Prognosis of Patients with Multifocal Glioblastoma: A Case-Controlled Study

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Introduction

The prognosis of patients with multifocal glioblastoma is not well documented. We aimed to determine whether multifocal disease on initial presentation is associated with worse survival.

Methods

We retrospectively reviewed records of 368 newly diagnosed GBM patients and identified 47 patients with multifocal tumors. Each multifocal patient was matched with a solitary GBM patient on the basis of age, KPS, and extent of resection using a propensity score matching methodology. Radiation and temozolomide treatments were also well matched between the two cohorts. Kaplan-Meir estimates and log-rank tests were used to compare survival.

Table 1. Characteristics of original and matched cohorts of newly diagnosed glioblastoma patients.

	Original Population			Matched Population		
	Multifocal	Unifocal		Multifocal	Unifocal	
Characteristics	N (%)	N (%)	p value	N (%)	N (%)	P value
Number of Patients	47	169		47	47	
Age in years			.76			.97
mean (SD)	62.9 (13.9)	60.2 (14.5)		62.7 (13.9)	62.8 (15.6)	
median	62	62		61	66	
Extent of Resection			<.0001			1.00
biopsy	27 (57.5)	41 (24.0)		27 (57.5)	27 (57.5)	
gross total resection	4 (8.5)	61 (35.7)		4 (8.5)	4 (8.5)	
near gross total resection	2 (4.3)	27 (15.8)		2 (4.3)	2 (4.3)	
partial resection	14 (29.8)	42 (24.6)		14 (29.8)	14 (29.8)	
Karnofsky Performance Score			.25			.80
KPS≤70	11 (23.4)	28 (16.2)		11 (23.4)	10 (21.3)	

Results

The median age of multifocal patients was 61 years, 76.6% had KPS>70, and 87.3% had either a biopsy or partial tumor resection. The 47 multifocal patients were almost perfectly matched on the basis of age (p=.97), extent of resection (p=1.0), and KPS (p=.80) with 47 solitary GBM patients. Age (>65), partial resection or biopsy, and low KPS (<70) were associated with worse median survival within the multifocal group. 19 multifocal patients had tumor progression on post-radiation imaging while 11 unifocal patients had tumor progression (p=0.08). Multifocal patients had a significantly shorter median overall survival of 6 months [95% CI: 4-10] compared to the 11 month [95% CI: 10-19] median survival of matched solitary GBM patients (log-rank test, p=.02). Two-year survival rates were 4.3% and 29.0% for the multifocal and unifocal cohorts, respectively. The hazard of death in the multifocal group nearly doubled that of the unifocal group (HR 1.8, CI: 1.1-3.1, p=.02). Tumor samples were analyzed for expression of pMAPK, PTEN, MGMT, Laminin Beta 1 and 2, as well as EGFR amplification with no significant differences detected in expression profiles between the multifocal and solitary GBM groups.

Table 2. Univariate analysis of the association between patient and tumor characteristics and median survival for the multifocal cohort.

Characteristics	Multifocal median survival	p value
Age in years		.0007
≤65	12 [5, 17]	
65+	4 [1, 6]	
Extent of Resection		.04
high	14 [6, NA]	
low	5 [4, 9]	
KPS Score		.04
KPS≤70	9 [5, 12]	
KPS>70	3 [0, 6]	

*23(48.9%) and 24 (51.1%) patients had age ≤65 and 65+, respectively.
**6(12.8%) and 41 (87.2%) patients had high and low, respectively.
***10 (21.3%) and 37 (78.7%) patients had KPS≤70 and KPS>70, respectively.

Learning Objectives

By the conclusion of this session, participants should be able to:

1. Discuss the difference in overall survival, prognosis, and tumor progression between newly diagnosed multifocal and unifocal GBM patients.

2. Discuss various proposed mechanisms of pathogenicity for multifocality in GBM.

3. Recognize the need for further molecular marker analyses for multifocal GBMs and recognize the possible implications of multifocal GBM having a separate tumor biology than that of unifocal counterparts.

Conclusions

Newly diagnosed GBM patients with multifocal disease on presentation have significantly worse survival than solitary GBM patients.

Table 3. Analysis of molecular markers in newly diagnosed GBM, multifocal and unifocal matched patients.

	Matched Population		
	Multifocal	Unifocal	
Characteristics	N (%)	N (%)	p
Laminin beta1			.23
normal	0 (0)	3 (7.5)	
over expressed	15 (57.7)	17 (53.1)	
under expressed	11 (42.3)	20 (50.0)	
Laminin beta2			.85
normal	3 (11.1)	4 (9.5)	
over expressed	13 (48.2)	18 (42.9)	
under expressed	11 (40.7)	20 (47.6)	
pMAPK Expression Level			.75
level 1 (≤10)	37 (75.5)	34 (73.3)	
level 2 (10<expression ≤40)	3 (6.1)	5 (10.6)	
level 3 (expression>40)	9 (18.4)	8 (17.0)	
EGFR Expression			.59
normal	6 (54.5)	11 (64.7)	
abnormal	5 (45.5)	6 (35.3)	
PTEN			.97
Loss	15 (60.0)	26 (60.5)	
Retained	10 (40.0)	17 (39.5)	
MGMT			.81
≤5	12 (38.7)	18 (40.0)	
≤20	6 (19.4)	11 (24.4)	
20+	13 (41.9)	16 (35.6)	

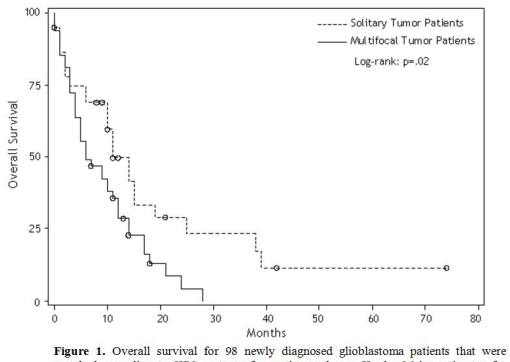

Figure 1. Overall survival for 98 newly diagnosed glioblastoma patients that were matched according to KPS, extent of resection and age. Kaplan-Meier estimates for overall survival in months for newly diagnosed multifocal (solid-line) and unifocal (dashed-line) GBM patients.