Analysis of Outcomes of Multidisciplinary Management of Gliosarcoma: A Single-Center Study, 2000–2013

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■ BACKGROUND: **Gliosarcoma is a rare tumor of the central nervous system with a reported incidence of ~2%–8% of all gliomas. We reviewed the outcomes of patients treated at our institution over a 14-year period from 2000 to 2013 to characterize overall survival (OS) and progression-free survival as well as to elucidate the additive effect of chemoradiotherapy.**

■ METHODS: **From January 1, 2000 to December 31, 2013, we retrospectively reviewed the clinical notes of all patients treated at our institution with a histopathologic diagnosis of gliosarcoma. This review yielded 21 patients whose clinicoradiologic data were analyzed with respect to age, sex, ethnicity, preoperative/postoperative Glasgow Coma Scale and Karnofsky Performance Scale, location, extent of resection, methylguanine DNA methyl transferase methylation status, and administration of adjuvant therapy.**

■ RESULTS: **The median age was 58 years (range, 40–80 years) with a male preponderance (1.6:1). Tumor location was mainly temporal ($n = 6$) but also parietal ($n = 5$), frontal ($n = 4$), multilobar ($n = 4$), and cerebellar ($n = 1$). Surgical resection was deemed to be total in 15 patients and subtotal in 6 patients. Methylguanine DNA methyl transferase methylation status was available for only 5 patients, with a methylation rate of 60% (3/5) and no impact on survival. Nine patients received both radiotherapy and chemotherapy (OS, 7.9 months), 7 received radiotherapy only (OS, 5.7 months), and 5 patients received no adjuvant therapy (OS, 1.4 months). The overall median survival was 5.7 months (range, 1–21.5 months) and median progression-free survival was 5 months (range, 1.4–12.4 months).**

■ CONCLUSIONS: **Despite an overall poor prognosis, a multimodality approach aiming for complete resection followed by radiotherapy and chemotherapy appears to be associated with better outcomes.**

INTRODUCTION

Gliosarcoma is a grade IV neoplasm variant of glioblastoma (GBM) with distinct biphasic glial and sarcomatous components as per the 2007 World Health Organization classification of brain tumors.[1,2] It was first described by Stroebe in 1895[1] as a GBM with sarcomatous elements. It gained wide acceptance through landmark studies by Feigin et al.[3] and Rubinstein et al.,[4] who discussed the origin of the sarcomatous components by presenting several cases in detail. The 2007 World Health Organization definition includes a variant of GBM showing biphasic tissue pattern with alternating areas showing glial and mesenchymal differentiation.[2] The glial component fulfils the criterion of a GBM and the mesenchymal differentiation can include osseous,[5,6] cartilaginous,[7] myoblastic, and lipomatous elements.[1,8] However, there is no consensus on the exact origin of the mesenchymal component or the minimum percentage of mesenchymal differentiation needed to consider a tumor gliosarcoma.

Much of the current literature related to gliosarcoma consists of case reports and there are only a few case series. We present a series of 21 patients diagnosed and treated at Auckland City Hospital over a 14-year period and analyze the impact of various clinicopathologic factors on the outcomes of this rare tumor.

Key words
- Chemotherapy
- Gliosarcoma
- MGMT
- Prognosis
- Radiotherapy

Abbreviations and Acronyms
GBM: Glioblastoma
KPS: Karnofsky Performance Scale
MGMT: Methylguanine DNA methyl transferase
OS: Overall survival
PFS: Progression-free survival

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Table 1. Patient Characteristics

Case	Age (years)	Sex	Preoperative Karnofsky Performance Scale	Location	Surgery	Radiotherapy	Chemotherapy	Methylguanine DNA Methyltransferase Methylation Status	Survival (months)
1	58	F	90	Parietal	GTR	EBR	N/A	Unknown	5.03
2	53	M	80	Temporal	GTR	EBR	N/A	Unknown	16.79
3	71	F	90	Parietal	GTR	N/A	N/A	Unknown	0.88
4	59	F	70	Temporoparietal	GTR	EBR	N/A	Unknown	7.46
5	53	F	70	Parietal	GTR	EBR	Lomustine	Unknown	11.07
6	71	M	70	Frontoparietal	STR	EBR	N/A	Unknown	4.34
7	50	M	40	Frontoparietal	STR	EBR	N/A	Unknown	5.68
8	53	M	90	Temporal	GTR	EBR	TMZ	Unknown	7.92
9	58	M	70	Parietal	GTR	EBR	N/A	Unknown	6.8
10	80	M	80	Temporal	GTR	N/A	N/A	Unknown	1.35
11	76	M	80	Temporal	STR	EBR	TMZ	Unknown	2.37
12	62	M	90	Temporal	GTR	EBR	TMZ	Unknown	10.65
13	43	F	90	Parietal	GTR	EBR	TMZ	Unknown	14.16
14	72	F	80	Frontal	GTR	EBR	TMZ	Unknown	7.56
15	40	M	80	Frontal	GTR	N/A	N/A	Unknown	21.36
16	53	M	80	Temporal	STR	EBR	TMZ	Unknown	21.55
17	61	M	90	Frontal	STR	EBR	TMZ	Methylated	5.19
18	65	M	80	Frontal	GTR	EBR	N/A	Nonmethylated	3.71
19	51	F	70	Parietotemporal	STR	EBR	Lomustine	Nonmethylated	3.94
20	73	F	50	Parietotemporal	GTR	N/A	N/A	Methylated	1.05
21	54	M	50	Cerebellar	GTR	N/A	N/A	Methylated	2.14

F, female; GTR, gross total resection; EBR, external beam radiation; N/A, not applicable; M, male; STR, subtotal resection; TMZ, temozolomide.

METHODS

The neuropathology records of the Department of Pathology, Auckland City Hospital, Auckland, New Zealand over a 14-year period between 2000 and 2013 were retrospectively analyzed. Twenty-one patients with histopathologically confirmed gliosarcoma who underwent treatment at the Department of Neurosurgery were identified. Original imaging studies were available in all cases.

The clinicopathologic features of these cases were analyzed with respect to age, sex, ethnicity, preoperative and postoperative Glasgow Coma Scale and Karnofsky Performance Scale (KPS) scores, tumor location, extent of resection, methylguanine DNA methyl transferase (MGMT) promoter methylation status and the type of adjuvant therapy.

Complete clinical follow-up from diagnosis until death was available for all patients through the electronic clinical records. Overall survival (OS) was calculated as the period from the date of surgery to the date of death using the product limit method of Kaplan and Meier.[9] Progression-free survival (PFS) was calculated as the date of surgery to date of increase in tumor size on follow-up imaging or symptomatic recurrence, whichever occurred earlier.

The log rank test was used to test for statistically significant differences[10] in survival and Kaplan-Meier survival curves were generated. A P value of <0.05 was considered significant. All statistical analyses were performed using the commercially available statistical software SPSS version 22 (IBM Corp., Armonk, New York, USA).

All patients underwent surgical resection as the primary treatment. This was defined as gross total or subtotal based on immediate postoperative imaging in the form of contrast-enhanced cranial magnetic resonance imaging and/or computed tomography scan, or the neurosurgeon's intraoperative opinion where no such imaging was available.

RESULTS

No patient was lost to follow-up and all patients were dead at the time of analysis. Patient characteristics are compiled in Table 1.

Age and Sex

The mean age at presentation was 60 years. The median age at presentation was 58 years (range, 40–80 years). Most patients in