Content available at: https://www.ipinnovative.com/open-access-journals

IP Indian Journal of Neurosciences

Journal homepage: https://www.ijnonline.org/

Case Report

Small cell GBM: Case report

P Vaishnavi[1]*, **Syed Fatima**[2]

[1] *Dept. of Radiation Oncology, Basavatarakam Indo American Cancer Hospital & Research Institute, Hyderabad, Telangana, India*
[2] *Yashoda Hospitals, Secunderabad, Telangana, India*

ARTICLE INFO

Article history:
Received 10-10-2024
Accepted 01-11-2024
Available online 20-11-2024

Keywords:
N-acetylaspertate
Basifrontal lobes
Bilateral caudate

ABSTRACT

A 33 year old male presented with complaints of Headache, vomiting, and two episodes of seizures with a history of loss of consciousness. The patient was brought to the emergency department and diagnostic MRI was suggestive of a diffuse soft tissue infiltrative neoplastic lesion occupying basifrontal lobes, corpus callosum, temporal lobes, bilateral caudate, and right lentiform nucleus with increased creatine peaks and relatively reduced N-acetylaspertate (NAA) peaks on MR spectroscopy, suggestive of Lymphoma/Glioma.

1. Introduction

Small cell glioblastoma is a rare variant of primary glioblastoma multiforme(GBM), constituting <10% of all GBM cases.[1] Due to its rare occurrence both clinical behavior and treatment guidelines are not standardized, Hence the treatment protocol is similar to classical GBM i.e. surgical resection followed by postoperative radiation with concurrent temozolomide (75mg/m^2) throughout the course of radiation followed by adjuvant Temozolomide (150-200mg/m^2) for five days every 28 days for 6-12 cycles. Small cell GBM behaves aggressively when compared with classical GBM. Pathologically it is characterized by highly proliferative monomorphic small glial tumor cells with round to slightly elongated nucleus with a high nuclear-to-cytoplasmic ratio. Markedly elevated mitotic count is a characteristic feature.[2]

2. Case Report

A 33 year old male was brought to ER with chief complaints of headache, vomiting, and two episodes of generalized tonic-clonic seizures (GTCS) with loss of consciousness, Diagnostic MRI was suggestive of soft tissue infiltrative lesion in basifrontal lobes and along the inferior aspect of the corpus callosum, temporal lobes, bilateral caudate and right lentiform nucleus in the midline which is seen extending along the subependymal location and intraventricular region of the left frontal horn of the lateral ventricle. Superiorly involving the region of corpus callosum and into the septum on T2 and FLAIR sequences, patchy nodular enhancement on post gadolinium T1 sequence.

Restricted diffusion on DWI sequences, significant increase in relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) in post gadolinium perfusion sequences, increased creatine peaks with relatively reduced NAA peaks on multivoxel MR Spectroscopy suggestive of Lymphoma/Glioma.

Neurosurgeon reviewed the patient and subsequently, he underwent a stereotactic biopsy which was suggestive

* *Corresponding author*.
E-mail address: drpakanativ@gmail.com (P. Vaishnavi).

https://doi.org/10.18231/j.ijn.2024.049

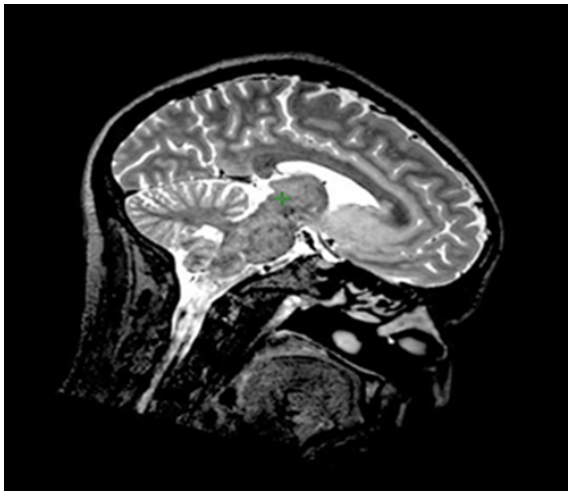

Figure 1: Soft tissue infiltrative lesion in basifrontal lobes and along the inferior aspect of the corpus callosum.

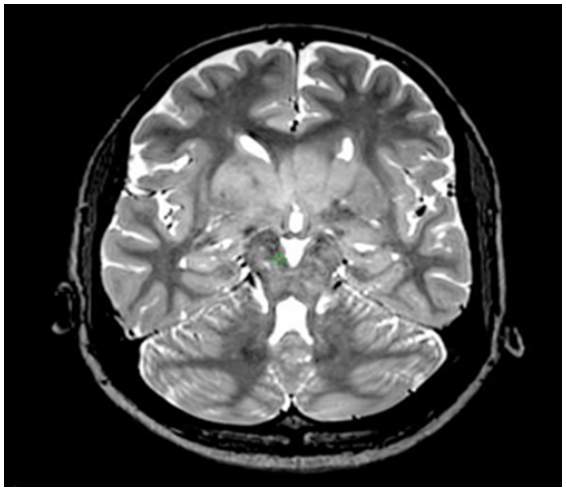

Figure 2: Soft tissue infiltrative lesion in basifrontal lobes

of High-grade neoplasm with predominant round cell morphology, IHC was advised for confirmatory diagnosis which was suggestive of GFAP-strong positive, LCA-negative, IDH1(R132H)-negative, ATRX-retained nuclear expression, P53 overexpressed (mutant phenotype), High Mib 1 index(20-22%), H3K27M-negative, Synaptophysin-negative, INI-1-retained nuclear expression which was suggestive of High-grade glioma, small cell variant-WHO Grade-IV, with methylated MGMT gene status.

He received adjuvant radiotherapy to Gross lesion with adequate margins as per RTOG guidelines to a total dose of 60Gy in 30 fractions with concurrent temozolomide (100mg) throughout the course of radiation followed by adjuvant temozolomide 250mg for 5 days, every 28 days for 6 cycles, post 6 cycles MRI brain showed significant interval increase in heterogeneously enhancing area with central necrosis with increased choline peaks,

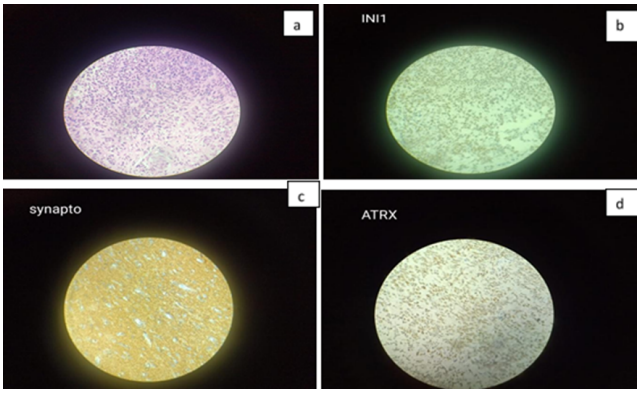

Figure 3: a: Increased cellularity showing small cells having scanty cytoplasmand hyperchromatic nuclei (40X); **b:** INI shows retained expression (40X); **c:** Positive Synaptophysin staining; **d:** ATRX shows retained expression.

choline/NAA with hyperperfusion suggesting interval increase in residual lesion with associated radiation necrosis. Interval development of subependymal nodular lesion along both lateral and fourth ventricle suggesting Metastatic deposits. Therefore he was advised to continue further adjuvant treatment. He received 2 more cycles of adjuvant temozolamide later lost for further follow-up.

3. Discussion

Histologically small cell glioblastoma is characterized by monomorphic densely packed small round neoplastic cells with high nuclear cytoplasmic ratio and increased mitotic activity.[3] It resembles anaplastic oligodendroglioma, therefore often misdiagnosed.[4–6] Till recent times CNS tumors as per WHO used histopathological classification by microscopic observation only. The new WHO 2016 classification of CNS tumors is based on the integration of histological and molecular criteria enabling more precise tumor categorization.[7] Hence the use of IHC and molecular markers in brain tumors made it easy for definitive diagnosis.

1p/19q codeletion or Loss of heterozygosity (LOH) is a genetic signature for oligodendroglial tumors. Mutations in IDH1 gene are most commonly seen on codon 132 while that of IDH2 gene on codon 172, is found in about 70% of secondary GBM tumors.IDH gene mutations are associated with better prognosis.[8] Malignant gliomas with Epigenetic silencing of MGMT (O-6-methylguanine-DNA methyltransferase) DNA repair gene by methylation is associated with longer survival when treated with temozolamide, an alkylating agent.[9] ATRX status (loss/retained) helps in defining the prognosis of astrocytic tumors where ATRX loss defines a favorable prognosis.H3k27M mutation is a feature of diffuse midline glioma(WHO CNS Tumors, 2016).

Guidelines for treatment of Small cell glioblastoma is not available despite the new molecular classification in CNS tumors and due to its rarity, hence patients are treated as per the guidelines of classical GBM. Treatment options for recurrent GBM are also limited, and as small-cell GBM shows EGFR amplification, the use of bevacizumab is questionable. Immunotherapy can be considered as there is a dull immune response seen in small cell GBM. [10]

4. Conclusion

Small cell GBM is a rare and aggressive variant of GBM with an extremely poor prognosis, with no clear guidelines for treatment. The role of immunotherapy can be explored for better results.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Takahashi K, Tsuda M, Kanno H, Murata J, Mahabir R, Ishida Y, et al. Differential diagnosis of small cell glioblastoma and anaplastic oligodendroglioma: a case report of an elderly man. *Brain Tumor Pathol*. 2014;31(2):118–23.
2. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol*. 2007;114(2):97–109.
3. Perry A, Aldape KD, George DH, Burger PC. Small cell astrocytoma: an aggressive variant that is clinicopathologically and genetically distinct from anaplastic oligodendroglioma. *Cancer*. 2004;101(10):2318–26.
4. Fflouis DN, Ohgaki H, Wiestler OD, Cavenee WK, Ellison D, Figarella-Branger D, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol*. 2016;131:803–20. doi:10.1007/s00401-016-1545-1.
5. Louis DN, Perry A, Reifenberger G, Deimling V, Figarella-Branger A, Cavenee D, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. *Acta Neuropathol*. 2016;131(6):803–20.
6. Korshunov A, Sycheva R, Golanov A. Molecular stratification of diagnostically challenging high-grade gliomas composed of small cells: the utility of fluorescence in situ hybridization. *Clin Cancer Res*. 2004;10(23):7820–6.
7. Bizu I, Georgescu M, Anghel R. Small cell glioblastoma: a glioblastoma subtype with an unexpected response. *Mod Med*. 2019;26(2):93–6.
8. Hartmann C, Hentschel B, Wick W, Capper D, Felsberg J, Simon M, et al. Patients with IDH1 wild type anaplastic astrocytomas exhibit worse prognosis than IDH1-mutated glioblastomas, and IDH1 mutation status accounts for the unfavorable prognostic effect of higher age: implications for classification of gliomas. *Acta Neuropathologica*. 2010;120(6):707–18.
9. Brady LW, Wazer DE, Perez CA. Perez & Brady's principles and practice. Lippincott Williams & Wilkins; 2013.
10. Yadav AK, Madan R, Chatterjee D, Dhiman S, Goyal S, Kumar N, et al. Small cell glioblastoma multiforme: a case series and clinicopathological update. *CNS Oncol*. 2020;9(4):63. doi:10.2217/cns-2020-0016.

Author's biography

P Vaishnavi, Consultant https://orcid.org/0000-0002-3370-0471

Syed Fatima, Associate Consultant

Cite this article: Vaishnavi P, Fatima S. Small cell GBM: Case report. *IP Indian J Neurosci* 2024;10(4):238-240.