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The role of ventriculoperitoneal shunting in patients with supratentorial glioma

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Abstract

Objectives: To assess the impact of ventriculoperitoneal (VPS) in patients with glioma. **Methods**: Retrospective review of patients with grade II-IV glioma who had VPS placement from January 1995 to November 2012. **Results**: We identified 62 patients. At time of VPS, 41 had gait disturbance, 40 cognitive impairment and 16 urinary incontinence; 10 had the classic triad. Thirty-eight (61%) improved after VPS. Median overall survival from VPS was 7 months for all patients, but 11 months for those who improved and 2 months for non-responders. Leptomeningeal disease, glioma grade or radiographic ventricular decompression did not predict benefit. **Conclusions**: VPS can improve functional status in some patients with symptoms suggestive of hydrocephalus.

Introduction

Gliomas account for 29% of all primary brain tumors and 80% of malignant tumors.[1–4] Neurological deterioration in these patients may be related to tumor progression, toxicity from treatment, edema, seizures, or infection. Communicating hydrocephalus (CH) is an infrequent complication that may cause gait disturbance, cognitive decline, and urinary incontinence; ventriculomegaly is a radiologic hallmark, but occasionally patients with brain atrophy have identical symptoms without convincing disproportionate ventricular enlargement.[5–10] The pathogenesis of CH in glioma patients remains unclear, but impaired Cerebrospinal Fluid (CSF) absorption due to radiotherapy (RT)-induced fibrosis, ventricular opening at craniotomy, number of previous surgeries, high CSF protein concentration, and leptomeningeal metastases (LM) are possible etiologies.[6,7,10]

Placement of a ventriculoperitoneal shunt (VPS) is often performed but clinical benefit is uncertain.[5,9] We sought to assess the impact of VPS in patients with glioma.

Materials and Methods

We retrospectively reviewed patients with gliomas who were treated with VPS at Memorial Sloan-Kettering Cancer Center from January 1995 to November 2012. These patients were shunted in an effort to reverse neurological decline that was not due to tumor progression or other processes. The patients were identified through our institutional database and included if they met the following criteria: (1) age ≥18; (2) histologic diagnosis of grade II–IV glioma; (3) supratentorial tumor location; and (4) a VPS. Patients who underwent VPS for obstructive hydrocephalus from tumor were excluded. Ventriculomegaly was diagnosed based on review of the preoperative neuroimaging and neuroradiology report. Evans' index (EI) was used to evaluate ventriculomegaly before and after VPS.[11] *T* test was performed to compare the differences in ventricle size before and after VPS. White matter abnormalities were evaluated using a modified Fazekas scale.[12] LM were diagnosed based on magnetic resonance imaging (MRI) findings and CSF cytology. The Kaplan–Meier method was used to examine survival from date of VPS to date of death or last follow-up. Neurological improvement was determined by the treating neurologist.

Results

We identified 2433 patients diagnosed with supratentorial WHO grade II–IV glioma between January 1995 and

November 2012, of whom 62 (2.5%) met the inclusion criteria. Median age at tumor diagnosis was 61 years (range, 20–75 years) and 40 patients were men (Table 1). Initial treatment included surgical resection in 58 (93%) patients of whom 29 (50%) had a second resection, eight (14%) a third, and one (2%) a fourth surgery. Four patients had biopsy alone. Opening of the lateral ventricle occurred in 23 of 58 patients (40%). Median time from tumor diagnosis to VPS was 10 months (range 0–263 months), from last craniotomy to VPS was 5 months, and from RT to VPS was 6.5 months; six patients required VPS before RT. All patients received RT; 58 received chemotherapy, 50 at diagnosis, and eight at recurrence. Twelve patients were treated with the vascular endothelial growth factor inhibitor bevacizumab, four before VPS placement and eight after, seven of whom received the drug at least 1 month after surgery and clinical assessment of VPS benefit; one patient started bevacizumab 2 weeks after VPS.

At VPS placement, median age was 64 years (range, 21–76 years) and median Karnofsky performance score (KPS) 60 (range, 40–90). All patients were symptomatic; 41 had gait disturbance, 40 cognitive impairment, and 16 had urinary incontinence; only 10 patients (16%) had the classical triad of gait disturbance, cognitive decline, and urinary incontinence. Other symptoms included drowsiness, headache, focal weakness, diplopia, and dizziness. Ventriculomegaly was observed in 59 patients (93%); three without ventriculomegaly had cognitive impairment with gait disturbance, drowsiness or headache. EI confirmed ventriculomegaly in 46 of the 57 patients (80%) who had scans available for measurement. Median EI at VPS was 0.32 (range, 0.23–0.43); median EI post-VPS was 0.28 (range, 0.19–0.38, P:<0.001). An MRI was available prior to VPS in 55/62 patients; Fazekas scale showed no white matter change (Grade 0) in 6 patients; minimal patchy white matter foci (Grade 1) in 17; start of confluence of white matter disease (Grade 2) in 18; large confluent areas (Grade 3) in 11 and confluence with cortical and subcortical involvement (grade 4) in 3 patients.

Table 1. Patient characteristics at ventriculoperitoneal shunting.

Median age, years (range)	64 (21–76)
KPS, median (range)	60% (40–90)
Pathology (%)	
Glioblastoma	41 (66)
Anaplastic glioma	18 (29)
Low grade glioma	3 (5)
Location (%)	
Temporal	26 (42)
Frontal	19 (31)
Parietal	10 (16)
Occipital	4 (6)
Other	3 (5)
Number of surgeries before VPS (%)	
1	31 (50)
2	19 (31)
3	7 (11)
4	1 (2)
Biopsy	4 (6)
Ventricle opened (%)	23 (37)
At first surgery	14 (61)
At second surgery	8 (35)
At fourth surgery	1 (4)
Clinical presentation (%)	
Gait disturbance	41 (66)
Cognitive impairment	40 (65)
Urinary incontinence	16 (26)
Other	18 (29)
Classical triad	10 (16)
Disease status	
Stable disease	35 (56)
Progression of disease	27 (44)

KPS, Karnofsky performance status; VPS, ventriculoperitoneal shunting.

CSF was available in 35 patients (56%), 27 samples were obtained through lumbar puncture, and 8 were ventricular. In the lumbar samples, median opening pressure was 20 mm H_2O (range, 11–55 mm H_2O), cytology demonstrated malignant cells in three patients and median protein level was 74 mg/dL (range, 16–306). Cytology was negative for malignant cells in all eight ventricular samples; median protein level was 229 mg/dL (range, 86–276) in these samples. LM was diagnosed in 10 patients on MRI; CSF cytology was available in eight of these, and three had malignant cells.

Thirty-eight patients (61%) improved after VPS; median duration of response was 6 months. The median overall survival (mOS) after shunting was 7 months. Patients who improved after VPS had a better performance status (mKPS 70%), higher rate of stable disease (63%) at time of VPS and a longer mOS (11 months) after VPS compared with those who did not improve (mKPS 60%, 45% stable disease, and mOS 2 months). However, 51% of the 27 patients who had tumor progression at time of VPS improved; six of 10 patients with LM also improved. Classical triad was associated with better outcome (8/10 improved after VPS). Patients with high opening pressure had a similar response rate (57%) to those with a normal opening pressure (66%). CSF removal trial was performed prior to VPS in 14 patients (23%), and 11 (79%) had transient improvement. After VPS, only four of these 11 patients improved; two of the three who did not improve after CSF removal trial improved after VPS. Age, LM or glioma grade did not predict improvement after VPS, but an increased number of surgeries was associated with worse outcome. The unequal distribution of these variables in such a small cohort precluded statistical analysis, so these relationships are descriptive.

Table 2. Complications associated with ventriculoperitoneal shunting.

Complication	Number of cases	Time from VPS (weeks)	Outcome
Meningitis	5	6	All patients: shunt removal and antibiotic therapy. Three VPS replacement with good outcome. Two poor outcome and comfort care.
Subdural hematoma/Hygroma	5	3	Four SDH evacuation and programmable valve. One with complete resolution.
Intraventricular hemorrhage	1	1	Coma/vegetative state
Others (wound infection, distal obstruction, wound dehiscence)	6	21	Appropriate treatment/good outcome

VPS, ventriculoperitoneal shunting; SDH, subdural hematoma.

Pre- and post-VPS imaging was available in 55 patients, and showed ventricular decompression in 45 (82%), 29 (64%) of whom improved. Ten had no improvement in ventriculomegaly post-VPS and five (50%) of these improved clinically.

Seventeen patients (27%) had complications related to VPS (Table 2). Five developed postoperative meningitis requiring shunt removal and antibiotic therapy; after appropriate treatment, three underwent VPS replacement with good outcome and the other two had poor outcome and received hospice care. Five developed postoperative hematomas/hygromas, four of which required evacuation and a programmable valve; the fifth was followed with complete resolution. One developed an intraventricular hemorrhage after VPS and never recovered. The other six patients had mild complications, recovered, and had a favorable outcome.

Discussion

CH is a known complication of glioma, but few data have been published on its frequency or optimal therapy. To our knowledge, our 62 patients represent the largest published series on VPS in patients with supratentorial glioma. The 2.5% incidence in our population is lower than reported previously, possibly because many prior studies excluded patients with lower glioma grades. Gliomas occur most frequently in the frontal lobe, but in our cohort receiving VPS, temporal lobe tumors were overrepresented.

The pathogenesis of CH in glioma patients remains unclear, but impaired CSF absorption due to RT fibrosis, high CSF protein concentration, and LM may all contribute. However, these causes do not explain all patients as six (10%) developed CH before RT, 14% of CSF samples had a normal protein level, and LM was confirmed in only 10 patients (16%).

The clinical presentation of CH in glioma patients mimics idiopathic normal pressure hydrocephalus (NPH), and it is similarly challenging to predict which patients will benefit from VPS. High-volume CSF drainage did not predict outcome after VPS in this study. Neither lumbar infusion nor Intracranial Pressure recordings were performed so it is unknown if either could predict benefit as has been reported in NPH.[13] However, patients with the classical triad or stable tumor had a higher rate of response. Disappointingly ventricular decompression after VPS was not associated with benefit as a similar proportion of patients improved whether they achieved radiographic decompression (64%) or not (50%).

This study is limited by its retrospective and subjective nature of outcome determination. Improvement after VPS could also reflect patient selection bias and not just VPS effectiveness. VPS complications were comparable to those reported by others in the glioma population and infections and subdural hematoma/hygroma were the most common.[10] Infection is likely related to prolonged steroid treatment and long hospitalization and subdural hematoma/hygroma related to pre-VPS brain tissue loss due to previous surgeries and RT. Despite frequent complications, only one was fatal (2%) in our cohort.

VPS can be an effective palliative measure for some patients with glioma and CH, particularly those with the classical triad of symptoms; however, shunt placement should not be delayed until a patient deteriorates so significantly as this reduces the chance of a good outcome. Radiographic improvement does not guarantee clinical improvement and patients who do not have ventricular decompression after VPS can also improve clinically. We continue to need better preoperative indicators to determine which patients will benefit from VPS so only those who qualify will undergo the procedure.

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Authorship Contributions

Study design: Macarena I. De La Fuente, Lisa M. DeAngelis; Data acquisition: Macarena I. De La Fuente; Data analysis: Macarena I. De La Fuente, Lisa M. DeAngelis; Manuscript preparation: Macarena I. De La Fuente, Lisa M. DeAngelis; Manuscript review: Macarena I. De La Fuente, Lisa M. DeAngelis.

Conflict of Interest

Dr. de la Fuente and Dr. DeAngelis report that they have no disclosures or conflict of interest.

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