Secondary gliosarcoma after diagnosis of glioblastoma: clinical experience with 30 consecutive patients

Clinical article

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Object. Gliosarcoma can arise secondarily, after conventional adjuvant treatment of high-grade glioma. The current literature on the occurrence of secondary gliosarcoma (SGS) after glioblastoma multiforme (GBM) is limited, with only 12 reported cases. The authors present a large series of histologically confirmed SGSs, with follow-up to describe the clinical and radiological presentation, pathological diagnosis, and treatment outcomes.

Methods. Gliosarcoma cases were identified using the University of California, San Francisco’s Departments of Neurological Surgery and Neuropathology databases. Through a retrospective chart review, cases of gliosarcoma were considered SGS if the following inclusion criteria were met: 1) the patient had a previously diagnosed intracranial malignant glioma that did not have gliosarcoma components; and 2) the histopathological tissue diagnosis of the recurrence confirmed gliosarcoma according to the most current WHO criteria. Extensive review of clinical, surgical, and pathological notes was performed to gather clinical and pathological data on these cases.

Results. Thirty consecutive patients in whom SGS had been diagnosed between 1996 and 2008 were included in the analysis. All patients had previously received a diagnosis of malignant glioma. For the initial malignant glioma, all patients underwent resection, and 25 patients received both external-beam radiation and chemotherapy. Three patients received radiotherapy alone, 1 patient was treated with chemotherapy alone, and 1 patient’s tumor rapidly recurred as gliosarcoma, requiring surgical intervention prior to initiation of adjuvant therapy. The median time from diagnosis of the initial tumor to diagnosis of gliosarcoma was 8.5 months (range 0.5–25 months). All but 1 patient (who only had a biopsy) underwent a second operation for gliosarcoma; 8 patients went on to receive radiotherapy (4 had brachytherapy, 3 had external-beam radiation, and 1 had Gamma Knife surgery); and 14 patients received additional chemotherapy. The median length of survival from the time of gliosarcoma diagnosis was 4.4 months (range 0.7–46 months). The median survival from the time of the original GBM diagnosis was 12.6 months (range 5.7–47.4 months). Patients who had received concurrent and adjuvant temozolomide for GBM had worse outcomes than those who had not (4.3 and 10.5 months, respectively; p = 0.045). There was no difference in time to diagnosis of gliosarcoma in these 2 groups (8 and 8.5 months; p = 0.387). Two patients who had not received radiation therapy for GBM had an anecdotally very prolonged survival (20.9 and 46.4 months).

Conclusions. The data underscore the difficulty associated with management of this disease. The strikingly poor survival of patients with SGS who had previously received combined radiation and temozolomide chemotherapy for GBM may reflect a unique molecular profile of GBM that eventually recurs as SGS. Further work will be required, controlling for multiple prognostic factors with larger numbers of patients. (DOI: 10.3171/2009.9.JNS09931)

Key Words • glioblastoma multiforme • secondary gliosarcoma • outcome analysis

Gliosarcoma is a rare malignant CNS tumor composed of distinct gliomatous and sarcomatous elements. It is considered a Grade IV neoplasm and a variant of GBM, according to the 2007 WHO classification scheme.12 Gliosarcomas are widely viewed as clinically similar to GBM; however, recent evidence suggests that gliosarcoma is a distinct entity. An epidemiological study by Kozak and colleagues10 reported a worse prognosis in patients with gliosarcoma than in those with GBM, and pathological and genetic studies have shown unique genetic profiles in gliosarcoma tissue distinct from those found in GBM.1,2,20

The currently accepted criteria for diagnosis of gliosarcoma include a well-circumscribed lesion with clearly identifiable glial and metaplastic mesenchymal components.16 Histologically, the glial component meets the cytological criteria of GBM, and the mesenchymal component may display a wide variety of morphological features, with origins from fibroblastic, cartilaginous, os-

Abbreviations used in this paper: AA = anaplastic astrocytoma; BCNU = carmustine; CCNU = lomustine; GBM = glioblastoma multiforme; GKS = Gamma Knife surgery; GTR = gross-total resection; PGS = primary gliosarcoma; SGS = secondary gliosarcoma; STR = subtotal resection; UCSF = University of California, San Francisco.
Secondary gliosarcoma after diagnosis of glioblastoma multiforme

Most reported cases of gliosarcoma develop de novo and are termed PGS, whereas those diagnosed subsequent to GBM that has been previously resected and irradiated are considered to be SGS. The SGS lesions are distinct from radiation-induced gliosarcoma, which are tumors that arise after intracranial radiation without the prior presence of GBM. Due to the rarity of gliosarcoma, experience reported in the literature is limited. Although early reports have suggested their clinical similarity to GBM, our own review of the published literature has identified a number of clinical and pathological characteristics that distinguish PGS from GBM. Despite these clear differences, all patients with gliosarcoma continue to be treated in a manner similar to patients with GBM, and SGS is managed in a manner similar to recurrent GBM.

The role of radiation in the induction of SGS remains speculative. Perry and colleagues first discussed the need to distinguish SGS from PGS by showing an anecdotal difference in survival between 7 patients with SGS and 25 with PGS. Our own review of the literature has revealed only 12 cases of SGS reported to date. In these patients, the mean survival was 57 weeks, and the mean latency from radiation to gliosarcoma diagnosis was 44.8 weeks. In this report, we present the largest series to date, which includes 30 confirmed cases of SGS.

**Methods**

Cases of SGS were initially identified by searching the database of the UCSF Department of Pathology, with dates of diagnosis ranging from 1996 to 2008. The clinical histories of these patients were collected by performing a retrospective chart review. The cases were deemed SGS and included in our analysis if the following criteria were met: 1) the patient had a history of GBM that was treated after diagnosis; and 2) the pathological diagnosis of samples obtained from subsequent resection confirmed gliosarcoma, according to the WHO criteria described below. Detailed clinical, radiological, and pathological features of the cases were collected through the chart review. The resection was deemed to be either a GTR or an STR, based on review of postoperative imaging. The final histological diagnosis was established using the 2007 WHO criteria, as follows: 1) the presence of dual morphological findings in the tumor on H & E staining (one finding of glial and the other of spindle morphological features); 2) positive staining of the area of glial morphological features by antibodies against glial markers (GFAP and Olig2); and 3) the area that appeared sarcomatous on H & E staining was negative for glial markers, yet positive for mesenchymal markers (reticulin). All cases received central pathology review. The time of survival was calculated from the date of diagnosis to the date of death (acquired through the Social Security Death Index). Statistical significance for differences in overall survival and time to progression to SGS was tested using the log-rank test (univariate analysis), and the t-test was used elsewhere when appropriate. The study protocol was reviewed and approved by the UCSF Institutional Review Board and Committee for Human Research (H41995–32867–01).

**Results**

**Clinical Characteristics of Patients**

Our series included 30 consecutive patients with SGS that was diagnosed and treated at UCSF between 1996 and 2008. There were 18 men and 12 women, and their mean age was 54 years at diagnosis of SGS (range 42–72 years). Secondary gliosarcoma was discovered in the left hemisphere in 16 cases (53%), and it most commonly localized in the temporal lobe (13 cases, 43% of patients). Other locations of SGS included the frontal lobe in 5 patients (17%), parietal lobe in 3 patients (10%), parietooccipital lobes in 3 patients (10%), and the occipital lobe, frontoparietal lobes, frontotemporal lobes, temporoparietal lobes, and in the scalp and subgaleal space in 1 patient each. In all but 1 patient with the scalp/subgaleal metastasis, SGS was diagnosed in the same location as the previous GBM diagnosis. Although studies were not uniformly performed, routine studies and examinations did not report other cases of extracranial metastases.

**Initial Management of Malignant Glioma/GBM**

All patients had a prior diagnosis of GBM. Two of the patients had a history of secondary GBM (one progressed from an AA after 18 months, and the other progressed from a low-grade astrocytoma 4 years after diagnosis [Cases 23 and 30]). The patient in whom AA was originally diagnosed was initially treated with resection and GKS, received resection and chemotherapy with tamoxifen, phosphonoacetic acid, and carboplatin for secondary GBM, and then underwent resection with 125I implants, followed by external-beam and etoposide therapies 8 months later when SGS was diagnosed. In the patient with the initial low-grade astrocytoma diagnosis, the disease was managed with surgery and external radiation, and the individual was given temozolomide for secondary GBM, and irinotecan and tamoxifen 17 months later when the tumor recurred as SGS.

As treatment for GBM, all patients underwent resection, and 28 patients received external-beam radiation. Chemotherapy was given to 26 patients, and the agents used included tamoxifen, carboplatin, BCNU, irinotecan, erlotinib, temozolomide, and bevazucimab. A total of 25 patients received radiotherapy followed by chemotherapy, 3 patients were treated postoperatively with radiation therapy alone, and 1 patient was treated with chemotherapy alone (Table 1). One patient’s tumor rapidly recurred as gliosarcoma within 1 month after STR of the primary glioma, and she did not receive any adjuvant therapy (Case 26). After SGS diagnosis, this patient went on to receive external-beam radiation, GKS, and temozolomide. Another patient did not receive adjuvant external-beam radiation therapy due to strong personal preference (Case 23). Radiation with concurrent and adjuvant temozolomide therapy was used in 16 patients.

**Time to Progression to SGS**

Gliosarcoma was diagnosed at the first recurrence in 18 patients, at second recurrence in 10, and at third recurrence in 2. The median latency of SGS induction,
calculated from time of diagnosis of GBM to time of SGS diagnosis, was 8.5 months (mean 9.56 months, range 0.5–25 months). There were no significant differences in time to progression to SGS between cohorts that received different modalities of therapy for the GBM. The time to diagnosis of SGS did not differ significantly in patients who received radiotherapy with concurrent and adjuvant temozolomide as management for GBM, compared with those not treated with this regimen (8 and 8.5 months, respectively; p = 0.387 [see Fig. 2]).

**Radiographic Characteristics of SGS**

All patients underwent preoperative MR imaging to characterize the SGS. An enhancing mass was discovered

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Initial Dx</th>
<th>Extent of Resection for GBM</th>
<th>Adjuvant Therapy for Glioma</th>
<th>Time to SGS (mos)</th>
<th>Location of SGS†</th>
<th>Survival From SGS (mos)</th>
<th>Therapy for SGS</th>
<th>Overall Survival After Initial Glioma Dx (mos)</th>
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<td>1</td>
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<td>EBR, hydroxyurea, carboplatin, tamoxifen</td>
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<td>lt P/O</td>
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<td>5.73</td>
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<td>2</td>
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<td>GBM</td>
<td>STR</td>
<td>EBR + concurrent temozolomide, BCNU, tamoxifen</td>
<td>5.5</td>
<td>rt F/T/P</td>
<td>1.6</td>
<td>none</td>
<td>7.1</td>
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<td>3</td>
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<td>GTR</td>
<td>EBR</td>
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<td>lt P</td>
<td>2.9</td>
<td>none</td>
<td>7.4</td>
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<td>GTR</td>
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<td>GBM</td>
<td>GTR</td>
<td>EBR</td>
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<td>rt T</td>
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<td>$^{125}$I implant</td>
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<td>GTR</td>
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<td>lt T</td>
<td>4.0</td>
<td>temozolomide</td>
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<td>7</td>
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<td>GTR</td>
<td>EBR + concurrent temozolomide, erlotinib, IL-13 pseudomonal toxin</td>
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<td>rt T</td>
<td>4.2</td>
<td>none</td>
<td>10.2</td>
</tr>
<tr>
<td>8</td>
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<td>GTR</td>
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<td>6.0</td>
<td>rt F</td>
<td>4.4</td>
<td>heat shock protein vaccine</td>
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<td>rt T</td>
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<td>GKS</td>
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<td>GTR</td>
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<td>scalp/sub-galeal</td>
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<td>EBR</td>
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<td>GTR</td>
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<td>rt F/P</td>
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<td>erlotinib</td>
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<td>STR</td>
<td>EBR, 6-dimethyl protocol</td>
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<td>rt P</td>
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<td>IL-13 pseudomonal toxin</td>
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<td>EBR, SU101, BCNU</td>
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<td>temozolomide</td>
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<td>STR</td>
<td>EBR + concurrent temozolomide, bevacizumab, pazopanib</td>
<td>10.0</td>
<td>rt sided</td>
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<td>bevacizumab, irinotecan</td>
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<td>GTR</td>
<td>EBR + concurrent temozolomide</td>
<td>12.0</td>
<td>lt P/O</td>
<td>2.8</td>
<td>none</td>
<td>14.8</td>
</tr>
<tr>
<td>17</td>
<td>66, F</td>
<td>GBM</td>
<td>STR</td>
<td>EBR + concurrent temozolomide, BCNU</td>
<td>15.0</td>
<td>lt F</td>
<td>2.5</td>
<td>none</td>
<td>17.5</td>
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<td>GTR</td>
<td>EBR, hydroxyurea, PCV</td>
<td>9.0</td>
<td>lt T</td>
<td>10.93</td>
<td>temozolomide, tamoxifen, irinotecan, $^{125}$I implant</td>
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<td>GTR</td>
<td>EBR + concurrent temozolomide, GKS, BCNU, isoretinoin</td>
<td>16.0</td>
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<td>4.9</td>
<td>carboplatin</td>
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<td>GTR</td>
<td>EBR, GKS, tamoxifen, $^{125}$I implant</td>
<td>13.5</td>
<td>rt T</td>
<td>8.5</td>
<td>$^{125}$I implant</td>
<td>22.0</td>
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<td>18.0</td>
<td>lt T</td>
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<td>BCNU, isoretinoin, carboplatin</td>
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<td>EBR, chemo (unknown agent)</td>
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<td>15.6</td>
<td>R125177</td>
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<td>GKS, tamoxifen, PAA, carboplatin</td>
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<td>lt P/O</td>
<td>20.9</td>
<td>EBR, VP-16, etoposide, $^{125}$I implant</td>
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<td>EBR, GKS</td>
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<td>lt P</td>
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<td>lt T</td>
<td>10.3</td>
<td>BCNU, carboplatin</td>
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</table>

(continued)
Secondary gliosarcoma after diagnosis of glioblastoma multiforme

### TABLE 1: Clinical data in 30 patients with secondary SGS* (continued)

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Initial Dx</th>
<th>Extent of Resection for GBM</th>
<th>Adjuvant Therapy for Glioma</th>
<th>Time to SGS (mos)</th>
<th>Location of SGS†</th>
<th>Survival From SGS (mos)</th>
<th>Therapy for SGS</th>
<th>Overall Survival After Initial Glioma Dx (mos)</th>
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<tbody>
<tr>
<td>26</td>
<td>51, F</td>
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<td>STR</td>
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<td>0.5</td>
<td>lt T</td>
<td>46.4</td>
<td>EBR, GKS, temozolomide</td>
<td>47.4</td>
</tr>
<tr>
<td>27</td>
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<td>STR</td>
<td>EBR, temozolomide</td>
<td>NA</td>
<td>lt T</td>
<td>4.6</td>
<td>none</td>
<td>NA</td>
</tr>
<tr>
<td>28</td>
<td>57, M</td>
<td>GBM</td>
<td>GTR</td>
<td>EBR + concurrent temozolomide</td>
<td>3.0</td>
<td>lt F/T</td>
<td>NA</td>
<td>thalidomide, BCNU</td>
<td>NA</td>
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<tr>
<td>29</td>
<td>45, F</td>
<td>GBM</td>
<td>GTR</td>
<td>EBR + concurrent temozolomide, irinotecan, BCNU, flutamide, Gliadel wafer</td>
<td>12.0</td>
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<td>temozolomide, erlotinib</td>
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<td>low-grade astrocytoma, GBM</td>
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<td>EBR, PCV, temozolomide</td>
<td>17.0</td>
<td>lt T</td>
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<td>irinotecan, tamoxifen</td>
<td>NA</td>
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<tr>
<td>mean; median</td>
<td>54; 53</td>
<td></td>
<td></td>
<td></td>
<td>9.7; 8.5</td>
<td>7.5; 4.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* EBR = external-beam radiation; F = frontal lobe; IL = interleukin; NA = not available through the Social Security Death Index or chart review; O = occipital lobe; P = parietal lobe; PAA = phosphonoacetic acid; PCV = procarbazine, CCNU, and vincristine; T = temporal lobe; VP-16 = etoposide.
† Forty-three percent temporal.

in a total of 26 patients (87%). The tumor had an irregular enhancement pattern in 13 cases (43%), it was rim enhancing in 7 patients (23%), and 6 had homogeneous enhancement. A large proportion of patients showed significant surrounding edema, seen by T2 prolongation (20 patients, 67%). Representative radiographic images are shown in Fig. 1.

**Gross Appearance at Surgery**

The operating surgeons’ descriptions of the gross appearance of SGS were available for 27 of the 30 cases; in 3 cases the surgeon’s operative report did not comment on the gross appearances of the tumors. The SGS was found attached to the dura mater in 5 patients. In 14 patients, the tumor was described as a firm, fibrous mass with distinct borders, which was likened to the appearance of a meningioma. The gross characteristics of the tumors in the other cases were more consistent with those of a GBM, which were described as infiltrative and necrotic masses. There was no statistically significant difference in survival of cohorts in these 2 groups.

**Treatment Modalities for SGS**

At the time of diagnosis, all but 1 patient underwent resection of the SGS (that patient [Case 13] underwent a stereotactic biopsy). A GTR of the enhancing area was achieved in 21 cases, whereas an STR was performed for 8 patients. The 125I implants were left in the resection cavities of 4 patients. External-beam radiation therapy was provided to 3 patients, 2 of whom had not received prior radiation therapy for the initial GBM. Two patients underwent GKS postoperatively. A total of 14 patients received chemotherapy, with agents including CCNU, thalidomide, etoposide, isotretinoin, temozolomide, carboplatin, irinotecan, bevacizumab, and pazopanib; these were distinct from the adjuvant therapy given for the primary tumor. One patient underwent immunotherapy with interleukin-13, and another was enrolled in a trial in which an autologously derived heat shock protein vaccine was used.

**Length of Survival**

The median length of survival from the time of SGS diagnosis was 4.4 months (mean 7.5 months). The median overall survival from the time of the original GBM diagnosis was 12.6 months (range 5.7–47.4 months). Anecdotally, the length of survival after diagnosis of SGS was unusually long in the 2 patients who had not received external-beam radiation therapy as treatment for their glioblastoma (20.9 and 46.4 months). Patients who had received the concurrent and adjuvant temozolomide regimen for the GBM had a significantly worse survival after SGS diagnosis in our series of 30 patients. Patients who had previously received temozolomide had a median length of survival of 4.3 months, compared with those who had not received temozolomide, who had a median survival of 10.5 months (p = 0.045; see Fig. 3). The 2 groups were equivalent in known prognostic factors, such as age and extent of resection. The survival times were similar between patients whose tumors were firm and likened to a meningioma by gross descriptions and patients whose tumors were infiltrative and necrotic (median 4 months and 4.6 months, respectively; p = 0.783). An analysis of survival by mode of management of SGS was not performed, due to the extensive heterogeneity of treatment modalities used.

**Discussion**

We report a series of 30 confirmed cases of SGS. The published literature to date contains 12 cases of this disease, and the current series represents the largest
collective experience with SGS. Our series also includes 2 first reported cases of SGS that progressed from secondary GBM (Cases 6 and 23, Table 1). The mean age of the patients in our series was slightly younger than that in previous reports of patients with either PGS or SGS, who were in their 6th to 7th decade of life. A greater proportion of our patients with SGS were male, and the most common location of SGS was in the temporal lobe, findings consistent with previous studies of PGS.

A number of studies of PGS cases have found a more favorable prognosis in patients with tumors that appeared firm, like a meningioma, at operation, probably because of the relative ease of resection. There were, however, a greater proportion of patients who underwent a GTR in the meningioma-mimicking group. In our series, there was also a distinct division into 2 subgroups, depending on the appearance of the tumor at operation, with proportions similar to those previously reported (roughly half in each group). However, there was no statistically significant difference in survival of cohorts in these 2 groups. This lack of difference may be due in part to equivalent proportions of GTR/STR in both groups. Our results support previous hypotheses in which it was observed that survival differences in subgroups of gliosarcoma are primarily related to their difference in relative ease of achieving GTR. In our series of 30 patients with SGS, the 2 morphological subtypes do not appear to carry prognostic significance.

The large number of SGS cases encountered at our single institution over the span of 10 years, compared with the relative paucity of cases reported in the literature over the past 3 decades, may represent a possible increase in the incidence of SGS. This increased incidence in turn may be a result of the increase in the aggressiveness with which GBM is managed, and the associated prolonged survival. Beaumont and colleagues described an increase in the extracranial metastasis of gliosarcoma since its first report. Alternatively, the large volume of SGS cases may reflect an increased awareness of this pathological diagnosis. Although there seems to have been a possible increase in the incidence of SGS over time in association with increased aggressiveness of GBM management, the incidence of metastasis has remained stable. Our series includes 1 case of metastatic SGS, which was found in the subgalea and scalp. Hence, in our study the rate of metastasis of SGS is 3%, which is consistent with rates reported in the literature for PGS, but lower than those found in the review by Beaumont and colleagues. It remains unclear, however, what role the prolonged survival of patients with GBM has had and will have on the epidemiological aspect of SGS. There was no difference in time to progression from GBM to SGS between those groups of patients who received a more aggressive treatment regimen, that is, the currently accepted standard regimen of radiotherapy with concurrent and adjuvant temozolomide, compared with previously accepted modalities. If the method of GBM management has a direct role in the progression from GBM to SGS, differences in time to recurrence as SGS would be expected.

The survival of our patients (mean 8 months, median 4.6 months) was shorter than in previously reported cases of SGS (13.1 months), as found in our recent review. However, considering the large number of consecutive patients included in our study, our data more accurately reflect the actuarial mortality rates in patients with this disease. The survival of our patients was also relatively poor when

![Fig. 1. Axial MR images illustrating the appearance of SGSs. A: A T1-weighted image obtained with contrast, revealing a large left-sided parietooccipital GBM. B: A T2-weighted FLAIR image demonstrating edema surrounding a GBM. C: A T1-weighted image obtained with Gd enhancement, demonstrating a large left-sided heterogeneously enhancing mass around the previous resection cavity. D: The surrounding T2 prolongation was diagnosed at resection as SGS. E: A T1-weighted image obtained with contrast. F: Another patient’s frontal SGS, also showing significant associated T2 prolongation. G: A T1-weighted image revealing SGS in the scalp/subgaleal space. H: A T1-weighted image with contrast of the same scalp/subgaleal SGS.](image-url)
Secondary gliosarcoma after diagnosis of glioblastoma multiforme

compared with the survival data reported for PGS in the literature (median 6.25–11.25 months).\textsuperscript{7,13,15,17–19,22} Perry and colleagues,\textsuperscript{19} however, compared 25 patients with PGS and 7 patients with SGS, and noted longer survival in patients with SGS. However, comparisons of survival between patients with SGS and PGS are difficult, because all cases of SGS are recurrent gliomas, and these patients are not eligible for a number of therapeutic modalities, such as radiation therapy. The overall poor survival of patients with SGS compared with those with PGS may reflect the paucity of effective treatments available for recurrent malignant glioma, and hence SGS.

Our analysis suggests worse outcomes in SGS patients who had received radiotherapy and temozolomide initially for GBM, potentially representing an effect of a unique pathogenetic and molecular profile of GBMs that are destined to recur as SGS. Although analyses of molecular profiles of GBMs and SGS, such as status of methyguanine-methyltransferase and epidermal growth factor receptor, were not performed here, our findings stress the necessity of detailed molecular and genetic analyses that may identify unique features of GBMs that will recur as SGS, as well as mutations associated with or that drive progression to SGS. These studies will ultimately guide therapy for these unique patients.

Limitations of our study include the retrospective nature of the analysis as well as the heterogeneity of baseline prognostic factors and treatment modalities used in patients. Ideally, a multivariate Cox proportional hazards model would have been applied to control for previously established prognostic factors in patients with malignant glioma; however, the small sample size of our series prevented proper application of such a model. These limitations, along with the relatively low statistical strength and power, may confound our analysis of prognostic factors. Ultimately, despite the rarity of these tumors, large prospective studies will be necessary for adequate evaluation of the impact of various treatment modalities while controlling for age, baseline performance status, extent of resection, and other relevant prognostic factors.

Conclusions

In this study, we report a modern series of 30 consecutive patients in whom SGS was diagnosed, representing the largest collective experience with this tumor type. Secondary gliosarcoma shares many clinical similarities...
with PGS, including its clinical presentation, male predominance, location, and radiographic characteristics; however, our survival data show a younger age at onset for SGS and a worse prognosis. Although SGS also appears to have 2 distinct morphological subtypes, these groups seem to be of little prognostic significance. The large number of cases encountered at our institution may be indicative of a rising incidence of SGS. This rise may be in part due to the prolonged survival of patients with GBM and an increased awareness of this diagnostic entity. Our results suggest poor survival in patients with SGS who had received radiation and temozolomide chemotherapy for GBM; however, the small sample size of our series limits firm survival comparisons of these groups. Our results may represent an effect of unique molecular pathological characteristics of GBM that ultimately progress to SGS. These findings stress the necessity of further molecular and cytogenetic analyses aimed at distinguishing which GBMs will recur as SGS, to identify the optimal treatment regimen for these unique patients.

Disclosure
Dr. McDermott is a consultant for Nycomed. The authors report no other conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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