Gliosarcoma

- Magnetic Resonance Imaging for Improved Brain Tumor Detection
- Combinational Radiotherapies Improve Brain Cancer Treatment at High Dose Rates In Vitro
- Next generation sequencing unravels a gliosarcoma mimicking cerebral osteosarcoma
- Three-dimensional bioprinted in vitro glioma tumor constructs for synchrotron microbeam radiotherapy dosimetry and biological study using gelatin methacryloyl hydrogel
- Ependymosarcoma presenting as recurrence in a primary left parieto-occipital ependymoma
- A rare case of gliosarcoma: Comprehensive radiological, histopathological, and clinical insights into diagnosis and management
- Oligosarcoma with chondroid metaplasia in a French bulldog
- Molecular Characteristics of a ZFTA::RELA Fusion Gliosarcoma: A Case Report

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Gliosarcoma is a classic variant of glioblastoma (along with epithelioid glioblastoma and giant cell glioblastoma) which, although not a distinct diagnosis, remains recognized in the World Health Organization Classification of Tumors of the Central Nervous System 2021 as a variant of glioblastoma

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Gliosarcoma was first reported by Strobe in 1895 but did not gain wide acceptance until 1955 when Feigin and Gross described, in detail, three patients with this malignancy [1) 2)].

Defined as a glioblastoma consisting of gliomatous and sarcomatous components.

Epidemiology

A rare variant of glioblastoma IDH wildtype, comprising 2–8% of glioblastomas. Histology features a biphasic tissue pattern consisting of areas of glial differentiation alternating with areas of mesenchymal differentiation.

May arise de novo, or can develop following glioblastoma treatment.

It is estimated that approximately 2.1% of all glioblastomas are gliosarcomas.

Gliosarcomas have an epidemiology similar to that of glioblastomas, with the average age of onset being 54 years, and males being affected twice as often as females. They are most commonly present in the temporal lobe.

Classification

Primary gliosarcoma PGS and secondary gliosarcoma SGS had distinct clinicopathological profiles and prognoses but shared similar genetic profiles. A study by Vuong et al. facilitates our understanding of how these two malignant brain tumors behave clinically, but future studies will be required to elucidate the genetic pathways of PGS and SGS [3].

Childhood's gliosarcoma

Salvati et al. described three cases of gliosarcoma in three patients of 13, 15, and 16 years old, in an attempt to identify any distinctive aspects of the “juvenile” variety. On the basis of their personal experience and in the light of the available literature, the authors review the salient features of this pathological condition in young patients to identify any distinctive aspects as well as to define the significance of the extent of the sarcomatous component and of a “meningioma-like” appearance of the lesion, in terms of survival.

In particular, they emphasized how modern diagnostic-therapeutic protocols make it possible to achieve a massive cytoreduction of the lesion in absolute safety in many cases, while avoiding further deficits in others, thus ensuring not only significant survival times but also a good quality of life [4].

Pathology

Trichrome staining and reticulin stain: Both delineate the sarcomatous component of gliosarcomas.

DNA aptamers

Wu et al have selected a group of DNA aptamers with high affinity and selectivity against gliosarcoma cells K308 using cell-SELEX. All the dissociation constants of these aptamers against gliosarcoma cells were in the nanomolar range and aptamer WQY-9 has the highest affinity and good selectivity among them. Furthermore, truncated aptamer sequence, WQY-9-B, shows similar recognition ability to aptamer WQY-9. In addition, WQY-9-B was found to be able to bind selectively and internalize into cytoplasm of target cancer cell at 37°C. More importantly, compared to a random sequence, aptamer WQY-9-B showed excellent recognition rate (73.3%) for tissue sections of clinical gliosarcoma samples. These data suggests that aptamer WQY-9-B has excellent potential as an effective molecular probe for gliosarcoma diagnosis [5].

Differential diagnosis

Glioblastoma: Gliosarcoma is a subtype of glioblastoma, so these two tumors can be difficult to distinguish. Glioblastoma tends to have a more uniform appearance on imaging studies than gliosarcoma, which often has a more heterogeneous appearance.

Meningioma: Meningiomas are tumors that arise from the meninges, the membranes that cover the brain and spinal cord. They are usually benign but can sometimes be malignant. Meningiomas tend to have a more well-defined border than gliosarcoma and are often easier to remove surgically.

Metastatic brain tumors: These are tumors that originate in other parts of the body and spread to the brain. They can often be distinguished from gliosarcoma based on their appearance and location.

Lymphoma: Primary central nervous system lymphoma is a rare type of brain cancer that can sometimes be confused with gliosarcoma. Lymphomas tend to have a more homogeneous appearance in imaging studies and are often located in the deep structures of the brain.

Stroke: Some of the symptoms of gliosarcoma, such as weakness or numbness on one side of the body and difficulty speaking, can also occur with a stroke. Imaging studies can usually distinguish between these two conditions.

Infection: Certain infections, such as meningitis or encephalitis, can cause symptoms similar to those of gliosarcoma. However, infections tend to have a more rapid onset and are often associated with fever and other systemic symptoms.

May also appear in conjunction with ependymoma (ependymosarcoma) and oligodendroglioma (oligosarcoma). Gliosarcomas that are predominantly sarcomatous may enhance homogeneously and can mimic a meningioma.

Treatment

Gliosarcoma treatment.

Outcome

Gliosarcoma (GS) is a rare subtype of glioblastoma, characterized by a shorter clinical course and poorer prognosis compared to glioblastoma

Dissemination

In contrast to glioblastoma, it is characterised by its propensity for extracranial metastases (11% of the cases) due to its sarcomatous component, most commonly spreading through the blood to the

lungs, and also liver and lymph nodes.

An extensive analysis of the characteristics, treatments and outcomes of the gliosarcoma (GS) patients with central nervous system (CNS) metastases reported in literature until April 2013. PubMed and Web of Science searches for peer-reviewed articles pertaining to Glioblastoma/GS patients with metastatic disease were conducted using predefined keywords. Additionally, a hand search following the references from the selected papers. Cases in which the metastases exclusively occurred outside the CNS were excluded. 110 publications reporting on 189 patients were eligible. There was a significant increase in the number of reported cases over the last decades, with a median overall survival from diagnosis of metastases (from initial diagnosis of Glioblastoma/GS) of 3.0 ± 0.3 (11 ± 0.7) months. On univariate analyses, gender, age, the histological subtype, the time interval between initial diagnosis and the occurrence of metastases and the location of CNS metastases (intracranial versus spinal and parenchymal versus leptomeningeal, respectively) did not influence survival after diagnosis of metastases. There was no substantial treatment progress over the recent decades. Glioblastoma/GS with CNS metastases are associated with a dismal prognosis. Crucial treatment progress is not evident. A central registry should be considered to consecutively gain more information about the ideal therapeutic approach [6].

Case series

Forty-five GSM patients were included. Median overall survival was 25.6 months (95% CI 8.0-43.1), and median relapse-free survival was 15.2 months (95% CI 9.7-20.8). In multivariable analysis, total resection (p = 0.023, HR = 0.192, 95% CI 0.046-0.797) indicated an improved prognosis. And low expression of Ki-67 (p = 0.059, HR = 2.803, 95% CI 0.963-8.162) would be likely to show statistical significance. However, there might be no statistically significant survival benefit from radiotherapy with concurrent temozolomide (n = 33, 73.3%, log-rank p = 0.99) or adjuvant temozolomide (n = 32, 71.1%, log-rank p = 0.74).

This single-center retrospective study with a limited cohort size has demonstrated the treatment of gross total resection and low expression of Ki-67 which are beneficial for patients with GSM, while radiotherapy or temozolomide is not [7].

The National Cancer Database was queried for patients histopathologically diagnosed with gliosarcoma between 2010 and 2019. The associations between MGMT promoter methylation, first-line single-agent chemotherapy-presumed to be temozolomide herein-and overall survival (OS) were examined using log-rank tests and Cox regression, with correction for multiple testing ($p < 0.01$ was significant).

580 newly-diagnosed gliosarcoma patients with MGMT status were available, among whom 33.6% were MGMT promoter methylated. Median OS for gliosarcoma patients that received standard-of-care temozolomide and radiotherapy was 12.1 months (99% confidence interval [CI] 10.8-15.1) for MGMT promoter unmethylated and 21.4 months (99% CI 15.4-26.2) for MGMT promoter methylated gliosarcomas (p = 0.003). In multivariable analysis of gliosarcoma patients-which included the potential confounders of age, sex, maximal tumor size, extent of resection, and radiotherapy-receipt of temozolomide was associated with improved OS in both MGMT promoter methylated (hazard ratio [HR] 0.23 vs. no temozolomide, 99% CI 0.11-0.47, $p < 0.001$) and unmethylated (HR 0.50 vs. no temozolomide, 99% CI 0.29-0.89, p = 0.002) gliosarcomas. MGMT promoter methylation was associated with improved OS among temozolomide-treated gliosarcoma patients ($p < 0.001$), but not

in patients who did not receive chemotherapy (p = 0.35).

In a national analysis of gliosarcoma patients, temozolomide was associated with prolonged OS irrespective of MGMT status. These results provide support for the current practice of trimodal therapy for gliosarcoma [8].

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18 patients with gliosarcomas, all Grade 4 (World Health Organization classification), were compared with the entire group of 730 patients with Glioblastoma and a control group of 18 patients with Glioblastoma matched for known prognostic factors including patient age, randomization date, performance status, extent of resection, and protocol number. Patients in all treatment groups received radiation and nitrosourea-based chemotherapy. The median time to progression and the median survival times for the patients with gliosarcoma were 28.0 and 35.1 weeks as compared with 24.7 and 41.6 weeks for the entire group of patients with Glioblastoma (log rank test, p = 0.94 and 0.27, respectively) and 16.7 and 34.4 weeks in the control group (p = 0.20 and 0.84, respectively). In previous molecular cytogenetic analyses of gliosarcoma these authors have shown similar genetic changes in the gliomatous and sarcomatous components.

The data obtained in this study support the conclusion that gliosarcoma shares significant clinical and genetic similarities with Glioblastoma and that the same principles should be applied for patient enrollment in research protocols and treatment for these two kinds of tumor [9].

Morantz et al. reviewed the clinical and pathological features of 24 patients with gliosarcoma. The study revealed the following findings. Gliosarcoma occurs more frequently than is indicated in the literature, and in our series was present in 8% of all cases of glioblastoma multiforme. The presenting features are not significantly different from those of glioblastoma multiforme. The lesion often presents itself at surgery as a firm, well circumscribed mass within the temporal lobe, and at surgery it is commonly mistaken for a meningioma. There is an increased likelihood of metastasis compared to that of glioblastoma. The prognosis is no worse than that of glioblastoma, in spite of the addition of sarcomatous elements [10].

Case reports

2025

The combination of ependymoma and gliosarcoma elements in the same tumor is extremely rare, and the molecular characteristics of these entities are not clear. Here, we present a rare aggressive brain tumor in a 12-year-old boy harboring a ZFTA::RELA gene fusion, a characteristic feature of supratentorial ependymomas. On the other hand, the histopathological, molecular, and methylation profiles were compatible with a diagnosis of a mesenchymal type, IDH wild-type glioblastoma multiforme (GBM). Additional somatic alterations provide evidence of RAS/MAPK signaling pathway activation. Overall, this report highlights the histopathological and molecular characteristics of a rare and aggressive glial tumor [11].

2024

Secondary IDH-mutant gliosarcoma in a patient with prior IDH-mutant grade 2 astrocytoma [12)]

A 50-year-old male patient who presented with episodic loss of consciousness and left-sided limb weakness for one month. MRI revealed a complex neoplastic lesion in the right fronto-parietal region. Postoperative pathology confirmed GS, and the patient underwent adjuvant radiotherapy and chemotherapy. This case highlights the characteristic features of GS through a combination of imaging and pathological findings, providing valuable insights for radiologists [13)].

2021

Hong et al. described a patient initially diagnosed with a low-grade brain glioma via biopsy, followed by adjuvant radiation and temozolomide treatment. Nearly 2 years after diagnosis, she developed neurological deficits from an intradural, extramedullary tumor anterior to the spinal cord at T4, which was resected and diagnosed as gliosarcoma. Whole-exome sequencing (WES) of this tumor revealed a hypermutated phenotype, characterized by somatic mutations in key DNA mismatch repair (MMR) pathway genes, an abundance of C>T transitions within the identified somatic single nucleotide variations, and microsatellite stability, together consistent with temozolomide-mediated hypermutagenesis. This is the first report of a hypermutator phenotype in gliosarcoma, which may represent a novel genomic mechanism of progression from lower grade glioma [14)].

2017

A rare case of gliosarcoma arising from oligodendroglioma, isocitrate dehydrogenase (IDH) mutant and 1p/19q codeleted. A 36-year-old man presented with a non-enhanced calcified abnormal lesion on the right frontal lobe. The patient underwent subtotal surgical resection, PAV chemotherapy (procarbazine, nimustine (ACNU) and vincristine), and fractionated radiotherapy with 50 Gy. The pathological diagnosis was oligodendroglioma, IDH mutant and 1p/19q codeleted, World Health Organization 2016 grade II. Six years later, a new enhanced lesion appeared, and the recurrent tumor was surgically removed. Although the histopathological findings indicated gliosarcoma, the recurrent tumor still demonstrated the IDH mutation and 1p/19q codeleted. Thus, the recurrent tumor was considered to originate from oligodendroglioma, rather than being newly generated after chemoradiotherapy. Interestingly, the second recurrent tumor responded well to temozolomide chemotherapy. Based on the findings of this case, oligodendrogliomas have the potential for mesenchymal transformation on progression, while keeping their genotype [15)].

2012

A 31-year-old Chinese woman with cranial gliosarcoma metastatic to the liver, lymph nodes and the spinal cord. Initially, the patient presented with dizziness, headache and vomiting and after surgery and histological examination, was diagnosed with cranial gliosarcoma. The patient was treated with surgical resection followed by chemotherapy and radiotherapy. Three years after completing treatment, the patient again presented with similar symptoms with the addition of a seizure. Test

revealed recurrence of the gliosarcoma, and the same treatment was prescribed. Three years after treatment completion, the patient again presented with dizziness and headache. Masses at the right temple and in the right side of the neck were found. Tumors were surgically removed from the brain, skull, scalp and neck, the latter three diagnosed as metastatic gliosarcomas. The patient received both chemotherapy and radiotherapy following resection. One month after treatment, bone scans revealed possible metastases in the right skull, lumbar and left ileum, soft neck tissue, lungs, collarbone, humeri, vertebrae, liver and abdominal lymph nodes. No further therapy was recommended due to the poor condition of the patient. The patient died 5 months later [16].

1989

A 68-year-old male was hospitalized because of headache, nausea, and disturbance of consciousness. Neurological examination on admission disclosed somnolence, disorientation, marked neck stiffness, papilledema, and quadriparesis. Computed tomography (CT) scanning demonstrated a round mass with marked contrast enhancement in the right sylvian fissure and small contrast-enhanced masses in the interpeduncular, quadrigeminal and ambient cisterns. CT also showed marked peritumoral edema, a midline shift, and hydrocephalus. The patient's consciousness level and respiration deteriorated 3 days after admission and a craniotomy was performed. The tumor, which was well demarcated, firmly attached to the sphenoidal ridge, and grossly appeared to be a meningioma, was totally removed. Histologically, the tumor had two well defined components, glioblastoma and fibrosarcoma. The patient underwent ventriculoperitoneal shunting, chemotherapy, and radiotherapy after surgery, but the primary tumor soon recurred, with scalp metastases, and he died 5 months postoperatively. Autopsy revealed metastases to the liver, spleen, and spinal cord [17].

A report of array-based comparative genomic hybridization (aCGH) analysis of spinal gliosarcoma metastases and the correlation to the clinical disease course shows that genotypic profiling may serve as a supplementary diagnostic tool in improving our knowledge of the biologic behavior of rare tumor variants [18].

Intramedullary gliosarcoma metastases

Few cases of intramedullary gliosarcoma metastases are described in the literature. This extremely rare entity should be suspected with the onset of spinal cord symptoms during the course of primary cerebral gliosarcoma [19] [20].

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