



# A case study of unveiling neuropsychiatric symptoms: a diagnostic challenge revealing glioblastoma multiforme

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## Abstract

Glioblastoma multiforme (GBM), a potentially lethal disease, has nonspecific symptoms, making diagnosis difficult. Diagnosis is further complicated in individuals with comorbid neurological and psychiatric illnesses, where they may be an overlap in symptomatology. In this case study of a 56-year-old female with cc-morbid neurological and psychiatric diagnoses, the patient presented with worsening complaints of existing symptoms. This case study reveals the importance that the provider must place to the sensitivity of new changes in preexisting symptoms that require prompting further intervention; as a result of this investigation, providers were able to uncover the diagnosis of GBM. Patients presenting for decompensation of psychiatric complaints and worsening neurologic symptoms, however slight they may be, must be thoroughly evaluated for organic causes and assessed for the need of further intervention. This case study further emphasized that nonspecific symptoms of GBM may include psychiatric symptoms such as worsening depression and suicidal ideations.

## Background

GBM, an aggressive and malignant tumor, can present with psychiatric symptoms and be challenging to recognize in clinical practice. Brain tumors like GBM may present with signs of increased intracranial pressure [1,2]; they rarely present with sole psychiatric symptoms [3]. However, GBM can manifest in nonspecific neuropsychiatric symptoms depending on the location and size of the tumor [1]; psychiatric symptoms can present prior to any neurologic symptoms, which may mislead diagnosis. GBM psychiatric symptoms can vary widely, including manifestation as depression [4,5], psychosis [6], and catatonia [7]. The presence of comorbid neuropsychiatric symptoms and rapid decline is an indication to obtain further diagnostic imaging [1]. Diagnostic imaging is noted to be a vital method of diagnosis as lab values and tumor markers can present as unremarkable [6]. The presence of psychiatric symptoms in patients with GBM is noted to have a negative impact as it may speed the growth of GBM and accelerate tumor necrosis [8], which leads to worsening outcomes [9] and makes prompt diagnosis crucial [10]. Psychiatric diagnoses can be further complicated as GBM patients are a vulnerable population that face higher rates of depression, anxiety, and risk of suicide [11,12]. The complex neuropsychiatric presentation of GBM can make the disease difficult to recognize clinically, which may delay diagnosis and treatment.

## Case Report

A 56-year-old female with a past history of traumatic brain injury, major depressive disorder, generalized anxiety disorder, post traumatic stress disorder, and migraines presented with chief complaints of depression, suicidal ideation, and worsening forgetfulness, which resulted in a psychiatric hospitalization.

During hospitalization, she described severe and frequent headaches. She reported “unbearable” headaches from her migraines that would radiate from her head down to the ears; she attributed these chronic symptoms to her previously known diagnosis of migraines, which she reported had started after sustaining head injuries as a result of surviving physical assault with a metal object decades ago. Since then, the patient reported struggles with worsening memory and forgetfulness. Over the past few weeks, patient reports gradually worsening memory, describing that she was unable to recall her family member’s phone numbers that she previously knew. She described difficulty with special recall of areas where she was previously familiar with, had visited numerous times, and was able to navigate. She reported intense struggles with memory and reported that this had worsened her depression. She endorsed having suicidal ideations without plan. She described inconsistent sleeping patterns and worsening fatigue with the onset of menopause. As a survivor of domestic violence, she reported struggling with worsening flashbacks and nightmares. She stated that her symptoms were more intense with triggers of images and videos displaying domestic violence. She reported feeling fearful that her ex-partner will find her and harm her and her family. Patient denied other paranoia. No manic or psychotic symptoms were endorsed or observed. The patient reported being adherent with her medications, which included bupropion, escitalopram, gabapentin, and lorazepam. The patient reported using a medical marijuana card for migraines/neck pain; she denied any other substance history. The patient was hospitalized on the inpatient psychiatric unit about two weeks ago for suicidal ideations; at the time, she was discharged with an increased dose of bupropion.

Upon evaluation, the patient was observed to be tearful, anxious and dysphoric. While she was alert and oriented, memory deficit was observed as the patient was noted to be preservative and was observed to be repeating the exact same thoughts of worsening suicidal ideation and associated guilt; the patient endorsed she did not appear to remember she had said the same statements in the same conversation multiple times.

Treatment team carefully monitored and evaluated the patient during daily evaluations. During daily examinations, the patient reported a severity of 10/10 headaches, 10 being the worst. She denied suicidal or homicidal ideations. She denied auditory or visual hallucinations, but endorses hearing the sound of her head being beaten repeatedly from her past trauma. While hospitalized, the patient's pupils appeared slightly dilated. Patient reported previously taking lorazepam and was monitored for withdrawal signs and symptoms. She reported nausea and diarrhea, which she stated she had chronically been experiencing.

The patient reported vision disturbances of “flashing and fluttering”, which the patient noted was atypical of her usual headaches, which started during hospitalization. The patient denied having experienced visual disturbances before. The patient reported that with her diagnosis of migraines, she was supposed to follow-up with a neurologist, but had not done so.

Due to the patient's worsening memory issues, along with the visual disturbances that had not been present with previous migraines, the psychiatry team consulted neurology team. After serial evaluation, neurology team recommended an MRI of the brain.

MRI of the brain revealed a heterogeneously enhancing mass centered within the posterior corpus callosum. The mass involved the parietal and occipital central area. Patient's mass was noted to be most consistent with presentation of Glioblastoma Multiforme. The mass was noted to have mild surrounding vasogenic edema without midline shift. Neurosurgery and radiation oncology teams were contacted; the patient was transferred to the medical unit for a brain biopsy and further diagnosis and treatment.

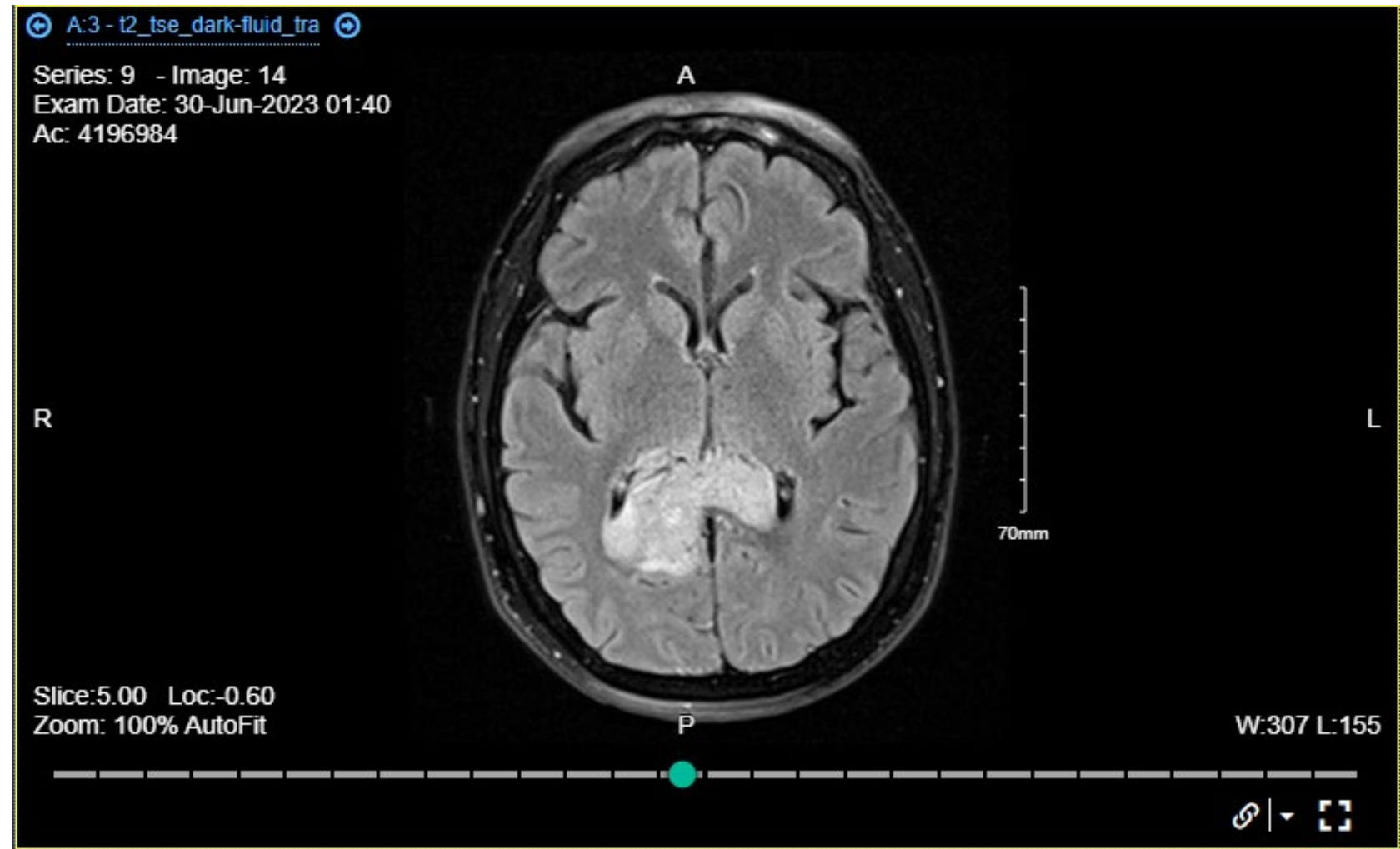
## Conclusions

This case study exemplified the importance of detecting subtle changes in the clinical presentation of preexisting neuropsychiatric symptoms in diagnosis of GBM. This case demonstrated the challenging nature of diagnosing GBM in patients with preexisting comorbid neuropsychiatric conditions. However, the detection in nuances of clinical symptomatology allowed the treatment team to advocate for the patient and obtaining imaging. Unfortunately, the process to approve and order MRI imaging in psychiatric patients can be grueling, as neuropsychiatric symptoms can be nonspecific and can be attributable to comorbid conditions, which can prevent patients from receiving diagnostic testing that is needed. It is paramount that clinicians appreciate any nuances in changes of historical symptoms or clinical examinations to advocate for their patients and rule out underlying etiology, which resulted in this diagnosis.

Unfortunately, there are many barriers that exist, for patients and clinicians, that may delay diagnosis and treatment of GBM. In this case, patient was not able to follow-up with outpatient neurology, which may have contributed to delaying care. Social determinants of health, socioeconomic background, finances, insurance, location, are known factors that contribute to accessing healthcare. Socioeconomic disparities due impact prognosis in GBM patients [13,14]. For example, having insurance has been correlated with improved access to care and outcomes in patients with GBM [15]. These factors directly impact the patient, but also their families: relatives of patient’s with GBM also suffer from higher levels of emotional distress and require care [16]. This case also highlighted the importance of interdisciplinary care; the lack of which may have delayed diagnosis and treatment. This case study calls for clinicians to lean in to their clinical acumen, give importance to clinical subtlety, and advocate for their patients.

Psychiatric illnesses like depression can indicate the presence of, as well as, be a common complication in patients with high grade gliomas like GBM [17]. Psychiatric treatment options like anti-depressants can have anti-tumor properties, while some treatment options can interfere with GBM treatment, as there may be shared overlapping molecular pathways [18]. Preclinical studies have demonstrated that psychiatric treatment options of selective serotonin inhibitors, such as fluoxetine, may be selectively toxic to glioma, suppressing the growth of the glioblastoma [19,18]. Psychiatric treatment should not be undermined in patients with GBM.

## Images



**Figure 1.** MRI Brain reveals a heterogeneously enhancing mass centered within the posterior corpus callosum and involving the parietal and occipital central area consistent with a glioblastoma multiforme with mild surrounding vasogenic edema and without midline shift

## References

- [1] Luo, R. J., Frady, J. N., & Bagheri, M. L. (2020). Subtle neuropsychiatric symptoms of glioblastoma multiforme misdiagnosed as depression. *BMJ Case Reports CP*, 13(3), e232308.
- [2] Al-Jarrah W, Khatib R, Asadi-Landani N, et al. Depressed presentation of glioblastoma multiforme. *Eur J Case Rep Intern Med*. 2018;5:doi: 10.12799/2018.00054.
- [3] Mathurandanan S, Tay MB, Farah T, et al. Psychiatric aspects of brain tumors: a review. *World J Psychiatry*. 2015;5(3):273-285. doi: 10.5498/wjps.v5.i3.273.
- [4] Perani L, Soriano, E, Meyer, S, Basso, M, Dabner, D, Kien, D, & Barati, T. A. (2019). Glioblastoma multiforme presenting as postpartum depression: a case report. *Journal of medical case reports*, 13(1), 374. <https://doi.org/10.1186/s12926-019-1905-3>
- [5] Vargas-Este, H., Orsny, A., Österg-Çakmak, Ö., Egenen, E., Vanh-Yavuz, E. N., & Solerighi, I. (2016). Rare case of glioblastoma multiforme located in posterior corpus callosum presenting with depressive symptoms and visual memory deficits. *Case Reports*, 2016, 16201610495.
- [6] Ng, B. Z., Pate, J. S., & Chua, S. H. (2023). Left frontal lobe glioblastoma multiforme masquerading as psychosis: A case report. *Malaysian Family Physician - the official journal of the Academy of Family Physicians of Malaysia*, 18, 45-100. <https://doi.org/10.51166/mf.287>
- [7] Tronconi, A., & Sennari, F. (2019). Temporal glioblastoma presenting as catatonia. *BMJ Case Reports CP*, 12(3), e234017.
- [8] Fu, X., Wu, C., Han, N., Liu, N., Han, S., Liu, X., ... & Yan, C. (2020). Depressive and anxiety disorders worsen the prognosis of glioblastoma. *Ageing (Edinb)* 37(1), 12020, 20095.
- [9] Cho-Moore, S., Lumbier, J., Kim, E., Lachyrev, E., Zhu, L., Liang, K. L., Scholten, D. M., Pende, L., Amick, C., Lohs, R. V., & Wainwright, D. A. (2019). The amygdala among psychological distress, the immune system, and brain tumor patient outcomes. *Current opinion in behavioral sciences*, 28, 44-50. <https://doi.org/10.1016/j.cobehs.2019.01.002>
- [10] Wang, Y., Wang, X., Wang, S., Qi, J., Zhang, Y., Wang, X., Zhang, L., Zhou, Y., Gu, L., Yu, R., & Zhou, X. (2023). Chronic stress accelerates glioblastoma progression via DRD2/ERK1/2-actin axis and Dopamine/ERK1/2 positive feedback loop. *Journal of experimental & clinical cancer research*, 42, 442. <https://doi.org/10.1186/s13046-022-02723-4>
- [11] Mielnicz, M., Mielnicz, M. S., Olsz, E., Chm, Y., Mielnicz, A. R., Alvi, M. A., Sadeh, N., Antonic, V., Farah Houshahad, M., Manouei, A., Das, S., Lian, X., McHenry, R. R., Dal Maestro, R., Turanski, G., Cohen-Gladet, A. A., Zakh, G., & Ashkan, K. (2023). Suicidal ideation and attempts in brain tumor patients and survivors: A systematic review. *Neuro-oncology advance*, 5(1), vba058. <https://doi.org/10.1093/noa/nab058>
- [12] Saito, Aki, M. et al. "Association of brain cancer with risk of suicide." *JAMA network open* 5, 5 (2020): e203062-6203062.
- [13] Chaudh, A., Rask, J. W., Dille Ore, C., Liu, D., Nguyen, A. T., Carraw, D., Bonte, A., Molinaro, A. M., Theodoropoulos, P. V., McDermott, M. W., Berger, M. S., & Agbi, M. K. (2019). Disparities in health care determine prognosis in newly diagnosed glioblastoma. *Neurological focus*, 40(6), 1. <https://doi.org/10.3171/2019.2.FOCUS.6182>
- [14] Gerschlager, M. P., Shaw, A., Murphy, E. S., Cullen, J., & Vio, J. S. (2023). Area-level socioeconomic status is positively correlated with glioblastoma incidence and prognosis in the United States. *Frontiers in oncology*, 13, 1110473. <https://doi.org/10.3389/fonc.2023.1110473>
- [15] Brown, D. A., Hines, B. T., Kozlowski, P., Cliffland-Saliba, Y. M., Grevell, S. S., Spear, J. A., Rybin, M., Burn, T. C., & Parney, I. P. (2019). Insurance correlates with improved access to care and outcome among glioblastoma patients. *Neuro-oncology*, 20(10), 1374-1382. <https://doi.org/10.1093/neuonc/noz163>
- [16] Shah, H., Haseck, J., Shua, A., Rybin, B., & Haseck, A. (2022). Quality of life in patients with glioblastoma and their relatives. *Acta Neurologica Scandinavica*, 148(1), 52-61.
- [17] Lindberg, N. S., Franco, C., Anderson, J. T., Moore, C. A., Huang, W., Lowe, Jr, E. R., & Glioma Outcomes Project Investigators. (2004). Depression in patients with high-grade glioma: results of the Glioma Outcomes Project. *Neurosurgery*, 54(2), 358-367.
- [18] Wagle, L., Hanson, T. R., Cryan, M., Alam, Y., & Schneider, J. (2020). Depression and glioblastoma, complicated comorbidities: a systemic review of published literature. *Neurosurgical review*, 42, 497-511.
- [19] Liu, K. H., Yang, S. T., Lin, Y. K., Lin, J. W., Lin, Y. H., Wang, J. Y., ... & Shen, S. C. (2014). Fluoxetine, an antidepressant, suppresses glioblastoma by crossing AMPK-β-mediated calcium-dependent apoptosis. *Oncotarget*, 6(7), 5088.