Secondary gliosarcoma: a review of clinical features and pathological diagnosis

Clinical article

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Object. Although secondary gliosarcoma after treatment of primary glioblastoma multiforme has been described, little is known of these rare tumors. In this article the authors review the literature on secondary gliosarcoma, with attention to clinical course and pathological features.

Methods. A PubMed search of the key word intracranial “gliosarcoma” with and without “radiation” or “radiotherapy” in humans was performed. The 204 citations yielded were screened for relevancy to gliosarcomas that occur after treatment of previous intracranial neoplasms.

Results. A search of the literature yielded 24 relevant articles, combined for a total of only 12 cases of secondary gliosarcoma and 12 cases of radiation-induced gliosarcoma. Of the 12 cases of secondary gliosarcoma, all were previously treated with surgery and radiotherapy (mean dose 50.7 Gy), with a mean survival of 13 months since time of gliosarcoma diagnosis (range 6.9–19.4 months). In the cases of radiation-induced gliosarcoma, the mean dose of previous radiotherapy was 51.3 Gy (median 54 Gy, range 24–60 Gy), and the mean survival since gliosarcoma diagnosis was 6.7 months (median 6 months, range 2–10 months).

Conclusions. Secondary gliosarcoma and radiation-induced gliosarcoma are exceedingly rare. The literature on secondary gliosarcoma illustrates a more favorable survival than for primary gliosarcoma but remains limited regarding clinical and radiographic presentation, response to treatment, and pathogenesis. The results of the present review also support the notion that secondary gliosarcomas and radiation-induced gliosarcomas are distinct entities, with longer survival and shorter latency of gliosarcoma induction seen in the former. Efforts to elucidate the role of radiotherapy in the induction of gliosarcomas may yield new insights into therapeutic risks of cranial radiation and CNS tumor pathogenesis.

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Key Words • gliosarcoma • secondary gliosarcoma • radiation-induced gliosarcoma

Gliosarcoma is a rare variant of GBM containing distinct gliomatous and sarcomatous components. Gliosarcomas comprise 1.8–2.4% of GBMs and are clinically similar to them, affecting adults in the 5th to 7th decades of life, with a higher proportion found in males.3,19,23 The survival for patients with gliosarcoma is equally poor as for those with GBMs, and there is a greater propensity for extracranial metastasis in gliosarcomas.3,12,19,22,23 Clinical treatment-related experience reported in the literature is limited, and gliosarcomas are currently treated in a similar fashion to GBMs, with modalities including tumor resection, postoperative radiation therapy, and chemotherapy. Most gliosarcomas are de novo, and are hence termed primary gliosarcomas, whereas those detected at subsequent surgery for previously resected and irradiated GBMs are termed secondary gliosarcoma (Figs. 1 and 2).25

The causal relationship between therapeutic irradiation and the delayed induction of neoplastic processes is well established for meningioma, cerebral fibrosarcoma, other sarcomatous variants, and more rarely GBM.2,9,28 The criteria for radiation-induced tumors require that: 1) the tumor appear in the area of irradiation, with a significant latency period (years) between irradiation and the appearance of the tumor, 2) the tumor is absent prior to irradiation, and 3) the new tumor is of a histologically distinct type from the first tumor.25 Using these criteria, cases of gliosarcoma have been reported in patients with previous cranial radiotherapy for a variety of indications. Thus, it is important to distinguish a secondary gliosarcoma, which occurs after a GBM that has been treated, from a radiation-induced gliosarcoma, which is a gliosarcoma.
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diagnosed after radiation therapy in patients without any prior history of GBM. In this report we present a comprehensive review of the published literature to identify and consolidate previously described cases of both secondary gliosarcoma and radiation-induced gliosarcoma.

Methods

A PubMed search of the key word “gliosarcoma” with or without “radiation” or “radiotherapy” was performed. The query yielded 204 citations, which were screened using our criteria. The inclusion criteria for sources were as follows: 1) reports of gliosarcoma diagnosed in patients with a history of therapeutic cranial irradiation, or 2) review articles of gliosarcoma in humans that included a discussion of the role of irradiation in tumor induction. Articles that described experiments utilizing the rat 9L gliosarcoma model were excluded. The search identified 24 total references and 16 references containing 24 reported cases of gliosarcoma. 

The cases were considered secondary gliosarcomas if patients had had a radiotherapy-treated GBM and radiation-induced gliosarcomas if patients had undergone radiotherapy for any other indication.

Results

Clinical Features of Secondary Gliosarcoma

Secondary gliosarcoma is a subgroup of rare tumors, and experience in the literature is limited to case reports and series. In a large case series of 32 patients with gliosarcoma, Perry and colleagues found 7 patients meeting criteria for secondary gliosarcoma with the original tumor confirmed as a GBM. These patients presented with symptoms similar to those associated with their GBMs, and the gliosarcomas were found at the same locations as their GBMs. They underwent 50-Gy whole-brain irradiation of the GBM, and the mean time to diagnosis of gliosarcoma was 38 weeks. All 7 patients underwent repeat resection, 3 received chemotherapy (specific agent not indicated), and 2 received photodynamic therapy. In 5 additional cases of secondary gliosarcoma, cranial irradiation was used to treat the GBM (dose range 5.5–90 Gy). These patients also presented with neurological symptoms suggesting that their original GBMs had recurred, except in the case reported by Weaver and colleagues in which the patient presented with abdominal pain and was discovered to have abdominal metastases of gliosarcoma. Of these 5 cases, 3 were found to have extracranial metastases of gliosarcoma, and in 1 patient there were metastases that contained only the sarcomatous component. There is an interesting case of an 8-year-old patient diagnosed with giant cell GBM who originally underwent resection and 5.5-Gy radiotherapy; the patient suffered 2 recurrences 8 and 9 years later, and a gliosarcoma was discovered at the second recurrence.

In all, the mean time from cranial radiotherapy to diagnosis of the gliosarcoma in these 11 patients was 44.8 weeks and the mean radiation dose was 54.8 Gy (Table 1). The unusual case described by Deb and colleagues was excluded from analysis.

Perry and colleagues have reported a mean survival of 53 weeks in patients with secondary gliosarcoma and noted that the duration of survival was greater in patients with secondary gliosarcoma than in those with primary gliosarcoma (53 and 25 weeks, respectively). However, the results for survival were not statistically significant, and the authors recognized the likely presence of uneven prognostic variables and aggressiveness of treatment between groups. The data from the individual case reports regarding survival are also limited. In 2 cases, gliosarcoma was diagnosed after the patient had died. The patient with secondary gliosarcoma from giant cell GBM survived the 1-month period (from time of diagnosis of gliosarcoma) to the time the report was written. The patient reported by Lieberman and colleagues survived 24 months from diagnosis of secondary gliosarcoma. In our review, the mean survival from gliosarcoma diagnosis in 8 patients with secondary gliosarcoma was 57 weeks (Table 1). The case of the patient alive at time of report and the cases diagnosed during postmortem were excluded from analysis. Median survival and median time to diagnosis of gliosarcoma were not calculated because Perry and colleagues reported means for these values in their series.

Radiographic Features of Secondary Gliosarcoma

The radiographic descriptions of secondary gliosarcomas are limited because many reports predate MR imaging. Perry and colleagues described hyperdense, well-demarcated lesions in 5 of their 7 patients on CT scans. In the case reported by Lieberman and colleagues, the tumor appeared as a calcified lesion with significant associated edema and mass effect on CT scans. The patient described by Deb and colleagues had a well-circumscribed, heterogeneously enhancing lesion with solid and cystic components on MR imaging. Magnetic resonance imaging was also used in the patient reported on by Beaumont and colleagues. The tumor appeared as a...
contrast-enhancing mass with associated edema and midline shift. Radiographic descriptions were not included in the reports by Slowik and Balogh\textsuperscript{29} and Weaver and colleagues\textsuperscript{31}.

Clinical Features of Radiation-Induced Gliosarcoma

In a review of radiation-induced gliosarcoma, Kaschten and colleagues\textsuperscript{14} found that a tumor evolved after a mean dose of 37 Gy. The period between radiotherapy and diagnosis of radiation-induced gliosarcoma ranged from 1 to 12 years\textsuperscript{2,3,14}. To date, there have been 12 reported cases of radiation-induced gliosarcoma, 4 of which were included in the analysis by Kaschten and colleagues\textsuperscript{4,13–17,20,24}. The subsequent 8 cases included 2 patients with ependymomas, in whom the tumors were irradiated with 54 and 60 Gy and in whom a diagnosis

Fig. 2. Histological results of gliosarcoma. Photomicrographic samples were gathered from the same patient whose imaging studies are depicted in Fig. 1. A: The original photomicrographic sample was consistent with GBM. H & E, original magnification × 200. B: The gliomatous portion of gliosarcoma discovered at subsequent reoperation. H & E, original magnification × 200. C: The sarcomatous component of the gliosarcoma. H & E, original magnification × 200. D: The sarcomatous tissue lacks GFAP positivity. Original magnification × 100. E: Diffuse staining with MIB-1 antibody in tumor cells suggesting abundant proliferative process. Original magnification × 100. F: Positivity to S100 antibody supporting the sarcomatous phenotype of tumor cells. Original magnification × 100.
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Radiographic Features of Radiation-Induced Gliosarcoma

Published imaging features of radiation-induced gliosarcoma are limited to only 4 cases. Kawaguchi and colleagues described a new enhancing mass on CT scans, and Kaschten and colleagues reported on a hypodense lesion with significant mass effect shown on CT scans. Malde and colleagues described CT features of an enhancing lesion with perifocal edema and mass effect. Beute and associates discussed MR imaging features of a ring enhancing mass with associated edema and hydrocephalus.

Histopathology and Genetics of Secondary and Radiation-Induced Gliosarcomas

Immunohistological analysis using antibodies against GFAP was commonly used to establish the diagnosis of gliosarcoma through the presence of staining in the glial component and its absence in the sarcomatous component. Staining for reticulin, collagen, or S100 protein was used to highlight the sarcomatous elements. In the cases of secondary and radiation-induced gliosarcomas, the sarcomatous component was most commonly a fibrosarcoma. One secondary gliosarcoma contained a portion consistent with an osteosarcoma in which both spindle cells and bone were present. Deb and colleagues discovered immunoreactivity for p53 protein in both glial and sarcomatous areas, whereas overexpression of EGFR was found only in the glial component. In the case of radiation-induced gliosarcoma, Kepes and colleagues noted that the sarcomatous component stained strongly for CD34, a vascular endothelial marker. Behling et al. however, subsequently found that the immunohistochemical stains for CD31 and CD34 were negative in the sarcomatous portion of their patient’s radiation-induced gliosarcoma.

of gliosarcoma was made 29 and 22 months after irradiation. The survivals after diagnosis of gliosarcoma were 7 and < 1 month. Kawaguchi and colleagues have reported 1 case of radiation-induced gliosarcoma 4 years following 45-Gy radiotherapy for choriocarcinoma, and another case of gliosarcoma found 9 years following 60-Gy irradiation for protoplasmic astrocytoma. These patients survived for 12 and 2 months, respectively, following gliosarcoma diagnosis. A gliosarcoma was detected in a patient 8 years after treatment for a medulloblastoma in which 35-Gy whole-brain and 20-Gy posterior-fossa irradiation was used. There are also 3 reported cases of irradiated low-grade gliomas that developed into gliosarcomas. The tumors in these patients received 50.4–54 Gy of radiation, and in each a gliosarcoma was diagnosed 6 months–13 years thereafter. Pasquier and colleagues described a patient initially diagnosed with a left temporal oligodendroglioma; 54-Gy radiotherapy was performed; and 6 months later, after the patient died, multiple intramedullary and subarachnoid spinal metastases from gliosarcoma were diagnosed at autopsy. In this case, sampling error of the initial tumor may have been a factor. Of the 12 cases reviewed, in 6 cases the gliosarcoma was found in an area separate from the original tumor, but within the irradiated field. In the other 6 cases, gliosarcoma was discovered in the location of the original primary tumor and was initially believed to be a local recurrence. Overall, the mean time from radiotherapy to diagnosis of gliosarcoma was 5.2 years (median 6 years), and the mean survival was 6.7 months (median 6 months) (Table 2).

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### Table 1: Summary of cases of secondary gliosarcoma reported in the literature

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Radiation Dose</th>
<th>Time From Irradiation to Gliosarcoma Diagnosis</th>
<th>Survival From Gliosarcoma Diagnosis</th>
<th>Radiographic Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slowik et al., 1985</td>
<td>1</td>
<td>90 Gy</td>
<td>82.6 wks</td>
<td>diagnosed postmortem</td>
<td>NM</td>
</tr>
<tr>
<td>Weaver et al., 1984</td>
<td>1</td>
<td>50 Gy cranial &amp; 12.5 Gy local coned-down</td>
<td>24 wks</td>
<td>diagnosed postmortem</td>
<td>NM</td>
</tr>
<tr>
<td>Perry et al., 1995</td>
<td>7</td>
<td>mean 50 Gy</td>
<td>mean 38 wks</td>
<td>mean 53 wks</td>
<td>CT: well-demarcated, hyperdense lesions in 5 patients</td>
</tr>
<tr>
<td>Lieberman et al., 2001</td>
<td>1</td>
<td>59 Gy</td>
<td>52 wks</td>
<td>84 wks</td>
<td>CT: ossification at site of previous resection w/ edema and mass effect</td>
</tr>
<tr>
<td>Deb et al., 2006</td>
<td>1</td>
<td>5.5 Gy</td>
<td>9 yrs</td>
<td>alive at time of report (1 mo)</td>
<td>MRI: well-circumscribed, heterogeneously enhancing lesion</td>
</tr>
<tr>
<td>Beaumont et al., 2007</td>
<td>1</td>
<td>54 Gy cranial &amp; 104 Gy peripheral brachy therapy</td>
<td>68 wks</td>
<td>diagnosed postmortem</td>
<td>MRI: contrast-enhancing lesion w/ significant edema and midline shift</td>
</tr>
<tr>
<td>mean value</td>
<td></td>
<td>50.7 Gy (12 cases)</td>
<td>80.1 wks (12 cases)</td>
<td>57 wks (8 cases)</td>
<td></td>
</tr>
<tr>
<td>mean excluding Deb et al. case</td>
<td></td>
<td>54.8 Gy (11 cases)</td>
<td>44.8 wks (11 cases)</td>
<td>57 wks (8 cases)</td>
<td></td>
</tr>
</tbody>
</table>

* NM = not mentioned.
Discussion

The total of 12 reported cases of secondary gliosarcoma support the notion that these tumors are rare but real entities. The literature, however, being limited to case reports, fails to establish a firm causal relationship between radiation and the induction of sarcomatous components in GBMs. The natural course in the pathogenesis of gliosarcoma may require the genesis of a gliomatous component and subsequent induction of the sarcomatous component. Unfortunately, the mechanism of pathogenesis in gliosarcoma is unclear. It is notable that in our review we did not find any cases of secondary gliosarcoma that occurred after GBM managed without radiotherapy. Because it would be very rare for a diagnosed GBM not to have been treated with irradiation, this result is not surprising, especially considering the rarity of secondary gliosarcomas.

The cases of radiation-induced gliosarcoma identified by our review include gliosarcomas that were discovered after radiation therapy for a wide variety of indications, including low-grade glioma, meningioma, ependymoma, medulloblastoma, pituitary adenoma, leukemia, and nasopharyngeal carcinoma.2,4,5,13–17,20,24 The histories of these cases have little in common with each other or GBMs, except for therapeutic cranial irradiation, implicating radiation as the agent responsible for inducing gliosarcoma. In 6 cases, gliosarcoma was found within the radiation field but at a separate location from the primary tumor, again supporting the notion that, at least in these cases, the therapeutic radiation and not the original tumor had a greater role in the genesis of gliosarcoma.

Our results also support the idea that secondary gliosarcoma and radiation-induced gliosarcoma are separate entities. The latency period from irradiation to gliosarcoma diagnosis was longer in cases of radiation-induced gliosarcoma than in secondary gliosarcoma (5.2 years and <1 year, respectively). The anecdotal survival of patients with secondary gliosarcoma was also much more favorable than in those with radiation-induced gliosarcoma (13 and 6.7 months, respectively). However, our ability to draw conclusions regarding actuarial survival outcomes is limited by several factors: 1) the small number of patients reported; 2) the heterogeneity of patient populations, particularly those with radiation-induced gliosarcoma; and 3) unknown information on prognostic factors. The mean radiation doses given to the 2 groups were comparable—54.8 Gy for secondary gliosarcoma; and 51.3 Gy for radiation-induced gliosarcoma. This likely represents the relatively similar doses of therapeutic radiation given for intracranial tumors (with the exception of pediatric cases). Comparisons of imaging characteris-

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### Table 2: Summary of cases of radiation-induced gliosarcoma reported in the literature*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Indication for Radiation</th>
<th>Radiation Dose</th>
<th>Time From Irradiation to Gliosarcoma Diagnosis</th>
<th>Survival From Gliosarcoma Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Averback, 1978</td>
<td>2</td>
<td>A: meningioma; B: pituitary adenoma</td>
<td>A: 58 Gy; B: 54 Gy</td>
<td>A: 1 yr; B: 1 yr</td>
<td>A: 6 mos; B: 6 mos</td>
</tr>
<tr>
<td>Pasquier et al., 1978</td>
<td>1</td>
<td>oligodendroglioma</td>
<td>54 Gy</td>
<td>6 mos</td>
<td>diagnosed postmortem</td>
</tr>
<tr>
<td>Kawaguchi et al., 1991</td>
<td>2</td>
<td>A: choriocarcinoma; B: protoplasmic astrocytoma</td>
<td>A: 45 Gy; B: 60 Gy</td>
<td>A: 4 yrs; B: 9 yrs</td>
<td>A: 12 mos; B: 2 mos</td>
</tr>
<tr>
<td>Beute et al., 1991</td>
<td>1</td>
<td>mucoepidermoid carcinoma</td>
<td>50 Gy</td>
<td>8 yrs</td>
<td>5 mos</td>
</tr>
<tr>
<td>Kaschten et al., 1995</td>
<td>1</td>
<td>acute lymphoblastic leukemia</td>
<td>24 Gy</td>
<td>12 yrs</td>
<td>6 mos</td>
</tr>
<tr>
<td>Kepes et al., 1996</td>
<td>1</td>
<td>ependymoma</td>
<td>54 Gy external beam &amp; 15 Gy LINAC</td>
<td>2.5 yrs</td>
<td>7 mos</td>
</tr>
<tr>
<td>Lach et al., 1996</td>
<td>1</td>
<td>low-grade glioma</td>
<td>NM</td>
<td>10 yrs</td>
<td>NM</td>
</tr>
<tr>
<td>Behling et al., 2004</td>
<td>1</td>
<td>ependymoma</td>
<td>60 Gy</td>
<td>22 mos</td>
<td>NM (transferred to hospice)</td>
</tr>
<tr>
<td>Malde et al., 2004</td>
<td>1</td>
<td>medulloblastoma</td>
<td>35 Gy whole brain &amp; 20 Gy posterior fossa</td>
<td>8 yrs</td>
<td>6 mos</td>
</tr>
<tr>
<td>Jager et al., 2008</td>
<td>1</td>
<td>pilocytic astrocytoma</td>
<td>50.4 Gy</td>
<td>13 yrs</td>
<td>~10 mos</td>
</tr>
<tr>
<td>median</td>
<td></td>
<td></td>
<td>54 Gy (11 cases)</td>
<td>6 yrs (12 cases)</td>
<td>6 mos (8 cases)</td>
</tr>
<tr>
<td>mean</td>
<td></td>
<td></td>
<td>51.3 Gy (11 cases)</td>
<td>5.2 yrs (12 cases)</td>
<td>6.7 mos (8 cases)</td>
</tr>
</tbody>
</table>

* LINAC = linear accelerator.
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tics shared by secondary and radiation-induced gliosarcoma are difficult due to the limited number of detailed reports of radiographic features included in the reports. The radiographic descriptions provided are mostly consistent with features of a rapidly expanding malignant intracranial neoplasm.

The possibility of sampling error, failing to sample GBM, or gliosarcoma present at initial resection and leading to a misdiagnosis of radiation-induced gliosarcoma warrants consideration. This is of particular concern for patients with an initial diagnosis of a glioma and a relatively short latency period, such as in the aforementioned case described by Pasquier and colleagues. In the case presented by Behling and colleagues, however, gliosarcoma was found at the fourth recurrence with 3 prior resections that lacked any gliomatous element. The likelihood of sampling errors in all 3 previous resections is fairly low. However, in other cases, many years passed between the prior resections and the resections diagnostic for gliosarcoma without clinical evidence of original tumor recurrence or transformation into gliosarcoma. In these cases, the GBM may have developed during the period when close monitoring was absent, with subsequent development of gliosarcoma. If so, these cases may in reality represent secondary gliosarcomas, misdiagnosed by timing of diagnosis.

Gliosarcomas have a well-documented propensity for metastasis. Our review includes 3 cases of metastatic secondary gliosarcoma and 1 case of radiation-induced gliosarcoma with metastases. In a recent review of gliosarcomas, Beaumont and colleagues noted that there has been an increase in the extent of extracranial metastases of gliosarcoma since they were first described. They indicated that this increase is due to a greater metastatic potential of secondary gliosarcomas over primary gliosarcoma. They also suggested that increased aggressiveness in the treatment of GBMs has led to an increase in secondary gliosarcomas and hence is responsible for the increase in the number of metastatic gliosarcomas. This hypothesis is difficult to accept because there has been no clearly documented increase in the incidence of secondary gliosarcoma relative to primary gliosarcoma. Ultimately, this issue cannot be adequately addressed until the rates of both primary and secondary gliosarcoma, along with their respective rates of metastases, are observed over time.

Proposed Mechanisms of Pathogenesis

The pathogenesis of gliosarcoma has been a topic of debate and currently remains unclear. Since its initial descriptions, one prevalent hypothesis has been that the sarcomatous components originated from hyperplastic changes of vessels induced by the malignant glial cells. This concept was based mainly on morphological and histological studies, including the early descriptions by Feigin and colleagues of hyperplastic vessels and perivascular arrangement of sarcomatous elements. Subsequent reports showing reactivity of the sarcomatous portion to vascular endothelial markers including factor VII, von Willebrand factor, and CD34 continued to provide support for this biclonal origin of gliosarcoma. The presence of vascular markers, however, has not been consistently shown in other studies.

An alternative hypothesis that has recently gained favor is a monoclonal origin of both components of gliosarcoma, either from a common precursor cell or as a result of mesenchymal differentiation of the malignant glial cells. A number of genetic studies have supported the monoclonal hypothesis, specifically those finding identical p53 and PTEN mutations, p16 deletions, and CDK4 amplifications present in both components. Other genetic alterations common in GBMs have been found in both sarcomatous and glial elements, including gains on chromosomes 7, 9q, 20q, and X and losses on chromosomes 10, 9p, and 13q. One distinguishing genetic feature of gliosarcoma was the relative infrequency of EGFR amplification compared with GBM.

The findings of Deb and colleagues that p53 is expressed in both components also support a common progenitor for sarcomatous and glial elements in secondary gliosarcomas. However, the differential amplification of EGFR in the 2 portions in the same sample seems inconsistent with the monoclonal hypothesis. The low level of EGFR expression in the sarcomatous component may explain the infrequency of EGFR amplifications in gliosarcoma reported in previous genetic studies, particularly if those tumors contained dominant sarcomatous components. Inconsistent expression of vascular markers found in the sarcoma of radiation-induced gliosarcoma seen in our review is also consistent with previous findings.

Overall, the proposed mechanisms of pathogenesis of secondary and radiation-induced gliosarcomas remain similar to those of primary gliosarcoma. The roles of radiation include potentially facilitating the process of the following: 1) GBM converting local or circulating mesenchymal stem cells into sarcoma; 2) sarcoma converting local or circulating stem cells into GBM; or 3) one stem cell lineage ultimately giving rise to both GBM and sarcoma. The induction of sarcoma by GBM seems in part to be facilitated by radiation. There was a shorter latency period between radiotherapy and the diagnosis of gliosarcoma in patients in whom a glioma was already present compared with patients in whom a previous gliomatous component was absent. In addition, the equivalent doses of radiation in the 2 groups seen in our review highlight the differential latency periods of gliosarcoma induction by radiotherapy.

Alternatively, radiation may have different roles in the pathogenesis of secondary and radiation-induced gliosarcomas. Radiation may induce a simultaneous genesis of glioma and sarcoma from a common progenitor stem cell, resulting in a case of radiation-induced gliosarcoma. Elucidating the relationship between therapeutic cranial irradiation and gliosarcoma pathogenesis requires further detailed genetic studies, particularly comparing and contrasting the profiles of primary, secondary, and radiation-induced gliosarcomas.

Conclusions

Although the role of therapeutic radiation in the pathogenesis of gliosarcoma remains largely speculative,
many authors support distinguishing secondary gliosarcomas from primary gliosarcomas. Furthermore, secondary gliosarcomas and radiation-induced gliosarcomas seem to be distinct entities, with longer survival associated with secondary gliosarcomas and longer latency of gliosarcoma induction associated with radiation-induced gliosarcomas. The literature on these 2 groups of tumors is limited to case reports and provides little information regarding their clinical and radiographic presentation, response to treatment, and pathogenesis. Elucidating the mechanism by which radiation influences the evolution of gliosarcoma has great implications for the overall pathogenesis of these rare yet devastating tumors.

**Disclosure**

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**References**


