BRAIN. Broad Research in Artificial Intelligence and Neuroscience
e-ISSN: 2067-3957 | p-ISSN: 2068-0473
Covered in: Web of Science (ESCI); EBSCO; JERIH PLUS (hkdir.no); IndexCopernicus; Google Scholar; SHERPA/RoMEO; ArticleReach Direct; WorldCat; CrossRef; Peeref; Bridge of Knowledge (mostwiedzy.pl); abcdindex.com; Editage; Ingenta Connect Publication; OALib; scite.ai; Scholar9; Scientific and Technical Information Portal; FID Move; ADVANCED SCIENCES INDEX (European Science Evaluation Centre, neredataltics.org); ivySCI; exaly.com; Journal Selector Tool (letpub.com); Citefactor.org; fatcat!; ZDB catalogue; Catalogue SUDOC (abes.fr); OpenAlex; Wikidata; The ISSN Portal; Socolar; KVK-Volltitel (kit.edu)
2025, Volume 16, Issue 4, pages: 281-294
Submitted: July 29th, 2025 | *Accepted for publication:* October 26th, 2025

Gliosarcoma in Adults: A Ten-Case Single-Center Analysis of Clinical Presentation, Imaging, and Pathology

Ana-Maria Dumitrescu
Department of Morphofunctional Sciences I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. anna.dumitrescu91@gmail.com, https://orcid.org/0000-0002-6833-7430

Simona Alice Partene Vicoleanu
Department of Morphofunctional Sciences I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania.

Ana-Maria Slănină
Department of Preventive Medicine and Interdisciplinarity, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. ana_maria_slanina@yahoo.co.uk https://orcid.org/0000-0002-6456-9744

Nicoleta-Loredana Hilițanu
Department of Preventive Medicine and Interdisciplinarity, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. https://orcid.org/0000-0002-4336-5056

Ana-Maria Haliciu
Department of Morphofunctional Sciences I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania.

Crînguța-Mariana Paraschiv
Department of Medicals I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. cringutaparaschiv@yahoo.com

Roxana Gabriela Cobzaru*
Department of Preventive Medicine and Interdisciplinarity, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania roxanabahnea@yahoo.com. https://orcid.org/0009-0009-3856-1413

Ruxandra Teodora Stan
Department of Implantology, Removable restorations, Technology, Grigore T. Popa University of Medicine and Pharmacy Iasi, Faculty of Dental Medicine, Iasi, Romania.

Claudia Florida Costea
Department of Clinical Ophthalmology, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania, "Prof. Dr. N. Oblu" Emergency Clinical Hospital, Iași, Romania. costea10@yahoo.com https://orcid.org/0000-0002-2488-2154

Abstract: *Background and Objective: Gliosarcoma (GS) is a rare and aggressive variant of glioblastoma (GB), accounting for 1–2% of GB cases. Our objective is to analyse the clinical, radiological, histopathological, and immunohistochemical characteristics of primary gliosarcoma in a single-center cohort and compare findings with existing literature. Material and Methods: We retrospectively reviewed ten adult patients with histologically confirmed primary gliosarcoma (GS) diagnosed between 2012–2021 at "Prof. Dr. N. Oblu" Emergency Clinical Hospital, Iași, Romania. Data extracted included demographics, clinical presentation, magnetic resonance imaging (MRI) features, surgical management, pathology, and immunohistochemistry. Results: Mean age at diagnosis was 64.1 years (range 47–79), with male predominance (male:female ratio = 6:4). Common symptoms included speech disturbances (30%), seizures (20%), and headache (20%), with a median symptom duration of 7 days. Tumours were supratentorial, primarily frontal (40%) or temporal (10%), with 50% involving multiple lobes. Histologically, all cases demonstrated biphasic glial-sarcomatous architecture; 40% showed giant-cell glioblastoma features. Immunohistochemistry revealed glial fibrillary acidic protein (GFAP) and oligodendrocyte transcription factor 2 (Olig2) positivity in glial areas, vimentin positivity in both components, isocitrate dehydrogenase 1 (IDH1) wild-type status, alpha thalassemia/mental retardation syndrome X-linked (ATRX) positivity, intermediate Ki-67 (~21%), and variable p53 expression. Conclusion: Primary gliosarcoma is an aggressive central nervous system (CNS) tumour with characteristic biphasic morphology, frequent dural contact, and meningioma-mimic imaging. Accurate diagnosis relies on histopathology, guiding maximal safe resection and adjuvant chemoradiation.*

Keywords: *gliosarcoma; glioblastoma; biphasic tumour; IDH1 wild-type; meningioma mimic; MRI; immunohistochemistry; Ki-67; p53; surgical resection.*

How to cite: Dumitrescu, A.-M., Partene Vicoleanu, S. A., Slănină, A.-M., Hiliţanu, N.-L., Haliciu, A.-M., Paraschiv, C.-M., Cobzaru, R. G., Stan, R. T., Costea, C. F., Cozma, L. C. D., Rădulescu, A.-M., Lupușoru, R.-V., & Rîpă, C. V. (2025). Gliosarcoma in adults: A ten-case single-center analysis of clinical presentation, imaging, and pathology. *BRAIN. Broad Research in Artificial Intelligence and Neuroscience*, *16*(4), 281-294. https://doi.org/10.70594/brain/16.4/17

Lucia Corina Dima Cozma
Department of Medicals I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. cdimacozma@yahoo.com https://orcid.org/0000-0003-0897-8639

Ana-Marina Rădulescu
Department of Morphofunctional Sciences I, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. anamarina_r@yahoo.com

Raoul-Vasile Lupușoru
Department of Pathophysiology, Faculty of Medicine, Grigore T. Popa University of Medicine and Pharmacy, Iași, Romania.

Carmen Valerica Rîpă
Department of Preventive Medicine and Interdisciplinarity, Grigore T. Popa University of Medicine and Pharmacy, Iasi, Romania. carmenripa2002@yahoo.com

**Correspondence Author: Roxana Gabriela Cobzaru, e-mail : roxanabahnea@yahoo.com*

1. Introduction

In the updated World Health Organization (WHO) Classification of Tumours of the Central Nervous System (CNS5), where histopathological diagnosis is based on the integration of histology with molecular markers, gliosarcoma (GS) is recognised as a variant pattern within adult-type diffuse gliomas (Louis et al., 2021). It typically arises as an IDH1-wild-type glioblastoma (GB) with biphasic glial and sarcomatous components. GS accounts for approximately 1–2% of all glioblastomas, predominantly affecting adults in the fifth to seventh decades of life, with a slight male predominance (Frandsen et al., 2019; La Torre et al., 2024).

Given the rarity of this neoplasm, the literature predominantly comprises case reports (Awadalla et al., 2020; Langlois et al., 2019, Athinodorou et al., 2025), small series of fewer than ten cases such as the four-case series described by (Yildiz et al., 2010), or reports of a few dozen cases (Güney et al., 2010; Machuca et al., 2004). Very few studies have analysed more than one hundred cases of GS. Firm conclusions regarding this entity remain elusive not only due to its low incidence but also because some studies combine primary (de novo) GS with secondary GS that develop following treatment of an initial glioblastoma (GB) (Roohani et al., 2024; Kavouridis et al., 2022; Peckham et al., 2019). GS is a highly aggressive malignant brain tumour with a short overall survival (OS). Being a variant of GB, it is managed similarly. In cohorts uniformly treated according to the Stupp protocol (radiotherapy combined with temozolomide), OS for GS is comparable to that of glioblastoma multiforme (GBM), with median OS approximately 13–16 months (Frandsen et al., 2019). Glioblastomas with a highly methylated O-6-methylguanine-DNA methyltransferase (MGMT) promoter are associated with improved OS and progression-free survival (PFS) due to better treatment response. In contrast, GS frequently exhibits an unmethylated MGMT promoter (Kavouridis et al., 2022).

However, studies have demonstrated that temozolomide confers a survival benefit in GS regardless of MGMT status, with higher OS observed in tumours harbouring a methylated promoter. In other series, even with trimodal therapy—comprising surgical resection, radiotherapy, and chemotherapy—the prognosis remains poor, with median survival significantly lower than that of conventional GB (9 months versus 15 months) (Zaki et al., 2021). Consequently, the question of whether GS should be considered a pathologically distinct entity from GB remains under debate. Differences between these tumours have not yet been clearly defined at the molecular level, and the pathogenesis of GS remains largely unclear (Dardis et al., 2021).

Some insights into GS genetics reveal copy number alterations that are distinct from GBM, suggesting that GS may require specific therapeutic approaches separate from conventional GB treatment (Han et al., 2010; Cheng et al., 2022).

The aim of this study was to analyse the clinical presentation, radiological features, tumour histopathology, and immunohistochemical characteristics observed in ten cases of primary gliosarcoma, in order to establish the defining features of this rare central nervous system (CNS) neoplasm and compare them with previously published reports.

2. Material and methods

2.1. Study Design and Data Source

We conducted a retrospective, single-center descriptive study of primary GS grade 4 cases diagnosed over a ten-year period (January 1, 2012 – December 31, 2021) at the "Prof. Dr. N. Oblu" Emergency Clinical Hospital, Iași, Romania, a national reference centre for the management of brain tumours. All cases were extracted from the Laboratory of Pathology's electronic archive, and corresponding clinical and radiological data were obtained from the hospital's electronic medical records.

Of the initially identified 12 cases of pathologically confirmed primary GS, only those with complete clinical and radiological information were included, resulting in a final cohort of 10 patients (Figure 1).

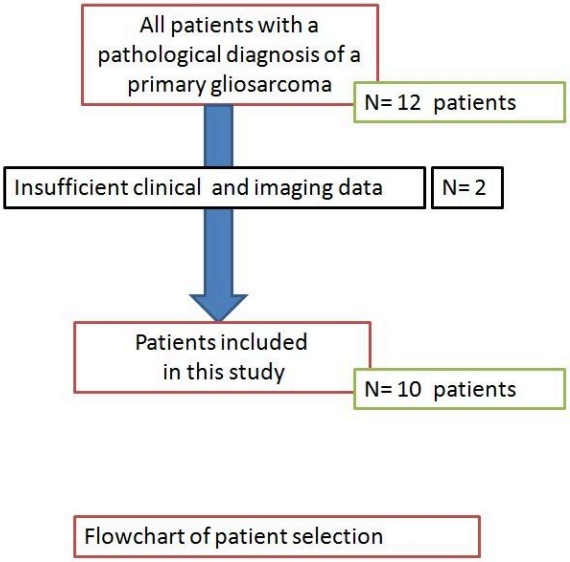

Figure 1. Flowchart of patient selection

2.2. Statistical Analysis

Demographic variables (age, sex), clinical data (presenting symptoms, duration of symptoms prior to surgery, comorbidities), imaging features (MRI characteristics including dural contact, perilesional oedema, bone involvement, tumour location and laterality, preoperative MRI diagnosis), pathological findings (microscopic description, histochemical and immunohistochemical profiles including glial fibrillary acidic protein (GFAP), oligodendrocyte transcription factor 2 (Olig2), vimentin, p53, isocitrate dehydrogenase 1 (IDH1), alpha thalassaemia/mental retardation syndrome X-linked (ATRX), and Ki-67, surgical interventions, and short-term postoperative outcomes were systematically recorded. Symptom duration was defined as the interval between the onset of the first neurological symptom and hospital admission for neurosurgical evaluation.

Inclusion criteria were: adult patients (≥18 years old) with histologically confirmed primary GS grade 4 and complete clinical, radiological, and pathological data available. Exclusion criteria included patients under 18 years of age and secondary GS cases developing after previous glioblastoma treatment.

All collected data were entered into an Excel spreadsheet and analysed using Python software. Continuous variables were expressed as mean, median, standard deviation (SD), and range. Categorical variables were summarised using counts and percentages. Data visualisation was performed using cumulative distribution plots, bar and pie charts, and boxplots with median values highlighted in red.

2.3. Ethics

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients prior to inclusion in the study.

2.4. Results

2.4.1. Demographics

The mean age at diagnosis was 64.1 years (range 47–79), with a median age of 65 ± 11.7 years (Figure 2). The cohort comprised six males and four females, resulting in a male-to-female ratio of 1.5:1 (Figure 3).

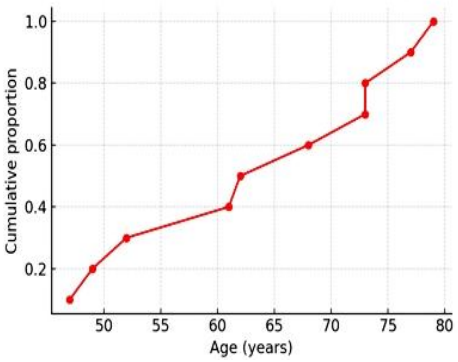

Figure 2. Age distribution (cumulative plot) of patients in the present series

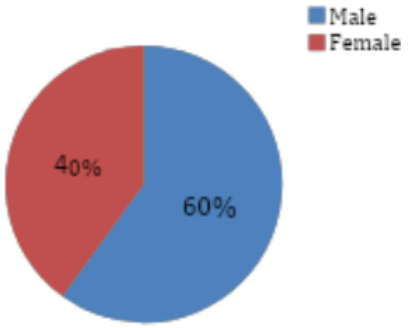

Figure 3. Gender distribution (pie chart) of patients in the present series

2.4.2. Clinical Symptoms

The most frequent initial clinical manifestation was speech disorder, observed in 3 patients (30%). Seizures were present in 2 patients (20%), and headache/cephalalgic syndrome was also reported in 2 cases (20%). One patient (10%) presented with a syncopal episode. In 2 cases (20%), symptoms were nonspecific or classified as other neurological complaints.

Most frequent initial manifestations were mostly speech disorder (n=3 cases; 30%), followed by seizures (n=2 cases; 20%) and headache (n=2 cases; 20%) (Figure 4).

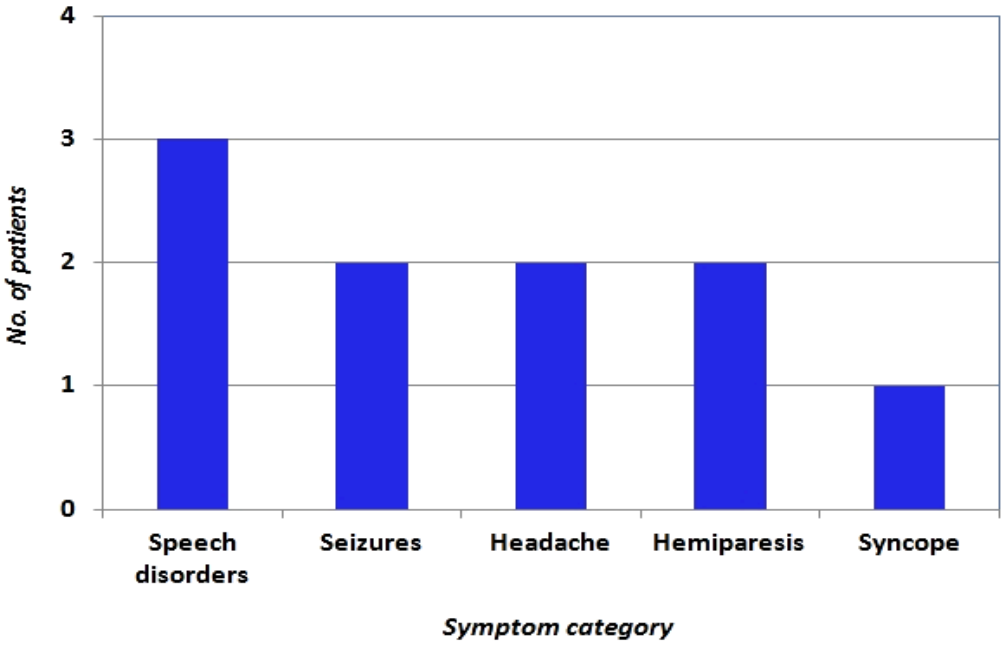

Figure 4. The initial symptoms in the present series

Average time period of clinical manifestations before hospital admission was 13.1 days, with a median of 7 days (range 2–30). This interval represents the number of days from symptom onset to hospital presentation. (Figure 5).

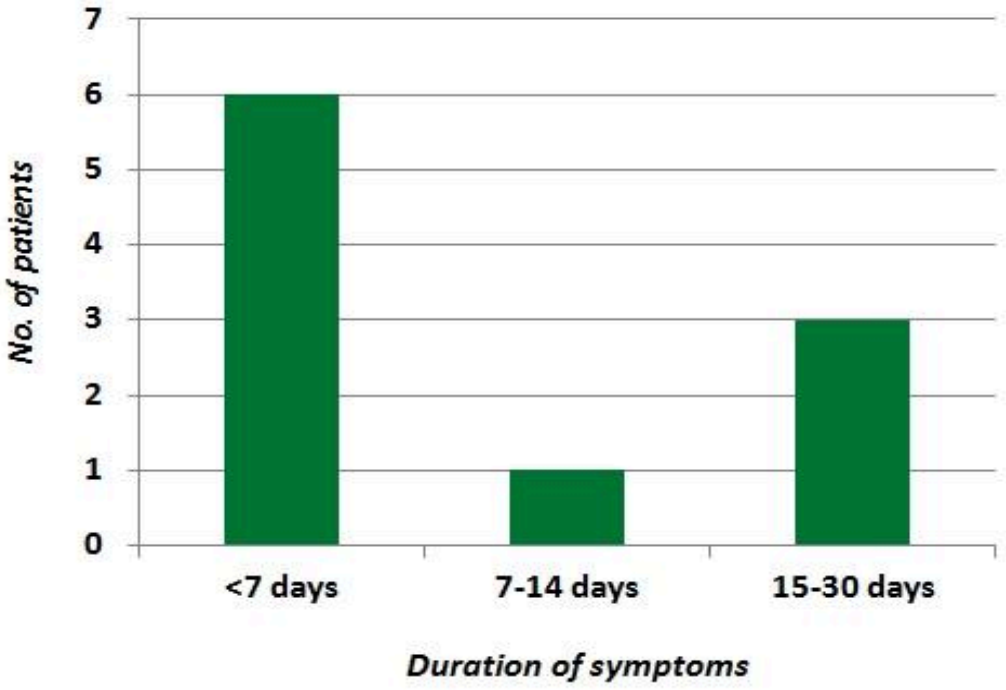

Figure 5. Period of time (days) from symptom onset to hospitalisation in the present series

Seven patients (70%) had at least one comorbidity. Cardiovascular diseases were the most frequent and accounted for 9 diagnostic instances across these patients (hypertension, dilated cardiomyopathy, ischaemic heart disease, atrial flutter). Metabolic conditions were identified in four patients (40%) (obesity, type II diabetes mellitus). One patient (10%) had preoperative SARS-CoV-2 infection. Minor comorbidities were documented in five patients (50%), whereas three patients (30%) had no comorbidities. (Figure 6).

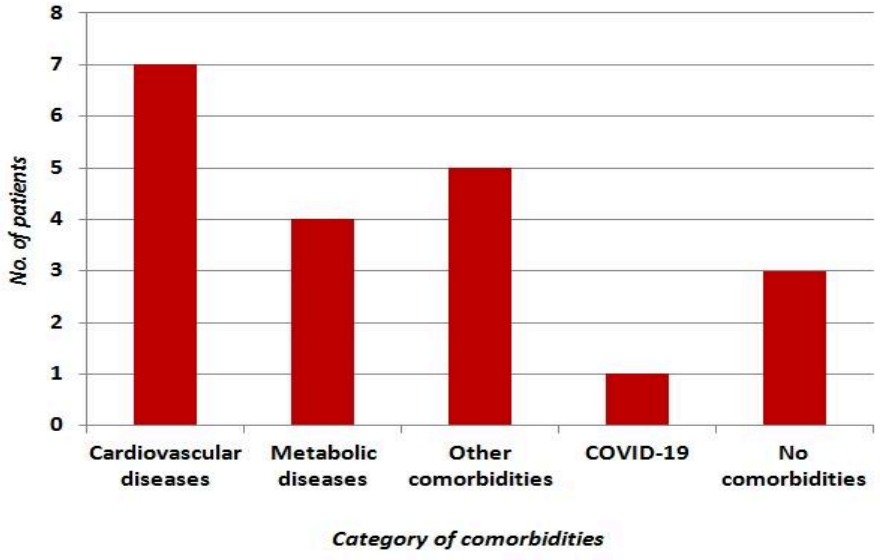

Figure 6. Comorbidities in gliosarcoma patients from the present series

3. MRI Diagnosis and Imaging Features

Preoperative MRI suggested glioblastoma in six cases (60%), meningioma in two cases (20%), and astrocytoma (grade 3 or 4) in two cases (20%) (Figure 7).

Regarding MRI features, dural or meningeal contact was noted in two cases (20%). Perilesional edema was present in all cases (100%), intratumoural necrosis in eight cases (80%), and midline shift in seven cases (70%). Bone involvement was observed in two cases (20%). One case explicitly described a cortical tumour in contact with the meninges, explaining occasional misclassification as meningioma.

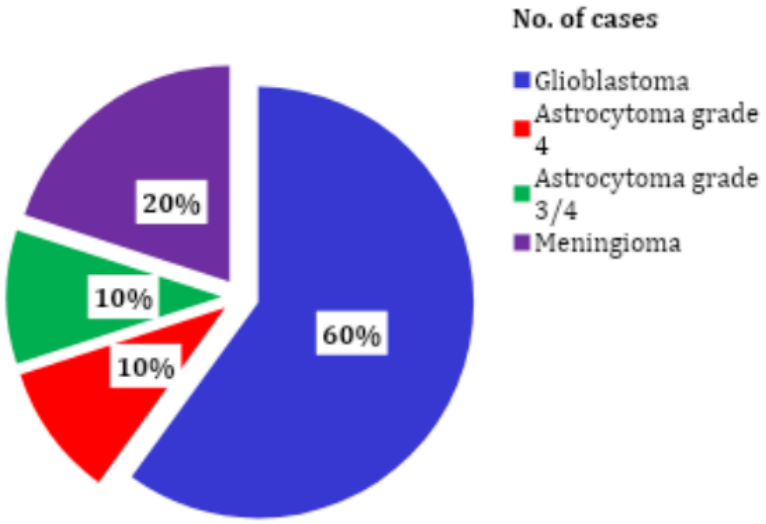

Figure 7. MRI-based diagnostic categories in the present series

One case explicitly described a 'cortical tumour in contact with the meninges,' confirming the propensity of gliosarcomas to abut or invade the dura mater. This feature explains why gliosarcomas are sometimes radiologically misclassified as meningiomas. Recognising this correlation is clinically relevant because it influences surgical planning and highlights the importance of histopathological confirmation.

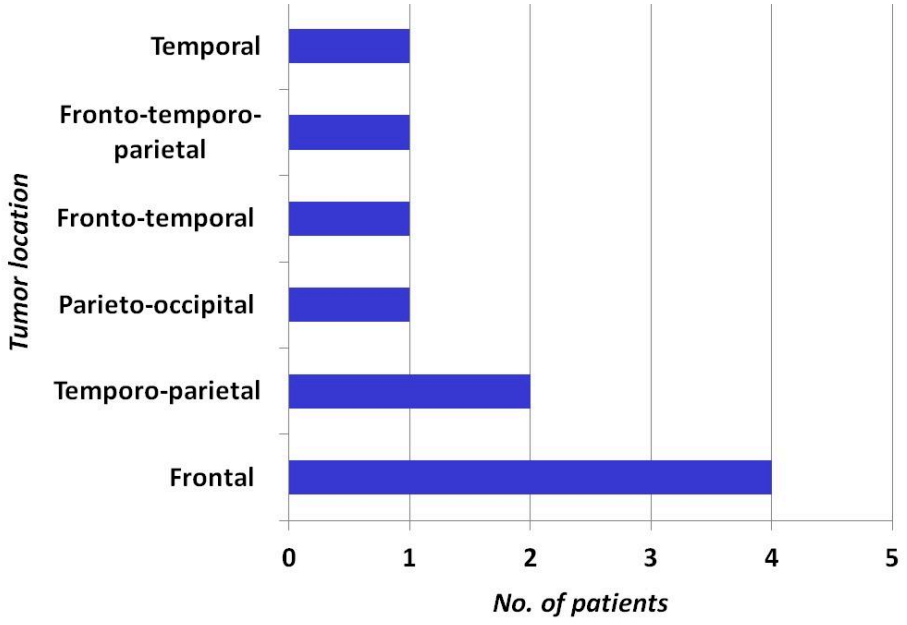

Figure 8. Gliosarcoma location in the present series

All tumours were supratentorial. Single-lobe involvement occurred in five cases (50%): frontal lobe in four (40%) and temporal lobe in one (10%). Multilobar involvement was observed in five cases (50%), most frequently temporo-parietal (n = 2; 20%) (Figure 8). Tumour laterality favoured the right hemisphere in six cases (60%), with the left hemisphere affected in four cases (40%) (Figure 9).

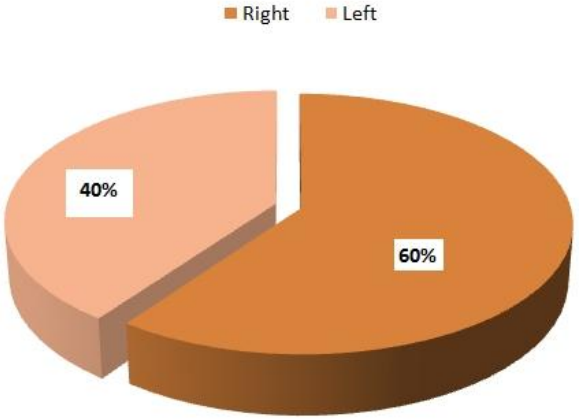

Figure 9. Tumour laterality in our gliosarcoma series

4. Histopathological Diagnosis

Histopathological examination confirmed gliosarcoma in 6 cases (60%). In 4 cases (40%), gliosarcoma with giant cells in the gliomal component was identified. This emphasises the morphological heterogeneity of gliosarcomas, which may combine sarcomatous areas with giant-cell glioblastoma features. Multi-level analyses and advanced structural characterisation techniques can highlight the differences between the glial and sarcomatous components of gliosarcoma and provide useful insights into tumour aggressiveness (Negrila et al., 2021).

Regarding the histopathological diagnosis, all cases exhibited a relatively well-delimited, mixed tumour, made up of glial and sarcomatous components, often arranged in a mosaic pattern. Glial components exhibited morphological features that were remarkably similar to those of a glioblastoma, including pleomorphic astrocytic cells, with nuclear atypia, mitosis. There were also foci of necrosis with peripheral pseudopalisading of glial tumour cells, and marked vascular proliferation in the form of glomeruloid vessels. In 4 cases (40%) the glial component was made up of giant astrocytic cells, with abundant eosinophilic cytoplasm and an eccentric, hyperchromatic nucleus or many nuclei.

The sarcomatous component showed bundles of densely packed, spindle-shaped tumour cells with nuclear atypia, mimicking a fibrosarcoma, arranged among glioblastoma-like tumor sheets.

A histochemical study with silver impregnation stain for reticulin fibres demonstrated a rich network of fibrils in sarcomatous components in all cases. The gliomal component was devoid of reticulin fibres, except for the intratumoural vessels in these areas, which showed a rich network of reticulin fibres in their walls.

Immunohistochemical stainings revealed the two different areas, each of them with a particular pattern of staining. GFAP and Olig2 were positive in the glial component, but negative in the sarcomatous component. Vimentin was positive in both components. IDH1 was negative and ATRX was positive in all cases (100%), both in gliomal and sarcomal components.

p53 was positive in both gliomal and sarcomal regions showing low values, but almost similar (p53 median value=42,5%; range 30–50%), while Ki-67 labelling indices (LI) showed high

values in both tumour components, but almost similar (Ki-67 LI averaged 20.8% (range 15–28%). The distribution of p53 expression levels and Ki-67 indices is illustrated in Figure 10.

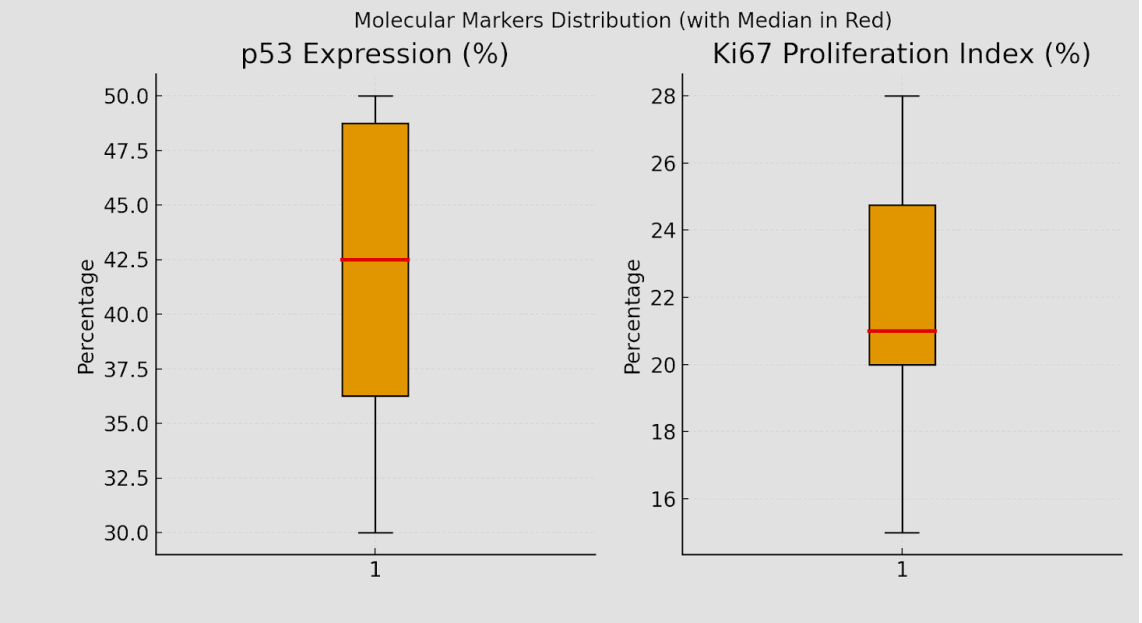

Figure 10. p53 expression (%) and Ki67 proliferation index (%) (with median values in red) in the present gliosarcoma series

5. Surgical Treatment and Outcomes

Surgical Treatment consisted in subtotal resection (n=7 cases; 70%), Gliolan-assisted total resection (n=2 cases; 20%) and total microscopical resection (n=1 case; 10%) (Figure 11). Short-term postoperative outcome was favourable in all cases (100%).

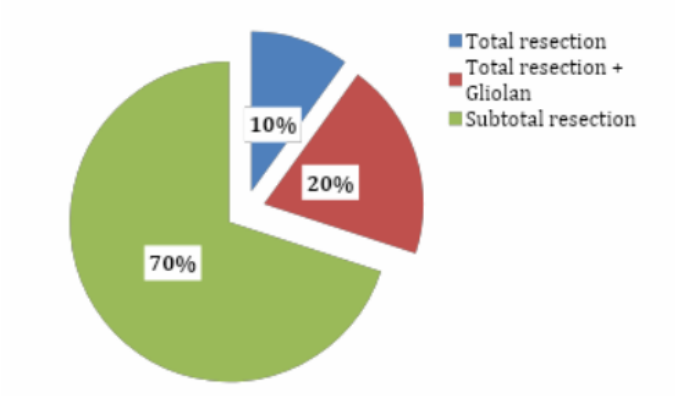

Figure 11. Types of surgical treatment in gliosarcoma patients from the present series

6. Discussion

The demographic characteristics of our series of ten primary GS cases—with a mean age in the seventh decade and a slight male predominance—align with previously published institutional series and large database analyses. GS typically presents in the fifth to seventh decades, with a modest male predominance (Frandsen et al., 2019; Kozak et al., 2009). Population-based studies show no substantial differences between GS and conventional GB regarding age or gender. However, some series report female predominance, highlighting the demographic heterogeneity of this rare neoplasm. Data from the *Surveillance, Epidemiology, and End Results Program* (SEER) program indicate that GS comprises ~2% of glioblastoma multiforme (GBM), with similar age and

gender distribution to GB, and that age and extent of resection remain important survival determinants (Kozak et al., 2009).

The clinical manifestations in our cohort were dominated by language disturbances, seizures, and headache, reflecting acute neurological compromise caused by rapidly expanding tumours. These findings align with previous reports describing symptoms related to mass effect and functional disruption of adjacent eloquent cortex. Symptom duration was short in most patients, emphasising the aggressive clinical course of gliosarcoma. It is important to note that features such as perilesional oedema, intratumoural haemorrhage, and necrotic areas are imaging characteristics on MRI, not clinical manifestations.

Symptom duration prior to admission was relatively short in our cohort (median 7 days), although some studies report longer intervals (median up to 75 days). Brain tumours present high mortality rates and this is the reason why there is an indication for the early detection of possible biomarkers, in regards to better evolution (Moroșan et al., 2024). As shown by Furnica et al., (2022), systemic healthcare factors strongly affect patient outcomes in time-sensitive diseases. This underscores the importance of multidisciplinary coordination and early intervention strategies, which are equally vital in gliosarcoma management.

In our cohort, the frontal lobe was the most frequently affected site (40%), while the temporal lobe was involved in only one case (10%). This pattern differs from several published series reporting temporal predominance (Frandsen et al., 2019; Han et al., 2010), highlighting the heterogeneity of gliosarcoma localisation in small cohorts. Some series describe frontal predominance or parietal localisation, reflecting heterogeneity across small samples. Right hemispheric involvement predominated in our series, paralleling other reports (Frandsen et al., 2019).

Unlike typical GBs, which are predominantly intra-axial, GS exhibits a higher propensity for dural and calvaria contact. MRI often demonstrates dural abutment or infiltration, occasionally producing a “dural-tail–like” appearance that may mimic meningioma (Frandsen et al., 2019; Chourmouzi & Drevelegas, 2012; Lyndon et al., 2019). In our cohort, MRI documented explicit dural contact in only 20% of cases, all misclassified preoperatively as meningioma; literature reports suggest the true frequency may be as high as 58% (Frandsen et al., 2019). This dural association has major implications for surgical planning, as neurosurgeons may anticipate an extra-axial lesion but encounter a parenchymal tumour with dural adherence. Histopathological confirmation is therefore essential.

Accurate diagnosis relies on biopsy and immunohistochemistry due to overlapping radiological features. In addition, gliosarcoma is a rare entity, while intracerebral metastases show an increasing incidence (Sava et al., 2021) and can originate from any carcinoma (Scripcariu et al., 2020), melanoma (Costea et al., 2014), or sarcoma (Jędrys et al., 2023).

On MRI, gliosarcoma may resemble glioblastoma, high-grade astrocytoma, metastases, or dural-based tumors such as anaplastic meningioma. Rare entities, including amyloidoma, have also been reported to mimic high-grade gliomas. These overlaps underline the importance of histopathological and immunohistochemical confirmation for establishing a definitive diagnosis. High-resolution MRI provides valuable structural detail that can help distinguish gliosarcoma from other high-grade brain tumors, especially when imaging features overlap. Careful analysis of asymmetries, regional atrophy, and involvement of commissural pathways can improve diagnostic accuracy and guide clinical decision-making (Iliuta et al., 2021).

In the population group in which gliosarcomas were identified in our study, almost one-third of cases showed an atypical Circle of Willis or anatomical variants, as identified in a previous study (Dumitrescu et al., 2022). In the field of neuroanatomy, anatomical variants are mostly encountered at the level of cerebral circulation (Nedelcu et al., 2024). This must be considered in the differential diagnosis of gliosarcoma and potential stroke. The sudden onset of clinical symptoms can lead to a misdiagnosis of ischemic stroke, particularly in the presence of mild cerebrospinal fluid lymphocytosis, middle cerebral artery stenosis on cerebral angiography, and absence of a properly

performed MRI (Züchner et al., 2003). Recent advances suggest that neuroinflammatory and neurodegenerative pathways—particularly chronic microglial activation and mitochondrial dysfunction—may contribute to glioma progression and influence cognitive decline in patients with high-grade tumors (Zheng & Graeber, 2022). Because of how the disease and its treatment directly affect brain function, patients typically show symptoms related to neurological, cognitive, and psychiatric issues (Moroșan et al., 2024). Moreover, recent clinical data support a clear association between tumour topography and psychiatric symptoms, particularly emphasising the impact of frontal lobe involvement on cognitive and behavioural function (Moroșan et al., 2024). Frontal and parietal tumours, as well as those extending into the corpus callosum, may produce motor and body-perception disturbances that can mimic psychiatric disorders. Clinical manifestations resembling the "alien hand" phenomenon may arise due to disruption of networks responsible for voluntary motor control, underscoring the need for careful clinico-radiological correlation in the differential diagnosis (Manea et al., 2024).

Because in imaging investigations GS can mimic glioblastoma, grade III/IV astrocytoma, and anaplastic meningiomas, histopathological confirmation is necessary. Its biphasic nature requires appropriate histochemical and immunohistochemical studies to identify the glial component (GFAP+, silver impregnation–) and sarcomatous component (CD34+, silver impregnation+), which are essential for a correct diagnosis and individualised treatment planning (Dumitrescu et al., 2025).

GS is classically IDH1-wildtype with biphasic glial and sarcomatous architecture. In our series, all cases were IDH1-negative, ATRX-positive, and exhibited intermediate proliferative activity (median Ki-67 ~22%), consistent with contemporary data (Frandsen et al., 2019; de Macedo Filho et al., 2020). P53 expression was variable but within ranges reported for high-grade gliomas. MGMT promoter methylation appears less frequent in GS compared with conventional GBM (~26% vs 55%), influencing response to temozolomide and survival outcomes (Frandsen et al., 2019; Roohani et al., 2024; Kavouridis et al., 2022). Recent genomic profiling highlights recurrent alterations in TERT-promoter (~92%), PTEN (~66%), and TP53 (~60%), with occasional actionable targets (BRAF, EGFR, CDKN2A, NF1) (Zaki et al., 2021).

Extent of resection is a key determinant of outcome in high-grade gliomas. Fluorescence-guided surgery using 5-ALA (Gliolan®) increases complete resection rates and progression-free survival (Stummer et al., 2006); (Stepp & Stummer, 2018). In our series, subtotal resection predominated (70%) due to tumour infiltration into adjacent brain, with only two 5-ALA–assisted total resections performed following its introduction in our hospital in 2015. Evidence from multi-institutional studies indicates that gross total resection (GTR), trimodal therapy (surgery + radiotherapy + temozolomide), younger age, smaller tumour size, and MGMT promoter methylation are associated with improved survival, with median OS ~13–17 months under standardised treatment (Frandsen et al., 2019; Roohani et al., 2024).

Based on current literature reviews, low-level laser therapy (LLLT) modulates cytokine signalling, mitochondrial function, and immune cell activation, potentially enhancing responsiveness to biologicals or immunotherapies (Al Balah et al., 2025). Meanwhile, monoclonal antibodies such as bevacizumab and nimotuzumab remain key adjuncts in glioblastoma and gliosarcoma management, targeting angiogenic and proliferative pathways (Wu et al., 2025). In this context, it is intriguing to consider LLLT, through its capacity to modulate immune responses and enhance the bioactivity of monoclonal agents, as previously illustrated in pediatric rheumatologic disorders (Chiran et al., 2013), may represent a conceptual framework worth exploring for augmenting monoclonal antibody–based or immune-targeted strategies in gliosarcoma.

Overall survival for primary GS treated with standardised chemoradiation is broadly comparable to GBM, though older registry studies suggested slightly worse outcomes (HR ~1.17) (Kozak et al., 2009). Age <65 years, GTR, and trimodal adjuvant therapy are consistently reported as favourable prognostic factors (Frandsen et al., 2018). Ki-67 and p53 indices provide supportive prognostic information, although their independent predictive value remains context-dependent

(Awadalla et al., 2020). MGMT promoter methylation appears to confer a survival advantage, though small series yield heterogeneous results (Kavouridis et al., 2022).

The study is limited by its small sample size, single-centre retrospective design, and lack of long-term follow-up and extended molecular profiling.

7. Conclusion

Primary gliosarcoma remains a rare and aggressive variant of glioblastoma, characterised by biphasic glial–sarcomatous morphology, IDH1-wild-type molecular status, and frequent dural contact that may mimic extra-axial tumours. In our cohort, the frontal lobe was the most commonly affected site, with patients typically presenting with rapidly progressive neurological symptoms.

Accurate diagnosis relies on detailed histopathological and immunohistochemical evaluation, while maximal safe resection followed by chemoradiation remains the standard approach. The small sample size and single-centre design represent inherent limitations; however, our findings add valuable clinical, imaging, and pathological data to the limited literature on gliosarcoma.

Future multicenter studies and comprehensive molecular analyses are needed to better define prognostic factors and explore potential targeted therapeutic strategies for this rare tumour entity.

References

Al Balah, O. F., Rafie, M., & Osama, A. R. (2025). Immunomodulatory effects of photobiomodulation: A comprehensive review. *Lasers in Medical Science, 40*(1), 187. https://doi.org/10.1007/s10103-025-04417-8

Athinodorou, I. P., Kolios, K., Koumoundourou, D., & Constantoyannis, C. (2025). A challenging diagnosis of gliosarcoma: A case report. *Cureus, 17*(6). https://doi.org/10.7759/cureus.85292

Awadalla, A. S., Al Essa, A. M., Al Ahmadi, H. H., Al Ojan, A., Muazen, Y., Alsayyah, A., Alsaif, H., & Alsafwani, N. S. (2020). Gliosarcoma case report and review of the literature. *Pan African Medical Journal, 35*, 26. https://doi.org/10.11604/pamj.2020.35.26.17577

Cheng, C.-D., Chen, C., Wang, L., Dong, Y.-F., Yang, Y., Chen, Y.-N., Niu, W.-X., Wang, W.-C., Liu, Q.-S., & Niu, C.-S. (2022). Gliosarcoma: The distinct genomic alterations identified by comprehensive analysis of copy number variations. *Analytical Cellular Pathology (Amsterdam), 2022*, 2376288. https://doi.org/10.1155/2022/2376288

Chiran, D. A., Ailioaie, L. M., & Ailioaie, C. (2013). New challenges in treating pediatric rheumatic diseases with lasers in the age of biologic therapy. In *Proceedings of the 9th World Association for Laser Therapy Congress (WALT): 9th Biennial Congress of the World Association for Laser Therapy, Gold Coast, Australia, 28–30 September 2012* (pp. 25–27). MEDIMOND, Monduzzi Editore, International Proceedings Division.

Chourmouzi, D., Potsi, S., Moumtzouoglou, A., Papadopoulou, E., Drevelegas, K., Zaraboukas, T., & Drevelegas, A. (2012). Dural lesions mimicking meningiomas: A pictorial essay. *World Journal of Radiology, 4*(3), 75. https://doi.org/10.4329/wjr.v4.i3.75

Costea, C. F., Anghel, K., Dimitriu, G., Dumitrescu, G. F., Faiyad, Z., Dumitrescu, A. M., & Sava, A. (2014). Anatomoclinical aspects of conjunctival malignant metastatic melanoma. *Romanian Journal of Morphology and Embryology, 55*(3), 933–937.

Dardis, C., Donner, D., Sanai, N., Xiu, J., Mittal, S., Michelhaugh, S. K., Pandey, M., Kesari, S., Heimberger, A. B., Gatalica, Z., Korn, M. W., Sumrall, A. L., & Phuphanich, S. (2021). Gliosarcoma vs. glioblastoma: A retrospective case series using molecular profiling. *BMC Neurology, 21*(1), 231. https://doi.org/10.1186/s12883-021-02233-5

de Macedo Filho, L. J. M., Barreto, E. G., Martins, P. L. B., Filho, E. N. S., Gerson, G., & de Albuquerque, L. A. F. (2020). IDH1-mutant primary intraventricular gliosarcoma: Case report and systematic review of a rare location and molecular profile. *Surgical Neurology International, 11*, 372. https://doi.org/10.25259/SNI_586_2020

Dumitrescu, A.-M., Eva, L., Haba, D., Cucu, A. I., Dumitrescu, G. F., Burduloi, V. M., Dima-Cozma, L. C., Vatavu, R., Moroşanu, G. C., & Sava, A. (2022). Anatomical study of Circle of Willis on fresh autopsied brains: A study of a Romanian population. *Romanian Journal of Morphology and Embryology, 63*(2), 395. https://doi.org/10.47162/RJME.63.2.10

Dumitrescu, A.-M., Sava, A., Eva, L., Chiran, D. A., Nour, M., Dumitrescu, G. F., Scripcaru, V., Ianole, V., Vatavu, R., Isac, C.-T., & Stan, C. I. (2025). Clinical, radiological, and histopathological insights into gliosarcoma: A case report and literature review. *Revista Română de Anatomie Funcţională şi Clinică, Macro- şi Microscopică şi de Antropologie, 24*(1), 56–61.

Frandsen, S., Broholm, H., Larsen, V. A., Grunnet, K., Møller, S., Poulsen, H. S., & Michaelsen, S. R. (2019). Clinical characteristics of gliosarcoma and outcomes from standardized treatment relative to conventional glioblastoma. *Frontiers in Oncology, 9*, 1425. https://doi.org/10.3389/fonc.2019.01425

Furnica, C., Chistol, R. O., Chiran, D. A., Stan, C. I., Sargu, G. D., Girlescu, N., & Tinica, G. (2022). The impact of the early COVID-19 pandemic on ST-segment elevation myocardial infarction presentation and outcomes: A systematic review and meta-analysis. *Diagnostics, 12*(3), 588. https://doi.org/10.3390/diagnostics12030588

Güney, Y., Hiçsönmez, A., Yilmaz, S., Adas, Y. G., & Andrieu, M. N. (2010). Gliosarcoma: A study of four cases. *Rare Tumors, 2*(2), e37. https://doi.org/10.4081/rt.2010.e37

Han, S. J., Yang, I., Tihan, T., Prados, M. D., & Parsa, A. T. (2010). Primary gliosarcoma: Key clinical and pathologic distinctions from glioblastoma with implications as a unique oncologic entity. *Journal of Neuro-Oncology, 96*(3), 313–320. https://doi.org/10.1007/s11060-009-9973-6

Iliuta, F. P., Manea, M. C., Budisteanu, M., Ciobanu, A. M., & Manea, M. (2021). Magnetic resonance imaging in schizophrenia: Luxury or necessity? *Experimental and Therapeutic Medicine, 22*, 765. https://doi.org/10.3892/etm.2021.10197

Jędrys, W., Leśniak, A., Borkowska, A., Rutkowski, P., & Sobczuk, P. (2023). Brain metastases of sarcoma: A rare phenomenon in rare tumours. *Journal of Cancer Research and Clinical Oncology, 149*(20), 18271–18281. https://doi.org/10.1007/s00432-023-05451-1

Kavouridis, V. K., Ligon, K. L., Wen, P. Y., & Iorgulescu, J. B. (2022). Survival outcomes associated with MGMT promoter methylation and temozolomide in gliosarcoma patients. *Journal of Neuro-Oncology, 158*(1), 111–116. https://doi.org/10.1007/s11060-022-04016-5

Kozak, K. R., Mahadevan, A., & Moody, J. S. (2009). Adult gliosarcoma: Epidemiology, natural history, and factors associated with outcome. *Neuro-Oncology, 11*(2), 183–191. https://doi.org/10.1215/15228517-2008-076

La Torre, D., Della Torre, A., Lo Turco, E., Longo, P., Pugliese, D., Lacroce, P., … Tomasello, F. (2023). Primary intracranial gliosarcoma: Is it really a variant of glioblastoma? An update of the clinical, radiological, and biomolecular characteristics. *Journal of Clinical Medicine, 13*(1), 83. https://doi.org/10.3390/jcm13010083

Langlois, A.-M., Alarfaj, A. K., Sagga, A., Findlay, J. M., & Das, S. (2019). Gliosarcoma in a young Filipino woman: A case report and review of the literature. *American Journal of Case Reports, 20*, 914–919. https://doi.org/10.12659/AJCR.916020

Louis, D. N., Perry, A., Wesseling, P., Brat, D. J., Cree, I. A., Figarella-Branger, D., Hawkins, C., Ng, H. K., Pfister, S. M., Reifenberger, G., Soffietti, R., von Deimling, A., & Ellison, D. W. (2021). The 2021 WHO classification of tumors of the central nervous system: A summary. *Neuro-Oncology, 23*(8), 1231–1251. https://doi.org/10.1093/neuonc/noab106

Lyndon, D. M. (2019). Dural masses: Meningiomas and their mimics. *Insights into Imaging, 10*(1), 1–11. https://doi.org/10.1186/s13244-019-0697-7

Machuca, T. N., Prevedello, D. M. S., Pope, L. Z. B., Haratz, S. S., Araújo, J. C., & Torres, L. F. B. (2004). Gliosarcoma: Report of four cases with immunohistochemical findings. *Arquivos de Neuro-Psiquiatria, 62*(3A), 608–612. https://doi.org/10.1590/s0004-282x2004000400008

Manea, M. C., Iliuta, F. P., Manea, M., Lacau, R. M., Varlam, C.-I., Mares, A. M., Ciobanu, C. A., & Ciobanu, A. M. (2024). Alien hand syndrome: Pathophysiology, semiology and differential diagnosis with psychiatric disorders. *Biomedical Reports, 20*, 74. https://doi.org/10.3892/br.2024.1762

Moroșan, G.-C., Moroșan, A.-C., Dobrin, R., Gavril, L.-C., Ciobică, A., & Sava, A. (2024). Distribution of astrocytic tumors and brain metastases by anatomical location: A study conducted on 91 patients. *Medico-Surgical Journal – Revista Medico-Chirurgicală a Societății de Medici și Naturaliști Iași, 128*(3), 577–586. https://doi.org/10.22551/MSJ.2024.03.16

Moroșan, G.-C., Moroșan, A.-C., Dobrin, R., Săcuiu, I., Petrariu, F. D., Dumitrescu, A.-M., Gavril, L.-C., Ciobică, A., & Sava, A. (2024). Psychiatric manifestations in the context of brain tumors: Study and findings. *BRAIN: Broad Research in Artificial Intelligence and Neuroscience, 15*(4), 231–252. https://doi.org/10.70594/brain/15.4/16

Moroșan, G.-C., Moroșan, A.-C., Ionescu, C., & Sava, A. (2024). Neuropsychiatric symptoms as early indicators of brain tumors. *Archives of Clinical Cases, 11*(4), 120–126. https://doi.org/10.22551/2024.45.1104.10302

Nedelcu, A. H., Bulgaru, D.-C., Partene Vicoleanu, S. A., Tepordei, R. T., Popa, C. G., Popa, R.-A., Moraru, M. C., & Ursaru, M. (2024). The limbic system in adult human brains – Comparative morphometric anatomo-imagistic study. *Romanian Journal of Oral Rehabilitation, 16*(4), October–December. https://doi.org/10.62610/RJOR.2024.4.16.32

Negrilă, C. C., Predoi, D., Ghita, R. V., Iconaru, S. L., Ciobanu, S. C., Manea, M., Badea, M. L., Costescu, A., Trusca, R., Predoi, G., Stanciu, G. A., Hristu, R., Dragu, L. D., Bleotu, C., Groza, A., Marinas, I. C., & Chifiriuc, M. C. (2021). Multi-level evaluation of UV action upon vitamin D enhanced, silver doped hydroxyapatite thin films deposited on titanium substrate. *Coatings, 11*(2), 120. https://doi.org/10.3390/coatings11020120

Peckham, M. E., Osborn, A. G., Palmer, C. A., Tsai, A., & Salzman, K. L. (2019). Gliosarcoma: Neuroimaging and immunohistochemical findings. *Journal of Neuroimaging, 29*(1), 126–132. https://doi.org/10.1111/jon.12565

Roohani, S., Mirwald, M., Ehret, F., Fink, C., König, L., Striefler, J. K., Jacob, N. S., Popp, I., Steffel, J., Handtke, J., Claßen, N. M., Rotermund, T., Zips, D., Vajkoczy, P., Schüller, U., Spałek, M. J., & Kaul, D. (2024). Gliosarcoma: A multi-institutional analysis on clinical outcomes and prognostic factors. *Cancer Medicine, 13*(22), e70347. https://doi.org/10.1002/cam4.70347

Sava, A., Costea, C. F., Vatavu, R., Grigore, M., Turliuc, M. D., Dumitrescu, G. F., Eva, L., Motoc, A. G. M., Stan, C. I., Gavril, L. C., & Scripcariu, S. I. (2021). Brain metastases originating in breast cancer: Clinical-pathological analysis and immunohistochemical profile. *Romanian Journal of Morphology and Embryology, 62*(2), 435–444. https://doi.org/10.47162/RJME.62.2.09

Scripcariu, V., Ciobanu Apostol, D. G., Dumitrescu, G. F., Turliuc, M. D., & Sava, A. (2020). Clinical, histopathological and immunohistochemical features of brain metastases originating in colorectal cancer: A series of 27 consecutive cases. *Romanian Journal of Morphology and Embryology, 61*(1), 81–93. https://doi.org/10.47162/RJME.61.1.09

Stepp, H., & Stummer, W. (2018). 5-ALA in the management of malignant glioma. *Lasers in Surgery and Medicine, 50*(4), 399–419. https://doi.org/10.1002/lsm.22933

Stummer, W., Pichlmeier, U., Meinel, T., Wiestler, O. D., Zanella, F., & Reulen, H. J. (2006). Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: A randomized controlled trial. *Lancet Oncology, 7*(5), 392–401. https://doi.org/10.1016/S1470-2045(06)70665-9

Wu, Y., Chen, Z., Shi, M., Qiu, S., & Zhang, Y. (2025). Nimotuzumab and bevacizumab combined with temozolomide and radiotherapy in patients with newly diagnosed glioblastoma

multiforme: A retrospective single-arm study. *Journal of Neuro-Oncology, 172*(2), 429–436. https://doi.org/10.1007/s11060-024-04932-8

Yildiz, G., Hiçsönmez, A., Yilmaz, S., Adas, Y. G., & Andrieu, M. N. (2010). Gliosarcoma: A study of four cases. *Rare Tumors, 2*(2), e37. https://doi.org/10.4081/rt.2010.e37

Zaki, M. M., Mashouf, L. A., & Woodward, E. (2021). Genomic landscape of gliosarcoma: Distinguishing features and targetable alterations. *Scientific Reports, 11*, 18009. https://doi.org/10.1038/s41598-021-97454-6

Zheng Y., Graeber M.B. (2022). Microglia and brain macrophages as drivers of glioma progression. *International Journal of Molecular Sciences, 23*(24):15612. https://doi.org/10.3390/ijms232415612

Züchner, S., Kawohl, W., Sellhaus, B., Mull, M., Mayfrank, L., & Kosinski, C. M. (2003). A case of gliosarcoma appearing as ischemic stroke. *Journal of Neurology, Neurosurgery & Psychiatry, 74*, 364–366. https://doi.org/10.1136/jnnp.74.3.364