BRAIN. Broad Research in Artificial Intelligence and Neuroscience
e-ISSN: 2067-3957 | p-ISSN: 2068-0473
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2025, Volume 16, Issue 3, pages: 282-296
Submitted: April 30th, 2025 | *Accepted for publication:* August 17th, 2025

From Neuropsychiatric Symptomatology to Oncological Diagnosis: Progression of Grade 2 to Grade 4 Cerebral Astrocytoma over a Four-Year Period and the Potential of AI in Precision Medicine

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Abstract: *The progression of low-grade gliomas, particularly IDH1-mutant diffuse astrocytoma, remains a complex and clinically relevant topic, especially when early manifestation are predominantly neuropsychiatric. In certain clinical scenarios, young individuals presenting with severe depressive and anxiety symptoms, initially suggestive of primary psychiatric disorders, may be found to harbour underlying low-grade brain tumours upon neuroimaging. Left temporal IDH-1 mutant astrocytoma (WHO grade II) are among such pathologies that can initially mimic affective or anxiety disorders, delaying appropriate diagnosis and intervention. Longitudinal clinical observation over a four-year period have shown that these tumours may undergo malignant transformation into high-grade (WHO grade IV) IDH-mutant astrocytoma, characterised histologically by increased cellularity, mitotic activity, vascular proliferation, and necrosis. Molecular analysis typically reveals continued IDH1 mutation, ATRX loss and p53 overexpression, with proliferative indices increasing significantly at the point of progression. The neuropsychiatric trajectory may parallel this evolution, transitioning from affective symptoms to more profound cognitive and personality disturbances associated with frontal lobe dysfunction. Despite multimodal treatment strategies including surgery, radiotherapy and chemotherapy, prognosis tends to worsen significantly upon transformation, particularly when early symptoms are misattributed to primary psychiatric conditions. A synthesis of current literature supports the recognition of early neuropsychiatric symptoms, particularly those resistant to conventional treatment, as potential early indicators of intracranial neoplasms. Systematic neuroimaging in such cases could facilitate early detection. Additionally, recent advances in artificial intelligence (AI) show promise in enhancing diagnostic precision through imaging analysis and multimodal clinical data integration, thereby contributing to more personalised and timely therapeutic approaches in neuro-oncology.*

Keywords: *diffuse astrocytoma grade 2; diffuse astrocytoma grade 4; immunohistochemistry; neuropsychiatric symptoms; depression; organic personality disorder; neuro-oncology.*

How to cite: Moroșan, A.-C., Dăscălescu, G., Ciobîcă, A., Ichim, D. M., & Moroșan, G.-C. (2025). From neuropsychiatric symptomatology to oncological diagnosis: Progression of a grade 2 to grade 4 cerebral astrocytoma over a four-year period and the potential of AI in precision medicine. *BRAIN. Broad Research in Artificial Intelligence and Neuroscience*, *16*(3), 282-296.
https://doi.org/10.70594/brain/16.3/20

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1. Introduction

Diffuse astrocytoma (WHO grade II-IV) is a type of infiltrative glial neoplasm of the central nervous system. Grade IV astrocytoma, also known as IDH-mutant glioblastoma (distinct from the more common IDH-wildtype glioblastoma), is an aggressive malignancy characterised by extensive invasion of the brain parenchyma and defining molecular alterations (Komori, 2022; Louis et al., 2021). In the 2021 WHO classification, the presence of an IDH1 or IDH2 mutation is a key feature that distinguishes these tumours from IDH-wildtype glioblastomas (Louis et al., 2021). Histologically, grade IV astrocytoma displays marked cellular pleomorphism, high mitotic activity, necrosis, and microvascular proliferation (Ohgaki & Kleihues, 2013). Common molecular alterations include ATRX loss and TP53 mutations, which contribute to tumour pathogenesis (Sampson et al., 2009). Classification by genetic markers has improved the stratification of patients and enables a more personalised therapeutic approach (Molinaro et al. 2019).

Diffuse grade IV astrocytomas are relatively rare, with an incidence of around 0.5 – 1 per 100.000 per year in adults (Ostrom et al., 2014). They are more often diagnosed in younger and middle-aged adults (30 – 50 years) and have a slight male predominance (Delgado-Lopez et al., 2017). Prognosis is generally poor, but IDH-mutant tumours tend to respond better to therapy and have longer median survival (on the order of 2 – 5 years) than their IDH-wildtype counterparts (Wick et al., 2017; Stupp et al., 2009). Known risk factors include hereditary cancer syndromes (e.g., Li-Fraumeni, NF1) and exposure to ionising radiation (Ohgaki & Kleihues, 2013). No specific environmental or lifestyle risk factors have been definitively linked to these tumours (van den Bent et al., 2017).

Clinically, symptomatology depends on tumour location and growth rate. The most frequent initial signs include seizures (in about half of cases, especially with IDH-mutant tumours) (Molinaro et al., 2019), followed by focal deficits (such as weakness, aphasia or visual field cuts), depending on the involved brain region (van den Bent et al., 2017). Headache due to raised intracranial pressure is common (Delgado Lopez et al., 2017). Cognitive impairment, memory loss, personality changes, and mood disturbances occur, particularly when the tumour affects frontal or temporal lobes (Sharma et al., 2022; Madhusoodanan et al., 2015). Nonspecific symptoms such as nausea, vomiting, and lethargy may develop with advanced intracranial hypertension (Delgado Lopez et al., 2017).

Diagnosis requires high-resolution Magnetic Resonance Imaging (MRI) (including advanced techniques such as spectroscopy for metabolites like 2-hydroxyglutarate (Ostrom et al., 2014) and ultimately histopathological confirmation. Surgical biopsy or resection provides tissue for both microscopic and molecular analysis. The histology of an IDH-mutant grade II astrocytoma will show relatively bland astrocytic cells with a low mitotic index, whereas conversion to grade IV is marked by increased cellularity, pleomorphism, mitoses, necrosis, and microvascular proliferation (Komori, 2022). Molecular testing for IDH, ATRX, TP53, and MGMT promoter methylation guides both prognosis and therapy (Komori, 2022).

Standard treatment for diffuse astrocytoma is maximally safe surgical resection followed by radiotherapy and chemotherapy. Surgical goals are gross total resection when feasible, as this correlates with longer survival (Stupp et al., 2009). Postoperative fractionated radiotherapy is typically administered to the resection cavity and residual tumour (Stupp et al., 2009). Chemotherapy regimens depend on tumour grade and molecular markers: temozolomide (TMZ) is standard for high-grade astrocytoma (Stupp et al., 2009), while lower-grade tumours may also often receive PCV (procarbazine, lomustine, vincristine) or other protocols (Delgado-Lopez et al., 2017; van den Bent et al., 2017). Ongoing clinical trials are exploring targeted therapies and immunotherapies for IDH-mutant gliomas. Despite aggressive treatment, recurrence is common and generally heralds transformation to a higher grade.

In recent years, Artificial Intelligence (AI) has rapidly entered the field of neuro-oncology. AI refers to computer algorithms, including machine learning and deep learning, that can interpret

complex data (Nakhate & Castro, 2023). In brain tumour management, AI-based systems have shown promise in enhancing MRI and pathological analysis, tumour classification, and outcome prediction (Khalighi et al., 2024; Nakhate & Castro, 2023). For example, AI algorithms can analyse medical images to detect subtle abnormalities, segment tumour boundaries, identify molecular subtypes from imaging, and predict patient outcomes (Khalighi et al., 2024). These tools could improve early tumour detection and guide personalised therapy. As technology matures, it may complement clinical decision-making in relevant clinical cases by alerting clinicians to evolving pathology or neuropsychiatric patterns that warrant further investigation.

2. Materials and Methods

2.1. Data Sources and Selection Criteria

A multidisciplinary approach was employed to investigate the clinical and neuropsychiatric dynamics associated with IDH1-mutant astrocytoma, alongside the utility of AI in early detection and disease monitoring. Clinical, neuroimaging, histopathological, and psychiatric data were synthesised from multiple patient management settings, with a focus on capturing longitudinal and multimodal information relevant to tumour evolution and neurobehavioural outcomes.

2.2. Clinical and Psychiatric Evaluation Framework

Baseline demographic and psychiatric characteristics were systematically recorded using validated instruments, the Hamilton Depression Rating Scale (HDRS) and Hamilton Anxiety Scale (HAM-A). Clinical consultations were analysed to identify psychiatric symptom trajectories, pharmacological interventions, and treatment stages.

2.3. Psychiatric Symptom Severity Scoring

To provide a structured and visual representation of the patient's longitudinal psychiatric trajectory and to synthesise the qualitative psychiatric evaluations, a numerical severity score (ranging from 1 to 5) was assigned to the primary symptom burden at each consultation point.
This scoring system, while inherently subjective, was developed to provide a standardised, visual representation of symptom progression and treatment response. The rationale for the score assignment is as follows:

- Score 1 (Minimal/Resolved Symptoms): Implies significant improvement or near-remission of symptoms, with minimal functional impairment. (Not used in this specific case, but available for future contexts.)
- Score 2 (Stable/Mild Symptoms): Indicates symptoms are stable or mildly present, generally well-managed by current treatment, with good functional capacity.
- Score 3 (Moderate/Persistent Symptoms): Represents the presence of clear and persistent symptoms, requiring ongoing management but without acute decompensation.
- Score 4 (Aggravated/Significant Symptoms): Denotes a clear worsening of symptoms, requiring dose adjustments or new medication classes. Functional impairment is notable.
- Score 5 (Severe/Decompensated Symptoms): Reflects acute and severe symptom exacerbation, treatment resistance, episodes of behavioural dysregulation, or emergent neurological signs directly linked to neurological deterioration. This score signifies a critical phase, which requires intensive intervention.

  The data for this trajectory was modelled and visualised using Microsoft Excel.

2.4. Neuroimaging Protocols

Neuroimaging data were acquired through standardised cranial non-contrast CT and 1.5 T MRI modalities. MRI sequences were T1-weighted, T2/ FLAIR, diffusion-weighted imaging and gadolinium-enhanced scans. Imaging studies were conducted during diagnostic, postoperative, and suspected recurrence stages, allowing for comprehensive temporal assessment of tumour morphology and response to treatment.

2.5. Histopathological and Molecular Characterisation

Tumour tissue obtained from surgical interventions was processed for haematoxylin-eosin staining and immunohistochemical profiling using GFAP, OLIG2, ATRX, p53, and Ki-67 (MIB-1). Molecular analyses focused on the IDH1 R132H mutation using polymerase chain reaction (PCR) testing followed by immunohistochemistry. WHO criteria were used to classify tumour grade, proliferation rates, and malignant features such as necrosis and microvascular proliferation.

2.6. Neuropsychiatric Symptoms Surveillance

Neuropsychiatric profiles were longitudinally monitored using standardised clinical instruments and qualitative observations. Atypical or treatment-resistant symptoms triggered neuroimaging reassessments to exclude tumour-related aetiology. This integrative protocol was intended to delineate the interface between primary psychiatric symptoms and neuro-oncological pathology.

2.7. AI-Assisted Literature Integration

A comprehensive literature review was undertaken across PubMed, Scopus, and Web of Science to contextualise current evidence on the neuropsychiatric manifestations of IDH-mutant astrocytoma and the implementation of AI in neuroimaging. Key search terms included „astrocytoma AND depression/anxiety", „IDH-mutant astrocytoma, and „artificial intelligence neuro-oncology". Inclusion criteria prioritised studies that employed AI for tumour characterisation, grading, or outcome prediction.

Emerging AI technologies, including radiomic texture analysis and convolutional neural networks (CNNs), were evaluated for their diagnostic accuracy, sensitivity, and clinical applicability. The review focused on AI's potential to enhance early detection, improve diagnostic accuracy, and integrate multimodal data for predictive modelling in neuro-oncology workflows.

3. Results

3.1. Initial Neuropsychiatric Presentation and Diagnostic Delay

A 34-year-old right-handed female with no prior psychiatric history presented with severe depressive symptoms, including affective dysregulation, marked anxiety, catastrophic thinking, and insomnia. These symptoms were documented consistently in clinical records across 46 psychiatric consultations, as detailed in *Table 1*. Standardised assessment recorded a score of 23 on HDRS and 24 on HAM-A, indicating moderate to severe depression and anxiety. Despite a progressive and varied psychopharmacological regimen, including alprazolam, clonazepam, sertraline, trazodone, mirtazapine, and risperidone *(Table 1)*, the symptoms persisted and frequently worsened, particularly following a surgical intervention unrelated to the later neuro-oncological findings. Initial treatment strategies failed to yield stable improvement, leading to repeated reassessment and ultimately the decision to initiate neuroimaging.

Table 1. Evolution of neuropsychiatric symptomatology and treatment plans throughout consultations

Consultation Number	Symptomatology	Treatment Plan	Comments
Phase 1: Initial Psychiatric Presentation			
1	Negative hypertensive affective disposition, diffuse anxious restlessness with marked anxiety attacks, affective dysregulation, easy crying, reduced tolerance to	Alprazolam 0.25 mg x 2 pills/day	Diagnosis: Severe depressive episode

	minor frustrations, memory and attention deficits, catastrophic anticipations, passive suicidal ideation, difficulty falling asleep, significantly diminished personal performance, reduced appetite, tendency towards isolation, and reduced communication.	Clonazepam 2 mg 1 pill/day Sertraline 50 mg 1 pill/day	
2	Improved sleep, aggravated symptoms post-surgery	Same as above	Severe depressive episode in a reactive context
3	Dysthymic disposition	Same as above	Organic depressive affective disorder
4	Significantly diminished personal performance	Same as above	Organic depressive affective disorder
Phase 2: Treatment Resistance			
5	Significantly diminished performance	Clonazepam 0.25 mg 3 pills/day	Clonazepam dose increased to 3 pills/day
8	Decompensated symptoms characterised by decreased vital drive and personal productivity, passive suicidal ideation	Trazodone 75 mg 1 pill/day added	A new antidepressant added to the treatment plan
9	Irritability, short temper	Same as above	Treatment adjustments maintained
10	Difficulty falling asleep	Clonazepam 3 mg/day Trazodone 75 mg 1 + 1/3 pill/day	Clonazepam and Trazodone doses increased
11	General condition affected	Sertraline increased to 150 mg/day Clonazepam reduced to 2 mg	Sertraline dose increased, Clonazepam reduced
12	Symptoms persist	Clonazepam 3 mg/day	Clonazepam dose increased
13	Symptoms stable	Clonazepam 2 mg/day	Clonazepam dose reduced
14	Symptoms stable	Trazodone increased to 150 mg/day Sertraline reduced to 100 mg/day Clonazepam 0.25 mg x 2 pills/day	Trazodone increased; Sertraline reduced
15	Symptoms stable	Mirtazapine 30 mg 1 pill/day added Sertraline reduced to 50 mg/day	A new antidepressant added, Sertraline reduced
16	Symptoms stable	Sertraline removed	An antidepressant introduced at the onset of symptoms is removed from the treatment plan
Phase 3: Neurological Deterioration			
19	Mixed insomnia resistant to treatment	Mirtazapine 45 mg/day Clonazepam 2 mg/day Bromazepam 1.5 mg x 2 pills/day Zolpidem 10 mg/day	Antidepressant dose increased, Alprazolam replaced with Bromazepam, Zolpidem added
20	Symptoms stable	Bromazepam replaced with Alprazolam 0.5 mg x 2 pills/day	Bromazepam replaced with Alprazolam

22	Episodes of impulsivity with explosive and aggressive behaviour, marked memory and attention deficits, significant psychoemotional lability	Clonazepam 2 mg/day	Due to explosive impulsive symptoms, the treatment plan is adjusted
		Zolpidem 10 mg/day	Diagnosis: organic depressive affective disorder, organic personality disorder
		Alprazolam 0.5 mg/day	
		Risperidone oral solution 0.25 ml/day	
		Mirtazapine 45 mg/day	
23	Worsened symptoms	Same as above, except for Risperidone	Organic mood/affective disorder, organic personality disorder
24	Symptoms stable	Alprazolam removed	Same as above
25	Symptoms stable	Alprazolam 0.5 mg/day added	Same as above
29	Impulsivity, irritability, reduced tolerance to minor frustrations	Trazodone 150 mg x 3 pills/day	Same as above
30	Dysthymic disposition alternating with depressive mood, excessive worries about daily activities, obsessive elements, reduced volition	Trazodone 150 mg x 3 pills/day	Same as above
31	Symptoms stable	Mirtazapine 45 mg/day	Same as above
		Alprazolam 0.5 mg/day	
		Zolpidem 10 mg/day	
		Clonazepam 1 mg/day	
32	Symptoms stable	Xanax removed	Same as above
Phase 4: Post-Oncological Diagnosis			
37-39	Telephone consultation	Same as above	
	The patient experienced 3 convulsive seizures, and was taken to the neurology and neurosurgery hospital.		
	Diagnosis: operated astrocytoma		
	Nitrazepam 5 mg 1 pill/day remains in the treatment plan, Risperidone oral solution 1 ml/day added		
40	Agoraphobia	Mirtazapine 30 mg/day	Same as above
		Carbamazepine 200 mg 1 pill/day	
		Lorazepam 1 mg x 2 pills/day	
		Clonazepam 2 mg/day	
41-42	Telephone consultation		
43	Symptoms stable	Clonazepam removed	Clonazepam removed
44	Symptoms stable	Same treatment plan maintained, Rivotril added back	Clonazepam added back
45	Recurrent panic attacks, agoraphobic elements	Clonazepam 0.5 mg x 4 pills/day increased	Clonazepam dose increased

		Quetiapine 50 mg/day added	
46	Symptoms stable	Quetiapine removed and replaced with Zopiclone 7.5 mg/day	Quetiapine removed and replaced with Zopiclone

The patient's complex clinical journey, characterised by the insidious onset and progressive exacerbation of neuropsychiatric symptoms, is meticulously documented in *Table 1*. To provide a clearer visual representation of this longitudinal evolution and to address the need for a more rigorous display of symptom trajectory, we developed a qualitative severity score, depicted in *Figure 1*. This figure illustrates the fluctuating intensity of psychiatric manifestations across the four distinct phases of the patient's illness, alongside key treatment adjustments.

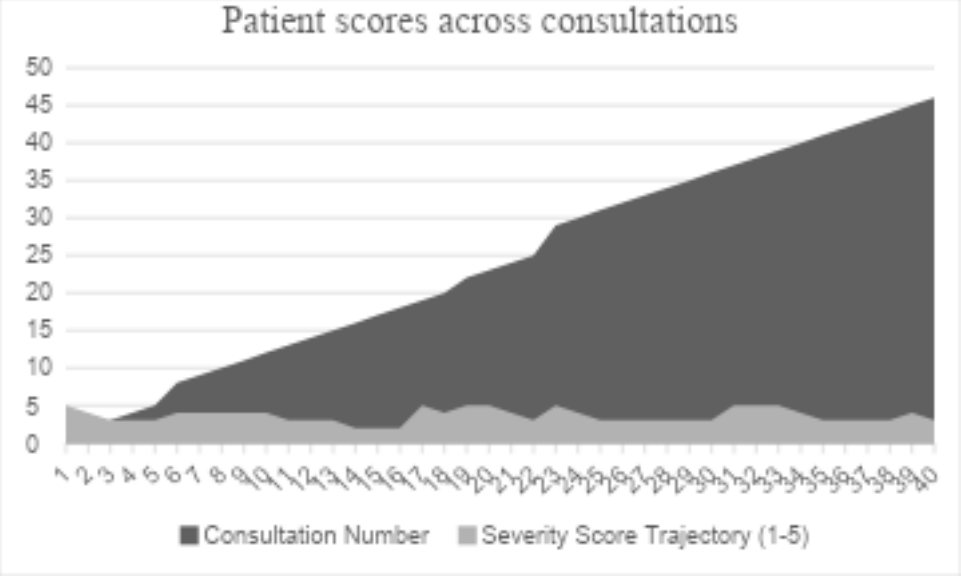

Figure 1. Patient score evolution

Figure 1 illustrates the patient's longitudinal psychiatric symptom burden across the consultations. The "Severity Score Trajectory (1-5)" visually captures the fluctuation in symptom intensity: it shows an initial high score, followed by periods of relative stability or slight improvement and, crucially, notable increases during phases of clinical worsening, particularly around consultation 22, indicating a significant exacerbation of symptoms. This visual trajectory highlights the patient's persistent symptom burden and treatment resistance, which eventually correlated with the neurological deterioration and subsequent oncological diagnosis.

3.2. Radiological Identification of IDH1-Mutant Astrocytoma

Cranial CT imaging revealed a hypodense lesion in the left temporal lobe (*Figure 2*), which was further characterised by MRI as a T1-hypointense lesion and T2/FLAIR-hyperintense lesion with no contrast enhancement and mild diffusion restriction, features consistent with a WHO grade II diffuse astrocytoma (*Figure 3*). Given the lesion's localisation in the dominant temporal lobe, it may have contributed to both subtle language deficits and persistent neuropsychiatric symptoms.

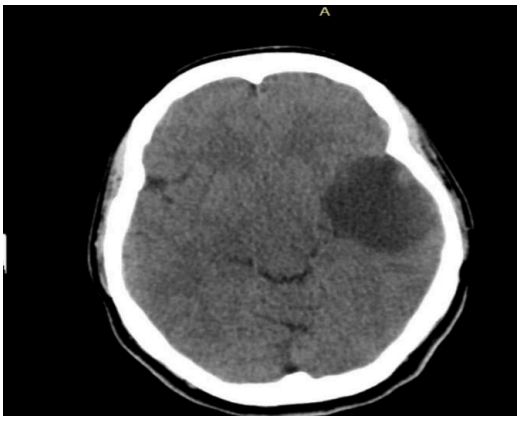

Figure 2. Native cranial CT (axial view) showing the initial left temporal hypodense lesion (white arrow) before the first surgery (Image from patient records.)

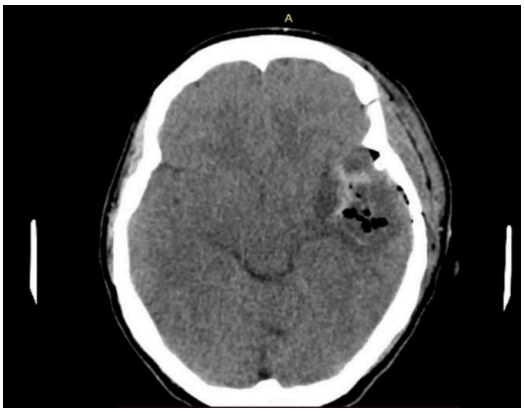

Figure 3. Native CT scan three weeks post-operation, showing the left temporal area with haemorrhagic and air inclusions, with the left temporal bone flap present

3.3. Surgical Resection and Molecular Profiling

The patient underwent a gross total resection with no major perioperative complications. Histopathological analysis (*Figure 4*) confirmed a WHO grade II astrocytoma characterised by low mitotic activity, showing a lack of necrosis and a low Ki-67 proliferation index (< 5%).

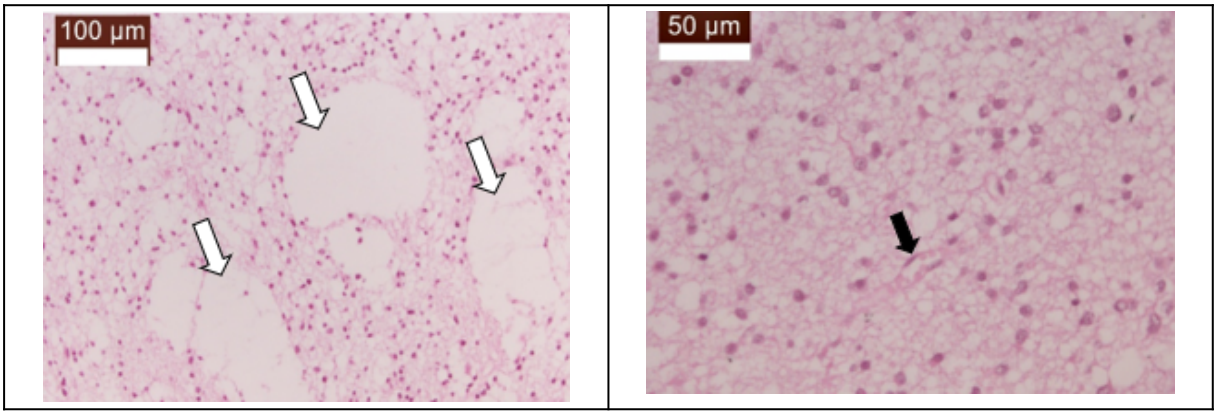

Figure 4. Diffuse astrocytoma, grade 2

A) Loose tumour, composed of astrocytes with modest nuclear atypia, arranged on a fibrillar background. Numerous pseudocysts are present intratumourally (white arrows), delimited by the tumour cells themselves and having the presence of weak basophilic material in their lumen (H-E, eyepiece x10, objective x20)

B) The tumour cells are of medium size, have round or oval nuclei, finely granular chromatin, sometimes a weakly visible nucleolus, but the mitotic activity is not visible. Intratumoural vessels (black arrow) are rarely represented and are of a capillary type, without endothelio-pericytic proliferation (H-E, eyepiece x10, objective x40)

Immunohistochemistry revealed IDH1 R132H mutation, loss of ATRX expression and positive p53 staining, with glial lineage markers GFAP and OLIG2 preserved. These findings confirmed the diagnosis of IDH1-mutant diffuse astrocytoma (*Figure 5*).

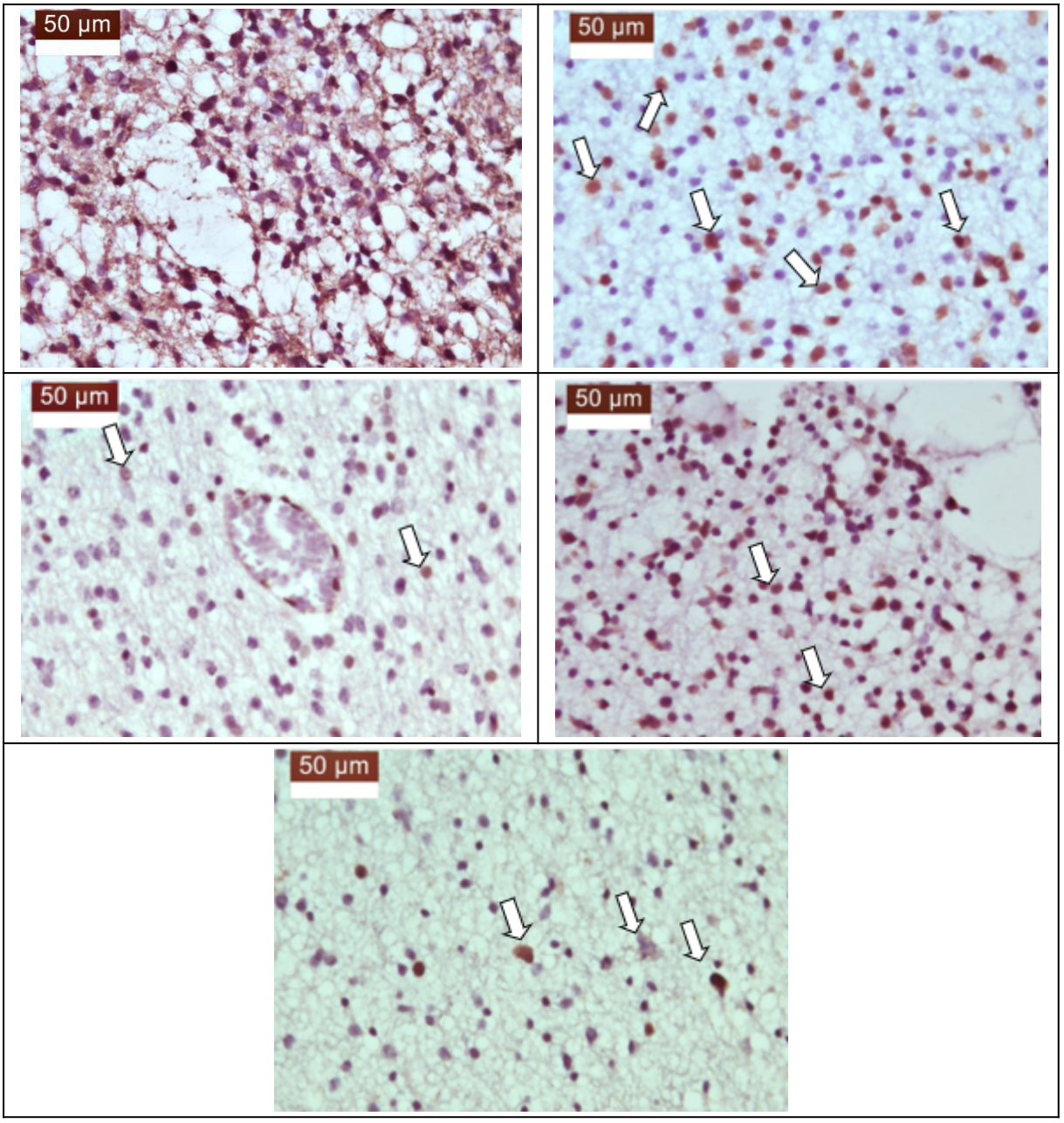

Figure 5. Same tumour stained by immunohistochemical technique
A) Glial fibrillary acidic protein (GFAP) is present in the cytoplasm of tumour cells (anti-GFAP antibody, eyepiece x10, objective x40)
B) Olig2 is intensely positive in the nuclei of cells with oligodendroglial phenotype (white arrows), which represent about 35% of tumour cells (anti-OLIG2 antibody, eyepiece x10, objective x40)
C) ATRX positive at the level of the nuclei of the endothelial cells of the vessels in the area (representing the control reaction) and very weakly positive at the level of rare tumoural nuclei (white arrows), which express an oligodendroglial phenotype (anti-Olig 2 antibody, eyepiece x10, objective x40)
D) p53 intensely positive at the level of 40% of tumour cell nuclei (white arrows) (anti-p53 antibody, eyepiece x10, objective x40)
E) The labelling index of Ki67 was below 5%, the positive nuclei for the antigen-antibody reaction being brown (white arrows) (anti-Ki67 antibody, eyepiece x10, objective x40)

3.4. Longitudinal Psychiatric Trajectory and Therapeutic Challenges

Postoperatively, the patient received adjuvant radiotherapy, a dose of 54Gy, followed by PCV chemotherapy. Despite these interventions, affective symptoms persisted across years of follow-up, including diminished drive, emotional blunting, and severe anxiety over the long term. Psychiatric symptoms were tracked across multiple consultations and treatment changes, as documented in *Table 1.* During this period, pharmacologic strategies were frequently adjusted. Notably, neuropsychiatric deterioration, marked by impulsivity, agitation, and affective dysregulation, occurred before any confirmatory imaging findings, as observed in *Figure 6,* which shows a hypodense area at the site of the previous lesion without mass effect.

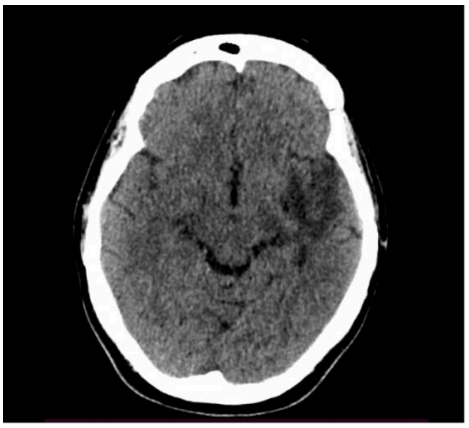

Figure 6. The CT images from 2023 indicate a hypodense area located in the left temporal region, at the site of the previous lesion, without any mass effect on the brain parenchyma

3.5. Tumour Recurrence and Malignant Transformation

CT imaging later revealed a new hyperdense nodular area superimposed on the previous lesion site, indicating recurrence *(Figure 7).* A second reaction was performed, with post-operative changes captured in *Figure 8*. Histopathological examination confirmed transformation to a WHO grade IV glioblastoma (secondary glioblastoma), supported by increased mitotic activity (~33 mitoses/HPF), necrosis, and glomeruloid microvascular proliferation. The tumour maintained IDH1 positivity. Microscopic analysis showed atypical tumour cells, pleomorphism, atypical mitoses, and vascular abnormalities, as illustrated in *Figure 9* (panels A-D).

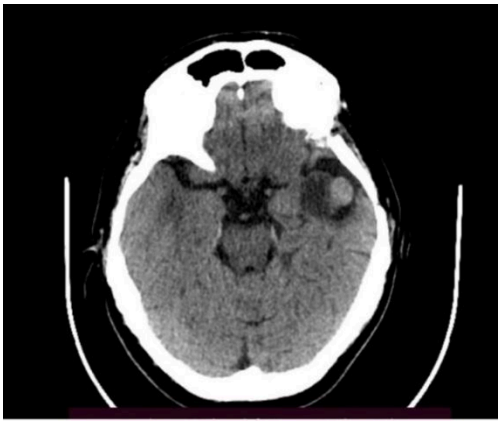

Figure 7. The CT images show a hypodense area located in the left temporal region, associated with a hyperdense nodular area, suggesting a possible recurrence

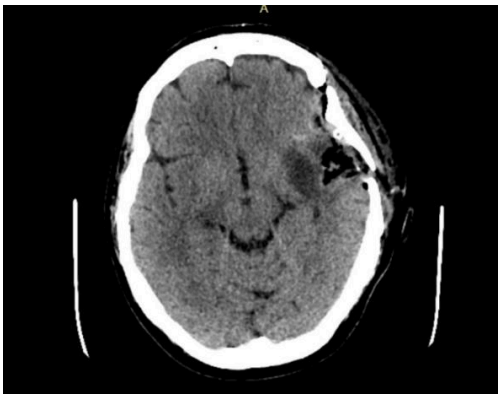

Figure 8. The CT images from 2023 present postoperative aspects corresponding to the second surgical intervention

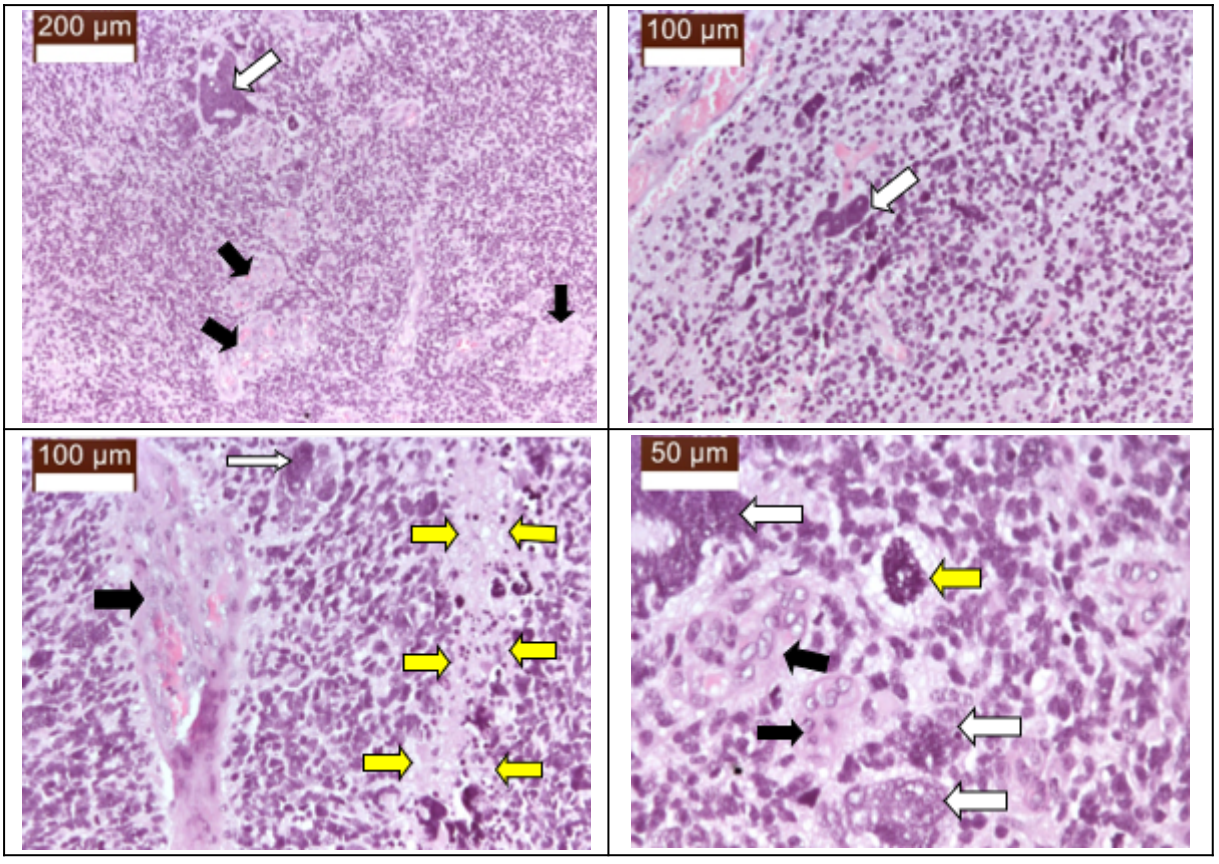

Figure 9. The recurrent tumour presented itself as a diffuse astrocytoma, grade 4

A) The tumour is very densely cellularised, being made up of medium-sized tumour cells, arranged in a diffuse pattern. The intratumoural vessels are numerous, richly branched and show glomeruloid endothelio-pericytic proliferation (black arrows). (H-E, eyepiece x10, objective x10)

B) Tumour cells do not have cell borders, but have pleomorphic nuclei with coarse chromatin, with high mitotic activity (33 mitoses/high power field). Between these tumour cells are present, from place to place, extremely bulky tumour cells, with one or more irregular, hyperchromic nuclei, with a "monstrous" appearance, and sometimes with obvious eosinophilic cytoplasm (white arrow). (H-E, eyepiece x10, objective x20)

C) The tumour is densely cellularised, being made up of cells with high cellular pleomorphism, some cells having a "monstrous" appearance (white arrow). It is noted the presence of an intratumoural vessel with marked endothelio-pericytic proliferation, which takes on a glomeruloid appearance (black arrow), and a microfocus of necrosis with nuclear debris, but without cell palisading in its periphery (yellow arrows) (HE, eyepiece x10, objective x20)

D) With a large objective, "monstrous"-looking tumour cells (white arrows), atypical mitosis (yellow arrow), and moderate endothelio-pericytic proliferation of intratumoural vessels (black arrows) are identified. (HE, eyepiece x10, objective x40).

3.6. Functional Decline and Palliative Management

Following the second surgery, the patient received temozolomide according to the Stupp et al. (2009) protocol. Although early post-treatment imaging showed radiological stabilisation, the patient's neuropsychiatric status declined with progressive apathy, cognitive deterioration, and emotional withdrawal, culminating in severe functional impairment and transition to palliative care.

3.7. Correlation of Psychiatric Symptoms with Oncological Progression

Table 1 offers a detailed chronology of psychiatric symptoms and pharmacologic interventions, revealing key decompensation episodes that temporally align with tumour recurrence and malignant transformation. Importantly, *Figures 6* and *7* show neuroimaging signs that exacerbations of symptoms suggest that certain psychiatric symptoms, such as disinhibition and affective lability, may precede radiological evidence of tumour progression.

3.8. AI-Assisted Imaging and Prognostic Tools

A structured literature review highlighted significant advancements in AI-driven glioma diagnostics. Deep learning and radiomic models leveraging multiparametric MRI have demonstrated the potential to outperform conventional imaging techniques in detecting low-grade gliomas and predicting malignant transformation. These AI tools may be particularly useful in identifying early psychiatric presentations in complex neuro-oncologic cases like the one described.

4. Discussion

This case illustrates several important lessons. First, diffuse astrocytoma (grade II) can transform into highly malignant grade IV tumours over time, underscoring the need for long-term surveillance even after initial treatment (Komori, 2022; Molinaro et al., 2019). The presence of an IDH mutation in our patient's tumour (retained in the recurrent tumour) is characteristic of "secondary" glioblastomas, which arise from lower-grade precursors (Ohgaki & Kleihues, 2013). Her molecular profile ($IDH1^+$, ATRX, $p53^+$, low MGMT methylation) fits with the known biology of this subset.

Second and central in this case are the neuropsychiatric symptoms. Depression and anxiety were the first manifestations of the disease, preceding neurological signs by weeks. The initial severe depressive episode in a young adult without prior psychiatric history was atypical, and standard antidepressant treatment produced only transient and partial improvement. As noted in the literature, depression is one of the most common psychiatric presentations of brain tumours (Madhusoodanan et al., 2015). For example, Nazli & Sevindik (2021) reported a case of frontal glioma diagnosed only after prominent depression and anhedonia. In meta-analyses, roughly 20 – 30% of brain tumour patients suffer clinical depression, which adversely affects their quality of life and survival (Sharma et al., 2022). Anxiety and mood lability are also frequent (Leo, Frodey, & Ruggieri, 2020). These symptoms often delay diagnosis when attributed to primary psychiatric illness.

Our literature review confirms that neuroimaging can unmask occult brain tumours in such scenarios. Al-Janabi et al. (2018) described a patient whose anxiety and coordination problems (misdiagnosed as a motor disorder) were later found to be from a frontal glioblastoma (Al-Janabi et al., 2018). Similarly, Leo, Frodey, & Ruggieri (2020) reported that individuals were treated for depression for months before imaging revealed an extensive frontal astrocytoma. Subtle cognitive changes and personality shifts should therefore prompt consideration of an organic cause. Third, this case highlights the need for integrative care. The progression of the patient's psychiatric diagnosis, from a primary mood disorder to an organic affective and finally to an organic personality disorder, mirrors her tumour's malignant transformation. Ongoing psychiatric support was essential, as treatment needed adjustment after each surgery and during adjuvant therapy.

Multidisciplinary management (neuro-oncology, neurosurgery, psychiatry, rehabilitative services) is vital for such complex cases.

Recent advances in AI-driven neuroimaging have enabled precise, automated analysis of gliomas. Deep neural networks (e.g., U-Net variants) can accurately segment tumour subregions, supporting quantitative volumetry for diagnosis and treatment planning. For example, Preetha, Priyadarsini, & Nisha (2025) used a multi-scale attention U-Net with an EfficientNet encoder to segment brain tumours, achieving a Dice coefficient ≈ 0.93 (Preetha, Priyadarsini, & Nisha, 2025). Similarly, Abd-Ellah et al. (2024) achieved ≈ 99% accuracy in classifying MRI scans as normal vs. low-grade vs. high-grade glioma and then segmenting the tumour (Abd-Ellah et al., 2024). Radiogenomic models extend AI's utility by predicting molecular markers for images: Choi et al. (2021) developed a CNN-radiomics pipeline that noninvasively predicted glioma IDH mutation status (AUC ≈ 0.96), and Yuan et al. (2024) combined structural and diffusion MRI features to predict IDH status in grade II–IV gliomas (AUC ≈ 0.85). Multimodal radiomics can predict multiple biomarkers at once. For example, a BraTS-trained DeepMedic model yielded AUC ≈ 0.93 for IDH and ≈ 0.999 for 1p/19q codeletion (Fan et al., 2024). AI models have also been applied longitudinally. Kickingereder et al. (2019) demonstrated a pipeline that automatically segmented tumours across serial MRIs and predicted time-to-progression, effectively automating volumetric response assessment. In this patient's case, such tools might have flagged subtle tumour growth or malignant transformation earlier. Finally, AI-driven "digital phenotyping" using passively collected data can monitor mood and cognition. For example, Kalisperakis et al. (2023) showed that smartwatch-derived metrics (heart rate, motor activity) could predict changes in psychotic patients' symptom severity, and Liu et al. (2025) used wearable-sensor features to classify psychiatric status more accurately than traditional measures. Although these studies focused on primary psychiatric disorders, similar approaches could be applied to a brain tumour patient to continuously track depression or cognitive decline. In summary, integrating AI-based imaging analysis (segmentation, radiogenomics) with digital symptom tracking could enable earlier detection of tumour progression and more objective monitoring of neuropsychiatric changes as observed in this case.

5. Conclusions

This case illustrates the complex interplay between diffuse astrocytoma and psychiatric symptoms. A high-grade astrocytoma (grade IV, IDH-mutant) can evolve insidiously from a lower-grade precursor, and its progression may be heralded by neuropsychiatric changes. Clinicians should maintain a high index of suspicion for brain tumours in patients with new, severe, or atypical psychiatric symptoms. Early neuroimaging and close neuropsychiatric follow-up are crucial. Our patient's experience highlights the need for adaptive, multidisciplinary care that addresses both oncological and mental health aspects.

In addition, this report underscores the potential role of emerging technologies. Artificial Intelligence methods, including advanced imaging analysis and predictive modelling, could facilitate earlier tumour detection and more personalised management in similar cases. As neuro-oncology advances, integrating AI tools with clinical expertise may improve outcomes by enabling faster diagnoses, tailored treatment plans, and proactive monitoring of neuropsychiatric and cognitive changes.

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