Case Report

IDH1-mutant primary intraventricular gliosarcoma: Case report and systematic review of a rare location and molecular profile

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Abstract

Background: Gliosarcoma (GS) is classified as an IDH-wild-type variant of glioblastoma (GBM). While GS is already an unusual presentation of GBM, IDH1-mutant cases are especially rare. We present an IDH1-mutant primary intraventricular GS case report and a systematic review of the molecular profile in GS correlating to the prognostic and pathogenesis of IDH1/2 mutations.

Case Description: A 44-years-old man presented with ongoing fatigue symptoms and a new-onset intense occipital headache. The patient complained of memory loss, dyscalculia, and concentration difficulties. An MRI revealed a bihemispheric intraventricular mass crossing the midline through the corpus callosum and infiltrating the trigone of the lateral ventricles, hypointense, and hyperintense on the T1- and T2-weighted image. We performed a microsurgical resection with a transparietal transsulcal approach; however, the contralateral mass was attached to vascular structures and we decided to reoperate the patient in another moment. The histopathological study showed a Grade IV tumor and the immunohistochemistry confirmed the diagnosis of GS. The patient presented progressive neurologic decline and died 45 days after the surgical approach.

Conclusion: We did two systematic reviews studies from PubMed, EMBASE, MEDLINE, Cochrane, and SCOPUS databases, and included molecular and intraventricular studies of GS. We performed further meta-analysis using OpenMeta Analyst software. We conducted a forest plot with the molecular profile of GS. When correlated IDH1 mutation versus tp53 mutation, we found an odds ratio (OR) of 0.018 (0.005–0.064) and P < 0.001. Moreover, we compared IDH1 mutation versus MGMT methylation (P = 0.006; OR = 0.138 [0.034–0.562]). The studies evaluating the molecular profile in GS prognostics are often extended from all GBMs despite specifics GBM variants (i.e., GS). We found a correlation between IDH1 mutation expression with tp53 and MGMT expression in GS, and future studies exploring this molecular profile in GS are strongly encouraged.

Keywords: Case report, Cerebral ventricle neoplasms, Gliosarcoma, Human IDH1 protein, Systematic review

Introduction

Gliosarcomas (GS) are rare primary high-grade brain tumors and a variant of GBM, constituting 2–8% of all GBM. They are classified as IDH-wildtype variant with two different components: gliomatous part (i.e., astrocytic with areas of necrosis, and fulfilling the criteria
for glioblastoma [GBM]) determined by the identification of GFAP; and a sarcomatous part that resemble a spindle cell sarcoma determined by the presence of the reticulin element.\textsuperscript{[15,16,31,45,46,48]} The exact pathogenesis is unknown, one theory suggests that sarcomatous components originated from the malignant transformation of hyperplastic blood vessels.\textsuperscript{[15,16,31,45,46,48]}

A modest propensity for temporal lobe involvement was observed in GS followed by the frontal, parietal, and occipital lobes. Cerebellum, pineal region, cerebellopontine angle, intraventricular, and spinal cord have been described as rare primary locations for these lesions.\textsuperscript{[15,16,24,31,45,46,48]}

Headache was the most common presentation of intraventricular GS, other clinical symptoms including aphasia hemiparesis, seizures, and cognitive decline depends on location, size of the tumor, and the existence of hydrocephalus.\textsuperscript{[16,21,42,46]} The age of onset is usually between 40 and 70 years and is more frequent in men than in women. GS has a poor prognosis and a median OS rate varying from 4 to 17.5 months.\textsuperscript{[8,16,17,26]}

We present a rare case of an IDH1-mutant primary intraventricular GS and a systematic review of the molecular profile in GS correlating to the prognostic and pathogenesis of IDH1/2 mutations.

**CASE REPORT**

**Patient**

A 44-years-old man presented with ongoing fatigue symptoms and a new-onset intense occipital headache which was worse in the night and was waking him up from sleep. The patient reported progressive deterioration of the symptoms with increased intensity and frequency of the headaches; moreover, he complained of memory loss, dyscalculia, concentration difficulties, psychomotor agitation, and aggressive behavior.

He was initially treated with dipyrone (4 g/day, oral), naproxen sodium (550 mg/day, oral), and dexamethasone (24 mg/day, oral) from urgent care, and referred to the neurosurgery department. He presented a normal mental status (GCS 15) without impairment on his physical examination and mild bilateral papilledema on his neurological examination.

**Imaging**

It was performed a brain MRI [Figure 1a-f] that revealed a hypointense bihemispheric intraventricular mass on the T1-weighted image and hyperintense mass on the T2-weighted image, crossing the midline through the corpus callosum and infiltrating the trigone of the lateral ventricles. The brain MRI also revealed a heterogeneous contrast enhancement with an important cystic component. The volume of the lesion (manual segmentation) was 63.1 cc and the estimated mean diameter was 50.15 mm. The initial hypothesis was GBM or anaplastic ependymoma. We discussed with the patient about the option of stereotactic biopsy to obtain samples for diagnostic purposes. However, the patient opted for microsurgery for maximum resection of the lesion; however, the gross-total resection was not achievable due to tumor extension.

**Surgery**

We decided to perform a microsurgical resection with a right transtemporal transsulcal approach, reaching the trigone of the right ventricle and the infiltrative mass. We resected the ipsilateral brain lesion; however, the contralateral ventricle resection was limited due to a deep surgical corridor and the need to manipulate vascular structures (i.e., vein of Galen). The immediate postoperative MRI revealed a residual tumor volume of 14.03 cc (estimated mean diameter of 30.58 mm) in the left ventricular trigone [Figure 2a-f]. The histopathological study [Figure 3a-d] showed a GS - Grade IV tumor and the immunohistochemistry [Figure 4a-i] confirmed the diagnosis of GS (WHO - 2016).

**Postoperative evaluation**

After 20 days of the procedure, the patient presented an improvement of headache and psychomotor agitation; however, he continued with progressive worsening of memory loss and showed a diminished spatial awareness.

We started adjuvant radiotherapy and chemotherapy with temozolomide. However, one month after the tumor resection, a new MRI revealed a residual lesion growing on the trigone of the left ventricle with a tumor volume of 41.6 cc (estimated mean diameter of 43.65 mm) and an impressive growth rate estimated in 176.68 mm/year [Figure 5a-c]. The patient had a progressive neurologic decline and died 45 days after the surgical approach.

**MATERIALS AND METHODS**

We performed two systematic reviews of the literature using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and protocol. A literature search was performed using PubMed, EMBASE, Ovid MEDLINE, Cochrane Library, and SCOPUS databases. Search terms included (GS) AND [(idh1) OR (idh2) OR (atrx) OR (p53) OR (tert) OR (1p19q) OR (Ki-67)] in our first systematic review [Figure 6], and (GS) AND (intraventricular) in our second systematic review [Figure 7]. We selected full-text articles published from January 1990 to February 2020. Screening of titles and abstracts was performed, and further evaluation of full-text publications was used to select studies.
The inclusion criteria in our first systematic review were case series studies with at least ten patients containing GS with molecular profile study (IDH1/2, ATRX, tp53, TERT, 1p19q, or Ki-67). Cases series without any molecular profile were excluded from the study.

In our second review, we included only case series studies containing primary GS in the intraventricular location, the exclusion criteria were case series without exclusive GS intraventricular location.

Included studies were assessed by two authors (L. J. M. F and L. A. F. A.) to ensure that cases were correctly included in the study. Patient data from multiple studies were combined into two tables for comparison [Tables 1 and 2].

We used the maximal tumor diameter as a parameter of a possible outcome. In this case, we transformed the tumor volume (V) in an equivalent mean tumor diameter (MTD) using the formula \[\text{MTD} = (2 \times V)^{1/3}\] to standardize our study. The OpenMetaAnalyst™ meta-analysis software (Brown University, RI, USA) was used to perform a forest plot correlating IDH1 versus tp53 and IDH1 versus MGMT methylations in the case series of [Table 1]. The results were expressed as mean ± SD. The differences were considered statistically significant when \(P < 0.05\).
RESULTS

A total of 8 series were included in our first systematic review focused mainly on GS molecular signature. A total of 192 patients were identified [Table 1], most of them were male (64.06%). The mean diameter size was 4.87 (±0.91) cm. Only five case series (132 patients) had reported the tumor location: the temporal lobe was the most common location (39.46%), followed by frontal lobe (29.93%), parietal lobe (14.29%), occipital lobe (6.80%), other locations – nonspecified (4.08%), corpus callosum (2.72%), cerebellum (1.36%), cingulate gyrus (0.68%), and brainstem (0.68%).

Regarding the GS molecular profile studies found in the collected articles, we identified IDH1 mutations in 5.88% ($n = 4/68$) and TP53 mutations in 57% ($n = 57/100$) of patients. TERT mutations and 1p/19q codeletion were reported, respectively, in 70.3% ($n = 26/37$) and 35.3% ($n = 6/17$) of patients. Ki-67 index ≥23% was measured in 46.15% ($n = 12/26$) of evaluated patients. Methylated MGMT was identified in 22.68% ($n = 22/97$) of the patients. The mean OS of these patients was 12.51 (± 3.02) months and the median was 12.3 months.

![Figure 3](image1.png)

**Figure 3**: (a) Sarcomatous component, with marked pleomorphic spindle cells and mitotic activity (H and E, ×10). (b) Glial component, presenting hypercellularity, pleomorphism, mitotic figures, and nuclear atypia (H and E, ×20). (c) Glial component. Featuring hypercellularity, a high degree of anaplasia, presence of bizarre multinucleated cells, nuclear atypia, and evident mitotic figures (H and E, ×40). (d) Sarcomatous component, presenting mitotic figures, and nuclear atypia (H and E, ×20).

![Figure 4](image2.png)

**Figure 4**: Immunohistochemical stains. (a) Focal positivity for GFAP, only in glial component (×10). (b) IDH was positive in the glial component (×10). (c) SMA (Smooth Muscle Actin) was positive in the sarcomatous component (×10). (d) Partial loss of ATRX expression (intact) in tumor cells (×10). (e) S100 was positive in the glial component (×10). (f) Vimentin was positive in the sarcomatous component (×20). (g) Diffuse positivity for p53 stain - approximately 80% of neoplastic cells (×10). (h) Ki-67 stain showed more than 60% proliferative activity in the tumor nuclei - 35% of neoplastic cells (×10). (i) Gomori silver stain highlights reticulin, negative in the glial component, and positive in the sarcomatous component.
We conducted a forest plot with the molecular profile of GS [Figure 8]; crossing IDH1 mutation versus tp53 mutation we found an estimated odds ratio of 0.018 (0.005–0.064) and $P < 0.001$. Moreover, we compared IDH1 mutation versus MGMT methylation and found a $P = 0.006$ and an odds ratio of 0.138 (0.034–0.562).

Our second systematic review included a total of ten intraventricular GS and we included our case for further evaluation [Table 2]. Out of 11 patients, seven were male (63.63%) and the mean diameter was 4.01 (±1.01) cm. The molecular profile study revealed tp53 mutations on four out of five patients (80%), IDH1 mutation was positive in only one patient (50%). ATRX was retained in two patients. Ki-67 index ≥ 23% was measured in 50% of patients. The mean OS of intraventricular GS was 4.75 (± 2.59) months and the median was 5 months. Transcortical approach was the most common neurosurgical technique in intraventricular GS (71.42%) and gross-total resection was achieved in only 50% of patients.
IDH1/2 has an important role in chemo and/or radiotherapy in many types of tumors, and this unique molecular signature (i.e., IDH1/2 mutations) need further studies regarding the impact on GS treatment efficacy and prognosis. Moreover, they seem to explain the cellular metabolism, DNA repair, and epigenetic regulation, which contribute to GS carcinogenesis. These mutations are common in more than 80% of DLGG and are considered biomarkers in secondary GBM; however, they are rare in primary GS and GBM. It is interesting to observe that the presence of IDH mutation in some GS probably means that some of these rare tumors also may arise from a low-grade glioma and follow the course of secondary gliomagenesis like in GBM.

Both components (i.e., gliomatous and sarcomatous) of GS present tp53 mutations or overexpression and are found in patients with primary and secondary GS, suggesting that they may occur early in gliomagenesis. These mutations increase the vulnerability to mesenchymal differentiation through cancer epithelial-to-mesenchymal transition-like processes that are also associated with cancer aggressiveness and could be a key in GS pathogenesis. These mutations are rare in GS, however, some study findings slightly differed with these data, demonstrating tp53 positivity in the majority of lesions. Our analysis showed an association between IDH1 and tp53 mutations in GS [Table 1]. The frequent DNA copy number losses in GS, mainly in regions containing CDKN2A genes (i.e., chromosomes nine and ten) that encode tumor suppressors and regulate the tp53 gene may explain why those mutations are so frequent in these tumors and were related to treatment resistance and poor patient OS.

Some studies suggest that ATRX is expressed in all GS. ATRX maintains genome stability, gene expression, and cell cycle regulation. ATRX loss in elderly patients is associated with IDH-mutation in GBM. Despite that, it is not well established if this ATRX loss is more prevalent in primary or secondary GBM.

TERT promoter mutations were majorly present in both glial and mesenchymal tumor areas in GS, and they play a crucial role by conferring these tumors unrestricted growth properties, contributing to the tumorigenesis. Therefore, telomerase activation may be an underlying mechanism...
### Table 1: Molecular profile of patients presenting with gliosarcoma.

| Authors (ref)         | n    | Median age (IQR) | Male sex (%) | Mean diameter (cm) | Tumor Location                                                                 | IDH1 mutation (%) | TP53 (% based on n of patients) | TERT (% based on n of patients) | MGMT (% based on n of patients) | 1p/19q codeletion | Ki67 index ≥23,0% (%) | Overall survival (months) |
|-----------------------|------|------------------|--------------|-------------------|---------------------------------------------------------------------------------|-------------------|--------------------------------|---------------------------------|-----------------------------|-----------------|------------------------|--------------------------|
| Adeberg et al., 2016[1] | 37   | 62.0 (42–82)     | NR           | NR                | 18 temporal lobe; 14 frontal lobe; 7 parietal lobe; 3 occipital lobe             | 0                 | NR                             | 70.3%                           | 27.0%                        | NR              | NR                     | 13.4                     |
| Ahmed et al., 2019[2]  | 11   | 63.0 (41.8–81.7) | 64.0         | 3.85              | 9 temporal lobe; 10 frontal lobe; 5 parietal lobe; 2 occipital lobe; 2 others   | 0                 | 82%                           | NR                             | NR                          | NR              | 50%*                   | 12.6                     |
| Biernat et al., 1995[3] | 12   | 51.5 (32–52)     | 66.7         | NR                | 18 temporal lobe; 14 frontal lobe; 7 parietal lobe; 3 occipital lobe             | NR                | 16.6%                          | NR                             | NR                          | NR              | NR                     | NR                       |
| Cachia et al., 2015[4] | 34   | 55 (35–74)       | 0.71         | NR                | 18 temporal lobe; 14 frontal lobe; 7 parietal lobe; 3 occipital lobe             | NR                | NR                             | 7.1%                           | (1/14)                       | NR              | NR                     | 17.5                     |
| Cho et al., 2017[5]    | 28   | 51.5 (42–64)     | 67.9         | 5.16              | 9 temporal lobe; 10 frontal lobe; 5 parietal lobe; 2 occipital lobe; 2 others   | 3.50              | 71.0%                          | NR                             | (7/18)                       | NR              | 38.9%*                  | 43.7%*                   | 12.0                     |
| Lee et al., 2012[6]    | 26   | 51.0 (11–84)     | 61.5         | NR                | 18 temporal lobe; 14 frontal lobe; 7 parietal lobe; 3 occipital lobe             | 7.7               | NR                             | 11.5%                          | NR                          | NR              | NR                     | 11.3                     |
| Peckham et al., 2019[7] | 25   | 65 (52.5–74)     | 52.0         | 5.6               | 18 temporal lobe; 14 frontal lobe; 7 parietal lobe; 3 occipital lobe             | 0                 | 81.25%*                        | (13/16)                        | NR                          | NR              | 12.5%*                  | 8.25                     |
| Reis et al., 2009[8]   | 19   | 56.0 (51–67)     | 57.9         | NR                | 18 temporal lobe; 14 frontal lobe; 7 parietal lobe; 3 occipital lobe             | NR                | 26%                            | NR                             | NR                          | NR              | NR                     | NR                       |

*Values referring to the fractions of the patients in which the researches were carried out for a given biomarker. †Average value, data provided by the authors. n: Number of patients. NR: Not reported. IQR: Interquartile range.
Table 2: Patients presenting with gliosarcoma in intraventricular location.

| Authors (ref)          | n  | Median age (IQR) | Male sex (%) | Mean diameter (cm) | Tumor Location                                                                 | Surgical Approach                                                                 | Gross total resection | Cyst Component | IDH1 mutation (%) | ATRX | TP53 | KI67 index ≥23% (%) | Overall survival (months) |
|------------------------|----|------------------|--------------|--------------------|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------|-----------------------|-----------------|-------------------|------|------|-------------------|--------------------------|
| Baldawa et al., 2013    | 1  | 18.0             | 0            | 3                  | Temporal horn of the left ventricle and left atrium                           | Left temporal craniotomy (trans temporal - middle temporal gyrus)                 | No                    | Yes             | NR                | NR    | NR    | NR                | 4 (Alive)                |
| Doddamani et al., 2016  | 1  | 23               | 100          | 6.23               | Occipital horn of right lateral ventricle                                    | Right parietal craniotomy (trans cortical transventricular)                      | Yes                   | Yes             | NR                | NR    | NR    | NR                | 6 (Alive)                |
| Govindan et al., 2008   | 1  | 55.0             | 0            | NR                 | Septum and both frontal horns of lateral ventricle                           | NR                                                                               | Yes                   | No              | NR                | NR    | NR    | Positive in both components | 0.33 (Died)               |
| Han et al., 2008        | 2  | 45 (36-54)       | 50           | 6.07               | Left posterior horn of lateral ventricle                                    | NR                                                                               | NR                    | No              | NR                | NR    | NR    | NR                | 8 (Alive)                |
| Huo et al., 2014        | 1  | 47               | 100          | 4.33               | Frontal lobe + anterior horn and body of left lateral ventricle               | NR                                                                               | NR                    | Yes             | NR                | NR    | NR    | Positive in both components | 0% 130.0 (Alive)          |
| Moiyadi et al., 2009    | 1  | 65.0             | 100          | NR                 | Right temporal horn                                                          | Right temporal craniotomy (trans cortical)                                      | No                    | No              | NR                | NR    | NR    | Positive in both components | 2.0 (Alive)               |
| Poyuran et al., 2017    | 1  | 68.0             | 100          | NR                 | Frontal horn of right lateral ventricle                                      | Right frontal craniotomy (trans sulcal transventricular)                         | Yes                   | No              | 0%                | Retained Negative | NR    | NR    | 2.0 (Died)         |
| Salunke et al., 2017    | 1  | 28.0             | 100          | NR                 | Bilateral lateral ventricles                                                 | Parasagittal craniotomy (trans cortical)                                         | No                    | No              | NR                | NR    | NR    | NR                | NR                       |
| Sarkar et al., 2013     | 1  | 60.0             | 0            | NR                 | Septal region extending into body and frontal horn of both lateral ventricles | Right frontal craniotomy (transfrontocortical transventricular)                 | Yes                   | No              | NR                | NR    | NR    | NR                | NR                       |
| Our case                | 1  | 44               | 100          | 5.02               | Lateral ventricles trigone                                                  | Right parietal craniotomy (trans parietal transsulcal)                          | No                    | Yes             | 100%              | Intact/Partial loss | 100% 100% | 2.76 (Died)       |

n: Number of patients, NR: Not reported, IQR: Interquartile range.
in GBM; moreover, TERT mutations are more frequent in IDH-mutant GBM and presented a better OS in these tumors.\(^{27}\) 1p/19q codeletion is strongly associated with TERT mutations in malignant gliomas\(^{27}\) and it is typically associated with mutations in IDH1/2.\(^{31}\)

Ki-67 is a nonhistone nuclear protein and a cellular marker associated with ribosomal RNA transcription in cell proliferation\(^{3,47}\) and the increasing Ki-67 expression may be the final event in the progression of these tumors.\(^{10}\) Ki-67 index with values below 23% indicating better OS in GBM and IDH1 mutations were associated with low Ki-67 expression in primary GBM.\(^{10}\)

MGMT is a DNA repair protein and its loss is correlated to increased survival in malignant gliomas.\(^{15}\) However, the MGMT methylation may vary between GBM and GS which can impact overall and progression-free survival.\(^{25,44}\) We observed that IDH1 mutations, a rare finding in GS (that is also correlated with better survival), are also associated with higher frequencies of methylated MGMT.

In our case, the tumor was in the atrium and the occipital horn of the lateral ventricles and we decided to achieve a maximal resection minimizing the risks to the relevant subcortical tracts through a transsulcal approach. A gross total resection of the tumor without significant complication requires a thorough understanding of available surgical approaches and their relative advantages and disadvantages.\(^{14}\)

Limitations

We may point some relevant limitations in our paper.

Since there are many nonrecorded IDH1 statuses in prior studies in both overall and intraventricular group, the percentages as described may have errors. Although we found a statistical correlation between IDH1 mutation and tp53 and between IDH1 mutation and MGMT, we must alert that with so few numbers of IDH1 positive cases data might be erroneous.

Due to the great limitation of data related to GS in the literature, many comparisons and analogies in the discussion were made in relation to GBM, including the cutoff point used for the Ki-67 of 23%, which is not entirely adequate because they are distinct pathologies, despite some similarities.

CONCLUSION

There is a lack of data in the literature related to molecular profiles specific to GS, with an inappropriate tendency to compare their behavior and molecular profile with GBM. More molecular studies are needed for GS.

We found a correlation between IDH1 mutation expression with p53 and MGMT expression in GS, and future studies exploring this molecular profile in GS are strongly encouraged.

Our study validates the need to perform IDH1 analysis in all GS cases and assess other molecular and clinical associations and outcomes, respectively.

Declaration of patient consent

Patient’s consent not required as patients identity is not disclosed or compromised.

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Conflicts of interest

There are no conflicts of interest.
REFERENCES

1. Adeberg S, Bernhardt D, Harrabi SB, Diehl C, Koelsche C, Rieken S, et al. Radiotherapy plus concomitant temozolomide in primary gliosarcoma. J Neurooncol 2016;128:341-8.

2. Ahmed FI, Abdullah KG, Durgin J, Salinas RD, O’Rourke DM, Brem S. Evaluating the association between the extent of resection and survival in gliosarcoma. Cureus 2019;11:e4374.

3. Alkhaiary A, Alasiri AH, AlSuﬁani F, Alhari MB. Ki-67 labeling index in glioblastoma; does it really matter? Hematol Oncol Stem Cell Ther 2019;12:82-8.

4. Arita H, Narita Y, Fukushima S, Tateishi K, Matsushita Y, Yoshida A, Miyakita Y, et al. Upregulating mutations in the TERT promoter commonly occur in adult malignant gliomas and are strongly associated with total 1p19q loss. Acta Neuropathol 2013;126:267-76.

5. Baldawa S, Kasegaonkar P, Vani S, Kelkar G. Primary intraventricular gliosarcoma. Clin Neuropathol 2013;32:525-8.

6. Biernat W, Aguzzi A, Sure U, Grant JW, Kleihues P, Hegi ME. Identical mutations of the p53 tumor suppressor gene in the gliomatous and the sarcomatous components of gliosarcomas suggest a common origin from glial cells. J Neuropathol Exp Neurol 1995;54:651-6.

7. Cachia D, Kamiya-Matsuoka C, Mandel JJ, Olar A, Cykowski MD, Armstrong TS, et al. Primary and secondary gliosarcomas: Clinical, molecular and survival characteristics. J Neurooncol 2015;125:401-10.

8. Cai J, Chen J, Zhang W, Yang P, Zhang C, Li M, et al. Loss of ATRX, associated with DNA methylation pattern of chromosome end, impacted biological behaviors of astrocytic tumors. Oncotarget 2016;7:16805-15.

9. Chaureasia A, Park SH, Seo JW, Park CK. Immunohistochemical analysis of ATRX, IDH1 and p53 in glioblastoma and their correlations with patient survival. J Korean Med Sci 2016;31:1208-14.

10. Cho SY, Park C, Na D, Han JY, Lee J, Park OK, et al. High prevalence of TP53 mutations is associated with poor survival and an EMT signature in gliosarcoma patients. Exp Mol Med 2017;49:e317.

11. Cikla U, Swanson KI, Tumturk A, Keser N, Uluc K, Cohen-Gadol A, et al. Microsurgical resection of tumors of the lateral and third ventricles: Operative corridors for difﬁcult-to-reach lesions. J Neurooncol 2016;130:331-40.

12. Souza LC, Nicoletti AL, Leao CM, de Lima JT, de Souza JT, Coutinho SL. Long-term metastatic gliosarcoma survival after meningioma resection: Case report and literature revision. J Neurosurg 2017;96:291-4.
33. Molenaar RJ, Maciejewski JP, Wilmink JW, van Noorden CJ. Wild-type and mutated IDH1/2 enzymes and therapy responses. Oncogene 2018;37:1949-60.

34. Ning L, Wang PF, Song HW, Kong LW, Yao K, Qi XL, et al. Immunostaining of IDH-1 R132H and ATRX proteins in the classification of adult glioblastomas. Int J Clin Exp Pathol 2016;9:12849-54.

35. Oh JE, Ohta T, Nonoguchi N, Satomi K, Capper D, Piercionek D, et al. Genetic alterations in gliosarcoma and giant cell glioblastoma. Brain Pathol 2016;26:517-22.

36. Pain M, Wang H, Lee E, Strahl M, Hamou W, Sebra R, et al. Treatment-associated TP53 DNA-binding domain missense mutations in the pathogenesis of secondary gliosarcoma. Oncotarget 2017;9:2603-21.

37. Pallud J, Taillandier L, Capelle L, Fontaine D, Peyre M, Ducray F, et al. Quantitative morphological magnetic resonance imaging follow-up of low-grade glioma: A plea for systematic measurement of growth rates. Neurosurgery 2012;71:729-40.

38. Peckham ME, Osborn AG, Palmer CA, Tsai A, Salzman KL. Gliosarcoma: Neuroimaging and immunohistochemical findings. J Neuroimaging 2019;29:126-32.

39. Poyuran R, Bn N, Reddy YV, Savardekar AR. Intraventricular gliosarcoma with dual sarcomatous differentiation: A unique case. Neuropathology 2017;37:346-50.

40. Reis RM, Köntü-Leblebicioglu D, Lopes JM, Kleihues P, Ohgaki H. Genetic profile of gliosarcomas. Am J Pathol 2000;156:425-32.

41. Salunke P, Singh H, Vaiphei K. Lateral ventricular gliosarcoma with attachment to septum pellucidum. Asian J Neurosurg 2017;12:82-4.

42. Sampaio L, Linhares P, Fonseca J. Detailed magnetic resonance imaging features of a case series of primary gliosarcoma. Neuroradiol J 2017;30:546-53.

43. Sarkar H, K S, Ghosh S. Pure intraventricular origin of gliosarcoma—a rare entity. Turk Neurosurg 2013;23:392-4.

44. Singh G, Mallick S, Sharma V, Joshi N, Purkait S, Jha P, et al. A study of clinico-pathological parameters and O⁶-methylguanine DNA methyltransferase (MGMT) promoter methylation status in the prognostication of gliosarcoma. Neuropathology 2012;32:534-42.

45. Smith DR, Wu CC, Saadatmand HJ, Isaacson SR, Cheng SK, Sisti MB, et al. Clinical and molecular characteristics of gliosarcoma and modern prognostic significance relative to conventional glioblastoma. J Neurooncol 2018;137:303-11.

46. Witwer BP, Salamat MS, Resnick DK. Gliosarcoma metastatic to the cervical spinal cord: Case report and review of the literature. Surg Neurol 2000;54:373-9.

47. Wong E, Nahar N, Hau E, Varikatt W, Gebski V, Ng T, et al. Cut-point for Ki-67 proliferation index as a prognostic marker for glioblastoma. Asia Pac J Clin Oncol 2019;15:5-9.

48. Zhang G, Huang S, Zhang J, Wu Z, Lin S, Wang Y. Clinical outcome of gliosarcoma compared with glioblastoma multiforme: A clinical study in Chinese patients. J Neurooncol 2016;127:355-62.

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