Low Grade Gliomas: Defining The Best Clinical Approach in the Multiply Deleted Patient

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Introduction

Recent advances in our understanding of the biology of low grade gliomas (LGGs) have highlighted the importance of molecular classification of these tumors. 1p/19q co-deletion and IDH mutational status have emerged as positive prognosticators. However, clinical strategies are lagging behind and continue to be debated. We present preliminary results of our twenty-year low grade glioma experience and our proposal to create an interactive database that integrates clinical and molecular annotations allowing multi-parameter queries for future clinical and research purposes.

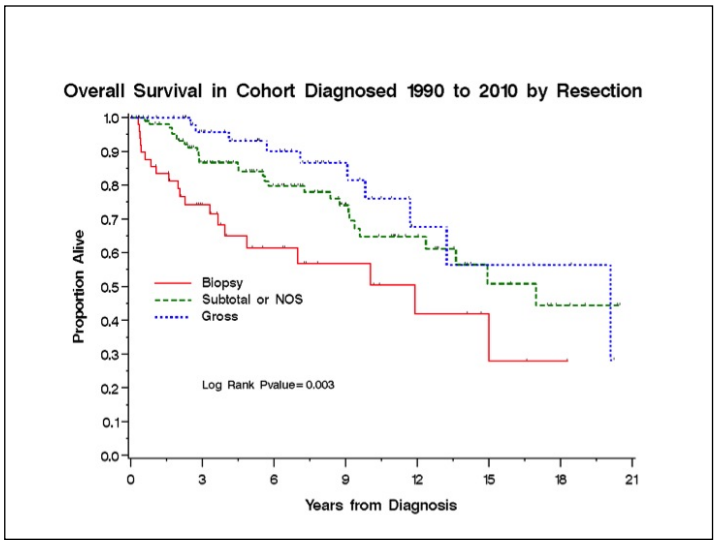
Methods

All available cases of pure grade II (WHO classification) gliomas, including oligodendrogliomas, astrocytomas and oligoastrocytomas were extracted from an existing cancer database at Memorial Sloan Kettering Cancer Center (MSKCC). Key clinical parameters were entered into a new database comprised only of patients with tissue diagnosed grade II gliomas. Grade I, mixed grade II/III and cases with indeterminate histologic grades were excluded. Availability of pathology information varied from simple histologic WHO grading to FISH for 1p/19q and immunohistochemistry for IDH status. Retrospective testing for 1p/19q and IDH status was performed whenever possible. In addition, we imported a more comprehensive molecular profile that uses a Nanostring platform for the multiplexed profiling of multiple genes.

Table 1. Demographics and Characteristics of Patients Diagnosed with Low Grade Glioma 1990-2010

Variable	Level	N	%
Histology	Astrocytoma	88	40
	Oligodendroglioma	90	41
	OligoAstrocytoma	41	19
Extent of Resection	Biopsy	50	23
	Subtotal	103	47
	Gross	57	26
	NOS	9	4
Gender	Male	118	54
	Female	101	46
Race	W	178	81
	B	13	6
	H	7	3
	A	10	5
	O	5	2
	Unk	6	3
IDH	Negative	1	0.5
	Positive	27	12
	Null	191	87
1p19q	Negative	42	19
	Positive	58	26
	Null	119	54
Radiation	No	93	42
	Yes	126	58
Chemotherapy	No	80	37
	Yes	139	63
Age*	<Median	111	51
	Median+	108	49

*Median age was 37; Mean age was 40; Minimum age was 18; Maximum age was 77.



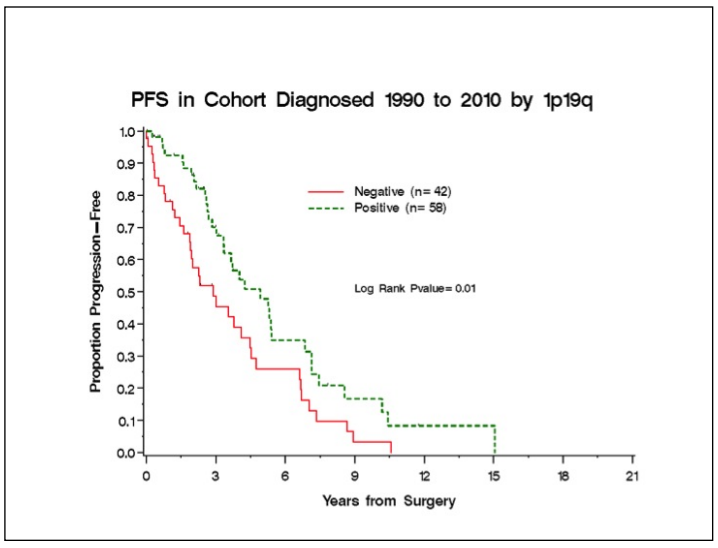
Results The median overall survival (OS) for the gross total group was 20 years, compared to 11.9 years for the biopsy group. The median survival for the subtotal group was 17 years. Progression free survival (PFS) for the biopsy, subtotal and gross total groups were 2.9, 3.8 and 5.4 years respectively-all statistically significant. Median PFS was 4.9 years for the 1p/19q positive group, and 6.7 years for the IDH positive group. However only 22% of our patient sample had completed IDH testing by the time of this analysis. Nanostring results revealed an overwhelming proneural designation in the analyzed sample.

Table 2. Overall Survival and PFS for Low Grade Glioma Patients Diagnosed from 1990-2010

Cohort	N (%)	Median OS	95% CI	Log Rank Pvalue	Median PFS	95% CI	Log Rank Pvalue
1990-2010	219	15 years	11.9-no UL	N/A	4.1 years	3.4-4.7	N/A
Biopsy	50 (23)	11.9 years	3.9-no UL	0.003	2.9 years	1.9-5.8	0.30
Subtotal or NOS	112 (51)	17 years	12.3-no UL		3.8 years	3.1-4.7	
Gross	57 (26)	20 years	11.7-no UL		5.4 years	3.3-6.8	
1p19q Negative	42 (19)	9.6 years	7.0-15.0	0.001	2.9 years	1.9-4.5	0.01
1p19q Positive	58 (26)	Median Not Reached			4.9 years	3.3-6.8	
IDH Negative	1 (0.5)	No Events		N/A	No Events		N/A
IDH Positive	27 (12)	Median Not Reached			6.7 years	3.0-8.1	
Astrocytoma	88 (40)	9.6 years	7.3-no UL	0.0003	3.3 years	2.7-4.1	0.009
Oligodendroglioma	90 (41)	Median Not Reached			5.4 years	4.0-6.8	
OligoAstrocytoma	41 (19)	15 years	9.1-20.1		3 years	2.0-4.6	

Conclusions

Our results were used to initiate an interactive database. The database is a catalogue of low grade glioma patients treated at MSKCC and will be a resource to track trends and investigate treatment responses in patients with these classically slow growing tumors. Complete analysis of the database will allow us to answer more specific research questions, such as whether biopsy only IDH positive tumors perform as well as those initially treated with open resection. Eventually we will use these results to design prospective trials aimed at predicting the best overall treatment strategy with regards to timing of surgery, radiation and chemotherapy in low grade gliomas with a known molecular profile. The addition of the Nanostring platform has allowed for the profiling of multiple genes. This platform was developed in house to allow rapid and cost efficient classification along TCGA subtypes and is a unique feature of our database.



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