Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Radiation Oncology

Gemistocytic Differentiation in an IDH-Mutant Astrocytoma in a 21-Year-Old Woman: A Case Report and Literature Review

Dr Elfehmi Kaoutar[1]*, Dr Alkama Sanaa[1], Pr Saadoune Mohammed[1], Pr Oussalem Rajaa[1], Pr Igarramen Tarik[1], Pr Barkich Samir[1], Pr Darfaoui Mouna[1], Pr Elomrani Abdelhamid1, Pr Khouchani Mouna[1]

[1]Department of Radiation Oncology, Mohammed VI University Hospital, Marrakech, Morocco

DOI: https://doi.org/10.36347/sjmcr.2026.v14i11.088 | **Received:** 25.09.2026 | **Accepted:** 18.11.2026 | **Published:** 21.11.2026

***Corresponding author:** Dr Elfehmi Kaoutar
Department of Radiation Oncology, Mohammed VI University Hospital, Marrakech, Morocco

Abstract **Case Report**

Background: Gemistocytic differentiation is an uncommon morphological pattern of diffuse astrocytic gliomas, whose independent prognostic significance remains uncertain. ***Case Presentation:*** A 21-year-old woman presented with a seizure in January 2025. MRI revealed a left frontoparietal lesion with corpus callosum infiltration and mass effect. Following interrupted follow-up, she developed headaches and diplopia and underwent extensive resection in October 2025. Histopathology supported an IDH-mutant astrocytoma with gemistocytic differentiation, reported as CNS WHO grade 2; CDKN2A/B status was unavailable. Radiotherapy with temozolomide was initiated in January 2026. Subsequently, no further seizures were reported and the central scotoma resolved. Post-treatment MRI findings were not yet available. ***Conclusion:*** Integrated histomolecular diagnosis and long-term imaging surveillance are essential for this uncommon astrocytic pattern.

Keywords: Gemistocytic Differentiation, IDH-Mutant Astrocytoma, Diffuse Glioma, Radiotherapy, Temozolomide, Case Report.

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution **4.0 International License (CC BY-NC 4.0)** which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

1. INTRODUCTION

Gemistocytic astrocytoma is an uncommon histological variant of diffuse astrocytic gliomas, characterized by the presence of gemistocytes, which are neoplastic astrocytes exhibiting abundant eosinophilic cytoplasm and eccentrically displaced nuclei. Historically classified as a distinct subtype of diffuse astrocytoma, gemistocytic astrocytoma is now recognized as a morphological pattern rather than a separate tumor entity. According to the 2021 World Health Organization (WHO) classification of central nervous system tumors, these neoplasms are classified primarily according to their molecular characteristics, particularly isocitrate dehydrogenase (IDH) mutation status, and are incorporated into the category of IDH-mutant astrocytomas when the appropriate diagnostic criteria are fulfilled [1, 2].

Although gemistocytic differentiation has traditionally been associated with low-grade astrocytomas, its biological behavior remains a subject of considerable interest. Several studies have suggested that astrocytomas exhibiting gemistocytic morphology may demonstrate a more aggressive clinical course than their non-gemistocytic counterparts, with an increased risk of tumor progression, malignant transformation, and reduced overall survival [3, 4]. However, the independent prognostic significance of gemistocytic differentiation in the era of integrated molecular classification remains incompletely established.

The diagnosis and management of these tumors require a multidisciplinary approach combining neuroimaging, histopathological examination, immunohistochemical and molecular characterization, and individualized therapeutic strategies. Surgical resection remains a cornerstone of management, while the indications for adjuvant radiotherapy and chemotherapy depend on tumor grade, molecular profile, extent of resection, and patient-related risk factors [2-5].

We report the case of a 21-year-old woman diagnosed with an IDH-mutant astrocytoma exhibiting gemistocytic differentiation, initially presenting with seizures and subsequently developing signs of intracranial hypertension. Through this observation and a review of the relevant literature, we aim to highlight the diagnostic challenges, prognostic implications, and therapeutic considerations associated with this uncommon histological pattern.

2. CASE PRESENTATION

A 21-year-old woman with no significant medical or surgical history and no family history of malignancy was referred to our radiation oncology department for further management of a histologically diagnosed astrocytoma with gemistocytic differentiation.

The patient's clinical history began in January 2025, when she experienced a sudden-onset seizure, prompting admission to the emergency department. Brain magnetic resonance imaging (MRI), performed on January 29, 2025, revealed a left frontoparietal intra-axial lesion measuring 31 × 30 mm. The lesion appeared hypointense on T1-weighted images, hyperintense on T2-weighted and fluid-attenuated inversion recovery (FLAIR) sequences, and demonstrated mild contrast enhancement and restricted diffusion. It was associated with moderate perilesional edema and a mass effect on the ipsilateral lateral ventricle and midline structures, resulting in early subfalcine herniation. Infiltration of the corpus callosum was also noted. Magnetic resonance spectroscopy demonstrated increased choline and decreased N-acetylaspartate levels, supporting the suspicion of a neoplastic process. The initial radiological differential diagnosis included oligodendroglioma and primary central nervous system lymphoma.

Following symptomatic management, the patient was referred for neurosurgical evaluation. A subsequent MRI with spectroscopy, performed in March 2025, demonstrated a left frontal expansile lesion suggestive of a low-grade oligodendroglioma. However, the patient was subsequently lost to follow-up.

In October 2025, approximately nine months after the initial presentation, the patient was readmitted with persistent, treatment-resistant headaches and diplopia, suggestive of increased intracranial pressure. A brain computed tomography (CT) scan performed on October 20, 2025, revealed a left frontoparietotemporal lesion with both solid and cystic components, causing mass effect on the ipsilateral lateral ventricle, midline shift, and subfalcine herniation.

The patient underwent extensive macroscopic surgical resection on October 28, 2025. Histopathological examination initially suggested a high-grade glial neoplasm, prompting further immunohistochemical investigations. Tumor cells showed positive immunostaining for glial fibrillary acidic protein (GFAP) and OLIG2, supporting their glial origin. Immunostaining for mutant IDH1 (R132H) was positive, while ATRX expression was lost and p53 showed diffuse nuclear positivity. CD34 and synaptophysin immunostaining were negative. Neurofilament staining highlighted the diffuse infiltrative growth pattern of the tumor. The Ki-67 proliferation index was estimated at 3–5%.

Based on the morphological and immunohistochemical findings, the tumor was diagnosed as an IDH-mutant diffuse astrocytoma with gemistocytic differentiation, reported as CNS WHO grade 2. The CDKN2A/B homozygous deletion status was unavailable.

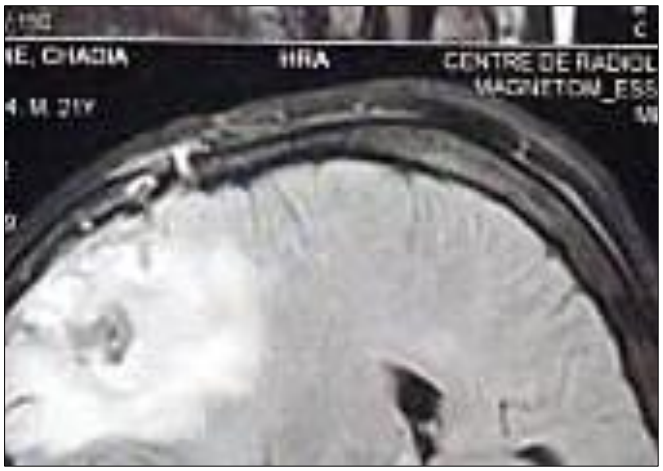
Postoperative brain MRI performed on November 24, 2025, demonstrated heterogeneous T2/FLAIR hyperintensity in the left frontoparietal corticosubcortical region, associated with postoperative hemorrhagic changes. No pathological contrast enhancement, diffusion restriction, significant mass effect, or midline shift was identified. There was no evidence of an evolving lesion on this examination.

At the time of referral to our department, the patient was conscious, hemodynamically stable, and had an Eastern Cooperative Oncology Group (ECOG) performance status of 1. Neurological examination revealed preserved muscle strength (5/5) in all four limbs, normal muscle tone, and an intact gait, without clinically detectable cranial nerve deficits. Ophthalmological assessment revealed a central scotoma in the left eye and a left visual hemifield defect in the right eye. The remainder of the physical examination was unremarkable.

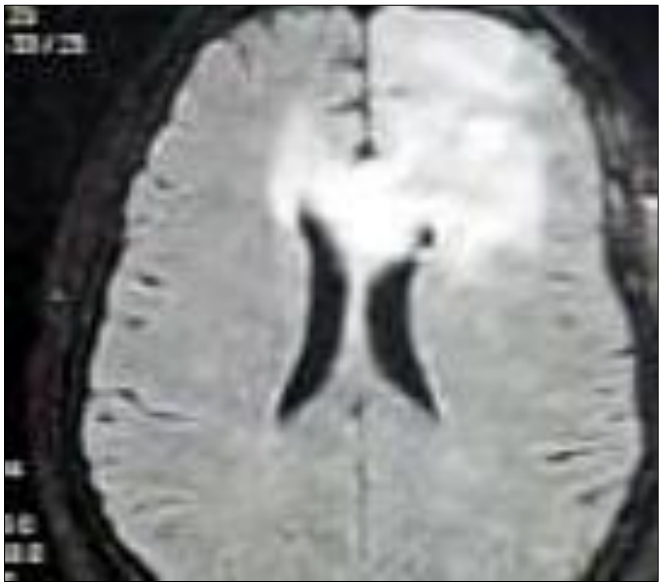
Adjuvant radiotherapy was initiated in January 2026, approximately three months after surgical resection, in combination with concomitant temozolomide. The total radiation dose and fractionation schedule were not available at the time of manuscript preparation. The last documented temozolomide treatment was administered on October 6, 2026. However, the exact chemotherapy schedule and whether additional adjuvant cycles were administered after completion of radiotherapy remain to be confirmed.

Following treatment, the patient experienced favorable clinical improvement, characterized by the absence of further reported seizures and resolution of the previously documented central scotoma. A follow-up brain MRI was planned for approximately one month after the last documented chemotherapy treatment to assess radiological response and disease status.

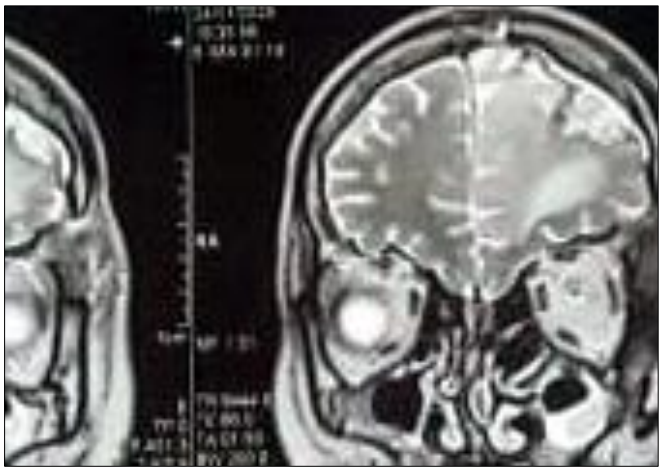
Representative postoperative MRI images are provided in Figure 1;



(A) Sagittal FLAIR



(B) Axial FLAIR



(C) Coronal T2

Figure 1: Representative postoperative MRI images

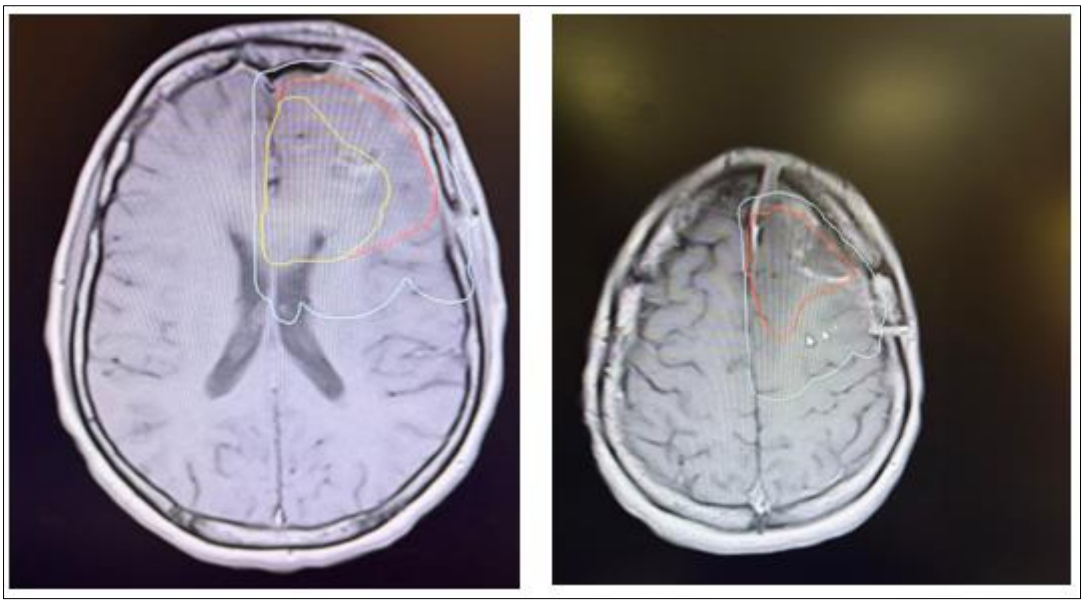


Figure 2: Axial images from the radiotherapy planning process showing the delineated volumes

3. DISCUSSION

Gemistocytic differentiation represents an uncommon histopathological pattern encountered in diffuse astrocytic gliomas. Historically considered a distinct variant of diffuse astrocytoma, gemistocytic astrocytoma is no longer recognized as an independent tumor entity in the 2021 World Health Organization (WHO) classification of central nervous system tumors. Instead, these tumors are classified according to their integrated histological and molecular characteristics, particularly their isocitrate dehydrogenase (IDH) mutation status [1]. Nevertheless, gemistocytic differentiation remains clinically relevant because of its potential association with a more aggressive biological behavior and unfavorable prognosis.

Gemistocytic astrocytomas are characterized histologically by the presence of neoplastic astrocytes with abundant, glassy eosinophilic cytoplasm and eccentrically displaced nuclei. These cells are typically embedded within an infiltrative astrocytic tumor. Although gemistocytic morphology has traditionally been associated with lower-grade diffuse astrocytomas, its presence does not necessarily indicate indolent biological behavior. Several studies have suggested that gemistocytic differentiation may be associated with an increased tendency toward tumor progression and shorter survival compared with conventional diffuse astrocytomas [4].

In a retrospective comparative study published in 2023, Hassan *et al.,* evaluated 56 patients with IDH-mutant astrocytomas, including tumors with and without gemistocytic differentiation. The authors reported a significantly shorter median overall survival among patients with gemistocytic differentiation compared with those without this morphological feature (2 versus 6 years, respectively; $p = 0.005$). Furthermore, tumors exhibiting gemistocytic differentiation demonstrated a higher mean Ki-67 proliferation index (4.4% versus 2.0%; $p = 0.005$). However, the proportion of gemistocytes within the tumor was not significantly associated with survival [4]. These findings suggest a possible adverse prognostic role of gemistocytic differentiation, although larger molecularly characterized studies are required to establish whether this association is independent of tumor grade and other prognostic factors.

Clinically, diffuse astrocytomas frequently present with seizures, headaches, or focal neurological deficits, depending on tumor location, size, and growth pattern. Seizures are particularly common in younger patients with supratentorial diffuse gliomas and may represent the first manifestation of the disease. In our case, the initial presentation consisted of a seizure in a previously healthy 21-year-old woman. Brain MRI revealed a left frontoparietal lesion associated with corpus callosum infiltration, perilesional edema, and early subfalcine herniation. The initial imaging findings raised the possibility of oligodendroglioma or primary central nervous system lymphoma, highlighting the difficulty of establishing an accurate diagnosis based on radiological features alone.

The subsequent clinical course was characterized by a period of interrupted follow-up, followed by the development of persistent headaches and diplopia approximately nine months after the initial presentation. Repeat imaging demonstrated a lesion with solid and cystic components, accompanied by mass effect and subfalcine herniation. Although these findings raised concern for clinically significant tumor progression, malignant transformation could not be established from imaging alone. This evolution emphasizes the importance of regular clinical and radiological surveillance in patients with suspected

diffuse gliomas, even when the initial radiological assessment suggests a lower-grade lesion.

The definitive diagnosis of diffuse gliomas increasingly relies on the integration of histopathological findings and molecular biomarkers. According to the 2021 WHO classification, IDH-mutant astrocytomas are assigned CNS WHO grades 2, 3, or 4 based on histological and molecular criteria [1]. In our patient, immunohistochemical analysis demonstrated positivity for GFAP, OLIG2, and mutant IDH1 (R132H), together with loss of ATRX expression and diffuse p53 immunoreactivity. This profile strongly supported the diagnosis of an IDH-mutant astrocytoma. The Ki-67 proliferation index was estimated at 3–5%, and the tumor was reported as CNS WHO grade 2 with gemistocytic differentiation.

An important consideration in the molecular classification of IDH-mutant astrocytomas is the homozygous deletion of CDKN2A/B, which is recognized as a criterion sufficient for assigning CNS WHO grade 4, even in the absence of necrosis or microvascular proliferation [1-3]. In the present case, the CDKN2A/B deletion status was unavailable, representing a limitation in definitive molecular grading. Furthermore, although the immunohistochemical profile strongly favored an astrocytic lineage, complete molecular characterization would provide additional diagnostic and prognostic information.

Surgical resection remains a fundamental component of the management of diffuse astrocytomas, with the aim of obtaining tissue for diagnosis, reducing tumor burden, alleviating neurological symptoms, and achieving maximal safe resection. In our patient, extensive macroscopic resection was performed following the development of intracranial hypertension. Postoperative MRI demonstrated surgical changes without an identifiable progressive lesion or persistent mass effect. Nevertheless, the infiltrative nature of diffuse astrocytomas means that the absence of a visible residual lesion does not necessarily indicate complete microscopic tumor eradication.

The role of adjuvant treatment in IDH-mutant astrocytomas depends on several factors, including tumor grade, extent of resection, patient age, neurological status, and molecular characteristics. Current ASCO-SNO recommendations support radiotherapy combined with adjuvant chemotherapy, using either temozolomide or the procarbazine, lomustine, and vincristine (PCV) regimen, for patients with CNS WHO grade 2 IDH-mutant astrocytomas requiring postoperative treatment [5]. However, treatment may be deferred in selected patients with favorable prognostic features, particularly younger individuals who have undergone complete resection, provided that appropriate surveillance is maintained.

Radiotherapy plays an important role in achieving local disease control in patients requiring adjuvant treatment. The ESTRO-EANO guidelines recommend a dose of 50.4 Gy delivered in 28 fractions for CNS WHO grade 2 IDH-mutant diffuse gliomas, with modern conformal techniques such as intensity-modulated radiotherapy preferred to optimize target coverage and limit irradiation of surrounding healthy brain tissue [7]. These recommendations are particularly relevant in young adults, for whom long-term treatment-related neurocognitive toxicity and quality of life must be considered.

In the present case, postoperative radiotherapy was initiated in January 2026, approximately three months after surgery, in combination with temozolomide. The decision to administer adjuvant treatment may be considered in the context of the patient's symptomatic disease course, infiltrative tumor characteristics, and concerning preoperative radiological findings. However, the precise radiotherapy dose, fractionation schedule, and complete chemotherapy regimen were unavailable, limiting a detailed comparison with established treatment protocols. In addition, the benefit of concomitant temozolomide specifically in CNS WHO grade 2 IDH-mutant astrocytoma remains less clearly established than that of radiotherapy followed by adjuvant chemotherapy.

Following treatment, our patient experienced favorable clinical improvement, with no further reported seizures and resolution of the previously documented central scotoma. These findings suggest an improvement in neurological symptom burden and functional status. Nevertheless, clinical improvement alone cannot be considered evidence of complete tumor response. Long-term follow-up with serial brain MRI is essential to evaluate disease control, detect recurrence or progression, and assess potential delayed treatment-related complications.

More recently, the development of targeted therapies has introduced new therapeutic perspectives for IDH-mutant diffuse gliomas. The 2025 ASCO-SNO guideline update incorporated vorasidenib, an oral inhibitor of mutant IDH1 and IDH2, as a treatment option for selected patients with CNS WHO grade 2 IDH-mutant astrocytomas in whom radiotherapy and chemotherapy can be deferred [8]. Although this approach was not applicable to the treatment already administered in our case, it highlights the growing importance of molecular characterization in individualized therapeutic decision-making.

Our observation illustrates several important aspects of IDH-mutant astrocytomas with gemistocytic differentiation. First, these tumors may present in young adults with seizures and subsequently develop significant neurological symptoms and mass effect. Second, radiological appearances and proliferative indices do not

always provide a complete assessment of tumor behavior, emphasizing the importance of integrated histomolecular diagnosis. Finally, the favorable early clinical evolution observed after surgery and oncological treatment is encouraging, but prolonged radiological surveillance remains essential, particularly given the uncertain independent prognostic significance of gemistocytic differentiation.

Further studies incorporating comprehensive molecular profiling, standardized therapeutic strategies, and long-term follow-up are needed to clarify the prognostic implications of gemistocytic differentiation and optimize the management of this uncommon morphological pattern.

4. CONCLUSION

Astrocytomas with gemistocytic differentiation represent an uncommon histological pattern of diffuse astrocytic gliomas, characterized by distinct morphological features and potentially unfavorable biological behavior. This case highlights the diagnostic and therapeutic challenges associated with these tumors, particularly in young adults presenting with progressive neurological manifestations. Accurate diagnosis requires an integrated histopathological and molecular approach, while optimal management relies on multidisciplinary collaboration involving neurosurgery, radiation oncology, and neuro-oncology. Although our patient demonstrated favorable clinical improvement following surgical resection and adjuvant treatment, long-term clinical and radiological surveillance remains essential. Further studies are needed to clarify the independent prognostic significance of gemistocytic differentiation and its potential implications for therapeutic decision-making.

REFERENCES

1. Louis DN, Perry A, Wesseling P, et al. 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.
2. Adult type diffuse gliomas in the new 2021 WHO Classification. Pathologica. 2022. https://pmc.ncbi.nlm.nih.gov/articles/PMC9763975/ [Complete bibliographic details to verify].
3. Low-grade astrocytomas: the prognostic value of fibrillary, gemistocytic, and protoplasmic tumor histology. J Neurosurg. 2013. https://pubmed.ncbi.nlm.nih.gov/23662821/ [Complete bibliographic details to verify].
4. Gemistocytic Differentiation in Isocitrate Dehydrogenase Mutant Astrocytomas: A Histopathological and Survival Analysis. Cureus. 2023. https://pmc.ncbi.nlm.nih.gov/articles/PMC10182877/ [Complete bibliographic details and quoted statistics to verify].
5. Mohile NA, Messersmith H, Gatson NT, et al. Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline. J Clin Oncol. 2022. doi:10.1200/JCO.21.02036.
6. The 2021 WHO classification of central nervous system tumors: what neurologists need to know. Neuro Oncol. 2022. https://pmc.ncbi.nlm.nih.gov/articles/PMC9669114/ [Complete bibliographic details to verify].
7. ESTRO-EANO guideline on target delineation and radiotherapy for IDH-mutant WHO CNS grade 2 and 3 diffuse glioma. Radiother Oncol. 2025. https://pubmed.ncbi.nlm.nih.gov/39454886/ [Complete bibliographic details to verify].
8. Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline Rapid Recommendation Update. Neuro Oncol. 2025;27(6):1412–1418. doi:10.1093/neuonc/noaf072.