Neurosurgical Review
https://doi.org/10.1007/s10143-021-01578-2

ORIGINAL ARTICLE

Characteristics and management of hydrocephalus in adult patients with cerebellar glioblastoma: lessons from a French nationwide series of 118 cases

Thiébaud Picart[1,2,3] · Chloé Dumot[1,2,4] · David Meyronet[2,3,5] · Johan Pallud[6,7,8] · Philippe Metellus[9,10] · Sonia Zouaoui[11,12] · François Ducray[2,3,13] · Isabelle Pelissou-Guyotat[1] · Moncef Berhouma[1,2,14] · Luc Bauchet[11,12,15] · Jacques Guyotat[1] · French Brain Tumor DataBase[16] · Club de Neuro-Oncologie of the Société Française de Neurochirurgie[17]

Received: 30 March 2021 / Revised: 19 May 2021 / Accepted: 2 June 2021

Abstract

The characteristics of hydrocephalus associated with cerebellar glioblastoma (cGB) remain poorly known. The objectives were to describe the occurence of hydrocephalus in a French nationwide series of adult patients with cGB, to identify the characteristics associated with hydrocephalus and to analyze the outcomes associated with the different surgical strategies, in order to propose practical guidelines. Consecutive cases of adult cGB patients prospectively recorded into the French Brain Tumor Database between 2003 and 2017 were screened. Diagnosis was confirmed by a centralized neuropathological review. Among 118 patients with cGB (mean age 55.9 years), 49 patients (41.5%) presented with pre-operative hydrocephalus. Thirteen patients (11.0%) developed acute (n=7) or delayed (n=6) hydrocephalus postoperatively. Compared to patients without hydrocephalus at admission, patients with hydrocephalus were younger (52.0 years vs 58.6 years, p=0.03) and underwent more frequently tumor resection (93.9% vs 73.9%, p=0.006). A total of 40 cerebrospinal-fluid diversion procedures were performed, including 18 endoscopic third ventriculostomies, 12 ventriculoperitoneal shunts and 10 external ventricular drains. The different cerebrospinal-fluid diversion options had comparable functional results and complication rates. Among the 89 patients surgically managed for cGB without prior cerebrospinal-fluid diversion, 7 (7.9%) were long-term shunt-dependant. Hydrocephalus is frequent in patients with cGB and has to be carefully managed in order not to interfere with adjuvant oncological treatments. In case of symptomatic hydrocephalus, a cerebrospinal-fluid diversion is mandatory, especially if surgical resection is not feasible. In case of asymptomatic hydrocephalus, a cerebrospinal-fluid diversion has to be discussed only if surgical resection is not feasible.

Keywords Cerebellar glioblastoma · Endoscopic Third Ventriculostomy · External Ventricular Drain · Hydrocephalus · Neuro-oncology · Ventriculoperitoneal shunt

Introduction

Ten to 50% of primary [1–3] and secondary [4, 5] adult posterior fossa tumors are associated with obstructive but also non-obstructive hydrocephalus in case of leptomeningeal tumor seeding [6]. In such patients, hydrocephalus, independently of the mechanism, can generate symptoms disabling enough to preclude systemic treatments to be performed and has consequently to be managed appropriately [6]. However, hydrocephalus management still remains controversial in this context, especially regarding surgical procedures [1, 5, 7, 8]. Adult cerebellar glioblastomas (cGB) are particularly rare, representing approximately 1% of *de novo* glioblastomas [9–14] and their characteristics remain relatively poorly known. The recent analysis of a series of 118 adult cases highlighted that total and subtotal tumor resection, performed in selected patients, were associated with improved onco-functional outcomes, compared with less invasive procedures (partial resection or biopsy), while complication rates

Luc Bauchet and Jacques Guyotat contributed equally to this work.

✉ Thiébaud Picart
thiebaud.picart@chu-lyon.fr

Extended author information available on the last page of the article

Published online: 01 July 2021

were comparable. Additionally, after total or subtotal resection, the functional outcomes were correlated with age, cerebellar hemispheric tumoral location but not with brainstem infiltration [15]. cGB are expected to be more frequently associated with hydrocephalus than their supratentorial counterpart and this parameter has also to be taken into account for patient management. Yet, the incidence, mechanisms, prognosis value, and management of hydrocephalus have never been studied in adult patients with cGB.

The aims of the present study were firstly to describe the occurence and management of hydrocephalus in a French nationwide retrospective series of adult cGB patients, secondly to identify the characteristics associated with hydrocephalus prior to and after cGB management, and thirdly to analyze the onco-functional outcomes associated with the different surgical strategies, in order to propose management guidelines.

Materials and methods

Identification of cerebellar glioblastoma patients

The French Brain Tumor Database (FBTDB) [16–19] and the Club of Neuro-Oncology of the Société Française de Neurochirurgie (CNO-SFNC) were screened in order to identify patients managed for a cGB from 2003 to 2017 [15].

Inclusion criteria were: (1) age ≥18 years at diagnosis, (2) tumor epicenter located within the cerebellum, with a brainstem invasion ≤5 mm, (3) surgical management between November 1st, 2003 and August 1st, 2017. The exclusion criteria were (1) the presence of a supratentorial or medullar tumor larger than the cerebellar tumor, (2) recurrent tumors.

Data collection

Data collection was performed in each neurosurgical center, by one senior neurosurgeon specialized in neuro-oncology (TP or one local neurosurgeon). Patients data were locally extracted from medical records using a chart designed for the study. The methodology used to assess the extent of resection was the same as previously detailed [15]. The diagnosis of leptomeningeal seeding was considered to be "documented" if CSF analysis demonstrated the presence of glial cells. When CSF analysis was not available, the diagnosis of leptomeningeal seeding was considered to be "suspected" if there were both clinical arguments for leptomeningeal seeding and a leptomeningeal contrast enhancement. Tumor progression was defined according to RANO criteria [20]. Follow-up data were centralized and completed (general practitioner or oncologist call) by one investigator (TP).

Centralized neuropathological review and molecular analysis

As previously detailed [15], a central pathological review was performed by a senior neuropathologist (DM) to ensure that characteristics of grade IV glioblastoma were met, according to the 2016 WHO classification of tumors of the central nervous system [21].

The molecular analysis locally performed at diagnosis was not comprehensive (screening for IDH1-2 mutations, ATRX status, TP53 status, histone H3 mutation, EGFR amplification, and TERT mutation were achieved in 35.6%, 6.8%, 27.9%, 19.5%, 35.6%, and 26.3% respectively). Consequently, IDH1-R132H, ATRX, TP53, and histone H3-K27M screenings were completed using immunostaining whenever possible (in 71.1%, 65.5%, 64.7%, and 67.4% of cGB without comprehensive molecular analysis, respectively). In all cases with available tissue samples, EGFR amplification was screened using next generation sequencing and TERT mutation was screened by droplet digital PCR (in 50% and 44.8% of cGB without comprehensive molecular analysis, respectively).

Standard protocol approvals and registrations

This study was approved by the French legislation (CCTIRS n°10.548; CNIL n°911013) and the CNO-SFNC.

Statistical analysis

Categorical comparisons were performed using the Chi-squared test or Fisher's exact test when the conditions of application of the Chi-squared test were not met. Quantitative variables were compared using the Mann-Whitney U test or the one-way ANOVA when appliable.

Overall Survival (OS) was measured from the date of the surgery to the date of death from any cause. Progression-free Survival (PFS) was measured from the date of the surgery to the date of progression or to the date of death. For surviving patients, these intervals were censored at the date of last follow-up. The actuarial data were represented with Kaplan-Meier plots and compared using the log-rank test.

The statistical tests were bilateral and the level of significance was set at 5% ($p < 0.05$). Statistical analyzes were conducted using R free software version 3.5.1 (R Core Team) and Graphpad software version 5 (Graphpad software corporation).

Results

After centralized neuropathological review, 118 patients were included. There were 55.1% of males and the median age at

diagnosis was 55.9 ± 16.6 years. Patients presented with raised intracranial pressure (*n*=60, 50.8%), cerebellar syndrome (*n*=95, 80.5%) and/or cranial nerve disorders (*n*=21, 17.8%) including diplopia and nystagmus (*n*=13) and swallowing disorders (*n*=8). cGB were classified as predominantly vermian (*n*=83, 70.3%) or predominantly hemispheric (*n*=35, 29.7%).

Occurrence and management of hydrocephalus

Based on clinical and MRI findings at admission, 69 patients (58.5%) did not display hydrocephalus of any cause (HAC) (group A), as detailed in Fig. 1. In group A, 56 patients (81.2%) did not develop HAC after cGB surgical management (group A1). Among the 13 remaining patients (18.8%, group A2), 7 patients (53.8%) developed acute postoperative obstructive hydrocephalus, caused by cerebellar swelling (*n*=6) or cerebellar hematoma (*n*=1), which was managed conservatively (*n*=3) or surgically by External Ventricular Drain (EVD) (*n*=3) or Endoscopic Third Ventriculostomy (ETV) (*n*=1). Six patients (46.2%) developed delayed hydrocephalus, linked to leptomeningeal seeding (*n*=3) or tumoral obstruction of the 4th ventricle (*n*=3), which was surgically managed by ETV (*n*=5) or Ventriculoperitoneal Shunt (VPS) (*n*=1). For non-obstructive hydrocephalus, VPS was preferred although ETV was performed in two patients in who hydrocephalus mechanism was not obvious, with a retrospective confirmation of leptomeningeal seeding. There were no complications related to Cerebrospinal Fluid (CSF) diversion procedures.

Conversely, 49 patients (41.5%) presented with hydrocephalus at admission (group B) that was mainly attributed to obstruction of the 4th ventricle by tumor mass (*n*=45) and more rarely to leptomeningeal seeding or subependymal tumor spread (*n*=4) (Fig. 2). Clinically, 32 patients (65.3%) presented with raised intracranial pressure and 17 patients (34.7%) had rather signs of subacute hydrocephalus including gait and cognitive disturbances. Twenty-nine patients (59.2%) underwent CSF diversion prior to cGB surgical management (group B1), that consisted of ETV (*n*=12, 41.4%), VPS (*n*=11, 37.9%) or EVD (*n*=6, 20.7%). EVD was proposed in patients with symptomatic acute obstructive hydrocephalus, in whom a large surgical resection was planned, allowing a large opening of the 4th ventricle. In case of non-obstructive hydrocephalus, VPS was always considered. In the remaining patients with obstructive hydrocephalus, the selection of CSF-diversion modalities (ETS vs VPS) was variable from one center to another in case of obstructive hydrocephalus, based on local habits. There were 3 treatment failures (10.3%) with postoperative hydrocephalus imputable to bacterial meningitis in a patient with VPS, postoperative hemorrhage in a patient with ETV and of unknown origin in another patient with ETV.

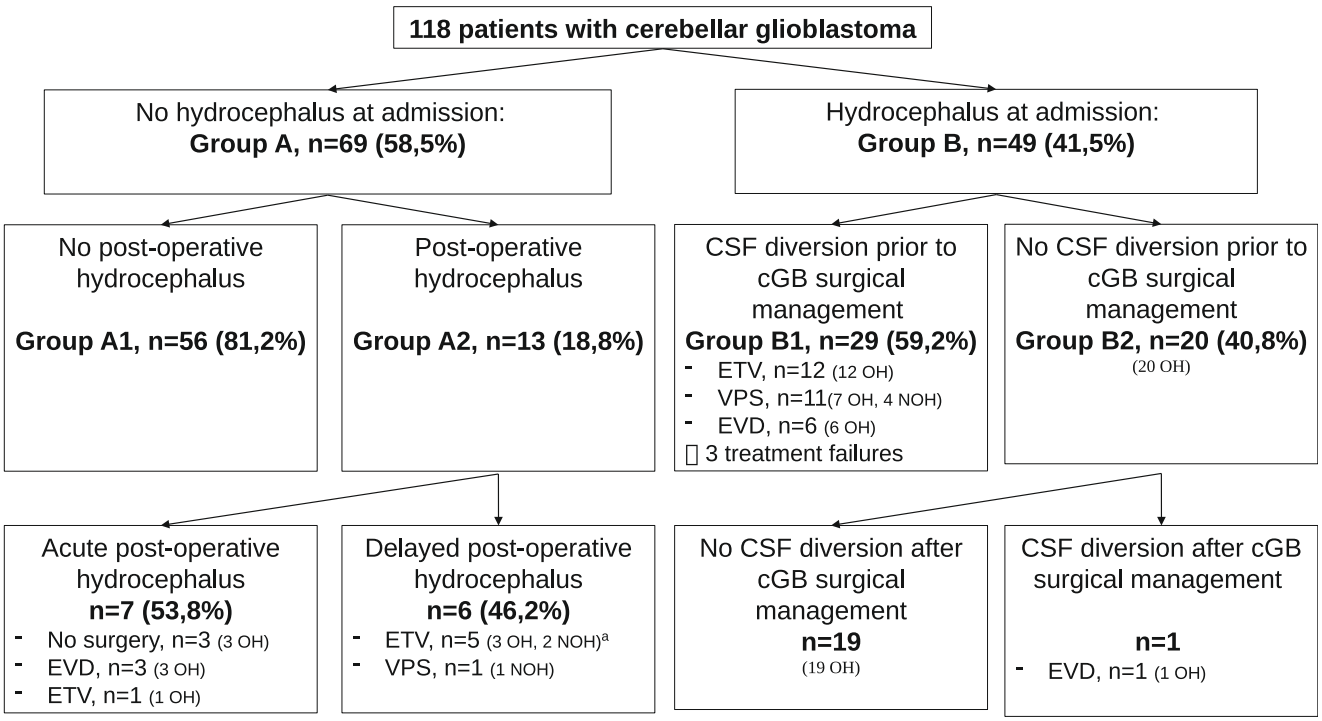
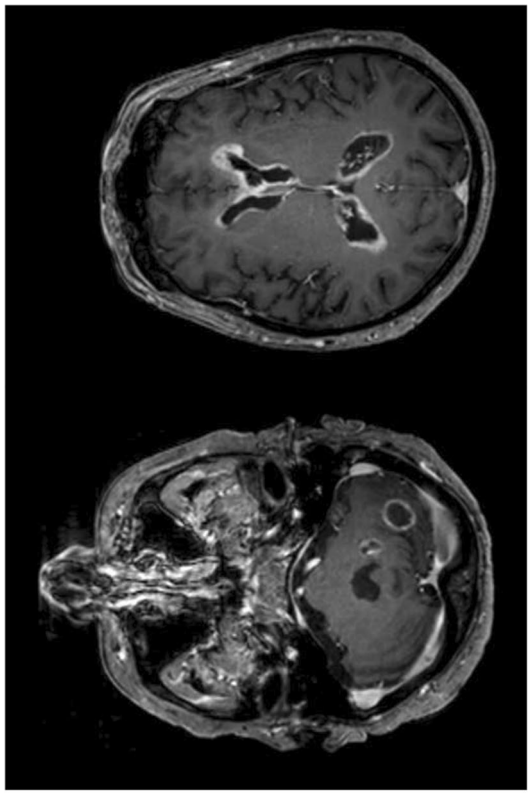
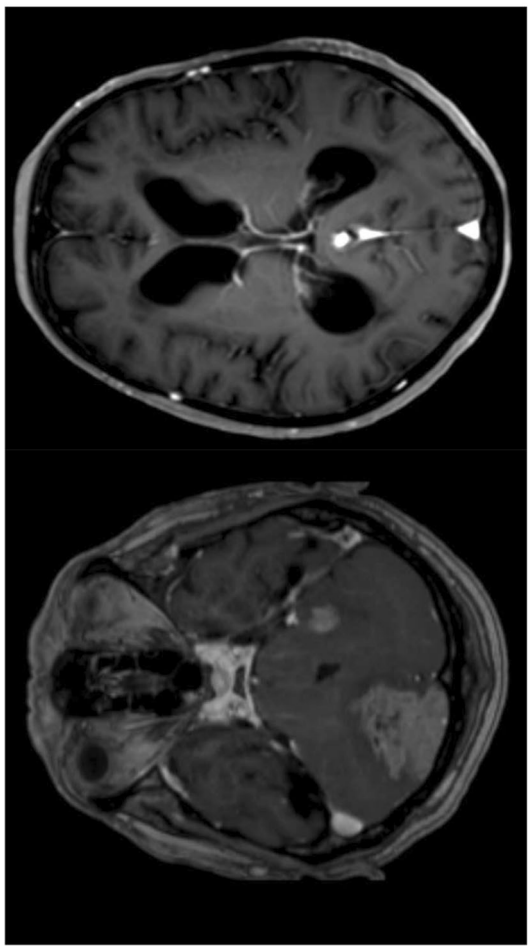


Fig. 1. Hydrocephalus incidence and management in the French nationwide series of cerebellar glioblastomas. ETV = Endoscopic Third Ventriculostomy, EVD = External Ventricular Drain, NOH = Non-Obstructive Hydrocephalus, OH = Obstructive Hydrocephalus, VPS = Ventriculoperitoneal Shunt. a. VPS was performed in two patients with non-obstructive hydrocephalus. In these two patients who had a poor general status, the mechanism of hydrocephalus was not really clear. "Palliative ETV" was performed and the diagnosis of leptomeningeal seeding was confirmed retrospectively thanks to the CSF that was harvested per-operatively





◀ **Fig. 2.** MRI features (contrast-enhanced T1-weighted MRI) in patients with hydrocephalus related to cerebellar glioblastoma. Left panel: Obstructive hydrocephalus with transependymal resorption in a 71-year-old male managed for a multifocal cerebellar glioblastoma. The clinical presentation was subacute with gait and cognitive disturbances Right panel: Subependymal spread of a multifocal cerebellar glioblastoma in a 72-year-old male who rapidly developed non-obstructive hydrocephalus with characteristic gait and cognitive disturbances

The 20 remaining patients (40.8%, group B2) were surgically managed for cGB without prior CSF diversion. In group B2, one patient (5%) developed acute postoperative obstructive hydrocephalus attributed to massive intra-ventricular postoperative hemorrhage, managed by EVD but no patient was long-term shunt-dependant.

Finally, in the entire series, the cumulative HAC rate reached 52.5% (62/118), with 55 cases (88.7%) of obstructive hydrocephalus and 7 cases (11.3%) of nonobstructive hydrocephalus. A total of 40 CSF diversion procedures were performed, including 18 ETV (45%), 12 VPS (30%), and 10 EVD (25%). Interestingly, among the 89 patients surgically managed for cGB without prior cerebrospinal-fluid diversion, only 7 (7.9%) were long-term shunt-dependant.

Differential characteristics of patients displaying hydrocephalus of any cause (HAC) at admission

Patients without (group A) and with HAC at admission (group B) were compared in order to decipher the characteristics associated with initial HAC in cGB patients (Table 1). Patients were younger in group B than in group A (52.0 years vs 58.6 years, $p=0.04$). Compared to group A patients, group B patients displayed more frequently signs of raised intracranial pressure (65.3% vs 40.6%, $p=0.01$) but less frequently cranial nerve disorders (4.1% vs 27.5%, $p=0.001$). Moreover, the postoperative KPS was more frequently improved compared to the preoperative KPS in group B than in group A (34.1% vs 15.2%, $p=0.02$).

Radiologically, tumor location ($p=0.06$), tumor volume ($p=0.71$), brainstem infiltration ($p=0.38$) and leptomeningeal seeding ($p=0.49$) did not differ in groups A and B.

The molecular profile was not similar as TP53 and TERT-mutations were more frequently found in group A than in group B (58.5% vs 33.3%, $p=0.03$ and 29.3% vs 6.9%, $p=0.03$, respectively) whereas H3-K27M-mutation was more frequently found in group B than in group A (27.8% vs 7.8%, $p=0.02$).

The surgical management was different as tumor resection was less frequently performed in group A than in group B (73.9% vs 93.9%, $p=0.006$) although the rates of total resection ($p=0.27$) and postoperative complications were not different ($p=0.84$). Postoperative management ($p=0.15$),

Table 1 Comparison of the characteristics of patients without hydrocephalus at admission (group A) with those of patients with hydrocephalus at admission (group B)

	cGBM without hydrocephalus at admission Group A (*n*=69)		cGBM with hydrocephalus at admission Group B (*n*=49)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	
CLINICAL AND RADIOLOGICAL PARAMETERS					
Mean age (years)	69	58.6 (15.3)	49	52.0 (17.7)	0.04*
Clinical presentation	28 (40.6%)		32 (65.3%)		0.01*
✓ Raised intracranial pressure	56 (81.2%)		39 (79.6%)		0.83
✓ Cerebellar syndrome	19 (27.5%)		2 (4.1%)		0.001*
✓ Cranial nerve disorders[a]					
One-month postoperative KPS vs Preoperative KPS (%)	10 (15.2%)		14 (34.1%)		0.02*
✓ Improved	56 (84.8%)		27 (65.9%)		
✓ Stable or worsened	3		8		
✓ Missing					
Tumor location	44 (63,8%)		39 (79,6%)		0.06
✓ Predominantly vermian	25 (36.2%)		10 (20.4%)		
✓ Predominantly hemispheric					
Initial tumor volume (mL)	43	16.7 (12.8)	32	18.4 (16.7)	0.71
✓ Missing	26		17		
Brainstem infiltration	22 (31.9%)		12 (24.5%)		0.38
✓ Yes	47 (68.1%)		37 (75.5%)		
✓ No					
Leptomeningeal seeding at diagnosis	2 (2.9%)		0 (0%)		0.49
✓ Yes	7 (10.1%)		5 (11.2%)		
✓ Suspected	60 (87%)		44 (89.8%)		
✓ No					
MOLECULAR PARAMETERS					
IDH status	57 (100%)		39 (100%)		0.99
✓ Wild-type	0 (0%)		0 (0%)		
✓ Mutated	12		10		
✓ Missing					
ATRX status	37 (77.1%)		22 (68.8%)		0.57
✓ Retained	11 (22.9%)		10 (31.2%)		
✓ Lost	21		17		
✓ Missing					
TP53 status	22 (41.5%)		24 (66.7%)		0.03*
✓ Wild-type	31 (58.5%)		12 (33.3%)		
✓ Mutated	16		13		
✓ Missing					
TERT mutation	12 (29.3%)		2 (6.9%)		0.03*
✓ Yes	29 (70.7%)		27 (93.1%)		
✓ No	28		20		
✓ Missing					
EGFR amplification	12 (25%)		4 (12.5%)		0.25
✓ Yes	36 (75%)		28 (87.5%)		
✓ No	21		17		
✓ Missing					
Histone H3 status	47 (92.2%)		26 (72.2%)		0.02*
✓ Wild-type	4 (7.8%)		10 (27.8%)		
✓ K27M mutation	18		13		
✓ Missing					
MANAGEMENT					
Surgical management	51 (73.9%)		46 (93.9%)		0.006*
✓ Resection	18 (26.1%)		3 (6.1%)		
✓ Biopsy					
Extent of resection	10 (19.6%)		5 (10.9%)		0.27
✓ Total	41 (80.4%)		41 (89.1%)		
✓ Subtotal/partial					

Table 1 (continued)

	cGBM without hydrocephalus at admission Group A (*n*=69)		cGBM with hydrocephalus at admission Group B (*n*=49)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	
Postoperative complication[b]	24 (34.8%)		18 (36.7%)		0.84
✓ Yes	45 (65.2%)		31 (63.3%)		
✓ No					
Postoperative management	55 (82.1%)		33 (68.8%)		0.15
✓ Adjuvant treatment[c]	12 (17.9%)		15 (31.2%)		
✓ Palliative cares	2		1		
✓ Missing					
OUTCOMES					
Progression	(*n*=43)		(*n*=35)		0.78
✓ Supratentorial	16 (37.2%)		15 (42.9%)		0.69
✓ Leptomeningeal	13 (30.2%)		13 (37.1%)		0.41
✓ Multifocal	10 (23.3%)		12 (34.3%)		
Progression-free survival (months)	*n*=69	5.1	*n*=49	5.2	0.96
Overall survival (months)	*n*=69	8.7	*n*=49	9.7	0.53

[a] Cranial nerve disorders consisted in visual disorders, including diplopia and nystagmus (*n*=12 in group A and *n*=1 in group B) and swallowing disorders (*n*=7 in group A, *n*=1 in group B)

[b] Postoperative complications consisted in hydrocephalus (*n*=12 in group A and *n*=1 in group B), neurological impairment (*n*=6 in group A and *n*=6 in group B), infection (local, meningeal, ventricular or pulmonary; *n*=5 in group A, *n*=6 in group B), intra-cranial haemorrhage (*n*=2 in group A and *n*=3 in group B) and gas embolism (*n*=2 in group A and *n*=2 in group B). Several complications sometimes co-existed in the same patients

[c] Adjuvant treatment consisted of Stupp radio-chemotherapy (*n*=37 in group A and *n*=25 in group B), chemotherapy (*n*=9 in group A and *n*=2 in group B), radiotherapy (*n*=6 in group A and *n*=4 in group B) and, radiotherapy followed by chemotherapy (*n*=3 in group A and *n*=2 in group B). The distribution did not differ significantly (p=0.57)

progression modes, PFS (5.1 months vs 5.2 months, p=0.96 – Fig. 3a) and OS (8.7 months vs 9.7 months, p=0.53 – Fig. 3b) were comparable in groups A and B.

Differential characteristics of group A patients displaying postoperative HAC

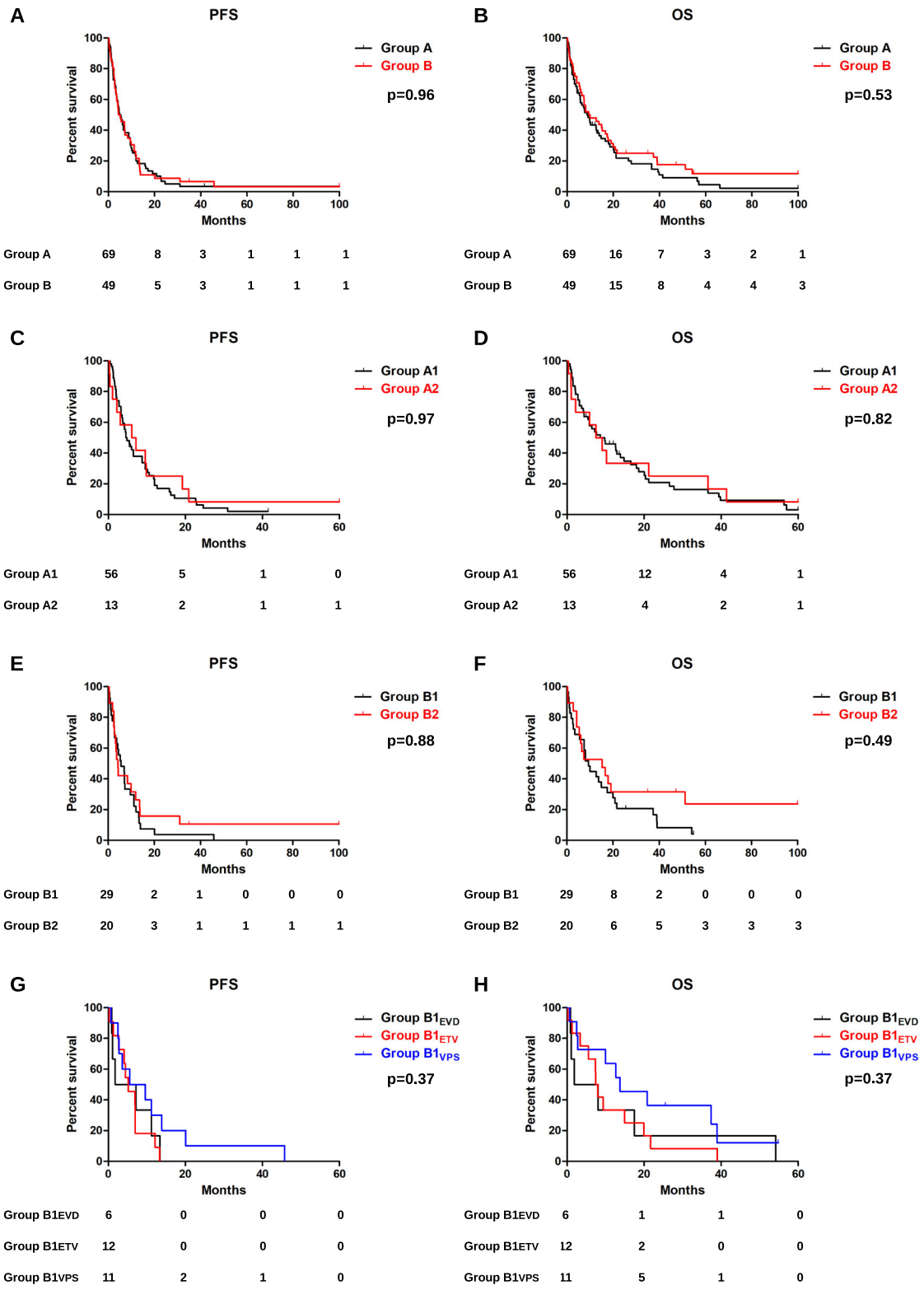
In group A, patients without postoperative HAC (group A1) were compared to patients with postoperative HAC (group A2) in order to determine the characteristics associated with the onset of postoperative HAC (Table 2).

Patients without postoperative HAC (group A1) and patients who developed postoperative HAC (group A2) did not differ in terms of age (p=0.16) and clinical presentation. The postoperative KPS was lower in group A2 than in group A1 (49.2% vs 67.1%, p=0.04).

Radiologically, there were no differences between groups A1 and A2 concerning tumor location (p=0.11), initial tumor volume (p=0.07), and leptomeningeal seeding (p=0.39) but brainstem infiltration was more frequent in group A2 than in group A1 (61.5% vs 25%, p=0.02). The molecular profile was similar in groups A1 and A2.

Tumor resection was performed as frequently in group A1 than in group A2 (75% and 69.2%, p=0.73). Total resection was more frequently achieved in group A1 than in group A2 although the difference was not significant (23.8% vs 0%, p=0.18). Postoperative management (p=0.21), progression modes, PFS (4.7 months vs 6.7 months, p=0.97 – Fig. 3c) and OS (8.7 months vs 8.3 months, p=0.82 – Fig. 3d) were comparable in groups A1 and A2.

Fig. 3 Kaplan-Meier survival analysis. **a**: Progression-free survival for cGB patients without hydrocephalus at diagnosis (group A) and patients without hydrocephalus at diagnosis (group B). **b**: Overall survival for cGB patients without hydrocephalus at diagnosis (group A) and patients without hydrocephalus at diagnosis (group B)**. c**: Progression-free survival for group A patients without postoperative hydrocephalus (group A1) and group A patients with postoperative hydrocephalus (group A2). **d**: Overall survival for group A patients without postoperative hydrocephalus (group A1) and group A patients with postoperative hydrocephalus (group A2). **e**: Progression-free survival for group B patients who underwent Cerebrospinal Fluid diversion prior to cGB management (group B1) and group B patients who did not (group B2). **f**: Overall survival for group B patients who underwent cerebrospinal fluid diversion prior to cGB management (group B1) and group B patients who did not (group B2). **g**: Progression-free survival for group B patients according to cerebrospinal fluid diversion modalities: external ventricular drain (group $B1_{EVD}$), endoscopic third ventriculostomy (group $B1_{ETV}$), and ventriculoperitoneal shunt (group $B1_{VPS}$). **h**: Overall survival for group B patients according to cerebrospinal fluid diversion modalities: external ventricular drain (group $B1_{EVD}$), endoscopic third ventriculostomy (group $B1_{ETV}$), and ventriculoperitoneal shunt (group $B1_{VPS}$)


A
PFS
Percent survival
Months
Group A
Group B
p=0.96
Group A 69 8 3 1 1 1
Group B 49 5 3 1 1 1
B
OS
Percent survival
Months
Group A
Group B
p=0.53
Group A 69 16 7 3 2 1
Group B 49 15 8 4 4 3
C
PFS
Percent survival
Months
Group A1
Group A2
p=0.97
Group A1 56 5 1 0
Group A2 13 2 1 1
D
OS
Percent survival
Months
Group A1
Group A2
p=0.82
Group A1 56 12 4 1
Group A2 13 4 2 1
E
PFS
Percent survival
Months
Group B1
Group B2
p=0.88
Group B1 29 2 1 0 0 0
Group B2 20 3 1 1 1 1
F
OS
Percent survival
Months
Group B1
Group B2
p=0.49
Group B1 29 8 2 0 0 0
Group B2 20 6 5 3 3 3
G
PFS
Percent survival
Months
Group B1EVD
Group B1ETV
Group B1VPS
p=0.37
Group B1EVD 6 0 0 0
Group B1ETV 12 0 0 0
Group B1VPS 11 2 1 0
H
OS
Percent survival
Months
Group B1EVD
Group B1ETV
Group B1VPS
p=0.37
Group B1EVD 6 1 1 0
Group B1ETV 12 2 0 0
Group B1VPS 11 5 1 0

Differential characteristics of group B patients according to the surgical strategy

In group B, patients who underwent CSF diversion prior to cGB management (group B1) were compared to patients who did not undergo CSF diversion prior to cGB management (group B2), in order to assess the onco-functional results of the different surgical strategies (Table 3).

Patients who underwent CSF diversion prior to cGB management (group B1) and patients who did not (group B2) were comparable in terms of age (p=0.71) and clinical presentation. The pre-operative KPS was lower in group B1 than in group B2 (63% vs 74%, p=0.04) but the difference was no longer significant postoperatively (59% vs 65%, p=0.46).

MRI parameters including tumor location (p=0.72), tumor volume (p=0.18), and leptomeningeal seeding (p=0.14) did not differ. The molecular profile was also homogeneous.

The surgical management was similar in groups B1 and B2 as resection was performed in 93.1% and 95% of cases, respectively (p=0.99), without difference in terms of patient positionning (p=0.48) and with total removal rates of 11.1% and 10.5%, respectively (p=0.99). Infection (p=0.99) and persistent postoperative HAC rates (p=0.64) were also comparable.

Postoperative management (p=0.99), progression modes, PFS (5.6 months vs 4.2 months, p=0.88 – Fig. 3e) and OS (9.4 months vs 15.2 months, p=0.49 – Fig. 3f) were comparable in groups B1 and B2.

Differential characteristics of group B1 patients according to CSF diversion modalities

In group B1, the surgical results associated with the different CSF diversion modalities (EVD, ETV, and VPS) were compared (Table 4).

Patients who underwent EVD (group $B1_{EVD}$), ETV (group $B1_{ETV}$), and VPS (group $B1_{VPS}$) did not differ in terms of age (p=0.20) and clinical presentation.

Radiologically, there were no differences between groups $B1_{EVD}$, $B1_{ETV}$, and $B1_{VPS}$ concerning tumor location (p=0.38), initial tumor volume (p=0.61), and leptomeningeal seeding (p=0.43). The molecular profile was similar in groups $B1_{EVD}$, $B1_{ETV}$, and $B1_{VPS}$.

The surgical management after CSF diversion (p=0.75), postoperative complications including infections (p=0.85) and CSF diversion failure (p=0.54) were comparable in groups $B1_{EVD}$, $B1_{ETV}$, and $B1_{VPS}$. Postoperative management (p=0.39), progression modes, PFS (4.5 months vs 5.2 months vs 7.6 months, p=0.37 – Fig. 3g) and OS (5.0 months vs 7.7 months vs 13.7 months, p=0.37 – Fig. 3h) did not differ.

Discussion

This study analyzed the characteristics of a unique nationwide series of 118 adult cGB patients with special emphasis on hydrocephalus. The overall perioperative HAC rate was 52.5%. Patients with HAC at admission had not the same clinical and molecular characteristics than patients without HAC. Among patients without HAC at diagnosis, patients who developed postoperative HAC had more frequently a brainstem infiltration than patients who did not. Patients with HAC at admission had the same outcomes, whether or not a CSF diversion was performed prior to cGB management. In patients with HAC at admission, all CSF diversion options provided comparable results. Finally, among the 89 patients surgically managed for cGB without prior cerebrospinal-fluid diversion, only 7 (7.9%) were long-term shunt-dependant.

Physiopathology and incidence of hydrocephalus in cGB patients

The frequency of HAC prior to and after the surgical management of posterior fossa tumor surgery remains poorly known [8]. In the present series of adult cGB, 41.5% of patients presented with HAC at diagnosis and 18.8% of cGB patients were not hydrocephalic at diagnosis but developed postoperative HAC. Consistently, HAC was present at diagnosis in 44.4% (4/9) and 40% (4/10) patients in two previous series of cGB [14, 22] but postoperative HAC rates are not known.

The rate of preoperative HAC is lower in extraparenchymal posterior fossa tumors and varies between 3.7%–33% [1, 2, 23–28]. Indeed, cerebello-pontine angle tumors are revealed by cranial nerve disorders preceding HAC which is correlated to increased tumor size [1, 23, 26, 27, 29]. Moreover, their greater distance to the 4th ventricule and their lower growth rate allow gradual molding of the 4th ventricle. In a series of 284 benign cerebello-pontine angle tumors, only two patients developed postoperative HAC [29]. Thus, the rate of postoperative HAC is also lower in patients with extraparenchymal posterior fossa tumors since postoperative cerebellar swelling may be more limited compared to cGB patients but also because hydrocephalus linked to local or leptomeningeal tumor progression is overrepresented in cGB patients. The incidence of HAC raises 50% in adult patients with medulloblastoma [3]. It varies between 20%–35% at diagnosis [8, 30–32] and around 15% postoperatively [31] in patient with posterior fossa metastasis. Consequently, the rate of HAC in cGB patients is close to this observed in adult intraparenchymal cerebellar tumors, independently of their histological nature but lower than this observed in children [33].

In this nationwide series of cGB, hydrocephalus was predominantly obstructive (88.7%) but 7 patients developed non-obstructive hydrocephalus, in the presence of tumor

Table 2 In group A, comparison of the characteristics of patients without post-operative hydrocephalus (group A1) with those of patients who developed post-operative hydrocephalus (group A2)

	cGBM without initial and postoperative hydrocephalus Group A1 (*n*=56)		cGBM without initial hydrocephalus but with postoperative hydrocephalus Group A2 (*n*=13)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	
CLINICAL AND RADIOLOGICAL PARAMETERS					
Mean age (years)	56	60.2 (14.0)	13	51.6 (19.0)	0.16
Clinical presentation	22 (39.3%)		6 (46.2%)		0.76
✓ Raised intracranial pressure	44 (78.6%)		12 (92.3%)		0.44
✓ Cerebellar syndrome	14 (25%)		5 (38.5%)		0.33
✓ Cranial nerve disorders					
One-month postoperative KPS (%)	54	67.1 (25.3)	12	49.2 (34.5)	0.04*
Tumor location	33 (58.9%)		11 (84,6%)		0.11
✓ Predominantly vermian	23 (41,1%)		2 (15,4%)		
✓ Predominantly hemispheric					
Initial tumor volume (mL)	39	15.3 (11.5)	4	19.8 (18.9)	0.07
✓ Missing	17		9		
Leptomeningeal seeding at diagnosis	1 (1.8%)		1 (7.7%)		0.39
✓ Yes	5 (8.9%)		2 (15.4%)		
✓ Suspected	50 (89.3%)		10 (76.9%)		
✓ No					
Brainstem infiltration	14 (25%)		8 (61.5%)		0.02*
✓ Yes	42 (75%)		5 (38.5%)		
✓ No					
MOLECULAR PARAMETERS					
IDH status	49 (100%)		8 (100%)		0.99
✓ Wild-type	0 (0%)		0 (0%)		
✓ Mutated	7		5		
✓ Missing					
ATRX status	32 (78%)		5 (71.4%)		0.65
✓ Retained	9 (22%)		2 (28.6%)		
✓ Lost	15		6		
✓ Missing					
TP53 status	20 (45.5%))		2 (22.2%)		0.28
✓ Wild-type	24 (54.5%)		7 (77.8%)		
✓ Mutated	12		4		
✓ Missing					
TERT mutation	10 (29.4%)		2 (28.6%)		0.99
✓ Yes	24 (70.6%)		5 (71.4%)		
✓ No	22		6		
✓ Missing					
EGFR amplification	9 (22.5%)		3 (37.5%)		0.39
✓ Yes	31 (77.5%)		5 (62.5%)		
✓ No	16		5		
✓ Missing					
Histone H3 status	39 (90.7%)		8 (100%)		0.99
✓ Wild-type	4 (9.3%)		0 (0%)		
✓ K27M mutation	13		5		
✓ Missing					
MANAGEMENT					
Surgical management	42 (75%)		9 (69.2%)		0.73
✓ Resection	14 (25%)		4 (30.8%)		
✓ Biopsy					
Extent of resection	10 (23.8%)		0 (0%)		0.18
✓ Total	32 (76.2%)		9 (100%)		
✓ Subtotal/partial					

Table 2 (continued)

	cGBM without initial and postoperative hydrocephalus Group A1 (*n*=56)		cGBM without initial hydrocephalus but with postoperative hydrocephalus Group A2 (*n*=13)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	
Postoperative management	47 (85.5%)		8 (66.7%)		0.21
✓ Adjuvant treatment	8 (14.5%)		4 (33.3%)		
✓ Palliative cares	1		1		
✓ Missing					
OUTCOMES					
Progression	(*n*=35)		(*n*=8)		0.13
✓ Supratentorial	11 (31.4%)		5 (62.5%)		0.68
✓ Leptomeningeal	10 (28.6%)		3 (37.5%)		0.07
✓ Multifocal	6 (17.1%)		4 (50%)		
Progression-free survival (months)	*n*=56	4.7	*n*=13	6.7	0.97
Overall survival (months)	*n*=56	8.7	*n*=13	8.3	0.82

leptomeningeal seeding or not. Nonobstructive hydrocephalus without leptomeningeal seeding has already been described in posterior fossa tumors but also in supra-tentorial glioblastomas and was attributed to arachnoiditis and to elevated CSF level resulting in clogging of the arachnoid granulations [23, 25–27, 29, 34, 35]. In the present study, CSF protein level was not available but this so-called "metabolic concept" may account for few cases of non-obstructive hydrocephalus associated with cGB with arachnoid contact.

Characteristics associated with HAC in cGB patients

In this nationwide series of cGB, several differences were observed between patients who were hydrocephalic at diagnosis and patients who were not. Firstly, group B patients were younger than group A patients. Consistently, the rate of cortico-subcortical atrophia and consequently the tolerance to 4th ventricle compression may be higher in group A. Secondly, the clinical presentation was different in groups A and B. As expected, signs of raised intracranial pressure were more frequent in group B. The increased frequency of cranial nerve disorders in group A is not explained by radiological parameters that were comparable in groups A and B but may result from an underestimation to these symptoms in group B patients in who raised intracranial pressure was clinically in the forefront. Thirdly, the molecular profile was not similar in groups A and B, which is explained by the difference in age as histone H3-K27M-mutant gliomas are generally found in young patients [36, 37] whereas TERT-mutant gliomas rather affect older patients [38]. Fourthly, tumor resection was more frequently performed in group B than in group A, undoubtedly because it was considered as the better strategy to alleviate raised intracranial pressure but also because patients were older in group A and did subsequently not constitute the best candidates for tumor removal [39].

Interestingly, tumor location and tumor volume were similar in groups A and B. Consistently, in 19 pooled cGB from 2 series, 50% of cGB were vermian and 50% were hemispheric in both hydrocephalic and non-hydrocephalic patients [14, 22]. Tumor volume was conversely a predictor of HAC in acoustic neurinomas [1, 23, 26, 27] but the predominant mechanisms leading to HAC may not be the same in cGB, as previously explained. Preoperative HAC did not influence the onco-functional outcomes in acoustic neurinomas [24]. This parameter was not studied in previous cGB prognosis studies [9, 10, 40] but did not significantly modify patient prognosis after appropriate management in the present series as the outcomes were the same in group A compared to group B.

In group A, the lower postoperative KPS observed in group A2 compared to group A1 may be linked to the presence of HAC itself but also to the causes of hydrocephalus onset, including serious surgical complications such as cerebellar swelling or hemorrhage. In group A, the only significant predictor of postoperative HAC was brainstem infiltration. Interestingly, total resection was never achieved in group A2 which is not surprising, given the high rate of brainstem infiltration (61.5%) [15]. Consistently, in a series mixing 320 benign or malignant posterior fossa tumors, brainstem compression was a predictor of postoperative HAC [41]. Intuitively, total resection offers the possibility to better unclog the 4th ventricle and has already been identified as inversely correlated with the risk of postoperative HAC in patients managed for posterior fossa tumors [42]. Thus, in patients with brainstem

Table 3 In group B, comparison of patients who underwent CSF diversion prior to glioblastoma management (Group B1) with patients who did not undergo CSF diversion prior to glioblastoma management (Group B2)

	Patients who underwent CSF diversion prior to glioblastoma surgical management Group B1 (*n*=29)		Patients who did not underwent CSF diversion prior to glioblastoma surgical management Group B2 (*n*=20)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	
CLINICAL AND RADIOLOGICAL PARAMETERS					
Mean age (years)	29	51.3 (17.0)	20	53.0 (18.0)	0.71
Clinical presentation	19 (65.5%)		13 (65%)		0.99
✓ Raised intracranial pressure	21 (72.4%)		18 (90%)		0.17
✓ Cerebellar syndrome	1 (3.4%)		1 (5%)		0.99
✓ Cranial nerve disorders					
Preoperative KPS (%)	25	63 (19)	18	74 (16)	0.04*
One-month postoperative KPS (%)	25	59 (28)	18	65 (29)	0.46
Tumor location	24 (82,8%)		15 (75%)		0.72
✓ Predominantly vermian	5 (17,2%)		5 (25%)		
✓ Predominantly hemispheric					
Initial tumor volume (mL)	17	18.4 (21.4)	15	18.4 (9.5)	0.18
✓ Missing	12		5		
Leptomeningeal seeding at diagnosis	1 (3.4%)		4 (20%)		0.14
✓ Suspected	28 (96.6%)		16 (80%)		
✓ No					
MOLECULAR PARAMETERS					
IDH status	22 (100%)		17 (100%)		0.99
✓ Wild-type	0 (0%)		0 (0%)		
✓ Mutated	7		3		
✓ Missing					
ATRX status	14 (77.8%)		8 (57.1%)		0.27
✓ Retained	4 (22.2%)		6 (42.9%)		
✓ Lost	11		6		
✓ Missing					
TP53 status	15 (71.4%)		9 (60%)		0.72
✓ Wild-type	6 (28.6%)		6 (40%)		
✓ Mutated	8		5		
✓ Missing					
TERT mutation	1 (6.7%)		1 (7.1%)		0.99
✓ Yes	14 (93.3%)		13 (92.9%)		
✓ No	14		6		
✓ Missing					
EGFR amplification	2 (11.1%)		2 (14.3%)		0.99
✓ Yes	16 (88.9%)		12 (85.7%)		
✓ No	11		6		
✓ Missing					
Histone H3 status	16 (76.2%)		10 (66.7%)		0.71
✓ Wild-type	5 (23.8%)		5 (33.3%)		
✓ K27M mutation	8		5		
✓ Missing					
MANAGEMENT					
Surgical management	27 (93.1%)		19 (95%)		0.99
✓ Resection	2 (6.9%)		1 (5%)		
✓ Biopsy					
Patient positionning for resection	5 (18.5%)		6 (31.6%)		0.48
✓ Ventral/lateral decubitus	22 (81.5%)		13 (68.4%)		
✓ Sitting					
Extent of resection	3 (11.1%)		2 (10.5%)		0.99
✓ Total	24 (88.9%)		17 (89.5%)		
✓ Subtotal/partial					

Table 3 (continued)

	Patients who underwent CSF diversion prior to glioblastoma surgical management Group B1 (*n*=29)		Patients who did not underwent CSF diversion prior to glioblastoma surgical management Group B2 (*n*=20)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	
Postoperative complications	3 (10.3%)		2 (10%)		0.99
✓ Meningitis / ventriculitis	3 (10.3%)		1 (5%)		0.64
✓ Postoperative hydrocephalus					
Postoperative management	20 (69.0%)		13 (68.4%)		0.99
✓ Adjuvant treatment	9 (31.0%)		6 (31.6%)		
✓ Palliative cares	0		1		
✓ Missing					
OUTCOMES					
Progression	(*n*=20)		(*n*=15)		0.99
✓ Supratentorial	9 (45%)		6 (40%)		0.74
✓ Leptomeningeal	8 (40%)		5 (33.3%)		0.99
✓ Multifocal	7 (35%)		5 (33.3%)		
Progression-free survival (months)	*n*=29	5.6	*n*=20	4.2	0.88
Overall survival (months)	*n*=29	9.4	*n*=20	15.2	0.49

invasion and without preoperative HAC, a closer monitoring of the ventricular volume is warranted given the higher risk of developing post-operative HAC.

Management of preoperative HAC in cGB patients

There is no real consensus regarding the management of symptomatic HAC in adult patients with benign [1, 24, 26, 29] or malignant [5, 7, 8, 30, 32, 43] posterior fossa tumors. Tumor removal has to be considered systematically in patients with posterior fossa tumors in order to optimize the onco-functional outcomes [2, 4, 5, 15, 25, 26] but to perform CSF diversion or not prior to tumor removal consequently remains a major question for the neurosurgeon.

The postoperative KPS was more frequently improved in group B than in group A. Consistently, in a series of 723 adult glioblastomas, 30 patients had HAC and CSF diversion provided a significant improvement of KPS in patients with lower preoperative KPS (<60%) [35]. These observation highlights the importance to optimally manage HAC in cGB patients.

The lower preoperative KPS was the only difference found in group B1 compared to group B2. Thus, the alteration of the general status was the main clinical argument that led to surgically managed preoperative HAC. Conversely, no radiological parameters or surgical parameter, including patient positioning, had significant influence on decision-making. The onco-functional results and complications rates were similar in groups B1 and B2. The increased infectious rate associated with CSF diversion prior to tumor management, identified in some series of posterior fossa tumors [32] was not confirmed.

It is impossible to retrospectively determine whether CSF diversion was really mandatory or not in groups $B1_{ETV}$ and $B1_{VPS}$. Interestingly, in group $B1_{EVD}$, no patient was long-term shunt-dependent. Consistently, in patients with hydrocephalus related to posterior fossa tumor managed with EVD, the reported rates of postoperative shunt-dependence are low [28, 30, 32, 42] and predisposing factors remain poorly known [7]. In group B2, the surgical strategy was appropriate as 0% of patients were long-term shunt-dependant. The only case of acute postoperative hydrocephalus was attributed to massive intra-ventricular hemorrhage and managed by transient EVD. In accordance, in a series of 52 patients with HAC related to posterior fossa tumor of various histology, very few patients without CSF diversion prior to tumor removal required a CSF diversion after tumor removal (3/41 = 7.3%) [8]. In hydrocephalic patients with acoustic neurinomas, tumor removal was also sufficient to manage HAC in the majority of patients (87.5%) [24].

Finally, all options of CSF diversion seem equivalent as there were no differences between groups $B1_{EVD}$, $B1_{ETV,}$ and $B1_{VPS}$. Global complication rates were relatively high but it is difficult to differentiate complications directly imputable to CSF diversion *per se* or to cGB management. Comparable or higher complication rates were reported in patients with posterior fossa tumor after CSF diversion [4, 6, 44, 45] and in a series of patients with supratentorial glioblastoma who underwent CSF diversion for HAC [35], respectively. Additionally, there were no important neurological deterioration imputable to intratumoral hemorrhage or upward transtorial herniation following CSF diversion, as sometimes reported in children [33].

In the present series, EVD was not associated with an increased complication rate compared to other CSF diversion

Table 4 In group B, comparison of patients who underwent CSF shunt prior to glioblastoma management according to the surgical modalities (External Ventricular Drain vs Endoscopic Third Ventriculostomy vs Ventriculoperitoneal Shunt)

	Patients who underwent EVD before glioblastoma surgical management Group $B1_{EVD}$ (n=6)		Patients who underwent ETV before glioblastoma surgical management Group $B1_{ETV}$ (n=12)		Patients who underwent VPS before glioblastoma surgical management Group $B1_{VPS}$ (n=11)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	N (%)	Mean (SD)	
CLINICAL AND RADIOLOGICAL PARAMETERS							
Mean age (years)	6	42.1 (17.6)	12	57.2 (15.5)	11	50.1 (17.3)	0.20
Clinical presentation	5 (83.3%)		8 (66.7%)		6 (54.5%)		0.49
✓ Raised intracranial pressure	3 (50%)		9 (75%)		9 (81.8%)		0.36
✓ Cerebellar syndrome	0 (0%)		0 (0%)		1 (9.1%)		0.43
✓ Cranial nerve disorders							
Tumor location	5 (83.3%)		10 (83.3%)		9 (81.8%)		0.38
✓ Predominantly vermian	1 (16,7%)		2 (16.7%)		2 (18.2%)		
✓ Predominantly hemispheric							
Initial tumor volume (mL)	5	16.5 (21.6)	6	12.8 (7.9)	6	25.5 (30.6)	0.61
✓ Missing	1		6		5		
Leptomeningeal seeding at diagnosis	0 (0%)		0 (0%)		1 (9.1%)		0.43
✓ Suspected	6 (100%)		12 (100%)		10 (90.9%)		
✓ No							
MOLECULAR PARAMETERS							
IDH status	6 (100%)		10 (100%)		6 (100%)		0.99
✓ Wild-type	0 (0%)		0 (0%)		0 (0%)		
✓ Mutated	0		2		5		
✓ Missing							
ATRX status	3 (60%)		7 (77.8%)		4 (100%)		0.36
✓ Retained	2 (40%)		2 (22.2%)		0 (0%)		
✓ Lost	1		3		7		
✓ Missing							
TP53 status	5 (83.3%)		5 (55.6%)		5 (83.3%)		0.38
✓ Wild-type	1 (16.7%)		4 (44.4%)		1 (16.7%)		
✓ Mutated	0		3		5		
✓ Missing							
TERT mutation	0 (0%)		1 (14.3%)		0 (0%)		0.54
✓ Yes	3 (100%)		6 (85.7%)		5 (100%)		
✓ No	3		5		6		
✓ Missing							
EGFR amplification	1 (25%)		1 (11.1%)		0 (0%)		0.49
✓ Yes	3 (75%)		8 (88.9%)		5 (100%)		
✓ No	2		3		6		
✓ Missing							
Histone H3 status	5 (83.3%)		7 (70%)		4 (80%)		0.81
✓ Wild-type	1 (16.7%)		3 (30%)		1 (20%)		
✓ K27M mutation	0		2		6		
✓ Missing							
MANAGEMENT							
Surgical management	6 (100%)		11 (91.7%)		10 (90.9%)		0.75
✓ Resection	0 (0%)		1 (8.3%)		1 (9.1%)		
✓ Biopsy							
Postoperative complication	1 (16.7%)		1 (8.3%)		1 (9.1%)		0.85
✓ Meningitis / ventriculitis	0 (0%)		2 (16.7%)		1 (9.1%)		0.54
✓ Persistent hydrocephalus							
Postoperative management	3 (50%)		8 (66.7%)		9 (81.8%)		0.39
✓ Adjuvant treatment	3 (50%)		4 (33.3%)		2 (18.2%)		
✓ Palliative cares							
OUTCOMES							
Progression	(n=4)		(n=8)		(n=8)		0.86
✓ Supratentorial	2 (50%)		4 (50%)		3 (37.5%)		0.11

Table 4 (continued)

	Patients who underwent EVD before glioblastoma surgical management Group $B1_{EVD}$ (n=6)		Patients who underwent ETV before glioblastoma surgical management Group $B1_{ETV}$ (n=12)		Patients who underwent VPS before glioblastoma surgical management Group $B1_{VPS}$ (n=11)		p
	N (%)	Mean (SD)	N (%)	Mean (SD)	N (%)	Mean (SD)	
✓ Leptomeningeal	2 (50%)		5 (62.5%)		1 (12.5%)		0.17
✓ Multifocal	3 (75%)		2 (25%)		2 (25%)		
Progression-free survival (months)	n=6	4.5	n=12	5.2	n=11	7.6	0.37
Overall survival (months)	n=6	5.0	n=12	7.7	n=11	13.7	0.37

ETV = Endoscopic Third Ventriculostomy, *EVD* = External Ventricular Drain, *VPS* = Ventriculoperitoneal Shunt

options. Consistently, in a series of 287 patients managed for posterior fossa tumors, EVD and VPS had similar complication rates (7%) [32]. These results consequently confirm that EVD constitutes a valid option, avoiding permanent shunt, in patients with poor clinical condition, pending tumor resection [5, 28, 32].

ETV is currently considered to provide good results with minimal complications in adult patients, regardless of the indication [5, 46–48]. In the present series, there were 2 ETV failures, one of which was attributed to postoperative hemorrhage which represent a predisposing mechanism for ventriculostomy occlusion in patients with posterior fossa metastasis [31]. VPS is also validated in patients with posterior fossa metastasis [5, 41, 43], especially in patients with history of resolved infection, ventricular hemorrhage or leptomeningeal carcinomatosis [5, 45]. In a series of 52 patients with HAC associated with posterior fossa metastasis, the outcomes and complication rates were similar in patients palliatively managed with ETV and VPS [45]. These two CSF diversion options appear to be also equivalent in cGB patients.

Limitations

The main limitations of this study are attributable to its retrospective design which was unavoidable given the rarity of the disease. Particularly, molecular data were not comprehensive. The results have to be cautiously interpreted as functional results and complications do not depend only on HAC management but also on cGB management.

Conclusion

HAC is frequent in cGB patients, with a cumulative incidence of 52.5%. Although HAC does not constitute a prognosis factor *per se*, it has to be carefully monitored and managed in cGB patients in order not to interfere with adjuvant oncological treatments [6]. The general guidelines available for the management of HAC in patients with posterior fossa metastasis [5] seem to be applicable to cGB patients and have to be integrated in an individual approach. In case of symptomatic HAC, a CSF diversion is mandatory, especially if surgical resection is not feasible. In case of asymptomatic HAC, the possibility to performed surgical resection should be firstly considered. If surgical resection is not feasible, a CSF diversion (ETV or VPS) has to be discussed.

Acknowledgements We thank all contributors from the French Brain Tumor Database and from the Club de Neuro-Oncologie of the Société Française de Neurochirurgie and Mr Julien Berthiller, biostatistician. Moreover, we thank the non-profit organizations that support the FBTDB: Ligue Nationale Contre le Cancer and comité 34, Associations pour la Recherche sur les Tumeurs Cérébrales (ARTC) Nord et Sud, Des étoiles dans la Mer ; as well as the French Glioblastoma biobank (FGB) and the French Institut National du Cancer-INCa.

Data Availability (data transparency) Anonymized data will be shared by request from any qualified investigator.

Code availability Not applicable

Authors' contributions Thiébaud Picart, Luc Bauchet and Jacques Guyotat designed and conceptualized the study.

Thiébaud Picart, Chloé Dumot, David Meyronet, Johan Pallud, Philippe Metellus, Sonia Zouaoui, François Ducray, Isabelle Pelissou-Guyotat, Moncef Berhouma and all members from the French Brain Tumor DataBase and the Club de Neuro-Oncologie of the Société Française de Neurochirurgie had a major role in the acquisition of data.

Thiébaud Picart and David Meyronet analyzed and interpreted the data.

Thiébaud Picart, Luc Bauchet and Jacques Guyotat drafted the manuscript.

All authors critically revised the manuscript for intellectual content and approved the final version.

Funding No funding was received for conducting this study.

Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the French legislation (CCTIRS n°10.548; CNIL n°911013).

Consent to participate (include appropriate statements) All patients provided written informed consent for study inclusion.

Consent for publication (include appropriate statements) All living patients provided written informed consent for data publication.

Conflicts of interest Drs. Thiébaud Picart, Chloé Dumot, David Meyronet, Johan Pallud, Philippe Metellus, Sonia Zouaoui, François Ducray, Isabelle Pelissou-Guyotat, Moncef Berhouma, Luc Bauchet, Jacques Guyotat, all members of the French Brain Tumor DataBase and Club de Neuro-Oncologie of the Société Française de Neurochirurgie declare that they have no conflict of interest.

References

1. Atlas MD, Perez de Tagle JR, Cook JA, Sheehy JP, Fagan PA (1996) Evolution of the management of hydrocephalus associated with acoustic neuroma. Laryngoscope 106:204–206. https://doi.org/10.1097/00005537-199602000-00018
2. Briggs RJ, Shelton C, Kwartler JA, Hitselberger W (1993) Management of hydrocephalus resulting from acoustic neuromas. Otolaryngol Head Neck Surg 109:1020–1024. https://doi.org/10.1177/019459989310900608
3. Chan AW, Tarbell NJ, Black PM, Louis DN, Frosch MP, Ancukiewicz M, Chapman P, Loeffler JS (2000) Adult medulloblastoma: prognostic factors and patterns of relapse. Neurosurgery 47:623–631; discussion 631-632. https://doi.org/10.1097/00006123-200009000-00018
4. Marx S, Damaty AE, Manwaring J, Refaee EE, Fleck S, Fritsch M, Gaab MR, Schroeder HWS, Baldauf J (2018) Endoscopic Third Ventriculostomy before Posterior Fossa Tumor Surgery in Adult Patients. J Neurol Surg A Cent Eur Neurosurg 79:123–129. https://doi.org/10.1055/s-0037-1608786
5. Roux A, Botella C, Still M, Zanello M, Dhermain F, Metellus P, Pallud J (2018) Posterior Fossa Metastasis-Associated Obstructive Hydrocephalus in Adult Patients: Literature Review and Practical Considerations from the Neuro-Oncology Club of the French Society of Neurosurgery. World Neurosurg 117:271–279. https://doi.org/10.1016/j.wneu.2018.06.084
6. Lee SH, Kong DS, Seol HJ, Nam D-H, Lee J-I (2011) Ventriculoperitoneal shunt for hydrocephalus caused by central nervous system metastasis. J Neuro-Oncol 104:545–551. https://doi.org/10.1007/s11060-010-0512-2
7. Mangubat EZ, Chan M, Ruland S, Roitberg BZ (2009) Hydrocephalus in posterior fossa lesions: ventriculostomy and permanent shunt rates by diagnosis. Neurol Res 31:668–673. https://doi.org/10.1179/174313209X380937
8. Marx S, Reinfelder M, Matthes M, Schroeder HWS, Baldauf J (2018) Frequency and treatment of hydrocephalus prior to and after posterior fossa tumor surgery in adult patients. Acta Neurochir 160:1063–1071. https://doi.org/10.1007/s00701-018-3496-x
9. Adams H, Chaichana KL, Avendaño J, Liu B, Raza SM, Quiñones-Hinojosa A (2013) Adult cerebellar glioblastoma: understanding survival and prognostic factors using a population-based database from 1973 to 2009. World Neurosurg 80:e237–e243. https://doi.org/10.1016/j.wneu.2013.02.010
10. Babu R, Sharma R, Karikari IO, Owens TR, Friedman AH, Adamson C (2013) Outcome and prognostic factors in adult cerebellar glioblastoma. J Clin Neurosci 20:1117–1121. https://doi.org/10.1016/j.jocn.2012.12.006
11. Jeswani S, Nuño M, Folkerts V, Mukherjee D, Black KL, Patil CG (2013) Comparison of survival between cerebellar and supratentorial glioblastoma patients: surveillance, epidemiology, and end results (SEER) analysis. Neurosurgery 73:240–246; discussion 246; quiz 246. https://doi.org/10.1227/01.neu.0000430288.85680.37
12. Picart T, Barritault M, Berthillier J, Meyronet D, Vasiljevic A, Frappaz D, Honnorat J, Jouanneau E, Poncet D, Ducray F, Guyotat J (2018) Characteristics of cerebellar glioblastomas in adults. J Neuro-Oncol 136:555–563. https://doi.org/10.1007/s11060-017-2682-7
13. Stark AM, Maslehaty H, Hugo HH, Mahvash M, Mehdorn HM (2010) Glioblastoma of the cerebellum and brainstem. J Clin Neurosci 17:1248–1251. https://doi.org/10.1016/j.jocn.2010.02.015
14. Takahashi Y, Makino K, Nakamura H, Hide T, Yano S, Kamada H, Kuratsu J-I (2014) Clinical characteristics and pathogenesis of cerebellar glioblastoma. Mol Med Rep 10:2383–2388. https://doi.org/10.3892/mmr.2014.2549
15. Picart T, Meyronet D, Pallud J, Dumot C, Metellus P, Zouaoui S, Berhouma M, Ducray F, Bauchet L, Guyotat J, French Brain Tumor DataBase, Club de Neuro-Oncologie of the Société Française de Neurochirurgie (2021) Management, functional outcomes and survival in a French multicentric series of 118 adult patients with cerebellar glioblastoma. J Cancer Res Clin Oncol 147:1843–1856. https://doi.org/10.1007/s00432-020-03474-6
16. Darlix A, Zouaoui S, Rigau V, Bessaoud F, Figarella-Branger D, Mathieu-Daudé H, Trétarre B, Bauchet F, Duffau H, Taillandier L, Bauchet L (2017) Epidemiology for primary brain tumors: a nationwide population-based study. J Neuro-Oncol 131:525–546. https://doi.org/10.1007/s11060-016-2318-3
17. Ng S, Zouaoui S, Bessaoud F, Rigau V, Roux A, Darlix A, Bauchet F, Mathieu-Daudé H, Trétarre B, Figarella-Branger D, Pallud J, Frappaz D, Roujeau T, Bauchet L (2019) An Epidemiology Report for Primary Central Nervous System Tumors in Adolescents and Young Adults: a nationwide population-based study in France, 2008-2013. Neuro-oncology. 22:851–863. https://doi.org/10.1093/neuonc/noz227
18. Rigau V, Zouaoui S, Mathieu-Daudé H, Darlix A, Maran A, Trétarre B, Bessaoud F, Bauchet F, Attaoua R, Fabbro-Peray P, Fabbro M, Kerr C, Taillandier L, Duffau H, Figarella-Branger D, Costes V, Bauchet L, Société Française de Neuropathologie (SFNP), Société Française de Neurochirurgie (SFNC), Club de Neuro-Oncologie of the Société Française de Neurochirurgie (CNO-SFNC), Association des Neuro-Oncologues d'Expression Française (ANOCEF) (2011) French brain tumor database: 5-year histological results on 25 756 cases. Brain Pathol 21:633–644. https://doi.org/10.1111/j.1750-3639.2011.00491.x
19. Zouaoui S, Rigau V, Mathieu-Daudé H, Darlix A, Bessaoud F, Fabbro-Peray P, Bauchet F, Kerr C, Fabbro M, Figarella-Branger D, Taillandier L, Duffau H, Trétarre B, Bauchet L, Société française de neurochirurgie (SFNC) et le Club de neuro-oncologie de la SFNC, Société française de neuropathologie (SFNP), Association des neuro-oncologues d'expression française (ANOCEF) (2012)

French brain tumor database: general results on 40,000 cases, main current applications and future prospects. Neurochirurgie 58:4–13. https://doi.org/10.1016/j.neuchi.2012.01.004

20. Wen PY, Macdonald DR, Reardon DA, Cloughesy TF, Sorensen AG, Galanis E, Degroot J, Wick W, Gilbert MR, Lassman AB, Tsien C, Mikkelsen T, Wong ET, Chamberlain MC, Stupp R, Lamborn KR, Vogelbaum MA, van den Bent MJ, Chang SM (2010) Updated response assessment criteria for high-grade gliomas: response assessment in neuro-oncology working group. J Clin Oncol 28:1963–1972. https://doi.org/10.1200/JCO.2009.26.3541
21. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW (2016) The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 131:803–820. https://doi.org/10.1007/s00401-016-1545-1
22. Kuroiwa T, Numaguchi Y, Rothman MI, Zoarski GH, Morikawa M, Zagardo MT, Kristt DA (1995) Posterior fossa glioblastoma multiforme: MR findings. AJNR Am J Neuroradiol 16:583–589
23. Fukuda M, Oishi M, Kawaguchi T, Watanabe M, Takao T, Tanaka R, Fujii Y (2007) Etiopathological factors related to hydrocephalus associated with vestibular schwannoma. Neurosurgery 61:1186–1192; discussion 1192-1193. https://doi.org/10.1227/01.neu.0000306096.61012.22
24. Gerganov VM, Pirayesh A, Nouri M, Hore N, Luedemann WO, Oi S, Samii A, Samii M (2011) Hydrocephalus associated with vestibular schwannomas: management options and factors predicting the outcome. J Neurosurg 114:1209–1215. https://doi.org/10.3171/2010.10.JNS1029
25. Harati A, Scheufler K-M, Schultheiss R, Tonkal A, Harati K, Oni P, Deitmer T (2017) Clinical features, microsurgical treatment, and outcome of vestibular schwannoma with brainstem compression. Surg Neurol Int 8:45. https://doi.org/10.4103/sni.sni_129_16
26. Miyakoshi A, Kohno M, Nagata O, Sora S, Sato H (2013) Hydrocephalus associated with vestibular schwannomas: perioperative changes in cerebrospinal fluid. Acta Neurochir 155:1271–1276. https://doi.org/10.1007/s00701-013-1742-9
27. Rogg JM, Ahn SH, Tung GA, Reinert SE, Norén G (2005) Prevalence of hydrocephalus in 157 patients with vestibular schwannoma. Neuroradiology 47:344–351. https://doi.org/10.1007/s00234-005-1363-y
28. di Russo P, Fava A, Vandenbulcke A, Miyakoshi A, Kohno M, Evins AI, Esposito V, Morace R (2020) Characteristics and management of hydrocephalus associated with vestibular schwannomas: a systematic review. Neurosurg Rev 44:687–698. https://doi.org/10.1007/s10143-020-01287-2
29. Pirouzmand F, Tator CH, Rutka J (2001) Management of hydrocephalus associated with vestibular schwannoma and other cerebellopontine angle tumors. Neurosurgery 48:1246–1253; discussion 1253-1254. https://doi.org/10.1097/00006123-200106000-00010
30. Ghani E, Zaidi GI, Nadeem M, Rehman L, Noman MA, Khaleeq-Uz-Zaman null (2003) Role of cerebrospinal fluid diversion in posterior fossa tumor surgery. J Coll Physicians Surg Pak 13:333–336. doi: 06.2003/JCPSP.333336
31. Sunderland GJ, Jenkinson MD, Zakaria R (2016) Surgical management of posterior fossa metastases. J Neuro-Oncol 130:535–542. https://doi.org/10.1007/s11060-016-2254-2
32. Taylor WA, Todd NV, Leighton SE (1992) CSF drainage in patients with posterior fossa tumours. Acta Neurochir 117:1–6. https://doi.org/10.1007/bf01400627
33. El-Gaidi MA, El-Nasr AHA, Eissa EM (2015) Infratentorial complications following preresection CSF diversion in children with posterior fossa tumors. J Neurosurg Pediatr 15:4–11. https://doi.org/10.3171/2014.8.PEDS14146
34. Bloch J, Vernet O, Aubé M, Villemure J-G (2003) Non-obstructive hydrocephalus associated with intracranial schwannomas: hyperproteinorrhachia as an etiopathological factor? Acta Neurochir 145:73–78. https://doi.org/10.1007/s00701-002-1021-7
35. Hong B, Polemikos M, Heissler HE, Hartmann C, Nakamura M, Krauss JK (2018) Challenges in cerebrospinal fluid shunting in patients with glioblastoma. Fluids Barriers CNS 15:16. https://doi.org/10.1186/s12987-018-0101-x
36. Ferguson SD, Xiu J, Weathers S-P, Zhou S, Kesari S, Weiss SE, Verhaak RG, Hohl RJ, Barger GR, Reddy SK, Heimberger AB (2016) GBM-associated mutations and altered protein expression are more common in young patients. Oncotarget 7:69466–69478. https://doi.org/10.18632/oncotarget.11617
37. Meyronet D, Esteban-Mader M, Bonnet C, Joly M-O, Uro-Coste E, Amiel-Benouaich A, Forest F, Rousselot-Denis C, Burel-Vandenbos F, Bourg V, Guyotat J, Fenouil T, Jouvet A, Honnorat J, Ducray F (2017) Characteristics of H3 K27M-mutant gliomas in adults. Neuro-oncology 19:1127–1134. https://doi.org/10.1093/neuonc/now274
38. Izquierdo C, Barritault M, Poncet D, Cartalat S, Joubert B, Bruna J, Jouanneau E, Guyotat J, Vasiljevic A, Fenouil T, Berthezène Y, Honnorat J, Meyronet D, Ducray F (2019) Radiological Characteristics and Natural History of Adult IDH-Wildtype Astrocytomas with TERT Promoter Mutations. Neurosurgery 85:E448–E456. https://doi.org/10.1093/neuros/nyy513
39. Di Carlo DT, Cagnazzo F, Benedetto N, Morganti R, Perrini P (2019) Multiple high-grade gliomas: epidemiology, management, and outcome. A systematic review and meta-analysis. Neurosurg Rev 42:263–275. https://doi.org/10.1007/s10143-017-0928-7
40. Weber DC, Miller RC, Villà S, Hanssens P, Baumert BG, Castadot P, Varlet P, Abacioglu U, Igdem S, Szutowicz E, Nishioka H, Hofer S, Rutz HP, Ozsahin M, Taghian A, Mirimanoff RO (2006) Outcome and prognostic factors in cerebellar glioblastoma multiforme in adults: a retrospective study from the Rare Cancer Network. Int J Radiat Oncol Biol Phys 66:179–186. https://doi.org/10.1016/j.ijrobp.2006.04.035
41. Won S-Y, Dubinski D, Behmanesh B, Bernstock JD, Seifert V, Konczalla J, Tritt S, Senft C, Gessler F (2019) Management of hydrocephalus after resection of posterior fossa lesions in pediatric and adult patients-predictors for development of hydrocephalus. Neurosurg Rev 43:1143–1150. https://doi.org/10.1007/s10143-019-01139-8
42. Won S-Y, Gessler F, Dubinski D, Eibach M, Behmanesh B, Herrmann E, Seifert V, Konczalla J, Tritt S, Senft C (2019) A novel grading system for the prediction of the need for cerebrospinal fluid drainage following posterior fossa tumor surgery. J Neurosurg 132:296–305. https://doi.org/10.3171/2018.8.JNS181005
43. Reddy GK, Bollam P, Caldito G, Willis B, Guthikonda B, Nanda A (2011) Ventriculoperitoneal shunt complications in hydrocephalus patients with intracranial tumors: an analysis of relevant risk factors. J Neuro-Oncol 103:333–342. https://doi.org/10.1007/s11060-010-0393-4
44. Chen CC, Kasper E, Warnke P (2011) Palliative stereotactic-endoscopic third ventriculostomy for the treatment of obstructive hydrocephalus from cerebral metastasis. Surg Neurol Int 2:76. https://doi.org/10.4103/2152-7806.82083
45. Gonda DD, Kim TE, Warnke PC, Kasper EM, Carter BS, Chen CC (2012) Ventriculoperitoneal shunting versus endoscopic third ventriculostomy in the treatment of patients with hydrocephalus related to metastasis. Surg Neurol Int 3:97. https://doi.org/10.4103/2152-7806.100185
46. Di Vincenzo J, Keiner D, Gaab MR, Schroeder HWS, Oertel JMK (2014) Endoscopic third ventriculostomy: preoperative considerations and intraoperative strategy based on 300 procedures. J Neurol Surg A Cent Eur Neurosurg 75:20–30. https://doi.org/10.1055/s-0032-1328953

47. Grand W, Leonardo J, Chamczuk AJ, Korus AJ (2016) Endoscopic Third Ventriculostomy in 250 Adults With Hydrocephalus: Patient Selection, Outcomes, and Complications. Neurosurgery 78:109–119. https://doi.org/10.1227/NEU.0000000000000994
48. Isaacs AM, Bezchlibnyk YB, Yong H, Koshy D, Urbaneja G, Hader WJ, Hamilton MG (2016) Endoscopic third ventriculostomy for treatment of adult hydrocephalus: long-term follow-up of 163 patients. Neurosurg Focus 41:E3. https://doi.org/10.3171/2016.6.FOCUS16193

Affiliations

Thiébaud Picart[1,2,3] · Chloé Dumot[1,2,4] · David Meyronet[2,3,5] · Johan Pallud[6,7,8] · Philippe Metellus[9,10] · Sonia Zouaoui[11,12] · François Ducray[2,3,13] · Isabelle Pelissou-Guyotat[1] · Moncef Berhouma[1,2,14] · Luc Bauchet[11,12,15] · Jacques Guyotat[1] · French Brain Tumor DataBase · Club de Neuro-Oncologie of the Société Française de Neurochirurgie

[1] Hospices Civils de Lyon, Hopital Neurologique Pierre Wertheimer, Department of Neurosurgery, 59 Boulevard Pinel, 69667 Bron, France

[2] Claude Bernard University, Lyon, France

[3] Department of Cancer Cell Plasticity–INSERM U1052, Cancer Research Center of Lyon, Lyon, France

[4] CarMeN laboratory, Inserm U1060, INRA U1397 INSA Lyon, Université Claude Bernard Lyon 1, Lyon, France

[5] Hospices Civils de Lyon, Groupe Hospitalier Est, Department of Neuropathology, Bron, France

[6] GHU Paris, Site Sainte-Anne, Department of Neurosurgery, Paris, France

[7] Universités de Paris, Paris, France

[8] IMA-Brain, INSERM U894, Institut de Psychiatrie et Neurosciences de Paris, Paris, France

[9] Privé Clairval, Ramsay Général de Santé, Marseille, France

[10] Institut de Neurophysiopathologie-UMR 7051, Université d'Aix-Marseille, Marseille, France

[11] Department of Neurosurgery CHU, Montpellier University Hospital, Montpellier, France

[12] FBTDB (French Brain Tumor DataBase), ICM, Montpellier, France

[13] Hospices Civils de Lyon, Hopital Neurologique Pierre Wertheimer, Department of Neurooncology, Bron, France

[14] CREATIS Laboratory, Inserm U1206, UMR 5220, Université de Lyon, Villeurbanne, France

[15] Institut des Neurosciences de Montpellier - INSERM U1051, Hôpital Saint Eloi, Montpellier, France

[16] Fabienne Bauchet (FBTDB, ICM Montpellier), Rim Ben Mhamed (CHU Montpellier), Faiza Bessaoud (Registre Tumeur Herault, Montpellier), Valerie Rigau (CHU Montpellier), Helene Mathieu-Daude (ICM Montpellier), Amélie Darlix (ICM Montpellier), Pascale Fabbro-Peray (CHU N mes), Brigitte Trétarre (Registre Tumeur Hérault), Montpellier, France

[17] Hugues Loiseau (CHU Bordeaux), Jean-Rodolphe Vignes (CHU Bordeaux), Mathilde Guibourd de Luzinais (CHU Bordeaux), Matthieu Peyre (APHP–Hopital La Pitie Salpetriere), Eric Bord (CHU Nantes), Edouard Samarut (CHU Nantes), Romuald Seizeur (CHU Brest), Walid Farah (CHU Dijon), Anne Herbrecht (APHP–Kremlin Bicetre), Nicolas Reyns (CHU Lille), Jimmy Voirin (CH Colmar), Helene Cebula (CHU Strasbourg), Evelyne Emery (CHU Caen), Adrien Simonneau (Fondation-Ophtalmologique Rothschild), Philippe Caillaud (CHU Bayonne), Philippe Menei (CHU Angers), Gwenaelle Soulard (CHU Angers), Bertrand Muckensturm (CH Orleans), Fabien Rech (CHU Nancy), Fabien Almairac (CHU Nice), Marie Onno (CHU Nice), Marine Lecorre (CHU Montpellier), Arnaud Dagain (HIA Sainte-Anne - Toulon), Francois Vassal (CHU Saint-Etienne), Benjamin Pommier (CHU Saint-Etienne), Emmanuel Gay (CHU Grenoble), Emmanuel De Schlichting (CHU Grenoble), Hassan El-Fertit (CHU Nimes), Andre Maillard (CH Perpignan), Emmanuel Mandonnet (APHP–Hopital Lariboisiere), Thibault Passeri (APHP–Hopital Lariboisiere), Jean-Jacques Lemaire (CHU Clermont-Ferrand), Remy Chaix (CHU Clermont-Ferrand), Mathilde Fouet (HIA Percy–Clamart), Jean-Christophe Sol (CHU Toulouse), Imene Djidjelli (CHU Toulouse), Stephane Gaillard (Paris–Foch), Olivier Langlois (CHU Rouen), Francois-Xavier Ferracci (CHU Rouen), Henri Dufour (APHM–La Timone) Pierre-Hugues Roche (APHM–Hopital Nord), Sebastien Boissonneau (APHM–La Timone), Christine Desenclos (CHU Amiens), Thierry Faillot (APHP–Beaujon), Ilyess Zemmoura (CHU Tours), Pierre-Jean Le Reste (CHU), Rennes, France