



# Journal of Health and Medical Sciences

**Ramos, M. E., De Leon, A. R., & Punzalan- Sotelo, Aubrey, M. (2022), Diffused Multifocal High Grade Glioma. *Journal of Health and Medical Sciences*, 5(2), 88-92.**

ISSN 2622-7258

DOI: 10.31014/aior.1994.05.02.216

The online version of this article can be found at:  
<https://www.asianinstituteofresearch.org/>

Published by:  
The Asian Institute of Research

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# Diffused Multifocal High Grade Glioma

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## Abstract

Multiple glioma represent approximately 2 to 5% of all high grade gliomas which are categorized as multifocal or multicentric which depends on its timing, location and pattern of spread. Most of the clinical manifestation of patient with High Grade Glioma are headache and seizures, however, some may present with cognitive symptoms like memory loss, personality changes, focal weakness or numbness related to the site of the mass. There are several ways on treating high grade glioma these include surgery, radiation and/or chemotherapy. This report is a case of 54-year-old male, without no known comorbidities who presented two months history of right hemi cranial headache, accompanied with left sided weakness. Cranial MRI revealed uni-hemispheric, non-contiguous high-grade gliomas. This case underwent surgical excision and concurrent chemo-radiotherapy.

**Keywords:** Multiple Multifocal Glioma High-Grade

## 1. Introduction

Glial tumors account for 42 percent of all primary adult CNS neoplasms, with malignant high-grade gliomas accounting for over 75 percent.<sup>4</sup> GBMs most commonly occur as solitary lesions with multiple GBMs occurring rarely (with reported incidence of 2–20%). Multiple GBMs are further categorized into multifocal and multicentric depending whether dissemination or growth by an established route, spread via commissural or other pathways, (i.e. corpus callosum, fornix, internal capsule, or massa intermedia), or spread via cerebrospinal fluid channels exists or not.<sup>4</sup>

To rule out any conceivable relationship between the neoplastic foci, multicentric tumors require comprehensive macro- and microscopic examination. Gliomatous tumors having many foci are known as multifocal gliomas. With or without evidence of cerebral spinal fluid spread, with microscopic continuity.<sup>10</sup> While multicentric gliomas are tumors arising independently in more than one site of the brain with absence of seeding along easily accessible routes.<sup>4</sup>

Despite the fact that the incidence of multicentric and multifocal glioblastomas is unknown, A series of 209 cases were studied by Batzdorf last 1963 and discovered a 2-4 percent and 25 percent for multicentric and multifocal gliomatous tumours, respectively.<sup>8</sup> Furthermore another 2 case study of multifocal glioblastoma was noted by Zhang et al., last 2021 at China.<sup>10</sup>

Currently, there is no noted literature regarding multiple multifocal high-grade glioma in Philippines. In this study we report a case of multiple multifocal high-grade glioma, we consider its course of illness, diagnostics, management and treatment and their outcome.

## 2. Case Report

This is the case of a 54 year old, male, who sought consult due to 2 months history of progressive right hemicranial headache, accompanied with left sided numbness and weakness. He had no comorbidities with no familial history of hereditary diseases.

### 2.1. Assessment

Upon consult patient was seen to be coherent, oriented with appropriate response. Vital signs and general physical examinations were unremarkable. On neuro examination, patient was awake, with, homonymous hemianopsia on the left, left hemiparesis and left hemisensory loss. The rest of the neurologic examination were normal.

### 2.2. Laboratory workup

Basic laboratory examinations such as CBC, electrolytes and coagulation studies all revealed unremarkable. Other ancillaries like random blood sugar, lipid profile, PSA, CEA and AFP were normal. A cranial CT scan was without contrast done showing a heterogenous predominantly hyperdensity focus in right parieto-occipital lobe measuring 4.9x 4.2x 4.9cm with surrounding hypodensity, which is considered as an intracranial mass. Furthermore, a cranial MRI with contrast was done showing a fairly defined nodule and mass in the right high parietal lobe and right temporo-parietal-occipital lobes exhibiting T1 hypo to isointense signal, interspersed with hyperintense signals and T2/ FLAIR heterogenous hyperintense signal abnormalities with respective measurement of 2.0x 1.4x2.1cm and 5.2x 4.5x 5.0cm. Surrounding vasogenic edema involving the right temporo-parieto-occipital lobes is observed, suggesting of a hemorrhagic metastatic process.

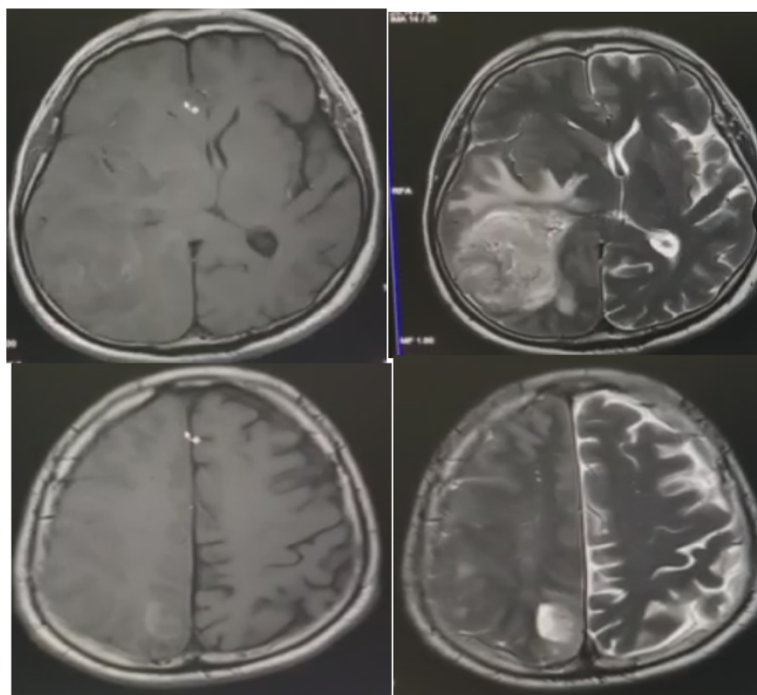


Figure 1 : Cranial MRI with contrast showed a fairly defined nodule and mass in the right high parietal lobe and right temporo-parietal-occipital lobes exhibiting on T1 a hypo to isointense signal, interspersed with hyperintense signals and on T2 showed heterogenous hyperintense signal abnormalities with respective measurement of 2.0x1.4x2.1cm and 5.2x 4.5x 5.0cm.

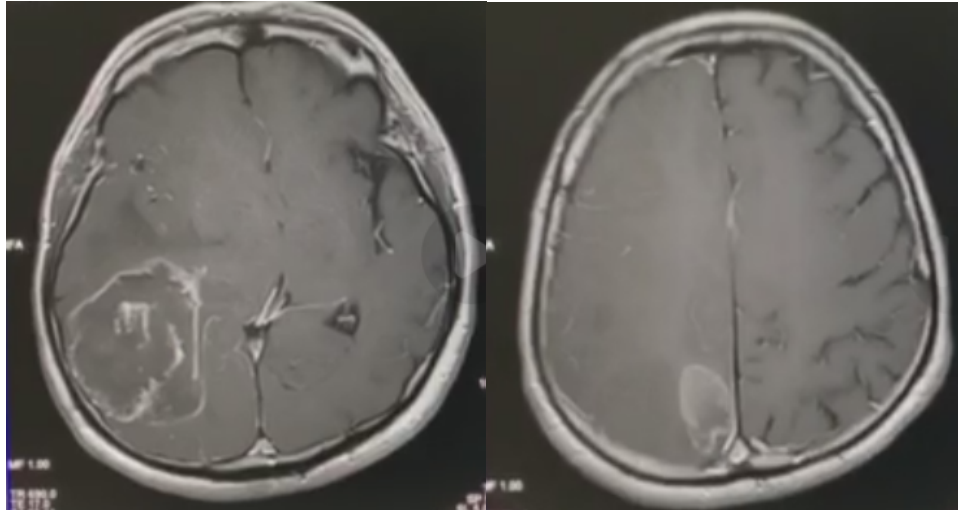


Figure 2: Cranial MRI with contrast on Post-gad contrast showed a hyperintense signal surrounding the fairly defined nodule on both right high parietal lobe and right parieto-temporo-occipital lobe.

Patient was managed with dexamethasone, omeprazole, paracetamol and lactulose. The patient was referred to neurosurgery service and underwent craniotomy, excision of tumor and biopsy was done revealing glioblastoma WHO GRADE IV, most likely wild type furthermore immunohistochemistry were also done revealing positive to GFAP and p53, negative in IDH-1, with retained nuclear stain of ATRX in tumor cells. The patient was then discharged with follow up on radiation-therapy and medical oncology.

### 2.3. Outcome

On follow up after 1 month since discharged, there was persistence of left hemiparesis but with resolution of left hemi sensory loss. Patient completed his chemo-radiation therapy with concurrent adjuvant chemotherapy sessions of Temozolomide. Unfortunately, the patient died after 3 months post treatment.

### 3. Discussion

Glioblastoma (GBM) is the most malignant diffuse glioblastoma of the astrocytic lineage, and according to the WHO classification, it is a grade IV glioma. GBMs account for 54 percent of all gliomas and 16 percent of all primary brain tumors, making them the most prevalent malignant primary brain tumor.<sup>10</sup>

For high-grade gliomas, a different pathway of propagation was seen. Multiple foci high-grade gliomas are considered tumors that spread through several pathways, including commissural fibers or the corpus callosum, and the CSF, and also by local metastasis. Multi focal high grade gliomas are fairly uncommon entities, with a reported incidence from 2–10% to 16% of all reported gliomas. The majority of instances occur supratentorially, whereas lesions in the posterior fossa have a documented prevalence of fewer than 4%.<sup>2</sup>

Multiple gliomas were initially classified by Budka into four categories: Diffuse, multiple, multicentric, and multi-organ. In 1963, Batzdorf and Malamud distinguished two types of multiple gliomas namely multifocal and multicentric gliomas. Multifocal gliomas are those which result from dissemination or growth of tumor cells by a preformed route like commissural fibers, cerebrospinal fluid pathway or by local metastasis. On the other hand, multicentric gliomas are located wide apart in different lobes or hemispheres, and their concurrence cannot be explained by previously mentioned mechanisms. The clinical significance of labeling multiple GBMs as either multifocal or multicentric is fading out. Various studies show that there is no apparent clinical utility in distinction between the two groups.<sup>5</sup>

Glioblastoma Multiforme's clinical manifestations are usually linked to the functional aspect of the brain area involved. Tumors in specific locations might create noticeable symptoms such as prolonged weakness, numbness,

visual loss, or language changes.<sup>1</sup> This is the same as the case presented which was gradual progression of headache accompanied by left hemisensory-motor deficit and left homonymous hemianopia upon examination

Imaging techniques that can be used for patients with intracranial tumors are non-invasive tests such as computed tomography (CT) and magnetic resonance imaging (MRI) scans. On a CT scan, the lesions appear as hypodense patches in comparison to neighboring brain tissue, with a midline shift due to moderate to severe edema. However, due to their higher soft tissue contrast, MRI scans are the gold standard imaging technique employed, allowing the complexity and heterogeneity of the tumor lesion to be better observed than a CT scan. T1-weighted MRI scans reveal hypointense lesions, but proton density weighted and T2-weighted imaging reveals hyperintense lesions. Moreover, a central area of necrosis surrounded by white matter edema can be seen on an MRI scan enhanced with gadolinium in patients with malignant gliomas. Tumors are usually unifocal but can be multifocal too.<sup>3</sup>

The best treatment for multifocal high-grade glioma is still up for debate. This is due to contradicting findings that urge no therapy at all on one hand and aggressive maximal surgical excision followed by chemo-radiotherapy(RT) on the other. Surgical biopsy is however, desirable to establish diagnosis and to decide further adjuvant therapy. Patients with multifocal disease in the modern temozolomide era had 1-year and 2-year survival rates of only 28.5% and 4.3%, respectively.<sup>5</sup>

The prognosis of multiple glioblastoma multiforme has remained unclear until now. There is no definitive study comparing the prognosis of multiple glioblastoma multiforme against a solitary glioblastoma multiforme. In a study by Parsa *et al.*, did not find any survival difference between the two. However, in another study, the authors found that patient with multifocal glioblastoma had a median overall survival of 6 months, compared to a solitary glioblastoma, of which was 11 months.<sup>7</sup>

#### 4. Conclusion

We report a rare case of a 54-year-old male who presented with focal neurologic deficit with no known comorbidities and no family history of familial disease. On neuroimaging a multiple intracranial mass on Cranial CT scan was seen, patient underwent surgery and completed his con-current chemo-radiotherapy. Although reports of this condition have been reported in other countries, there is still no known data recorded in the Philippines. Moreover, although multifocal high-grade glioma is rare and has a poor prognosis, one must give all the best treatment to the patient.

#### Acknowledgment

None

#### Funding

None

#### Ethical Consideration

Patient form was secured before submission of manuscript

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