

CASE REPORT

Large infratentorial cystic oligodendroglioma in a pregnant patient: A case report of a rare presentation and literature review

Salman Abbasi Fard¹ | Farhad Tabasi^{2,3}  | Pouria Pourzand⁴ | Arshia Vahedi⁵ | Mehrdad Heravi⁴ | Martin M. Mortazavi¹

¹Department of Neurosurgery, National Skull Base Foundation, Thousand Oaks, California, USA

²Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran

³Institute for Brain Sciences and Cognition, Tarbiat Modares University, Tehran, Iran

⁴School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran

⁵Chronic Respiratory Diseases Research Center (CRDRC), Masih Daneshvari Hospital, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), Tehran, Iran

Correspondence

Farhad Tabasi, Department of Physiology, Faculty of Medical Sciences, Tarbiat Modares University, Jalal Al-Ahmad Street, Nasr Bridge, 1411713116 Tehran, Iran.

Emails: f.tabasi@modares.ac.ir; tabasif@gmail.com

Martin M. Mortazavi, Department of Neurosurgery, National Skull Base Foundation, 2100 Lynn Road, Suite 120, Thousand Oaks, CA 91360, USA.
Email: m_mortazavi@hotmail.com

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Abstract

Oligodendrogliomas (ODGs) are rare brain tumors in adults, mostly presenting as a supratentorial solid mass, while less than 10% occur infratentorially. Infratentorial cystic ODGs are extremely rare. We reported a large partially cystic cerebellar ODG in a 31-week pregnant patient with an unusual presentation and discussed the challenging management.

KEYWORDS

cerebellar oligodendroglioma, cystic brain tumor, infratentorial mass, oligodendroglioma

1 | INTRODUCTION

Oligodendrogliomas (ODGs) originate from oligodendrocytes and comprise 4–8% of all brain tumors.¹ ODGs usually occur in the middle ages and males, similar to many primary brain tumors.¹ More than 90% of all ODGs in adults are supratentorial, mostly found in cerebral hemispheres, most commonly in frontal lobes. Though,

only a small fraction of ODGs is located infratentorially. Typically, ODGs present as solid tumors, whereas cystic ODG is less common. Infratentorial cystic oligodendroglioma, however, is considerably rare.²

ODGs are slow-growing tumors with insidious presentations and might remain silent for many years. Seizure is reported as the most common presenting symptom, ranging from 35% to 85% of all cases.¹ Presenting symptoms

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could vary based on location, growth rate, and tumor size. Infratentorial ODGs frequently present with cerebellar symptoms, or symptoms attributed to increased intracranial pressure (ICP) caused by the tumor's compressive effect on the ventricular system causing obstructive hydrocephalus.³

Initial diagnosis is mainly based on neuroimaging and preferentially gadolinium-enhanced magnetic resonance imaging (MRI). There is no diagnostic hallmark on neuroimaging, but some features such as tumor calcifications that are easily visible on computed tomography (CT), could differentiate an ODG from other brain tumors. Nevertheless, a significant portion of these tumors may not demonstrate typical presentations. Thus, the most accurate diagnosis is made by histopathological examinations. We reported a large partially cystic cerebellar ODG in a young pregnant woman, provided a comprehensive literature review, and discussed the importance, challenges, and critical management of posterior fossa ODG in late pregnancy.

2 | CASE PRESENTATION

A 21-year-old right-handed Caucasian woman at 31st weeks of gestation was presented with a 2-month history of headache, neck pain, nausea, vomiting, and progressive ataxia. On physical examination, papilledema, dysmetria, intentional tremor, and truncal ataxia were evident. Next, she underwent brain imaging to clarify the possibility of brain masses. Preoperative brain MRI without contrast showed a large right paracentral cerebellar cystic mass with compression of the fourth ventricle and brain stem, causing obstructive hydrocephalus (Figure 1).

Given the MRI result, juvenile pilocytic astrocytoma, hemangioblastoma, and brain metastasis were initially suspected as a primary diagnosis. Since the patient was in 31st weeks of gestation, pregnancy termination and safe delivery of the child were planned immediately after a ventriculostomy to treat hydrocephalus, divert the cerebrospinal fluid (CSF), and monitor ICP. Following that, her brain tumor resection was scheduled on the third day to reach the patient's optimized general condition.

Histopathological examination showed a diffusely infiltrating tumor with moderate cellularity and cystic space. Tumor cells were monomorphic with round nuclei and perinuclear halos caused by artefactual retraction of cytoplasm that provided a characteristic "fried egg" appearance. A dense network of fine branching capillaries (chicken wire) patterns, numerous small calcifications, hemorrhage, and scattered mitotic activity were identified. Additionally, gliosis in the surrounding parenchyma was noted. There was no evidence of necrosis,

microvascular proliferation, or nuclear atypia (Figure 2). Immunohistochemistry (IHC) confirmed the ODG diagnosis with strongly positive glial fibrillary acidic protein and S-100 protein. The sample was negative for inhibin. However, we could not check for markers such as 1p/19q co-deletion, isocitrate dehydrogenase (IDH) mutation, and alpha-thalassemia/mental retardation, X-linked.

3 | PATIENT MANAGEMENT AND TECHNICAL NOTE

The diagnosis of a brain tumor in a pregnant woman is a challenging event for the patient and her family, as well as the medical team taking care of the patient. Operating on a symptomatic brain tumor in a pregnant patient presents a unique challenge to the medical team. Since the patient was in 31st weeks of gestation, pregnancy termination and safe delivery of the child were primarily intended. Her general condition and hemodynamics were monitored and stabilized. In terms of medications, steroids, mannitol, and preoperative intravenous antibiotics were initiated. Ventriculostomy was placed to treat hydrocephalus, divert CSF, and monitor ICP. Subsequently, the delivery was performed through a cesarean section while ICP and neuro-exams were closely monitored.

The patient was monitored in the intensive care unit, receiving steroids and mannitol to keep her ICP within normal range. This enabled us to temporize surgical treatment for the brain tumor to ensure the safest possible management. Resection of her brain tumor was planned on day 3 unless her neurological examination or ICP would deteriorate. This strategy could allow her general condition to optimize and heal her abdominal incision to a more acceptable level.

On the operation day, right para-midline suboccipital craniectomy and C1 laminectomy were performed to obtain an adequate trajectory and viewing angle to the lesion. Once the dura was opened, the ventriculostomy was lowered to 5 mmHg, and cisterna magna was opened to reduce the pressure on the cerebellum. Intraoperative neuro-navigation and neuro-monitoring consisting of motor evoked potentials, somatosensory evoked potentials, and brainstem auditory evoked responses were performed. Tonsillo-medullary cisterns were opened to release the tension on the brain, and the posterior inferior cerebellar artery and the inferior retro-tonsillar vein were cautiously dissected along with the tonsils laterally. Cottonoid neurosurgical patties were placed in the interface between the mass and the cerebellum. When it came to resection, the cyst was punctured to relax and decrease the mass effect. Then, the cystic and solid part was carefully dissected off from the cerebellum first.

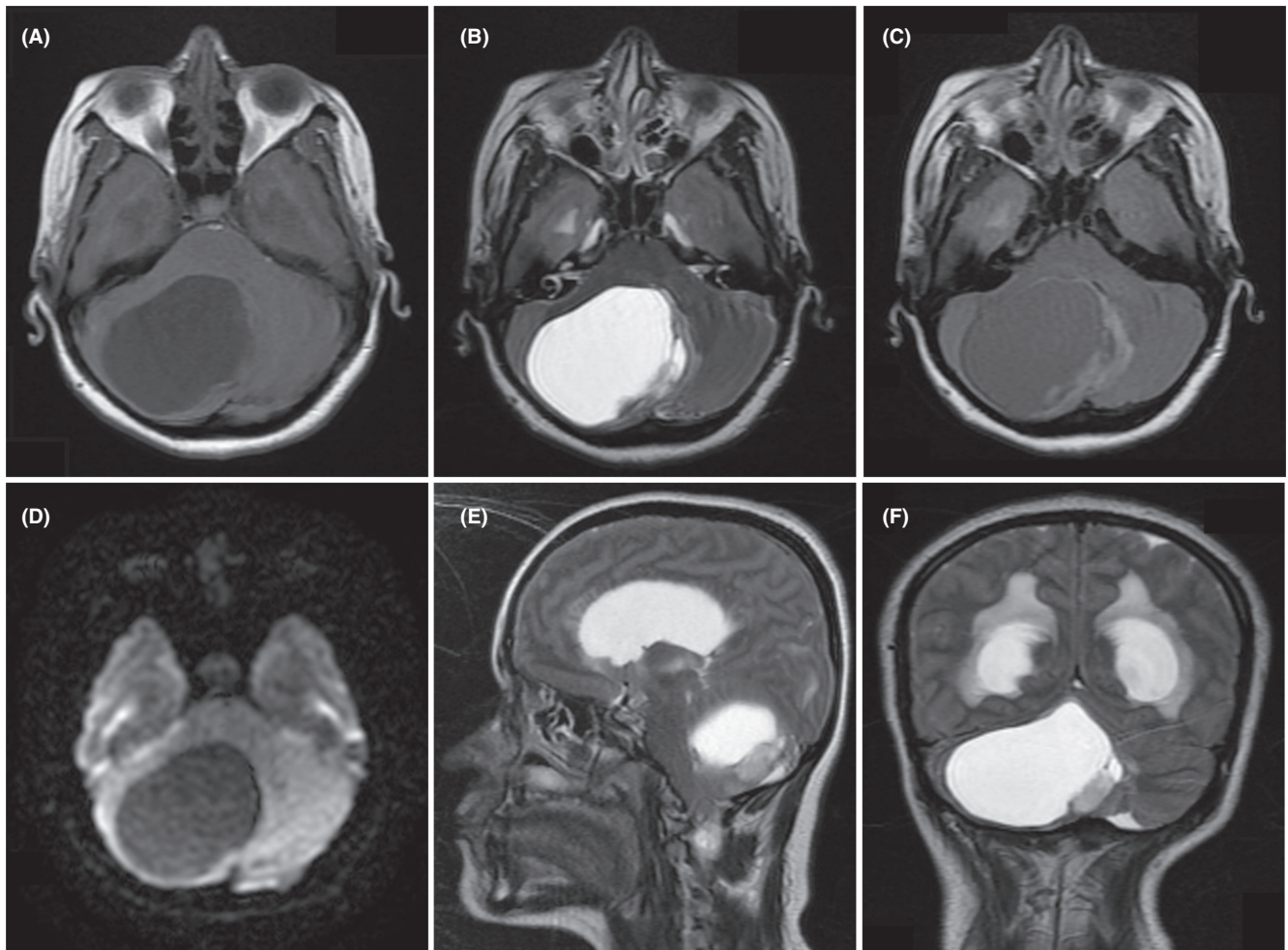
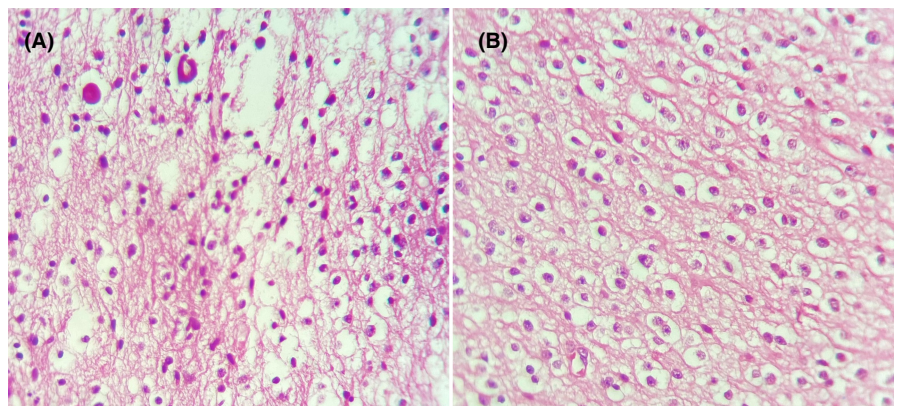


FIGURE 1 Preoperative brain MRI without contrast shows a large right paracentral cerebellar cystic mass with compression of the fourth ventricle and brain stem, causing obstructive hydrocephalus. (A) Axial T1-weighted image. (B) Axial fluid-attenuated inversion-recovery image. (C) Axial Diffusion-weighted image. (D) Axial T2-weighted image. (E) Sagittal T2-weighted image. (F) Coronal T2-weighted image

FIGURE 2 Histopathological examination shows monomorphic tumor cells with round nuclei, perinuclear halos, and numerous small calcifications. (A) Hematoxylin and eosin (H&E) $\times 100$ (B) H&E $\times 400$



Further cautious dissection of the cyst from the rhomboid fossa was performed. Finally, the resection of the tumor from the fourth ventricle floor and obex was performed with abundant precautions. A small superomedial residual attached to the inferior torcula was left to avoid venous

sinus complications. This technique and strategy allowed us to achieve a safe tumor resection. In the end, the dura was closed in a water-tight fashion and expanded with autologous pericranium. Ligamentum nuchae and subcutaneous tissue, followed by skin, were closed in anatomical layers.

4 | DISCUSSION

ODGs are uncommon brain tumors originating from the neuroepithelium, with diverse molecular pathology panels. Previously, ODGs were considered gliomas with distinctive morphology.¹ Some share the same pathological features with astrocytomas, but new molecular markers have separated ODGs from others.⁴ Glioma with *IDH* mutation and concurrent 1p/19q co-deletion is diagnosed as ODG.⁴ Though, *IDH* mutation and 1p/19q co-deletion may be seen less frequently in pediatric ODGs⁵; for instance, 1p/19q occurs about 10–35% in ODGs of this age group.^{6–8} Most ODGs tend to arise from cortical or subcortical white matter regions, including frontal (about 70%), parietal (about 20%), or temporal lobes.⁹ Infratentorial ODGs are infrequent in adults.^{1,3}

The infratentorial ODGs incidence is inconclusive and reported around 2–7%,¹⁰ primarily located in the cerebellum.¹¹ Posterior fossa ODGs seem to be more frequent in the pediatric population.¹² On the other hand, ODGs are typically solid, while cystic parts may be present.⁵ Notably, predominantly cystic ODGs are quite rare. We comprehensively searched for all infratentorial cystic ODGs in English literature and found that just eight cases of cystic ODG have been reported so far^{2,13–19} (Table 1). Notably, only four infratentorial cystic ODG cases were reported in cerebellar regions, with only a single case occurring in adult patients.²

Generally, the clinical presentations of ODGs are diverse, non-specific, and depend on the size, growth rate, location, and compressive effects on adjacent structures.⁹ Seizure has been reported as the most common presenting symptom of ODG, which may have existed several years before the diagnosis.²⁰ Headache, vertigo, nausea, vomiting, visual disturbances, cranial nerve impairment, sensory and/or motor deficit, or even altered mental status can be present in the disease course.²¹ Infrequently, patients may have no symptoms until a sudden onset loss of consciousness.²⁰ Further, infratentorial tumors can present even more insidiously.^{2,3}

In a pregnant patient, symptoms of elevated ICP, such as headache, nausea, and vomiting, can be challenging to distinguish from the expected pregnancy discomforts and may justify the tumor's large size, its compressive effect on the brain structures, and obstructive hydrocephalus in our case. This highlights the significance of detailed examination and clinical suspicion of long-lasting unusual neurological symptoms.

Initial diagnosis is mainly by neuroimaging. CT scan may have lower sensitivity than MRI but is more available, faster, and less expensive. The typical ODG calcifications are easily detectable on the CT; the lesions may appear as iso/hypodense lesions, and peritumoral

TABLE 1 Summary of reported cases of cystic oligodendroglioma

Report	Age/sex	Initial presentation	Location	Definite diagnosis
Greenfield and Robertson, 1933	Case series of five cases with cerebellar ODG	Headache, nausea, and vomiting	Cerebral hemisphere	Cerebral cystic ODG
Wycis, 1945	13-year-old/F	6 weeks of headache, dizziness, and staggering gait, falling to the left side	Cerebellum	Cerebellar cystic ODG
Hosono et al., 2001	6-year-old/F	3 months of psychomotor automatism and decreased LOC	Temporal lobe	ODG with multilocular cystic formation
Baysefer et al., 2004	7-year-old/F	1 month of vomiting, slight loss of tandem gait	Cerebellum	Cystic ODG
Das et al., 2006	59-year-old/F	5 days of intermittent confusion, memory problem, and headache	Pineal region	Anaplastic ODG
Levidou et al., 2010	37-year-old/F	Gaze impairment	Pineal region	Cystic ODG
El Ouni et al., 2010	8-year-old/F	2 weeks of headache, vertigo, nausea, and vomiting, mental status changed, and visual complaints	Cerebellum	Cystic ODG
Bhaskar et al., 2017	36-year-old/M	1 month of headache and vertigo	Cerebellum	Cystic ODG

Abbreviations: F, female; LOC, loss of consciousness; M, male; ODG, oligodendroglioma.

edema is uncommon.²² On the MRI, lesions may appear hypointense on T1-weighted and hyperintense on T2-weighted images.²³ ODGs have unique features that differentiate them from other brain lesions despite the lack of diagnostic radiological hallmarks. Tumor calcification is present in more than half of cases (range 60–90%) on preoperative neuroimaging and more than 70% on pathological examination.²² However, calcification may not be seen in posterior fossa ODGs.²⁴

Although ODGs may have cystic or necrotic parts, large cystic ODGs are uncommon.²⁵ Due to the paucity of infratentorial ODGs, the proposed radiological features are inconclusive and may not help distinguish them from other possible diagnoses such as astrocytoma preoperatively. We performed an emergent brain MRI without gadolinium in our case. According to the Society of Obstetricians and Gynecologists of Canada, there is level II evidence that fetal exposure to MRI is safe during the second and third trimesters, but gadolinium should only be used when the benefits outweigh the potential risks.²⁶ Based on imaging results, our initial preoperative diagnoses were pilocytic astrocytoma, hemangioblastoma, or brain metastasis.

Pilocytic astrocytomas (World Health Organization [WHO] grade I) are astrocytoma variants with a tendency in children and adolescents,²⁷ predominantly seen in the cerebellar region and may appear as a large cystic lesion with enhancing mural nodule, cyst wall, and calcification on imaging.²⁸ Cystic components usually appear as fluid signals on T1-weighted and hyperintensity on T2-weighted imaging and cyst wall enhancement with contrast T1-weighted imaging.²⁸ Therefore, distinguishing ODG and pilocytic astrocytoma based on neuroimaging findings alone is impractical and requires histologic and molecular assessments. Pilocytic astrocytomas demonstrate certain histopathological features, which help distinguish them from ODGs. These tumors usually have low-to-moderate cellularity, dense fibrillation, and characteristic Rosenthal fibers, as well as eosinophilic granular bodies, which are not present in ODGs. However, they may sometimes show foci with more rounded nuclei resembling ODG. Although IHC assessment may not be helpful due to overlaps in their patterns, genetic studies could be helpful in certain situations^{29,30}; though not definitive, considering the paucity of IDH mutation and 1p/19q co-deletion in ODGs occurring in children.³¹

On the other hand, hemangioblastomas are rare, low-grade (WHO grade I) lesions making 1–3% of cranial tumors.³² They commonly occur in the posterior fossa and are responsible for 10% of all posterior fossa tumors in young adults, known as the most common infratentorial tumors in this group.³² These tumors are well-circumscribed lesions with no real capsule, forming a solid mural nodule in a large cystic cavity abutting

pial matter.³³ Also, these tumors could be present as solid lesions without cyst formation.³³ The radiological features are the presence of the cystic part with T1-weighted isointensity, T2-weighted/fluid-attenuated inversion recovery hyperintensity, and mural nodule, which is iso/hypointense on T1-weighted and hyperintense on T2-weighted images.³⁴ Histologically, hemangioblastomas are distinguished by their vascularized appearance, composed of stromal and reactive vascular cells. Characteristically, microscopy shows thin-walled vessels in the background of connective tissue stroma and polygonal lipid-laden stromal cells.³³

The histological characteristics of ODGs are small, round cells with scant cytoplasm, perinuclear halos, and small nucleoli, the characteristic “fried egg” appearance.⁴ These features, along with cystic space, fine branching capillaries, hemorrhage, small calcifications, and scattered mitotic activity, were evident in the histopathological examination of the resected lesion from the case presented here, which established the diagnosis of cystic ODG (grade II). Based on mitotic activity, ODGs are categorized as grade II or grade III, according to the WHO classification of central nervous system tumors.⁴ About 75% of all ODGs are low-grade tumors.³⁵

The cornerstone of treatment is maximum surgical resection and, consequently, chemotherapy or radiotherapy. Because of its infiltrative nature, this tumor commonly involves adjacent gray matter and sometimes extends to the leptomeninges, which is a severe obstacle to surgical resection.³⁶ The amount of residual tumor following surgery is correlated with outcome in ODGs.³⁷ These tumors are typically chemosensitive,²¹ but molecular features can influence the chemosensitivity and prognosis.³⁸ The prognosis of patients with ODG is strongly correlated with 1p/19q co-deletion and IDH mutation.³⁹ The 1p/19q co-deletion is detected in 74% and 83% of well-differentiated and anaplastic ODGs, respectively.⁴⁰ Co-deletion of 1p/19q is associated with longer overall and progression-free survival, regardless of the treatment.⁴¹

Further, patients with 1p/19q co-deletion treated with radiation in addition to chemotherapy had a favorable prognosis and more prolonged overall survival.⁴² Proposed prognostic factors associated with worse overall survival rates are higher age, poor functional status, non-epileptic presentation, neurological deficits at presentation, tumor location other than frontal and parietal lobe, and tumor size greater than 4–5 cm.⁴³ However, the precise survival rate of patients with infratentorial ODG has not been elucidated yet, and most studies have reported a short outcome.

Since it has been suggested that posterior fossa ODGs can be potentially more aggressive, prophylactic craniospinal radiotherapy is required.^{3,12} ODGs tend to metastasize

outside the nervous system, probably throughout CSF, unlike other gliomas.²¹ Holladay and Fruin suggested that CSF cytology should be evaluated postoperatively to determine spinal radiotherapy's need since ODG could metastasize through the subarachnoid route.⁴⁴ However, patients can be observed before radiotherapy for the recurrence of the tumor.² The scarcity of data about posterior fossa ODGs has led to the absence of the exact treatment protocol.

Generally speaking, in most instances, radiation and chemotherapy can be postponed until after delivery due to potential harm to the developing fetus.⁴⁵ However, if radiation or chemotherapy is necessary during pregnancy, maximum precautions must be taken to protect the fetus as much as possible, and the patient must determine whether or not to proceed with pregnancy in conjunction with the treatment team after extensive and detailed counseling.⁴⁵ Patients with low-grade tumors similar to the presented patient should be carefully monitored over time for tumor behavior and receive radiation only at the time of progression.⁴⁵ Patients with high-grade lesions or anaplastic tumors should be irradiated upfront, although with maximal precautions.⁴⁵

4.1 | Resection of a brain tumor in pregnancy

Brain tumor incidence is very low during pregnancy, and pregnancy does not affect most brain tumors' overall risk or incidence, including gliomas.^{46,47} Likewise, gliomas seem not to negatively impact the delivery and even development of children.^{47,48} Progression of all grade gliomas is not associated with hormone expression and should be treated in pregnant women like non-pregnant persons, though with obstetrical consideration for the delivery,⁴⁹ as mentioned earlier. Intriguingly, it has been suggested that female sex hormones may have protective effects on glioma pathogenesis.^{47,50}

Surgery remains the first step in treating patients with oligodendroglial tumors⁵¹; however, it should be tailored to each patient individually. In a pregnant woman with a brain tumor, it is necessary to consider the patient's presenting symptoms, the nature of the tumor, and the timing of pregnancy to decide the best patient care and whether carrying out the pregnancy is feasible. Although there is no high-level evidence guiding the safe management of intracranial tumors during pregnancy, it is encouraged to observe stable patients, and gestational advancement could be permitted into the second trimester.⁵² In low-grade tumors with isolated seizures as initial presentation, an observational approach and anticonvulsant treatment until the third trimester have been suggested.^{49,53} Neurological

symptoms, presumed tumor histology, and gestational age can potentially affect the surgery timing.^{54,55}

Current evidence is scant and limited to observational studies or expert opinion, though any invasive procedure can be postponed to permit gestation advancement or until delivery as long as the patient is stable and the tumor is not rapidly growing.⁴⁵ In cases with a clear indication for neurosurgery, the second trimester may be preferred, given that fetus is less vulnerable than in the first trimester and has a lower risk of intraoperative hemorrhage than in the third trimester.⁴⁵ If obstructive hydrocephalus is causing increased intracranial pressure, a shunting procedure should be performed.⁴⁵ Nevertheless, urgent neurosurgery is indicated in unstable patients with impending brainstem herniation (e.g., in cases with large tumors causing increased intracranial pressure or mass effect), even in the first trimester, in which the fetus is not viable.⁴⁵ In an unstable patient in the late second or third trimester, delivery by cesarean section under general anesthesia followed by immediate neurosurgery might be necessary.⁵² The case presented here was consistent with the latter scenario.

4.2 | Concurrent fetus delivery and brain tumor resection

Pregnancy should not delay the neurosurgical intervention.⁵³ Overall, it is favorable to postpone neurosurgical procedures after delivery; but in life-threatening emergencies, simultaneous cesarean delivery of the viable fetus and maternal surgery can be planned,⁴⁹ which is a challenging condition. There are very few reports regarding concurrent cesarean section and neurosurgical procedures.^{56,57} Korula and Farling reported a case with cerebellar mass necessitating concurrent cesarean section and sub-occipital craniectomy. They indicated that posterior fossa operation might cause maternal hemodynamic instability and harm the fetus.⁵⁵ Thus, it is crucial to prevent ICP rise caused by anesthetic agents and avoid neonatal respiratory depression.⁵⁵

The cesarean section under general anesthesia is recommended in pregnant patients with a significant mass-occupying lesion.⁵⁸ There is little evidence regarding anesthesia for neurosurgical intervention in pregnant patients.^{56,57} The choice of anesthetic technique for concurrent cesarean section and neurosurgical procedures for a brain tumor depends on various factors, including the patient's condition, type and location of the tumor, gestational condition, and urgency of the intervention.⁵⁷ It requires a multidisciplinary decision of the care team, aiming to maintain cerebral perfusion and control intracranial pressure. Also, it is essential not to use anesthetic

agents that alter cerebral blood flow (such as nitric oxide and halothane), which may harm both the fetus and mother.⁵⁵

5 | CONCLUSION

We reported an unusual ODG presentation with challenging management due to gestation conditions. ODGs rarely manifest as a large infratentorial cystic lesion in adults, with insidious general symptoms and atypical radiological findings. In a young pregnant patient, these non-specific symptoms could be mistaken as common gestational symptoms, leading to delayed diagnosis and progression of the disease. Timely diagnosis, management, and brain tumor treatment during pregnancy are challenging situations that require expert teamwork.

AUTHOR CONTRIBUTIONS

SA was responsible for the patient's operation, involved in patient care and reviewed the literature. FT and PP were involved in patient documents and data collection. FT, PP, AV, MH, and MM reviewed the literature and drafted the manuscript. MM critically reviewed and edited the final version. SA and FT contributed to writing the manuscript. All authors read and approved the final manuscript.

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None.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICAL APPROVAL

The Institutional Review Board and Ethics Committee of Zahedan University of Medical Sciences waived the requirement for ethical approval.

CONSENT

Written informed consent was obtained from the patient to publish this case report and any accompanying images.

ORCID

Farhad Tabasi  <https://orcid.org/0000-0003-4877-0701>

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