

WHO Grade III Anaplastic Astrocytoma In A 72 Years Old Male-A Case Report

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Case Report

Keywords: Hypothalamic dysfunction, Neuro Tumor, Glioma, Choroid glioma

DOI: <https://doi.org/10.21203/rs.3.rs-352548/v1>

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Abstract

Glioma is a common type of tumor that originates in the glial cell in brain and is devastating in nature. It can affect all age groups but is more common in adults and has been found more in males than in females with a ratio of 1.3/1. Despite the aggressive treatment it relapsed and can cause mortality because of its infiltrative nature. This WHO type III Anaplastic Astrocytoma is more common in 40-50 years old with a median of 41 years.

Here, we report a new case of Glioma occurring in a 72 year old male, who presented with a right sided headache, forgetful, worsening memory, behavioral problem along with increased agitation and irritability. MRI Brain WO/W revealed a mass in the left thalamus and basal ganglia region with a thick rim of peripheral enhancement. Diagnosis of Anaplastic Astrocytoma (WHO Grade III) was confirmed by histology and immunohistochemical analysis of the tumor.

Conclusion:

It is a case of Left sided WHO GRADE III Anaplastic astrocytoma which is rare in this age group of 72 years. The patient was managed with gamma knife radiosurgery, chemotherapy with Temozolomide (TMZ), and targeted molecular therapy with Bevacizumab. The patient improved with remission of symptoms.

Background

Among brain tumors, rare ones are the those, arising from the deep brain and most of them likely to be low-grade astrocytoma. Possibility of ganglion cell tumors cannot be excluded. (1) Gliomas are rare low-grade primary brain tumors that are thought to derive from neuroglial stem or progenitor cells from the anterior wall or roof of the third ventricle representing 81% of malignant brain tumors. Gliomas are either astrocytic, oligodendrocytic, or a mix of these 2 cell types. However, there is no consensus definition of gliomas as a larger class of histology, which can make comparisons between studies challenging (2,3,4) Glial tumors which arise primarily in the thalamus, are rare, and only represent approximately 1% to 5% of all brain tumors.

Patients with thalamic gliomas usually develop their first symptoms of headache, vomiting due to mass effect of compression of tumor the adjoining ventricle, resulting in a blockage of the flow of cerebrospinal fluid (CSF). Tumors also commonly interfere with normal fibers surrounding the thalamus and can manifest with gait imbalance, motor weakness, or abnormal tones. These tumors are treated with radiation and adjuvant chemotherapy, either with or without a tissue diagnosis, due to their deep seated, midline location (5,6,7) Like most other gliomas of the brain, thalamic gliomas are generally treated using radiation therapy with or without chemotherapy. The inclusion or choice of chemotherapy is dependent on the result of tumor biopsy.

Clinical Presentation

Presenting History:

A 72 year old male with Past medical history presented with history of self-limiting, intermittent near daily pressure like Right Sided (frontotemporal region) headache radiating to left side, usually responding well to analgesics since 3 months. He has reported headache worsened in afternoon. Patient has reported to be more forgetful, worsening memory. Patient's primary caretaker (Daughter) has reported behavior changes with increased agitation/irritability and found the slowness of thinking. Patient has denied any vomiting, vision changes, dizziness, or vertigo, weakness or sensory changes. There was no history of seizures nor recent abnormal movements. No personal or family history of cancer was reported. Patient has reported being a long-term former smoker.

Physical Examination:

At admission to a local hospital, the patient had stable vitals and normal gross physical examination. His systemic examination including neurological examination was normal.

Neurological Exam:

Mental Status: AA OX3

follow commands:

- clear speech
- no dysphasia
- Cranial Nerves:
 - Pupils equal
 - eyes midline w/o gaze
 - preference
 - face symmetric
 - no gross visual field cuts
 - hearing intact grossly
 - Tongue is midline

Motor Exam:

- MAE AG and to resistance
- Sensory Exam:
 - LT/PP and pain intact

Coordination Exam:

- no gross ataxic movements

- no dysmetria

Reflexes Exam:

- DTR 2+ symm throughout.
- Gait: steady gait, able to tandem

Investigation:

CT brain is notable for left subcortical well circumscribed hypodensity involving thalamic region, concerning intracranial mass with perilesional edema and mass effect and MLS. Neurosurgery consulted which deemed not urgent immediate neurosurgical intervention. MRI brain w/wo GAD ordered for further evaluation for lesion. Decadron ordered and Keppra initiated seizure prophylaxis. Possible surgical intervention/planning pending MRI. Patient admitted to Neuro ICU for further monitoring.

His blood workup was within the normal range except for a mild leukocytosis. Since he had no acute infectious etiology of symptoms, it was possibly a reactive and most likely due to recent administration of steroids. **CT brain was notable for left thalamic and left basal ganglia low-attenuated mass with 3.7 cm anteroposterior diameter, 3.6 cm transverse diameter and 3.9 cm craniocaudal diameter. It had adjacent vasogenic edema and mass effect on the third ventricle with 7mm midline shift towards the right consistent with a malignancy primary versus metastatic etiology.**

MRI Brain WO/W Contrast showed a mass in the left thalamus and basal ganglia region with a thick rim of peripheral enhancement as well as internal septal and amorphous areas of enhancement. The mass measured approximately 3.9 x 3.8 x 3.7 cm. The central portions of the mass showed heterogeneous hyperintense T2 signal suggesting internal complex cystic or necrotic components. There was significant surrounding vasogenic edema with mass effect upon the brain structures and left-to-right subfalcine shift.

No malignancy or metastasis was found on both CT chest and CT Abdomen apart from an incidental left liver lobe cyst. The patient had moderate to severe valvular aortic stenosis on echocardiography.

Differential considerations for these findings are broad. Findings are concerning for primary or metastatic malignancy, however other etiologies including abscess/infection, lymphoma, or other etiologies would present a similar appearance and cannot be excluded.

Histopathology The biopsy was sent for a pathology examination. Microscopic sections showed cellular aggregates and minute fragments of hypercellular glial tissues with mild to moderate cytologic atypia but no evidence of increased mitoses and cell necrosis. The findings were consistent with Anaplastic Astrocytoma (WHO Grade III). On immunohistochemical staining, 100% cells were positive for cytoplasmic GFAP (3+) and 2% cells were positive for nuclear Ki-67 (3+).

Diagnosis: WHO GRADE III Anaplastic Astrocytoma

Treatment

The patient was managed with gamma knife radiosurgery, chemotherapy with Temozolomide (TMZ), and targeted molecular therapy with Bevacizumab. The patient improved with remission of symptoms. No more behavioural changes were noted.

Follow up:

Follow up in the outpatient neurology clinic was continued for six months with complete improvement in patient neurological status.

Discussion

WHO type III Anaplastic astrocytoma (AA) is a malignant, astrocytic, diffusely infiltrating primary brain tumor, mostly seen in an age group 40-50 years old patients with a median of 41 years. In this case it's a 72 years old patient. In old age this disease is quite rare. In this age group glioblastoma multiforme (GBM) is more common. In the neuro imaging in T1+Contrast (C) shows ring enhancement with central necrosis and oedema in the surrounding,

Histopathology generally shows densely hypercellular with nuclear atypia and increased mitotic activity. Nuclear pleomorphism increased with prominent nucleoli, abnormal mitosis with multinucleated tumor cells.

In Immuno-histochemistry tumor cells express GFAP, Vimentin and S-100 protein. Ki-67 labelling index is important.

Molecular Genetics includes, IDH mutation, TP53 mutation, P 16 deletion, RB alteration, PTEN mutation, CDK4 amplification, LOH on Chromosome 19q, 10q,22q and EGFR amplifications.

AA account for 4% of all malignant CNS tumors and 10% of all gliomas. (8) The prognosis for AA patients varies depending on the molecular biology. The median overall survival (mOS) and 5-year survival rates for conventional therapy are 3 years and 28%, respectively. (8,9). The only identified risk factors are ionizing radiation and rare genetic syndromes including neurofibromatosis type 1 and 2, tuberous sclerosis, and the Li-Fraumeni syndrome. Seizures at presentation are less frequent than in low-grade astrocytoma: 83 percent against 46%. (10)

Treatment is Surgery, Radiotherapy and Chemotherapy. Molecular Stratification is shown in the Fig2.

The treatment of AA is progressing as more molecular subgroups are established, as shown by the two broad categories of non-codeleted IDH1 mutated and IDH1 wild type AA. Despite major variations in outcome, it is unknown if care should vary with these two molecular subtypes of AA. (12) Based on the early findings of the CATNON trial, the initial treatment of AA after full healthy surgery involves field radiotherapy accompanied by 12 cycles of post-radiotherapy TMZ. (13) Alternatively, based on the results

of the RTOG 9813 analysis, either lomustine (CCNU) or carmustine (BCNU) may be used in place of TMZ and tend to have comparable survival benefits. (12)

In a Paper of Sean A Grimm et al (11) states that “There are no adjuvant therapies aside from TMZ or nitrosoureas (CCNU or BCNU) that have demonstrated a survival benefit in newly diagnosed AA, a significant unmet need not dissimilar to the up-front treatment of GBM. Whether immunotherapy (e.g. vaccines or check point inhibitors) will provide another adjunct treatment strategy is dependent in large part on success of these therapies in on-going trials in GBM. IDH1 small molecule inhibitors, a rationale targeted therapy for the majority of patients with IDH1 mutant AA awaits on-going clinical trials. Much as in GBM, salvage therapy for recurrent AA utilizes re-resection, re-radiation and cytotoxic chemotherapies in an appropriate context with only modest efficacy. A novel randomized trial in recurrent AA (sponsor Orbus Pharmaceutical) is comparing lomustine with or without the oral agent DFMO in patients having progressed on TMZ. New approaches for both the up-front and salvage treatment of AA remain a significant need in neuro-oncology.”

Conclusion

This is a case of WHO GRADE III Anaplastic astrocytoma in the left hemisphere of the brain. The patient was managed with gamma knife radiosurgery, chemotherapy with Temozolomide (TMZ), and targeted molecular therapy with Bevacizumab. The patient improved with remission of symptoms.

Declarations

Conflict of Interest: Authors don't have any COI

Funding: No Funding

Consent: Consent has been taken from the patient for the publications

Acknowledgements:

Thanks to Dr Sameer and Dr Vikash for guiding us in the case. Thanks to professors and parents for all the support.

References

1. ADDITIONAL INFORMATION

Figures

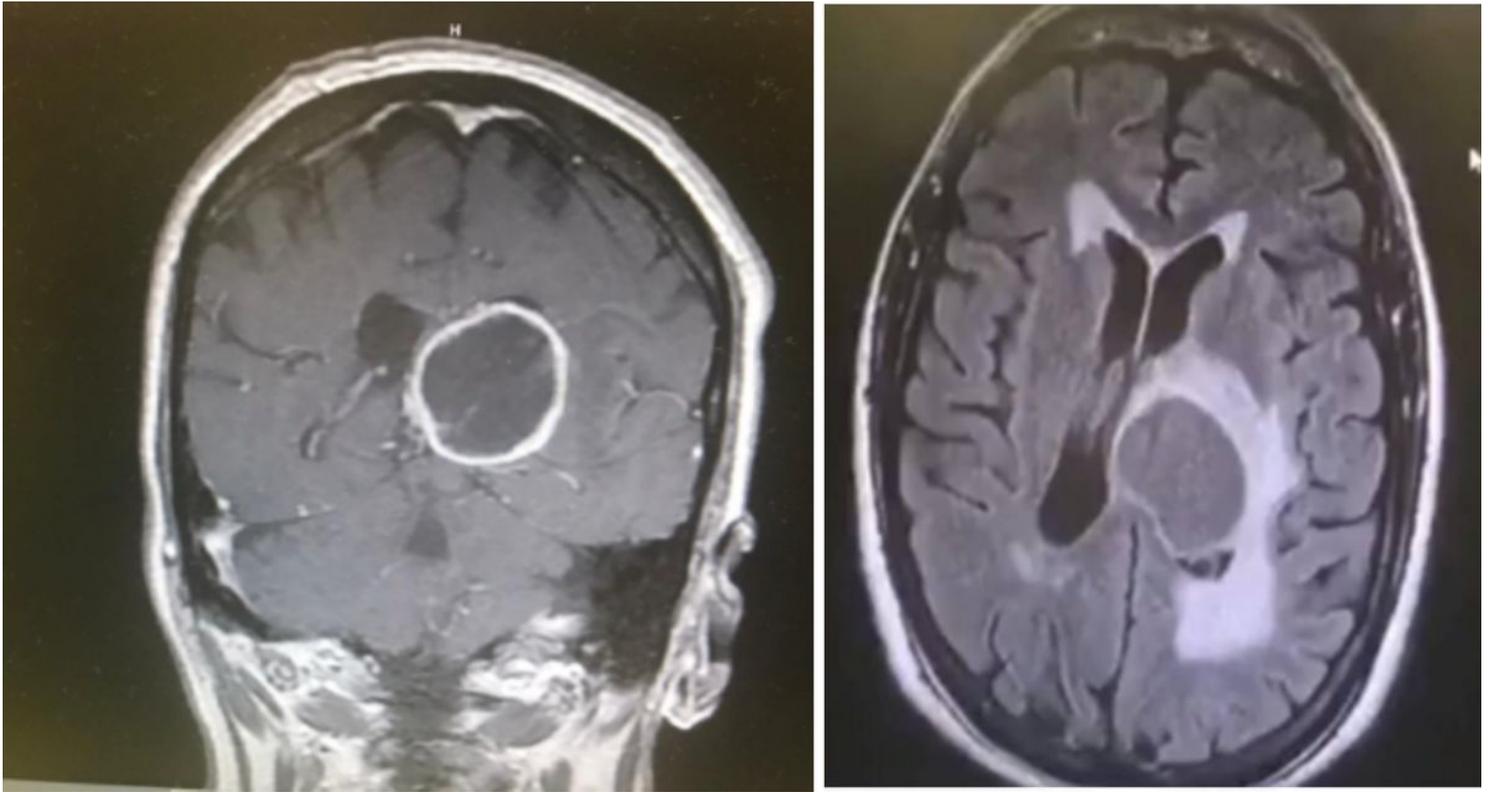


Figure 1

CT brain was notable for left thalamic and left basal ganglia low-attenuated mass with 3.7 cm anteroposterior diameter, 3.6 cm transverse diameter and 3.9 cm craniocaudal diameter. It had adjacent vasogenic edema and mass effect on the third ventricle with 7mm midline shift towards the right consistent with a malignancy primary versus metastatic etiology

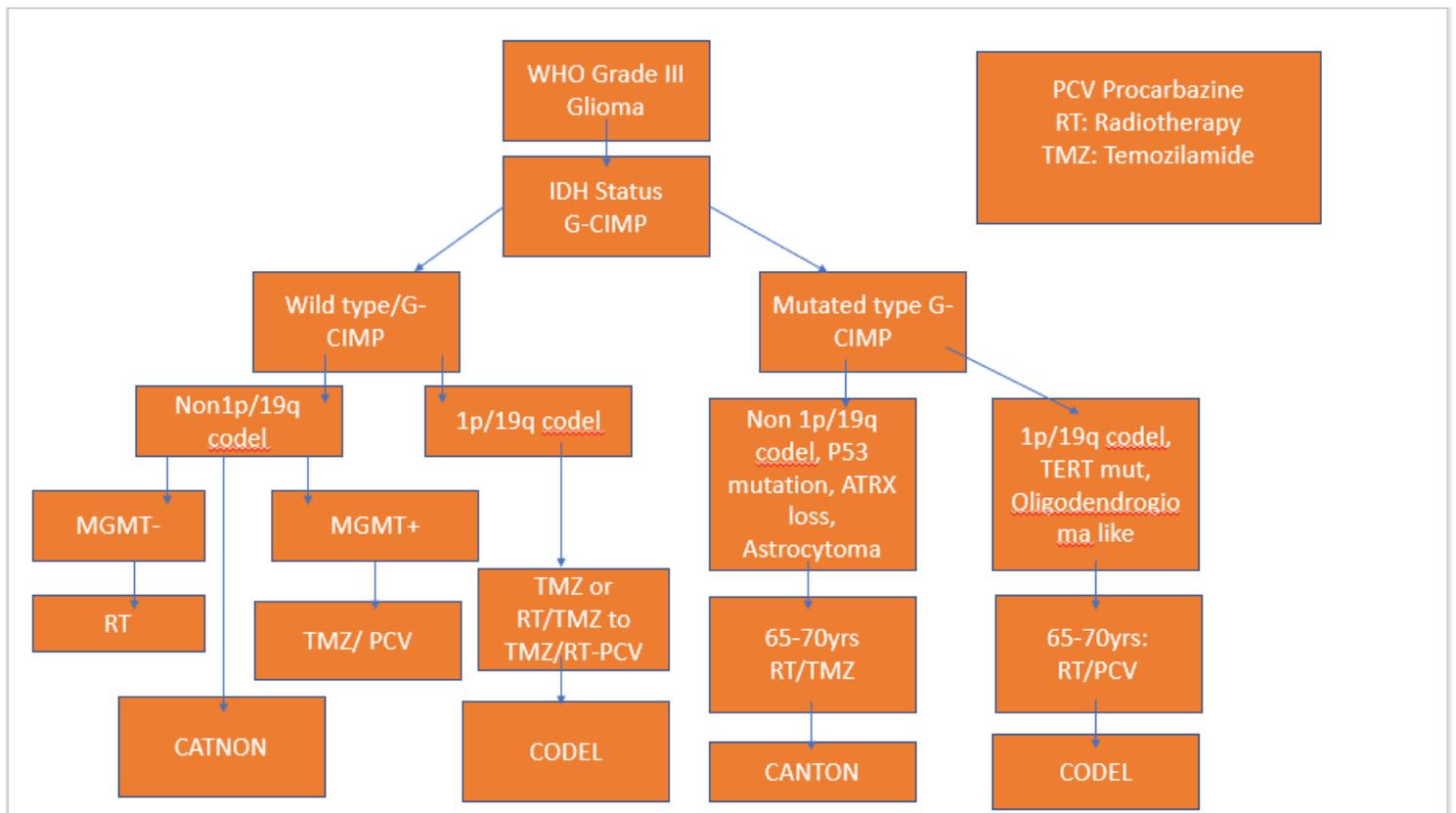


Figure 2

Molecular Stratification of AA

Supplementary Files

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- [AdditionalInformation.docx](#)