Lateral Intraventricular Glioblastoma Multiforme – Case Report

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Research Article

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Abstract

**Background:** Although glioblastoma multiforme is the most common malignant primary brain tumor, it rarely presents in the intraventricular region(s) of the brain.

**Case presentation:** We report a unique case of intraventricular glioblastoma multiforme in a 62-year-old Hispanic female, distinguished by her lack of substantial tumor recurrence.

**Conclusions:** Our report suggests the importance of understanding management and treatment of intraventricular glioblastoma multiforme in neurosurgical patients. In addition, our study emphasizes the importance of treating intraventricular glioblastoma multiforme in patients, as survival rates and post-operative quality of life can results in improved function.

Introduction

Glioblastoma multiforme (GBM) are high grade astrocytomas and the most common primary malignant brain tumors of the central nervous system (CNS), encompassing a quarter of all adult intracranial tumors and half of all glial tumors.\(^1\)\(^-\)\(^3\) The aggressive nature of the tumor results in a median survival approximately 14.6 months for adults treated with concurrent chemotherapy and radiation therapy.\(^4\) Although GBM can arise at any location in the CNS, intraventricular regions are relatively rare.\(^5\)

The subventricular zone (SVZ) is defined as a region located on the lateral wall of the lateral ventricle where neural stem cells are more vulnerable to tumor proliferation in comparison to cortical regions, and studies have shown worse prognosis with subependymal-spreading tumors, as opposed to non-subependymal-spreading tumors.\(^6\),\(^7\) Good prognostic factors include young age, high Karnofsky Performance Status (KPS), high mini-mental status examination score, \(O^6\)-methylguanine methyltransferase promoter methylation, and resection of > 98% of the tumor.\(^8\) There are only 16 reported adult intraventricular GBM cases to our knowledge.\(^1,2,5,9^-\)\(^{13}\)

In this case report, we describe a case of intraventricular GBM that is notable due to her prolonged survival of 20 months and lack of significant tumor mass recurrence.

Case Presentation

**History and Examination.** A 62-year-old Hispanic female admitted to the neurosurgery unit after presenting to the emergency department with complaints of headaches and reported behavioral changes. On initial presentation the patient was alert and orientated to person and place. She moved all extremities equally but had an unsteady gait. Cranial nerves II through XII were grossly intact. The remainder of her neurological exam did not include any focal deficits. Past surgical history was remarkable for colon cancer in remission after colectomy, cholecystectomy, hysterectomy, and bilateral knee arthroscopy repair x 3. Past medical history included osteoporosis, hyperlipidemia, steroid-induced hyperglycemia, and chronic anemia. She did not report any tobacco or alcohol use.

**Imaging.** A non-contrast computed tomography (CT) identified an intraventricular soft tissue mass centered at the anterior aspect of the septum pellucidum covering the foramen of Monro bilaterally and extended to the body of the corpus callosum (Figure 1). The left lateral ventricle was moderately enlarged. Multiplanar magnetic resonance imaging was significant for a large 4.6 x 4.3 x 2.9 cm mass extending from the foramen of Monro occupying the entire anterior aspect of the lateral ventricles (Figure 2). CT of the chest abdomen and pelvis was negative for any other masses. The patient had some complaints of back pain. The entire neuro axis was scanned as a primary intraventricular tumor was also in the differential.

**Operation and Pathological Findings.** The patient underwent a right frontal craniotomy. An interhemispheric transcallosal approach was used to reach the tumor. Frameless stereotactic navigation, microscope, and microsurgical techniques were employed. The dissection corridor was along the right side of the falx, and the right hemisphere was positioned downward to allow gravity to assist with retraction. The tumor was encountered upon the corpus callosotomy, and tumor dissection led to entry into the bilateral lateral ventricles. The mass was sub-totally resected with a small residual left on the side of the ventricle. The significant retraction required to reach this last piece of tumor, in addition to its adherence to the ventricular wall, weighed in our decision to leave this small residual. An external ventricular drain (EVD) was placed under direction visualization. The patient had unchanged Somatosensory Evoked Potentials (SEEP) continuous electroencephalogram (EEG) throughout the case. Post-operatively, the patient awoke with a 1/5 left hemiparesis. The tumor was found to be a high-grade IV intraventricular glioblastoma multiforme (GBM) with no \(O^6\)-methylguanine-DNA-methyltransferase (MGMT) gene methylation. Pathology immunohistochemical stains included neurofilament stain highlighting infiltrative tumor edges, strong glial...
fibrillary acidic protein (GFAP) reactivity, and nonspecific positive synaptophysin. Numerous mitotic figures were consistent with malignancy, where arrangements were in conspicuous perivascular, focal fascicular, palisading arrangements around areas of necrosis with myxoid stromal-type change and focal diffuse patterns. Proliferation index MIB-1 (Ki67) was elevated at approximately 35% (Figure 3). Prior to discharge, the patient had placement of a ventricular peritoneal shunt, as the ventriculostomy placed at surgery could not be weaned.

**Post-operative course to time of death.** Her initial outpatient visit, one month after discharge from the hospital demonstrated improvement in muscle strength from 2/5 to 3/5 in the left upper extremity (LUE), 1/5 to 2/5 strength in the left lower extremity (LLE), and consistent 5/5 strength in right upper and lower extremities. Sensation to light touch was intact throughout and the patient rated her pain a 0 on a scale of 10. Cranial nerves II through XII were all intact throughout with no upward gaze palsy. She was alert and oriented with ability to articulate her speech. As she continued her post-operative care her hemiparesis improved to 4/5 and she regained the ability to walk with a cane.

Two weeks after her surgery she was started on a chemotherapy and radiation therapy regimen. Chemotherapy included 120 mg PO daily of temodar (temozolomide) for one month. This was then followed with metronomic dosing of temodar at 80 mg for 10 months, due to the patient’s tolerance. Avastin (bevacizumab) was started for prevention of tumor recurrence and disease progression after completion of metronomic temodar. Radiation therapy consisting of 6000 cGy was administered concurrent with this chemotherapy. Since her disease was the rare intraventricular site, inclusion of the cerebrospinal fluid (CSF) similar to the approach for carcinomatous meningitis became a consideration. This was used for the initial approach after extensive literature search and discussion with experts. Treatment began with a 2-field approach to the whole brain and upper cervical spine to C2 to 3600 cGy. Then a 10 IMRT (intensity modulated radiation therapy) arrangement was used to complete the 6000 cGy (Figure 4). Before treatment each day IGRT (imaged guided radiation therapy) cone beam analysis was used to ensure precise treatment setup. The first MRI detected recurrence/progression of the tumor 4 months after completion of the initial course of therapy. This was occurring at the site of subtotal resection along the ventricular wall SRS (stereotactic radiosurgery) was planned with personal participation by the neurosurgeon to ensure correct treatment volumes were established. Treatment was administered using a 19 field SRS plan delivering 1800cGy as a single fraction. The patient responded well with treatment with first arrest, then regression of the residual mass. She remained relatively stable from 4 to 20 months, without signs of disease progression on MRI. Twenty months post-craniotomy, the patient's performance scale began to deteriorate significantly without signs of tumor recurrence. She was ultimately placed on hospice care and expired 20 months after her diagnosis.

**Discussion**

Intraventricular tumors are very rare and comprise less than 2% of all intracranial tumors. The most common presentation, generally occurs after the tumor grows significantly, includes signs of hydrocephalus and increased intracranial pressure, as the neoplasm can obstruct CSF movement and may require further intervention via a VP shunt. A majority of the case reports describe the location of the tumor to be in the lateral ventricle or the body of the corpus collosum. The reports do not describe any CSF dissemination where the tumor metastasizes to the spine via CSF. Various transcortical approaches were reported in the case reports to resect the intraventricular tumors. A majority of them required post-operative radiation and chemotherapy, therefore gross total resection is generally not completely achievable. The average age of survival from the case reports was found to be 14.75 months, which is comparable to the median survival age for parenchymal GBMs. Our patient survived for 20 months post-procedure. Some case reports did not include an average age of survival period: one report mentions a patient dying after 1 month; three do not report any time frame; and one mentioned 3 patients surviving at least two years post-surgery. Furthermore, three patients required ventriculoperitoneal shunts due to acute hydrocephalus. Table 1 summarizes characteristics of common intraventricular tumors.
<table>
<thead>
<tr>
<th>Type</th>
<th>Most common age Group</th>
<th>Most common Region</th>
<th>Typical Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choroid plexus tumors</td>
<td>Children &lt;10 yo</td>
<td>Lateral or fourth ventricles</td>
<td>Hyperdense on CT, lobulated, enhancing</td>
</tr>
<tr>
<td>Meningioma</td>
<td>40-60 yo, females&gt;males</td>
<td>Lateral ventricle</td>
<td>Hyperdense on CT, calcification (50%), enhancing</td>
</tr>
<tr>
<td>Ependymoma</td>
<td>Adults and children (1/3 in &lt;3 yo)</td>
<td>Fourth ventricle</td>
<td>Heterogenous, hemorrhage, necrosis, cyst, calcification</td>
</tr>
<tr>
<td>Subependymoma</td>
<td>40 – 60 yo</td>
<td>Lateral ventricle or fourth ventricle</td>
<td>Poor enhancement, calcification (30%)</td>
</tr>
<tr>
<td>Subependymal giant cell astrocytoma</td>
<td>0 – 20 yo</td>
<td>Foramen of Monroe</td>
<td>Enhancing</td>
</tr>
<tr>
<td>Central Neurocytoma</td>
<td>20 – 40 yo</td>
<td>Inferior septum pellucidum and anterior lateral ventricle</td>
<td>Lobulated, enhancing</td>
</tr>
</tbody>
</table>

Although GBMs are the most common primary brain tumors, intraventricular GBMs occur rather infrequently. Most GBMs happen in those who are 55-74 years of age and are more common in men\(^\text{17}\). The annual incidence in the US is approximately 3 in 100,000 people and account for 25% of all malignant nervous system neoplasms.\(^\text{17}\) A PubMed search was conducted using the following key words, “intraventricular glioblastoma multiforme” and “intraventricular GBM”. The search found only 16 adult known events of intraventricular GBMs to date.\(^\text{1,2,5-9-13}\)

Table 2 summarizes the features of the 16 cases of adult intraventricular GBM that have been documented in the literature.
<table>
<thead>
<tr>
<th>Authors and year</th>
<th>Sex and Age at diagnosis</th>
<th>Presentation</th>
<th>Survival time/post-operative follow-up findings</th>
<th>GBM location</th>
<th>Surgical Approach</th>
<th>Post-operative management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asha, M et al., 2014</td>
<td>M, 66</td>
<td>Epileptic patient with a one-month history of progressive vague Symptoms (i.e. nausea, ‘funny’ feeling in stomach, tingling associated with feeling cold and having ‘goose bumps’, visual disturbances and hallucinations)</td>
<td>approximately 14 months post-operatively</td>
<td>Posterior and temporal horn of the right lateral ventricle</td>
<td>neuronavigation-guided craniotomy and debulking of lesion</td>
<td>chemo/radiotherapy, ventriculoperitoneal shunt (due to hydrocephalus)</td>
</tr>
<tr>
<td>Lee, T.T et al., 1997</td>
<td>M, 59</td>
<td>Depression, anxiety, urinary incontinence, bilateral non-pulsatile tinnitus</td>
<td>7 months post-operatively</td>
<td>Third ventricle</td>
<td>Right craniotomy transcallosal approach</td>
<td>Whole brain radiation followed by a course of chemotherapy</td>
</tr>
<tr>
<td>Park P, et al., 2005</td>
<td>F, 32</td>
<td>Headache, intermittent short-term memory loss, mild nausea Neurologically intact (2-years post-operation)</td>
<td>Trigone of lateral ventricle</td>
<td></td>
<td>parietooccipital surgical approach</td>
<td>Whole brain radiation followed by a course of chemotherapy</td>
</tr>
<tr>
<td>Patnaik A, et al., 2014</td>
<td>M, 27</td>
<td>headache, vision loss in both eyes</td>
<td>Not reported</td>
<td>frontal horn and body of right lateral ventricle</td>
<td>right frontal transcortical approach</td>
<td>Not reported</td>
</tr>
<tr>
<td>Prieto R, et al., 2006</td>
<td>F, 29</td>
<td>Loss of consciousness, depression, polyuria, polydipsia</td>
<td>Recurrence of tumor 2 months post-operation</td>
<td>third ventricle</td>
<td>right craniotomy transcortical-transventricular route</td>
<td>Hormone replacement therapy, ventriculoperitoneal shunt (due to hydrocephalus)</td>
</tr>
<tr>
<td>Secer H.I., et al., 2008</td>
<td>M, 19</td>
<td>Headache, seizures, mental disturbance, high intracranial pressure, motor deficit, sensorial deficit, cerebellar signs</td>
<td>patient died 1 month post-operation; Five patients died after 12-28 months (mean 18.8 months) 3 patients survived post-operation</td>
<td>Body/thalamus Body/corpus callosum Septum pellucidum/thalamus Body/corpus callosum Body/corpus callosum Body/corpus callosum</td>
<td>R frontal transcortical R anterior transcallosal R frontal transcortical R anterior transcallosal L anterior transcallosal L anterior transcallosal R frontal transcortical R anterior transcallosal</td>
<td>Radiotherapy and chemotherapy, ventriculoperitoneal shunt (due to hydrocephalus 1 one patient)</td>
</tr>
<tr>
<td>Authors and year</td>
<td>Sex and Age at diagnosis</td>
<td>Presentation</td>
<td>Survival time/post-operative follow-up findings</td>
<td>GBM location</td>
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<tr>
<td>Kim, Y.J. et al, 2010</td>
<td>M, 64</td>
<td>Gait disturbance, progressive incontinence, memory difficulty and frequent episodes of disorientation, global headache, vomiting, and constant drowsiness</td>
<td>Discharged with some memory disturbance and mild hemiparesis</td>
<td>Occipital horn of lateral ventricle</td>
<td>parieto-occipital craniectomy with a transcortical approach</td>
<td>Whole brain radiation</td>
</tr>
<tr>
<td>Sarikaff Y, et al., 2015</td>
<td>F, 65</td>
<td>severe headache, gait disturbance, drowsiness, vomiting and urinary incontinence</td>
<td>Patient died 3 months post-operatively</td>
<td>Right lateral ventricle</td>
<td>posterior transcallosal approach</td>
<td>Radiotherapy and chemotherapy</td>
</tr>
</tbody>
</table>

Survival rates in GBM patients are very low: less than 30% at 1 year, 5% at 3 years, 3% at 5 years.\(^\text{17}\) One clinical trial reported a 5-year survival rate of 9.8% in patients who were treated with radiation therapy and temozolomide.\(^\text{18}\) The radiation therapy oncology group (RTOG) prognostic classification helps estimate median survival. RTOG class V can be used for our patient (i.e. patients older than 50 years of age with of the following: Karnofsky performance scale (KPS) of 70-100 and resection with neurologic deficits, KPS 70-100 and only biopsy followed by at least 54.4 Gy of radiation therapy, or KPS < 70 and no neurologic deficits)\(^\text{19,20}\). Median survival for the RTOG V group is 8.9-10.7 months. Tumor genetic expression has the potential to affect prognosis. The O\(^5\)-methylguanine-DNA methyltransferase (MGMT) gene is involved in DNA repair and reversal of any DNA damage, and when the promoter region of MGMT is hypermethylated, tumor cells more sensitive to treatment with alkylating agents, therefore a survival mechanism\(^\text{21}\). GBMs are pathologically poorly differentiated neoplastic astrocytes that consist of a diffuse infiltrative growth pattern, making it difficult for neurosurgeons to completely resect the tumor\(^\text{17}\). This patient's past chemotherapy and radiation exposure for diagnosis and treatment of colon cancer could have influenced tumor growth. Although it is not known if this is a definitive cause for this patient's GBM, it can play a role for potentially contracting future malignancies. Our patient survived for a total of 20 months post-surgical intervention, which is more than the current average lifespan of GBM; however, our literature review did find a few instances where the survival rate was similar or slightly more. Of note, some studies did not report full patient follow-up up to the time of death. This could be attributed to the patient's death and may have an impact interpreting an accurate post-operative lifespan.

Our patient had an increased proliferation index with several risk factors, including therapeutic radiation exposure and an increased KPS score. Some challenges involved with tumor removal include safely dissecting its external surface from surrounding neural structures obstructing ventricle cavity.\(^\text{9}\) Even with total tumor resection, minuscule remnants of tumor are frequently left behind.\(^\text{9}\) Typical GBM standard of care includes maximal tumor resection followed by adjuvant chemoradiation therapy. Stupp et al. advise the use of the chemotherapeutic agent, Temodar given at 75mg/m\(^2\) daily for 6 to 7 weeks, and 150-200 mg/m\(^2\) given for 5 days every 28 days for approximately 6 cycles.\(^\text{18}\) Although the incidence of GBM in a colon cancer survivor patient is unknown, effects of radiation and chemotherapy should be considered and revisited when determining possible causes. Changes in neurological examination should be followed-up with re-evaluation of the patient and additional surgical procedures should be considered with risks and benefits in mind. Furthermore, baseline neuroimaging should be included in initial assessment and additional imaging should regularly be conducted to monitor any future tumor growth.

**Conclusions**

This case report describes a neurosurgeon’s experience with intraventricular GBM in a patient with a history of colon cancer. Based on our experience and review of literature, this patient had no signs of gross tumor recurrence, and functionally benefits from her surgery and treatment. Although intraventricular tumors are rare, gross total resection can safely be performed with promising patient functionality.

**List Of Abbreviations**
Declarations

Ethics approval and consent to participate: informed patient consent was obtained

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials: not applicable

Competing interests: The authors declare no competing interests

Funding: none

Author contributions: AP and RA drafted, reviewed, and approved the final case report

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References


**Figures**

![Figure 1](image1.png)

**Figure 1**

Non-contrast axial CT images of 62 y/o female in 2009 (A), 2011 (B), 2015 (C).
Figure 2

(A) Non-contrast axial T1 MRI. (B) Axial T1 MRI with contrast. (C) T2 axial MRI without contrast. (D) T1 with contrast coronal T1 MRI.
Figure 3

Histopathologic examination of solid glial neoplasm (A) Bizarre nuclear features and vascular proliferation (10X magnification) (B) Broad coagulative type necrosis and focal areas of cellular necrosis associated with small cell and gemistocytic change. Bizarre nuclear features and necrosis (40X magnification) (C) Ki-67 (MIB1) immunohistochemical stain (10X magnification) showing approximately 35% staining in areas.
Figure 4

Intensity modulated radiation therapy (IMRT) to localize treatment of the tumor

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- CAREchecklistEnglishGBM.docx