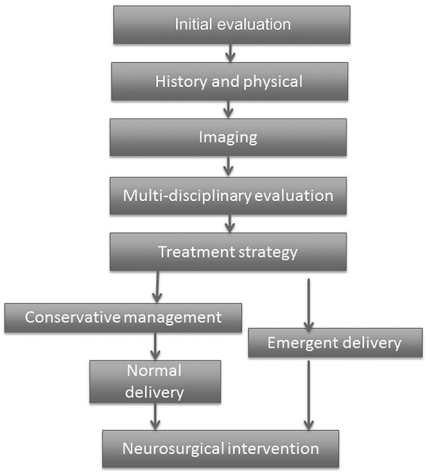

Figure 3: Potential evaluation algorithm for treatment of pregnant women with neurological signs and symptoms with intracranial lesion

Table 1: Review of series of intracranial tumors and pregnancy

Authors	No. of patients	Pathology (no. cases)	Gestational age (weeks)	Craniotomy/delivery (no. cases)	Delivery method (no. cases)
Roelvink *et al.* (1987)[30]	3	Astrocytoma (1) Medulloblastoma (2)	32-36	After	Unknown
Isla *et al.* (1997)[14]	6	Meningioma (2) Astrocytoma (4)	23-40	After (5)	Cesarean section (2) Vaginal (3) Termination (1)
Vougioukas *et al.* (2004)[40]	3	Glioma (2) Meningioma (1)	23-33	Before	Unknown
Ducray *et al.* (2006)[8]	3	Glioblastoma (2) Oligodendroglioma (1)	12-29	Before	Cesarean section
Lynch *et al.* (2010)[21]	10	Meningioma (2) Astrocytoma (4) Adenoma (1) Other (3)	16-40	Before (4) After (6)	Cesarean section (6) Vaginal (4)
Verheecke *et al.* (2014)[39]	27	Glioma (10) Low-grade astrocytoma (6) Meningioma (2) Others (9)	30-36	Before (12) After (7)	Cesarean section (16) Vaginal (5) Deceased (2) Termination (4)
Present case	1	Ganglioglioma	39	Biopsy before, craniotomy after	Cesarean section

primarily due to mass effect. The principal presenting symptom for our patient was unremitting headache, which was accompanied by blurred vision and left-sided weakness. In general, headaches are the primary presenting symptom in 36–90% of patients with brain tumors.[11] Symptoms of increased ICP, including nausea and vomiting, can be confused with hyperemesis gravidum. Women who present with generalized symptoms, which could be attributable to neurological pathology or normal pregnancy, are generally investigated with neuroradiologic imaging. The modality of choice is MRI because it does not utilize ionizing radiation and scanners used in most medical facilities have demonstrated no demonstrable harm to human tissue.[9] Specifically, cranial MRI has been demonstrated to be safe for both the mother and the fetus. Gadolinium contrast material does cross the placenta but has not been associated with birth defects at conventional doses.[36] Most centers, however, will not use it for pregnant patients.

Management of vascular pathology

Cerebrovascular disease is the most common cause of intracranial pathology during pregnancy; the most prevalent conditions include AVMs, aneurysms, and intracranial bleeding due to preeclampsia.[6] Treatment of vascular pathology requires immediate, in some cases emergent, attention and places extra emphasis on gestational age and both fetal and maternal stability. There is no class I or class II evidence to guide management of AVMs during pregnancy. Treatment options include surgery, radiosurgery, and endovascular techniques; however, individualized therapy based on location, grade, patient condition, and gestational age remains a controversial topic.[38] Previous reports have demonstrated that early surgical resection of AVMs did not confer a better outcome during pregnancy when compared with conservative treatment.[6]

Aneurysm rupture during pregnancy is rare, with an incidence of 0.01–0.05%; however, it accounts for 5–12% of maternal mortality.[6,12] Treatments for ruptured aneurysms during pregnancy may be surgical or endovascular, and the modality of treatment depends on the patient's clinical status, the location of the aneurysm, and gestational age. Endovascular management requires consideration of radiation exposure; however, good maternal and fetal outcomes have been reported with endovascular treatment.[16,17,24,28,29,37] Regular fetal monitoring should be performed during the vasospasm period to ensure fetal safety.

Preeclampsia is a common occurrence, but progression to eclampsia can occur in 2% of pregnancies and is present in 14–44% of cases of intracranial hemorrhage.[32] The mainstay of management includes intensive blood pressure control and close fetal monitoring.

Pregnant women are also at increased risk for cerebral venous sinus thrombosis (CVST), which has a variable mortality rate that has been reported as high as 30%. Treatment for CVST includes hydration, anticonvulsant therapy, and anticoagulation.[33] More extensive thrombosis may require endovascular thrombolysis or thrombectomy. Pregnant women diagnosed with CVST should be screened for thrombophilia and monitored carefully for their response to anticoagulation.

Role for surgical intervention

Whether or not to intervene surgically or with radiation therapy is case dependent. Our case involved a symptomatic patient with signs of tumor growth. There is scant evidence in the literature about neurosurgical operative outcomes in pregnant women. Johnson *et al*.[15] described 22 patients with 25 pregnancies; 13 of these patients had been diagnosed prior to pregnancy and 3 patients had tumor growth or recurrence during their pregnancy. In this series, seven patients underwent neurosurgical intervention at a mean gestational age of 27 weeks, with two patients experiencing permanent visual loss. Cohen-Gadol *et al*.[2] also addressed these issues as they relate to neurosurgery in a review of 34 pregnant patients treated over a 36-year span. Every patient had neurosurgical pathology: 12 had vascular lesions, 14 had tumors, 4 had traumatic lesions, 2 had primary intracerebral hematomas, and 2 had hydrocephalus. The average age of the 14 patients with tumors was 29.8 years, and the gestation at presentation varied from 2 to 34 weeks. Initial presenting symptoms included seizure, headache, nausea, vomiting, papilledema, hemiparesis, various cranial nerve palsies, and even respiratory distress. Additional information exists about the presence of pituitary neoplasms present during pregnancy, which are associated with lower morbidity and mortality when compared with other brain neoplasms. Higher rates of cesarean delivery in a macroadenoma cohort versus a microadenoma cohort are thought to be driven by symptoms caused by increased ICP.[31] The relationship between other brain neoplasms and cesarean delivery is not clear, but we would reason that the same principle would apply. Evidence has shown that neurologic deterioration during pregnancy can manifest with many symptoms and may be associated with increased rates of cesarean delivery, preterm delivery, and neonatal intensive care unit admission for the child.[15]

Delivery method

While definitive therapy may be delayed until the postpartum period, the actual type of delivery must be considered as well. In healthy pregnant women, increases of 33 cm H_2O in ICP during the first stage of labor and 70 cm H_2O during the second stage are typical.[36] The accentuation during the second stage can be attributed not only to increasing Valsalva pressure with pushing, but also to spontaneous uterine contractions. An induced increase in ICP in a patient with an elevated baseline ICP can lead to rapid neurologic decline and cerebral herniation.[36] The patient presented in this case delivered via cesarean section and experienced no complications. It must also be noted that no matter what decision is made for the type of delivery, epidural anesthesia is generally contraindicated in patients with intracranial mass because of the associated morbidity with possible cerebral herniation due to a wet tap. While accidental lumbar puncture can occur and is cause for concern during placement of an epidural catheter, earlier research has indicated it is uncommon. Korein *et al*.[18] evaluated 418 patients with papilledema, 83% of whom had a brain tumor, and noted that lumbar puncture occurred in only 5 (1.2%) patients. The conclusion of these authors, often referenced, was that a mass lesion in the brain was not an absolute contraindication to lumbar puncture.[18] Our patient was given spinal anesthesia with careful surveillance of her neurological status.

Tumor pathology

During the second operative intervention, we were able to obtain enough tissue to make a definitive diagnosis of a WHO grade II ganglioglioma. While the epidemiology of the tumor type fits the patient's profile, the region to which the tumor was localized is quite unique. Ganglioglioma is a rare glial–neuronal tumor composed of neoplastic glial cells and dysplastic neuronal elements. Histopathological differential diagnosis for these tumors includes both high-grade and low-grade neoplasms, such as diffuse astrocytomas, oligodendrogliomas, dysembryoplastic neuroepithelial tumors, pilocytic astrocytomas, and pleomorphic xanthoastrocytomas.[22]

Gangliogliomas have been reported to occur throughout the central nervous system, including the temporal lobe, spinal cord, brainstem, 3rd and 4th ventricles, pineal region, thalamus, intrasellar region, optic nerve, and cerebellum. In most cases, tumors are localized to the temporal lobe.[5] Supratentorial, cortically based lesions often present with focal or generalized seizures, whereas posterior fossa lesions present with hydrocephalus, cranial nerve palsy, speech or gait changes, myoclonus, and cerebellar seizures.[26] A review of six case reports of patients with intracerebral ganglioglioma showed that all six patients initially presented with seizure episodes, two with headache, one with hemiparesis and dysphasia, and one with behavioral difficulties.[5] The chief presenting symptoms in our patient were headaches, blurred vision, and left-sided numbness and tingling.

Surgical resectability depends on the exact location and behavior of the tumor. For those in the posterior fossa, gross total resection is often not possible without marked neurological deficit.[1,19,23,25,26,35,41] Several studies have suggested a benign clinical course in most patients with ganglioglioma, but tumor recurrence, malignant progression, and secondary glioblastoma have been observed in some patients. In a study of 58 patients with gangliogliomas by Lang *et al*.,[20] 40 tumors were assigned histologic grade I, but 16 tumors were grade II, and 2 tumors were grade III. The event-free 5-year survival rate in that cohort was 95% for gangliogliomas of the cerebral hemispheres; however, there is little data about thalamic region gangliogliomas.[20]

CONCLUSIONS

Pregnancy presents a challenge for any patient requiring neurosurgical intervention. In every aspect of care, including imaging, tissue diagnosis, and treatment strategies, the pregnant patient requires extra thought and consideration. We present a case example with a rare central nervous system neoplasm in a difficult location that represented a diagnostic and surgical dilemma to illustrate how the unique situation of each patient must determine the appropriate management in that case.

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