Malaysian Family Physician
Official Journal of the Academy of Family Physicians of Malaysia
and Family Medicine Specialist Association of Malaysia

CASE REPORT

Left frontal lobe glioblastoma multiforme masquerading as psychosis: A case report

Bee Zhen Ng, Jeremiah Sunderaj Peter, Sze Hung Chua

Ng BZ, Peter JS, Chua SH. Left frontal lobe glioblastoma multiforme masquerading as psychosis: A case report. *Malays Fam Physician.* 2023;18:45. https://doi.org/10.51866/cr.287

Keywords:
Glioblastoma, Frontal lobe, Psychosis

Authors:

Bee Zhen Ng
(Corresponding author)
MD, MRCPsych (UK)
Psychiatry & Mental Health Unit, Hospital Bentong, Jalan Padang, Bentong, Pahang, Malaysia.
Email: beezhen_ng@hotmail.com

Jeremiah Sunderaj Peter
MD, FRCR (UK)
Radiology Specialist Clinic, 25 & 26, SEDCO Complex, Jalan Albert Kwok, Kota Kinabalu, Sabah, Malaysia.

Sze Hung Chua
MD, MPM (UM)
Fellowship in Forensic Psychiatry
Department of Psychiatry and Mental Health, Hospital Mesra Bukit Padang, Kota Kinabalu, Sabah, Malaysia.

Abstract

Brain tumours often present with a variety of early subtle, non-specific symptoms. This can obscure an organic origin of the illness, which deters timely referral and management. We report a rare case of psychosis in a patient with a left frontal lobe tumour, preceded by 2 months of lethargy and word-finding difficulty with minimal neurological deficits, who was referred to our psychiatric unit from a primary care facility. Blood investigation findings including tumour marker levels were normal. Prompt neuroimaging revealed a left frontal lobe lesion with findings indicating a glioblastoma. The patient was subsequently referred to the neurosurgical team for surgical resection of the tumour. A high index of suspicion is paramount among atypical sociodemographic groups of patients with atypical psychiatric presentations. The primary care setting, which is often the first point of contact for patients, provides an avenue for early detection of such cases and timely referral to the appropriate healthcare system to ensure an optimal outcome.

Introduction

The diversity and subtlety in the presentations of intracranial tumours often confer a diagnostic challenge. It is common for patients with only psychiatric presentations to be referred initially to psychiatric facilities despite an acute presentation. This may result in years of inappropriate diagnosis, an impediment towards effective management culminating in higher rates of morbidity and mortality especially for aggressive brain tumours.[1] Brain tumours constitute one tenth of all adult tumours.[2] Gliomas (excluding grade I) represent the most common primary malignant tumour of the brain.[3] Psychiatric manifestations of brain malignancy are prevalent. While a fifth of patients with brain tumour present with psychosis, frontal lobe tumours are more commonly associated with mood symptoms.[4] Herein, we highlight a rare case of psychosis due to left frontal lobe glioblastoma multiforme (GBM) with non-specific neurological deficits, which was swiftly detected and managed.

Case presentation

A 51-year-old woman with no history of medical or psychiatric illnesses was referred from a primary care facility immediately to our psychiatric department upon presenting with complaints of visual hallucination, persecutory delusion and delusion of control lasting for 1 week. There were no other investigations conducted prior to referral. On our assessment, there were no mood symptoms elicited in addition to the aforementioned psychotic symptoms. Collaborative history-taking revealed further history of one episode of word-finding difficulty and lethargy for 2 months before the onset of psychotic symptoms. No history suggestive of seizure was reported. There was no family history of psychiatric illnesses. On examination, her vital signs were normal, and she was orientated to time, place and person. There were no specific neurological deficits apart from a generalised muscle power of 3/5. Biochemical investigation findings including tumour marker levels were normal. Urgent computed tomography (CT) of the brain demonstrated a left frontal lobe lesion measuring 3.2×4.2 cm. This prompted magnetic resonance imaging of the brain, which was performed 8 days later, revealing a left frontal lobe lesion favouring a glioblastoma (**Figure 1**). The patient was then referred to the neurosurgical team for further management. No psychotropics were prescribed for her psychotic presentation.

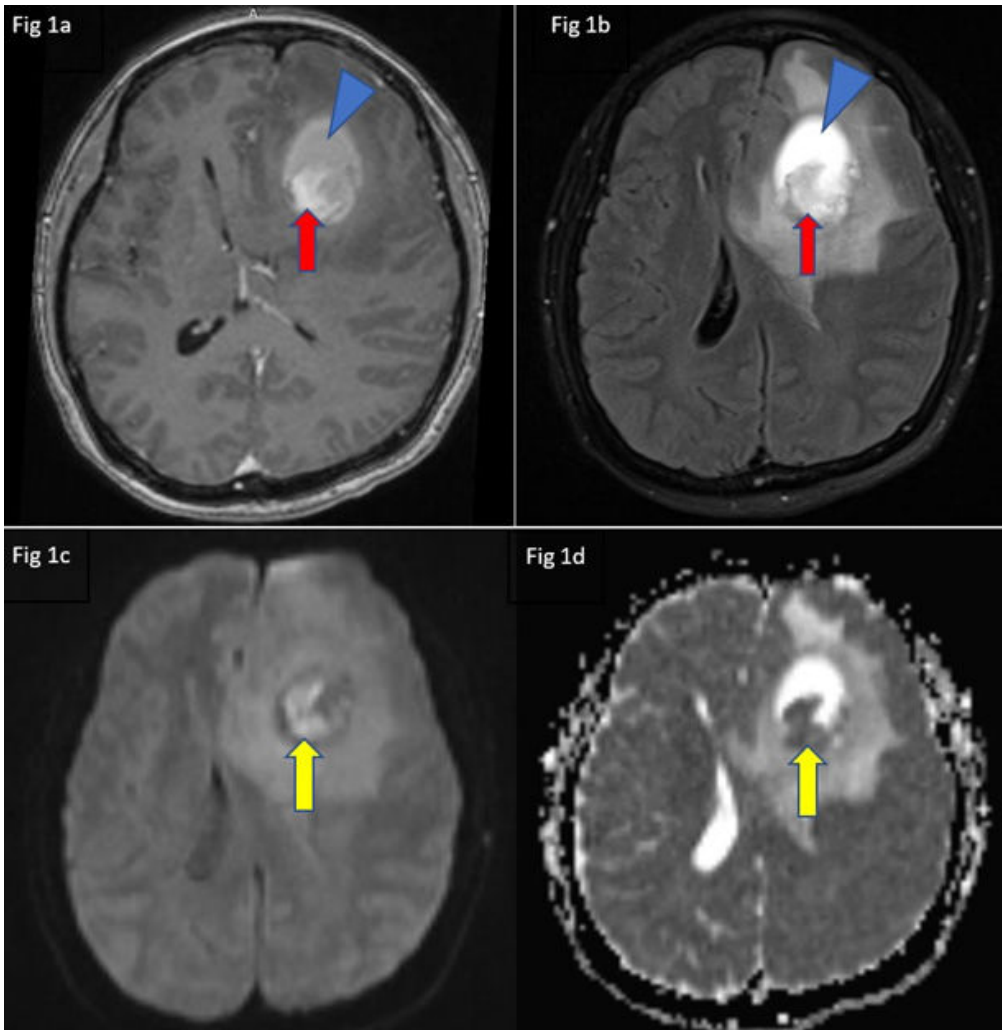

Figure 1. Axial plane magnetic resonance images: (a) contrasted T1, (b) FLAIR, (c) DWI and (d) ADC map. Figure 1a and b show a left frontal lobe mass with associated white matter oedema. The mass has a solid enhancing component located peripherally (red block arrow), which demonstrates restricted diffusion (yellow block arrow in Figure 1c and d). A large portion of the mass shows high signal intensity in the T1, T2 and FLAIR images, suggestive of necrotic components (blue arrowhead in Figure 1a and b). These findings favour a glioblastoma.

Soon after her psychotic presentation, the patient continued to develop progressively worsening cognitive dysfunction of expressive dysphasia, apathy, echolalia, agraphia and acalculia. The patient underwent left craniotomy and excision of the tumour 9 days after her presentation to our service. Histopathological examination (HPE) confirmed a diagnosis of GBM. She received chemoradiotherapy after surgical intervention and fully recovered thereafter.

Discussion

Gliomas are the most common group of primary brain tumours, with GBM or astrocytoma grade IV accounting for the subgroup of malignant gliomas with the poorest prognosis in view of a rapidly evolving course.[3] While neurological symptoms vary, the generalised features of raised intracranial pressure are frequently noted as the tumour enlarges.[5,6] The patient's initial psychiatric manifestation with minimal neurological deficits may be attributed to physiological ageing and brain atrophy compensating for the features of raised intracranial pressure.[4,7]

Psychiatric presentation as the only manifestation of brain neoplasm is rare.[8] In their meta-analysis, Madhusoodanan et al. reported mood symptoms to be predominant, accounting for 36% of cases, while psychotic symptoms accounted for 22% of cases.[4] Psychotic symptoms were more commonly found in association with tumours in the temporal lobes and pituitary gland.[4,8] The review on psychiatric symptoms in relation to GBM by Leo et al. found that 62% of cases

presented with depression and 35% with psychosis. Psychotic symptoms in patients with GBM were reported to be localised predominantly in the temporal lobes. Psychosis in association with GBM of the frontal lobes is uncommon. Two reports of psychosis were described in association with GBM in the frontal lobes; however, in one case, the chronic presentation of psychosis rendered it challenging to distinguish between organic and functional psychoses.[6,9]

In this study, the patient presented with an acute onset of psychosis in the context of a frontal lobe lesion. The mass effect of the tumour encroaching into the left lateral ventricle and third ventricle may be a plausible explanation for the psychotic symptoms. While there are reports of psychosis in relation to other groups of brain tumours (i.e. meningiomas localised at the ventricular system), there are none reported in patients with GBM to our knowledge.[6] Another possible explanation for the atypical presentation is the phenomenon of diaschisis, wherein the tumour has affected circuits to distant areas of the brain, resulting in psychiatric manifestations.[8,10] The absence of mood symptoms in the present patient further fuels a clinical conundrum.[6,8] Metastatic brain tumours, which more often present with psychiatric symptoms as compared to primary tumours, may also explain the patient's presentation; however, the results of the HPE and CT of the thorax, abdomen and pelvis post-surgery revealed a primary brain tumour.

The present case further illustrated a rapidly evolving and aggressive tumour with psychotic symptoms preceding cognitive impairment in a short span of time. Studies have demonstrated that this fast-growing tumour can double in size within 2 days.[11] The domains of cognitive impairment in the present case are consistent with the functions of the frontal lobe and left parietal lobe. The involvement of the left parietal lobe may arise from the effects of the enlarging tumour size or from the mass effect exerted by the tumour. The patient provided an account of word-finding difficulty and lethargy 2 months prior to the onset of psychosis. This demonstrates a non-specific presentation that could often be mistaken as benign, especially in the general or primary care setting where patients are more likely to make the first contact with. The absence of a formal neuropsychological assessment further precludes the identification of subtle neuropsychiatric presentations that would easily evade clinical diagnosis.[12]

Patients with psychiatric presentations in the context of brain neoplasm are typically referred initially to psychiatrists. A high index of suspicion is paramount especially when a patient presents with atypical symptoms (i.e. perceptual disturbances of atypical modality such as visual or olfactory hallucinations, late onset of psychiatric symptoms that are inconsistent with the usual epidemiological age, neuroleptic sensitivity, treatment refractory cases, evolving psychiatric presentations between episodes and subtle neurological deficits). In this study, the patient had a late onset of acute psychosis with atypical presentation and minimal neurological deficits in the absence of a family background of mental illness. Vigilance in an organic aetiology prompted neuroimaging, which confirmed the presence of a left frontal lobe mass. This prevented needless administration of psychotropic medications that could result in more risks than benefits whilst delaying effective management.

While brain tumours may be neurologically silent with only psychiatric manifestations, routine neuroimaging is controversial. One study recommended neuroimaging for patients above 40 years old with neuropsychiatric and behavioural changes, whereas the review by Albon et al. on the clinical and cost-effectiveness of neuroimaging did not recommend routine neuroimaging.[13,14] A previous systematic review found neuroimaging abnormalities in only 0.4% of patients with first-episode psychosis.[15] Further studies are warranted given that brain tumours at a later stage herald a poorer prognosis. In the present case, timely neuroimaging aided in accurate diagnosis and management, which subsequently improved the prognosis.

Conclusion

It is important for primary care clinicians, who serve as gatekeepers to further healthcare services, to have a high index of suspicion in patients with non-specific, subtle or atypical presentations. Secondary causes of psychiatric manifestations (i.e. organic aetiologies) must be considered initially in this subset of patients. Nevertheless, good history-taking including collaborative history-taking coupled with a thorough physical examination is imperative in good clinical practice. Missing an organic aetiology in a patient who presents with only

psychiatric symptoms would inadvertently delay diagnosis, and subsequently referral to the appropriate team for further prompt management. An inaccurate diagnosis also prevents the judicious use of psychotropics, which heralds more risks than benefits.

Acknowledgements
We would like to thank the Director General of Health Malaysia for his permission to publish this article.

Conflicts of interest
The authors declare no conflicts of interest.

Author contributions
All authors contributed equally to the production of this manuscript.

Patient's consent for the use of images and content for publication
Informed consent was obtained from the patient prior to the writing of this article for publication.

What is new in this case report compared to the previous literature?

- Psychosis as the presenting symptom of glioblastoma multiforme and frontal lobe tumour is rare but possible.
- Primary care clinicians should be vigilant about acute psychiatric presentations especially in patients with atypical features (i.e. late-onset psychosis, visual or olfactory hallucinations and subtle neurological deficits).
- The localising neurological presentation of increased intracranial pressure was absent in the early stage. Such presentation can occur in senior adults owing to physiological ageing and brain atrophy.
- While no amount of investigations can replace clinical skills, neuroimaging is valuable in modern medicine. Prudent and indicated use should be encouraged to ensure that an organic aetiology is ruled out.

What is the implication to patients?

- Early symptoms of brain tumours may be subtle and non-specific, and such tumours are easily mistaken as benign. The primary care setting, which is often the first point of contact for patients, provides an avenue for early detection through a high index of suspicion of atypical presentations. Thorough assessments and investigations, including good collaborative history-taking, provide an excellent opportunity for the diagnosis of such cases and timely referral to the appropriate healthcare system to ensure an optimal prognosis.

References

1. Betul O, Ipek M. Brain tumor presenting with psychiatric symptoms. *J Neuropsychiatry Clin Neurosci*. 2011;23(4):E43–E44. doi:10.1176/jnp.23.4.jnpe43
2. Zajączkowska M, Kryszkowski W, Talarowska M, et al. Psychiatric symptoms as possible brain tumor complications: a case report. *Med Sci Tech*. 2015;56:73.
3. Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumors of the central nervous system. *Acta Neuropathol*. 2007 Aug;114(2):97–109. doi:10.1007/s00401-007-0243-4
4. Madhusoodanan S, Opler MG, Moise D, et al. Brain tumor location and psychiatric symptoms: is there any association? A meta-analysis of published case studies. *Expert Rev Neurother*. 2010 Oct;10(10):1529–1536. doi:10.1586/ern.10.94
5. Al-Janabi W, Krebs R, Arcila-Londono X, et al. Atypical presentation of glioblastoma multiforme. *Eur J Case Rep Intern Med*. 2018;5. doi:10.12890/2018_000954
6. Leo RJ, Frodey JN, Ruggieri ML. Subtle neuropsychiatric symptoms of glioblastoma multiforme misdiagnosed as depression. *BMJ Case Rep*. 2020;13(3):e233208. doi:10.1136/bcr-2019- 233208
7. Madhusoodanan S, Patel S, Reinharth J, et al. Meningioma and psychiatric symptoms: a case report and brief review. *Ann Clin Psychiatry*. 2015;27(2):126–133.
8. Madhusoodanan S, Ting MB, Farah T, et al. Psychiatric aspects of brain tumors: a review. *World J Psychiatry*. 2015;5(3):273–285. doi:10.5498/wjp.v5.i3.273
9. Lyra A, Cordeiro Q, Shiozawa P. Catatonia after glioblastoma multiforme in a patient with schizophrenia: the importance of establishing etiology. *J Neuropsychiatry Clin Neurosci*. 2015;27:e216–e217. doi:10.1176/appi.neuropsych.14120388

10. Singh D, Kapoor A, Khadda S, et al. Psychotic manifestations as an initial presentation in glioma: two case reports and review of literature. *Neuropsychiatr Neuropsychol*. 2014;9(1):1–3.

11. Furneaux CE, Marshall ES, Yeoh K, et al. Cell cycle times of short-term cultures of brain cancers as predictors of survival. *Br J Cancer*. 2008;99:1678–1683. doi:10.1038/sj.bjc.6604716

12. Hendrix P, Hans E, Griessenauer CJ, et al. Neurocognitive status in patients with newly-diagnosed brain tumors in good neurological condition: the impact of tumor type, volume, and location. *Clin Neurol Neurosurg*. 2017;156:55–62. doi:10.1016/j.clineuro.2017.03.009

13. Madhusoodanan S, Danan D, Brenner R, et al. Brain tumor and psychiatric manifestations: a case report and brief review. *Ann Clin Psychiatry*. 2004 Apr–Jun;16(2):111–113. doi:10.1080/10401230490453770

14. Albon E, Tsourapas A, Frew E, et al. Structural neuroimaging in psychosis: a systematic review and economic evaluation. *Health Technol Assess*. 2008 May;12(18):iii–iv, ix–163. doi:10.3310/hta12180

15. Forbes M, Stefler D, Velakoulis D, et al. The clinical utility of structural neuroimaging in first-episode psychosis: a systematic review. *Aust N Z J Psychiatry*. 2019 Nov;53(11):1093–1104. doi:10.1177/0004867419848035