

ROMANIAN NEUROSURGERY

Vol. XXXX | No. 3

September 2026

Synchronous coexistence of low-grade
and high-grade gliomas in a single
patient: a case report and literature
review

Alejandra Arévalo-Sáenz,
Gloria de Antonio Palomo,
Elisa González Romero,
Fernando José Rascón-Ramírez,
Pedro Alonso Lera



Synchronous coexistence of low-grade and high-grade gliomas in a single patient: a case report and literature review

A. Arévalo-Sáenz, G. de Antonio Palomo, E. González Romero,
F. J. Rascón-Ramírez, P. Alonso Lera

Department of Neurosurgery, Hospital Clínico San Carlos,
Complutense University of Madrid, Madrid, SPAIN

ABSTRACT

Background: The simultaneous occurrence of low-grade and high-grade gliomas in different brain regions of the same patient is exceedingly rare. This phenomenon may represent malignant progression of a pre-existing low-grade glioma, true synchronous gliomas, or multicentric gliomagenesis. Distinguishing among these entities has important diagnostic, prognostic, and therapeutic implications.

Case description: A 53-year-old man with no significant neurological history had been followed for several years for a stable left thalamic lesion radiologically suggestive of a low-grade glioma. He presented with acute visual impairment and was diagnosed with a left occipital hemorrhagic lesion. Subsequent magnetic resonance imaging revealed a contrast-enhancing occipital mass with radiological characteristics suggestive of a high-grade glial neoplasm, while the thalamic lesion remained unchanged. Perfusion imaging demonstrated increased vascularity within the occipital lesion. The patient underwent gross total resection of the occipital tumor, and histopathological examination confirmed a high-grade glial neoplasm. Given the long-term radiological stability and deep location of the thalamic lesion, no surgical intervention was performed.

Conclusions: The synchronous coexistence of low-grade and high-grade gliomas in distinct cerebral locations is exceptionally uncommon. This case highlights the diagnostic challenges associated with multiple gliomas and emphasizes the importance of integrating clinical, radiological, histopathological, and molecular findings to differentiate malignant progression from truly synchronous tumors. Further molecular characterization is essential to improve our understanding of glioma pathogenesis and multicentric tumor development.

INTRODUCTION

Gliomas are the most common primary tumors of the central nervous system and comprise a heterogeneous group of neoplasms characterized by distinct histological, molecular, and clinical features [5,6]. According to the current World Health Organization (WHO) classification, gliomas are stratified based on both histopathological and molecular characteristics, which have significant implications for prognosis and treatment strategies [9].

Keywords

glioma,
low-grade glioma,
high-grade glioma,
multicentric glioma,
synchronous glioma,
neuro-oncology



Corresponding author:
Alejandra Arévalo-Sáenz

Hospital Clínico San Carlos, Madrid,
Spain

praimale@hotmail.com

Copyright and usage. This is an Open Access article, distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License (<https://creativecommons.org/licenses/by-nc-nd/4.0/>) which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is unaltered and is properly cited.

The written permission of the Romanian Society of Neurosurgery must be obtained for commercial re-use or in order to create a derivative work.

ISSN 2344-4959 (online)
ISSN 1220-8841 (print)

© Romanian Society of
Neurosurgery



First published
September 2026 by
London Academic Publishing
www.london-ap.uk

Most gliomas present as solitary lesions; however, multiple gliomas occurring within the same patient represent an uncommon clinical entity [1].

The presence of more than one glial tumor may correspond to multifocal gliomas, multicentric gliomas, or malignant progression of a previously existing low-grade lesion [1,3]. Multifocal gliomas are thought to arise through dissemination along established anatomical pathways, whereas multicentric gliomas develop independently in separate regions of the brain without evidence of direct anatomical connection [3,8]. The simultaneous occurrence of lesions with different histological grades is particularly rare and raises important questions regarding glioma pathogenesis and tumor evolution [2,7].

Several mechanisms have been proposed to explain the coexistence of low-grade and high-grade gliomas in the same patient. These include malignant transformation of a pre-existing low-grade glioma, independent tumorigenesis from distinct precursor cells, and widespread molecular alterations predisposing different regions of the brain to neoplastic development [2,7]. Recent advances in

molecular neuropathology have demonstrated that some spatially separated gliomas share common genetic alterations, suggesting a common clonal origin, whereas others exhibit completely distinct molecular profiles consistent with independent tumor formation [4,7].

Distinguishing between these possibilities is clinically relevant because it may influence prognosis, therapeutic decisions, and follow-up strategies [6,9]. Neuroimaging plays a fundamental role in the initial evaluation of these patients; however, histopathological and molecular analyses remain essential for definitive diagnosis and characterization of the relationship between separate lesions [7,9].

We present the case of a 53-year-old man with a longstanding stable thalamic lesion suggestive of a low-grade glioma who subsequently developed a hemorrhagic occipital high-grade glial tumor. This unusual presentation highlights the diagnostic challenges associated with synchronous gliomas of different grades and underscores the importance of integrating clinical, radiological, and pathological findings in the management of these rare cases.

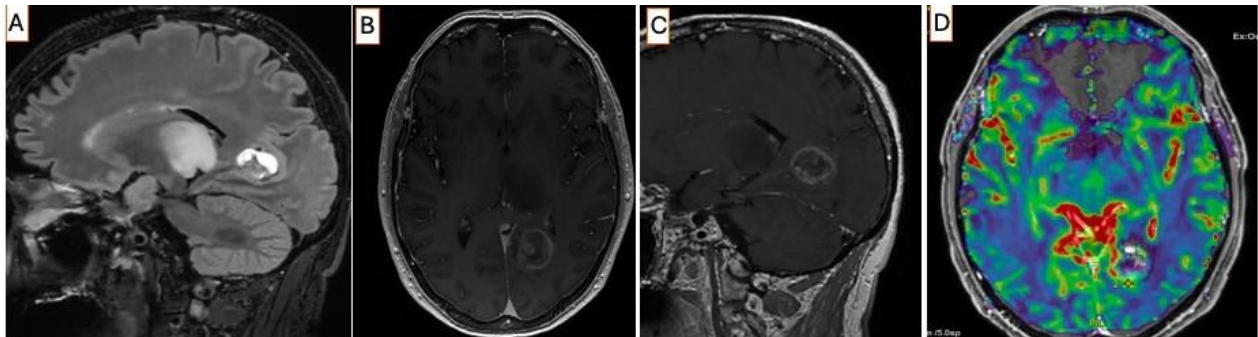


Figure 1. Preoperative MRI demonstrating a stable left thalamic lesion suggestive of low-grade glioma and a hemorrhagic left occipital contrast-enhancing lesion with increased perfusion, compatible with a high-grade glial neoplasm.

CASE REPORT

A 53-year-old man with no relevant neurological or oncological medical history was followed in our outpatient neurosurgical clinic for a left thalamic lesion that had remained radiologically stable for several years. Serial magnetic resonance imaging (MRI) studies demonstrated a diffuse infiltrative lesion involving the left thalamus, without contrast enhancement or significant interval growth, findings suggestive of a low-grade glioma. Given its deep-seated location and the absence of clinical or radiological progression, a conservative

management strategy based on periodic neuroimaging surveillance was adopted.

The patient presented to the emergency department with acute visual impairment. Neurological examination revealed visual disturbances without motor deficits, sensory abnormalities, language disturbances, or impairment of consciousness. Cranial computed tomography demonstrated a left occipital intracerebral hemorrhage. Subsequent MRI revealed a hemorrhagic lesion in the left occipital lobe associated with irregular contrast enhancement,

surrounding vasogenic edema, and increased perfusion, findings highly suggestive of a high-grade glial neoplasm (Figure 1).

The previously known thalamic lesion remained unchanged compared with prior examinations, maintaining the radiological characteristics of a diffuse low-grade glioma. No radiological continuity between the thalamic and occipital lesions was identified.

Considering the symptomatic presentation and the imaging characteristics of the occipital lesion, surgical treatment was indicated. The patient underwent a left occipital craniotomy and microsurgical resection of the lesion. Gross total resection was achieved without intraoperative complications. Postoperative MRI confirmed complete removal of the contrast-enhancing lesion with no evidence of residual tumor or surgical complications (Figure 2).

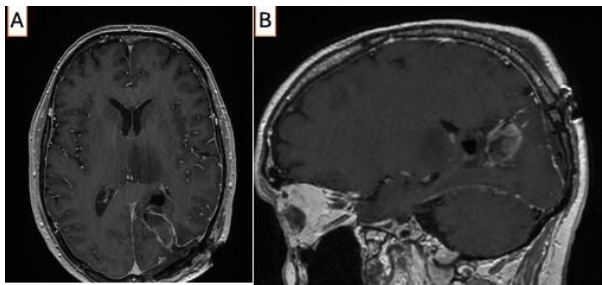


Figure 2. Postoperative contrast-enhanced MRI showing gross total resection of the occipital tumor without evidence of residual enhancing disease or postoperative complications.

Histopathological examination revealed a high-grade diffuse glial neoplasm. Immunohistochemical analysis demonstrated strong positivity for glial fibrillary acidic protein (GFAP), confirming astrocytic differentiation. ATRX expression was retained, while immunostaining for IDH1 R132H mutation was negative. Cytokeratin markers (CK AE1/AE3) were also negative, excluding an epithelial neoplasm or metastatic carcinoma. P53 expression was identified in approximately 5% of tumor cells, and the Ki-67 proliferation index reached approximately 20%, supporting a highly proliferative glial tumor. These findings were consistent with an IDH-wildtype high-grade glioma.

The postoperative course was uneventful, and the patient was referred to the multidisciplinary neuro-oncology board for further management and adjuvant treatment planning. Given the prolonged

radiological stability of the thalamic lesion, its deep anatomical location, and the absence of imaging findings suggestive of progression, no surgical intervention or biopsy was performed for this lesion. Continued radiological surveillance was recommended.

The coexistence of a longstanding radiologically stable thalamic lesion suggestive of a low-grade glioma and a newly diagnosed high-grade IDH-wildtype glioma in a separate cerebral location represents an unusual and diagnostically challenging presentation. The absence of radiological progression of the thalamic lesion over several years favors the hypothesis of synchronous gliomas rather than malignant transformation, although definitive confirmation would require molecular characterization of both lesions. This case highlights the complexity of glioma biology and emphasizes the importance of integrating clinical, radiological, histopathological, and molecular findings when evaluating multiple glial lesions within the same patient.

DISCUSSION

The occurrence of multiple gliomas within the same patient is an uncommon event, accounting for approximately 2–8% of all gliomas. These lesions may be classified as multifocal or multicentric depending on the presence or absence of anatomical continuity between tumors. While multifocal gliomas are thought to arise through dissemination along established white matter tracts, cerebrospinal fluid pathways, or commissural fibers, multicentric gliomas are considered independent neoplasms developing in separate brain regions without radiological evidence of connection [1,3,8].

The coexistence of low-grade and high-grade gliomas in distinct cerebral locations is exceptionally rare. Several mechanisms have been proposed to explain this phenomenon, including malignant transformation of a pre-existing low-grade glioma, independent tumorigenesis from distinct precursor cells, and widespread molecular abnormalities predisposing multiple areas of the central nervous system to neoplastic transformation [2,7]. Distinguishing between these possibilities is clinically relevant because it may influence prognosis, treatment strategies, and surveillance protocols.

In the present case, the patient had a left thalamic lesion that remained radiologically stable for several

years and was highly suggestive of a low-grade glioma. The subsequent development of a hemorrhagic occipital lesion with contrast enhancement, surrounding edema, and elevated perfusion parameters raised suspicion for a biologically distinct high-grade glial neoplasm. Importantly, no radiological continuity between the two lesions was identified. The prolonged stability of the thalamic lesion argues against conventional malignant transformation and favors the hypothesis of synchronous gliomas with different biological behavior.

Only a limited number of comparable cases have been reported in the literature. Nakhl *et al.* described a patient harboring a WHO grade II astrocytoma and

a synchronous glioblastoma in separate cerebral locations, demonstrating clear radiological-pathological correlation between lesions of different grades [10]. Similarly, Inoue *et al.* reported multicentric gliomas with distinct histological grades located in supra- and infratentorial regions [13]. Doğan *et al.* described synchronous multicentric astrocytomas with different histological subtypes, further supporting the concept that spatially separated gliomas may arise independently [12]. These reports, together with our case, suggest that gliomas of different grades may coexist in the same patient without necessarily representing progression from a single precursor lesion.

Table 1. Published cases of synchronous or multicentric gliomas with different histological grades (WHO, World Health Organization).

Author	Year	Age/sex	Location	Histology	Key findings
Nakhl <i>et al.</i>	2010	52/M	Left frontal and left temporal lobes	WHO grade II astrocytoma and glioblastoma	First report demonstrating radiological-pathological correlation between synchronous gliomas of different grades.
Inoue <i>et al.</i>	2016	42/F	Supratentorial and infratentorial regions	Diffuse astrocytoma (WHO grade II) and glioblastoma (WHO grade IV)	Multicentric gliomas with different histology and no anatomical continuity.
Doğan <i>et al.</i>	2021	26/M	Frontal lobe and posterior fossa	Anaplastic astrocytoma (WHO grade III) and pilocytic astrocytoma (WHO grade I)	Rare synchronous multicentric astrocytomas with distinct pathological features.
Perić <i>et al.</i>	2018	59/M	Multiple supratentorial lesions	Multicentric malignant gliomas	Distinct radiological behavior among lesions suggesting biological heterogeneity.
Cureus multicentric glioma series	2023	3 patients	Multiple cerebral locations	High-grade multicentric gliomas	Discussed independent tumor evolution and genetic divergence among lesions.
Present case	2026	53/M	Left thalamus and left occipital lobe	Presumed low-grade glioma and IDH-wildtype high-grade glioma	Longstanding stable thalamic lesion associated with a spatially distinct hemorrhagic high-grade glioma; findings favor synchronous gliomas rather than malignant progression.

Neuroimaging plays a crucial role in the evaluation of these patients. The thalamic lesion in our patient demonstrated the typical characteristics of a low-grade glioma, including the absence of contrast enhancement and long-term radiological stability. In contrast, the occipital lesion presented with hemorrhage, irregular enhancement, vasogenic edema, and increased perfusion, findings commonly associated with high-grade gliomas [4,11]. Such marked radiological differences strongly suggest divergent biological behavior and support the possibility of independent tumor development.

Histopathological analysis of the occipital lesion revealed a high-grade diffuse glial neoplasm. Immunohistochemistry demonstrated GFAP positivity, confirming glial differentiation. Retained ATRX expression and negative IDH1 immunostaining were consistent with an IDH-wildtype high-grade glioma. The Ki-67 labeling index of approximately 20% indicated a highly proliferative tumor, whereas p53 expression was limited to approximately 5% of

tumor cells. Negative AE1/AE3 staining excluded an epithelial neoplasm or metastatic carcinoma. Although molecular profiling was not available, the pathological findings confirmed the aggressive nature of the occipital lesion.

Recent advances in molecular neuropathology have significantly improved the understanding of multicentric gliomas. Genomic studies have demonstrated that some apparently separate lesions share common driver mutations, supporting a common clonal origin, whereas others exhibit completely distinct molecular profiles, suggesting independent tumorigenesis [4,7]. Unfortunately, molecular comparison between the thalamic and occipital lesions was not feasible because tissue from the thalamic lesion was unavailable. Nevertheless, the prolonged radiological stability of the thalamic lesion and the markedly different imaging characteristics of the occipital tumor support the hypothesis of synchronous gliomas rather than malignant progression.

Management of patients with multiple gliomas should be individualized. Surgical resection remains the standard treatment for accessible high-grade lesions because it provides histological diagnosis, cytoreduction, and symptomatic relief. Conversely, observation may be appropriate for stable lesions located in eloquent or deep-seated regions when the risks associated with biopsy or resection outweigh potential benefits. In our patient, gross total resection of the symptomatic occipital lesion was achieved, whereas the thalamic lesion continued to be managed conservatively due to its stability and anatomical location.

CONCLUSION

The synchronous coexistence of a longstanding thalamic lesion suggestive of low-grade glioma and a spatially distinct hemorrhagic IDH-wildtype high-grade glioma is exceedingly rare. The absence of radiological continuity and the prolonged stability of the thalamic lesion favor the diagnosis of synchronous gliomas rather than malignant transformation. This case highlights the importance of integrating clinical, radiological, histopathological, and molecular information when evaluating multiple glial lesions and contributes to the limited literature regarding gliomas of different grades occurring in the same patient.

Patient consent

Written informed consent for publication of the clinical information and accompanying images was obtained from the patient.

REFERENCES

1. Batzdorf U, Malamud N. The problem of multicentric gliomas. *J Neurosurg.* 1963;20:122-136.
2. Di Carlo DT, Cagnazzo F, Benedetto N, Morganti R, Perrini P. Multiple high-grade gliomas: epidemiology, management, and outcome. A systematic review. *Neurosurg Rev.* 2019;42:263-275. DOI: 10.1007/s10143-018-0994-2.
3. Djalilian HR, Shah MV, Hall WA. Radiographic incidence of multicentric malignant gliomas. *Surg Neurol.* 1999;51:554-557. DOI: 10.1016/S0090-3019(99)00008-0.
4. Lasocki A, Gaillard F, Tacey M, Drummond K, Stuckey S. Multifocal and multicentric glioblastoma: improved characterisation with contemporary imaging. *J Med Imaging Radiat Oncol.* 2016;60:530-538. DOI: 10.1111/1754-9485.12436.
5. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, Hawkins C, Ng HK, Pfister SM, Reifenberger G, Soffietti R, von Deimling A, Ellison DW. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol.* 2021;23(8):1231-1251. DOI: 10.1093/neuonc/noab106.
6. Ostrom QT, Price M, Neff C, Cioffi G, Waite KA, Kruchko C, Barnholtz-Sloan JS. CBRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2015-2019. *Neuro Oncol.* 2022;24(Suppl 5):v1-v95. DOI: 10.1093/neuonc/noac202.
7. Picart T, Barritault M, Berzero G, Meyronet D, Raverot G, Ducray F. Characteristics of adult multifocal gliomas: a review. *J Neurooncol.* 2018;136:189-198. DOI: 10.1007/s11060-017-2646-8.
8. Salvati M, Caroli E, Orlando ER, Frati A, Ferrante L. Multicentric glioma: our experience in 25 patients and critical review of the literature. *Neurosurg Rev.* 2003;26:275-279. DOI: 10.1007/s10143-003-0278-0.
9. Weller M, van den Bent M, Preusser M, Le Rhun E, Tonn JC, Minniti G, *et al.* EANO guidelines on the diagnosis and treatment of diffuse gliomas of adulthood. *Nat Rev Clin Oncol.* 2021;18:170-186. DOI: 10.1038/s41571-020-00447-z.
10. Nakhl F, Chang E, Shiao J, Alastrá AJ, Wrzolek MA, Odaimi M. A patient with multiple synchronous gliomas of distinctly different grades and correlative radiographic findings. *Surg Neurol Int.* 2010;1:46. DOI: 10.4103/2152-7806.66685.
11. Perić P, Pavličević G, Ostojić J, *et al.* Synchronous malignant multicentric cerebral glioma with atypical neuroradiological presentation and prolonged survival: case report and literature review. *Vojnosanit Pregl.* 2018;75:1007-1013.
12. Doğan A, Kutlay M, Safalı M, Kayhan S. Synchronous multicentric astrocytoma with different histological types in both supratentorial and infratentorial regions. *Gulhane Med J.* 2021;63:75-77.
13. Inoue A, Ohnishi T, Kohno S, Nishikawa M, Ohue S. Multicentric gliomas with different histological grades in supra- and infratentorial regions: case report and literature review. *World J Surg Oncol.* 2016;14:152.