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Original Research Paper

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EPITHELIOID GLIOBLASTOMA OF BRAIN: A RARE CASE REPORT WITH REVIEW OF LITERATURE

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ABSTRACT A 52 year old female presented with complains of headache, dizziness and vomiting. Her MRI revealed a heterogenously enhancing tumor in right temporal lobe. She underwent gross total resection followed by chemoradiotherapy, but later succumbed to her illness. Histopathology showed highly pleomorphic tumor cells with eosinophillic cytoplasm and pleomorphic vesicular nuclei. A diagnosis of Epithelioid Glioblastoma was made. Epithelioid Glioblastoma is a rare pseudoepithelial form of glioblastoma. It usually presents in younger age group, is more malignant, difficult to differentiate from usual GBMs on radiology and needs aggressive management. No streamlined protocols exist for their diagnosis and treatment. The following communication discusses its epidemiology, pathology, diagnosis and management.

KEYWORDS : Epithelioid glioblastoma, INI-1 retention, Pseudoepithelial glioblastoma

INTRODUCTION

WHO classification of brain tumors has recently included a new entity in the class of glioblastomas (GBMs) i.e. Epithelioid Glioblastoma (E-GBM)[1] **It is an arcane tumor, difficult to diagnose and differentiate from various other similar tumors.** They are extremely rare tumors, whose incidence rate has not been mentioned in literature; but a study of 3500 GBMs found, E-GBM to be present in 10 cases i.e. 1 in 3500 GBMs.[2] It presents in a younger population and has worse prognosis than classical GBMs.[1,3] Hence treatment protocols should be streamlined according to the aggressive and usually fatal tumor.

Case Report

A 52 year old patient presented with complaints of headache for 15 days; giddiness and vomiting for 5 days. There was no history of seizures, convulsions, loss of consciousness or any weakness of limbs. On examination, she was conscious, oriented, higher mental functions were intact. Cranial nerve and sensorimotor examination was normal. She had Frisen grade 3 papilloedema. She underwent an MRI, which on T2W image showed a heterogenous isointense lesion in right temporal lobe with areas of necrosis, significant perilesional edema compressing ipsilateral ventricles and causing mass effect. (Fig. 1)

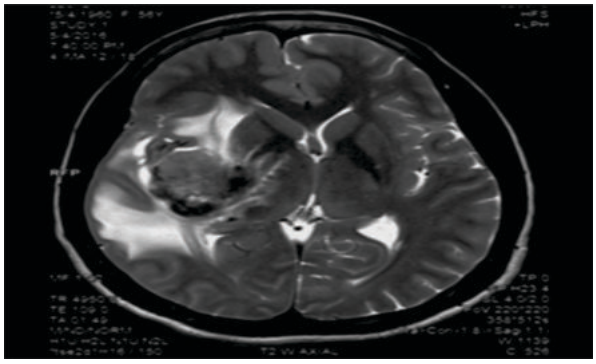

Figure 1: T2W image showing a heterogenous isointense lesion in right temporal lobe with necrosis, perilesional edema compressing ipsilateral lateral ventricles and causing mass effect

On T1W contrast it was a heterogenously enhancing lesion with areas of necrosis particularly along its medial border. (Fig. 2) Areas of restriction were present on DW1. On MRS, there was significant choline peak. So, a pre-operative diagnosis of GBM/Metastasis was made.

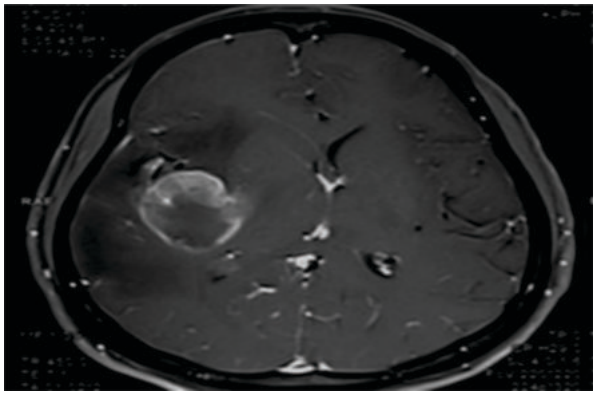

Figure 2: T1W contrast image shows heterogenously enhancing lesion with areas of necrosis along its medial border

Patient was evaluated with CT thorax and abdomen to rule out metastasis, both were normal. A right temporoparietal craniotomy and excision of right temporal intracranial space occupying lesion was done. Yellow-grey tumor of soft to hard consistency, suckable, CUSAble, moderately vascular with cystic changes was found in right temporal region just posterior to sylvian fissure. Intratumoral necrotic changes and hemorrhages were present.

On histopathological examination, a highly cellular neoplasm invading into ans surrounded by a thin rim of brain parenchyma was noted. The cells were large with abundant eosinophillic cytoplasm, large irregular vesicular nucleus, some showing bi and multinucleation and prominent nucleoli. These cells were arranged in sheets interspersed by vessles and extensive large areas of necrosis. (Fig.3)

There was marked anaplasia and brisk mitotic activity. Preserved tumor cells were present around the periphery. On immunohistochemistry cells were positive for Vimentin, S-100, p53 and focally for EMA; GFAP, Desmin and CK were negative. (Fig. 4)

The retention of nuclear stain INI-1 was observed. ATRX retention was also noticed. IDH-1 (R132H) was negative, signifying absence of mutant IDH-1, but MIB-1 labelling index was high. Immunoreactivity for BRAF V600E specific antibodies could not be tested. Adjuvant chemoradiotherapy was started in post-operative period, but patient succumbed to the disease 2 months after surgery.

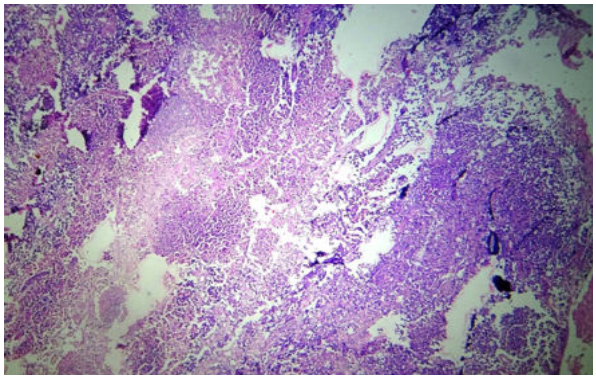

Figure 3: Microscopy showing highly pleomorphic tumor cells with eosinophilic cytoplasm and pleomorphic vesicular nuclei and conspicuous nucleoli, extensive areas of necrosis noted.

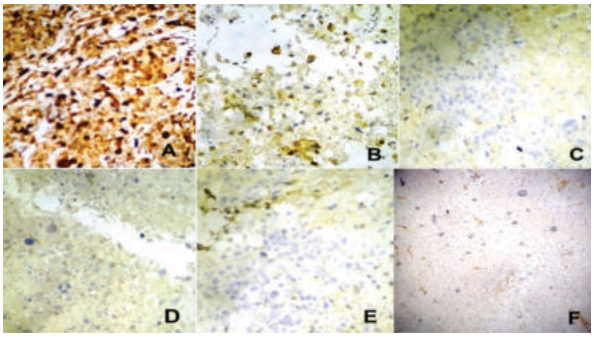

Figure 4: Immunohistochemical picture showing Vimentin positivity (A), focal EMA positivity (B), GFAP, Desmin, CK and SMA negativity (C, D, E & F).

DISCUSSION

E-GBMs are Grade IV WHO tumors classified under IDH-wild type glioblastomas.[1] As mentioned above these tumors are quite rare. **They are extremely rare tumors, whose incidence rate has not been mentioned in literature; but a study of 3500 GBMs found, E-GBM to be present in 10 cases i.e. 1 in 3500 GBMs.**[2] They show equal incidence in males and females.[2] GBM have vast morphological cell diversity. The majorities are compromised by small cell and giant cell glioblastoma but rare forms like granular cell, rhabdoid, signet ring and epithelial differentiation can also be seen.[3,4,5]

Amongst epithelial differentiation too true epithelial and pseudoepithelial variants exist. Epithelioid and adenoid GBMs comprise pseudoepithelial GBMs.[2]

E-GBMs tend to develop in children and young adults in contrast to the traditional GBMs.[1] They are most commonly found in the diencephalon and superficial cerebral hemispheric masses.[1]

In adults they are generally found in cerebral cortex while, those in pediatric age group are found in diencephalon.[3] Clinical features generally vary from headache, nausea, dizziness, syncope and constitutional symptoms.

Radiologically these tumors are indistinct from classical GBMs; but enhancement, superficial localization, sharp demarcation, necrosis, perilesional edema and restricted diffusion occurs in vast majority of tumors.[1,7]

Pathologically epithelioid variants show large epithelioid cells with abundant eosinophillic cytoplasm, vesicular nuclei and large melanoma like nucleoli.[1] Rhabdoid variants (R-GBM) closely mimic epithelioid GBMS under the microscope, though they can sometimes be differentiated by presence of eccentric nuclei and paranuclear inclusions.[1]

Some E-GBMs can be secondary and may show features of lower grade precursors like Pleomorphic Xanthoastocytoma in adjacent tissue.[8] Histologically E-GBMs can be difficult to distinguish from metastatic carcinoma and metastatic melanoma. Though, IHC can easily differentiate them; metastatic carcinoma are GFAP, S-100 negative and pancytokeratin positive, Metastatic melanoma are S-100, HMB-45 and Melan A positive and GBM is GFAP, S-100 positive and HMB45, Melan A positive.[9] IHC can also help distinguish epithelioid and rhabdoid variants as focal loss of INI-1 occurs in R-GBM.[7] Activating mutations in BRAF kinas gene (V600E) have been identified to occur in over 50% of E-GBM.[10]

Adequate treatment of these tumors is total gross resection whenever possible, followed by Stupp regimen of chemoradiotherapy. BRAF inhibitors like Vemurafenib, have also been tried in the tumors showing V600E mutation. Generally E-GBMs carry poor prognosis because of presence of hemorrhage and leptomeningeal seeding at the time of diagnosis, with median survival rate quoted at only 169 days in one of the studies.[3] A few sporadic studies have shown good survival rates in patients treated with BRAF inhibitors, one study even saw complete clinical regression.[11] It has been postulated that BRAF V600 E mutations are encountered in more favorable subtypes of GBM and they confer different biological properties to these tumors, resulting in improved outcomes.[12]

CONCLUSION

E-GBMs should be treated disparate from traditional GBMs. The conventional Stupp regimen has stood the test of time but a new regimen incorporating BRAF inhibitors should be constructed in order to provide more targeted therapy to these esoteric tumors. Further research is needed to give form to the inchoate postulates that have been developed germane to these entities.

REFERENCES:

1. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Weistler OD, Kleihues P, Ellison DW: The 2016 World Health Organization Classification of Tumors of Central Nervous System: a summary. Acta Neuropathol 131: 803-820, 2016.
2. Rodriguez FJ, Scheithauer BW, Giannini C, Bryant SC, Jenkins RB: Epithelial and pseudoepithelial differentiation in glioblastoma and gliosarcoma: A comparative morphologic and molecular genetics study Cancer 113: 2779-2789, 2008
3. Broniscer A, Tatevossian RG, Sabin ND, Klimo P Jr, Dalton J, Lee R, Gajjar A, Ellison DW: Clinical, radiological, histological and molecular characteristics of pediatric epithelioid glioblastoma Neuropathol Appl Neurobiol 40: 327-336, 2014.
4. Louis DN, Ohgaki H, Weistler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW, Kleihues P. The 2007 WHO classification of tumors of the central nervous system: Acta Neuropathol 114: 97-109, 2007
5. Shi Y, Morgenstern N: Granular cell astrocytoma: Arch Pathol Lab Med 132:1946-1950, 2008
6. Martin SE, Bonnin JM, Hall DC, Hattab EM: Glioblastoma with signet-ring morphology: a case report and review of literature. Hum Pathol 41: 443446,2010
7. Kleinschmidt-DeMasters BK, Alassiri AH, Birks DK, Newell KL, Moore W, Lillehei KO: Epithelioid versus rhabdoid glioblastoma are distinguished by monosomy 22 and immunohistochemical expression of INI-1 but not claudin 6 Am J Surg Pathol 34: 341-354, 2010
8. Tanaka S, Nakada M, Nobusawa S, Suzuki SO, Sabit H, Miyashita K, Hayashi Y: Epithelioid glioblastoma arising from pleomorphic xanthoastrocytoma with the BRAF V600E mutation Brain Tumor Pathol 31: 172 176, 2014
9. Leibelt B, Boghani Z, Takei H, Britz GW: Epithelioid glioblastoma presenting as massive intracerebral hemorrhage: Case report and review of the literature Surg Neurol Int 6: S97-S100, 2015.
10. Kleinschmidt-DeMasters BK, Aisner DL, Birks DK, Foreman NK: Epithelioid GBMs show a high percentage of BRAF V600E mutation Am J Surg Pathol 37: 685-698, 2013
11. Robinson GW, Orr BA, Gajjar A: Complete clinical regression of a BRAF V600E mutant pediatric glioblastoma multiforme after BRAF inhibitor therapy BMC Cancer 14; 258, 2014
12. Dahiya S, Emnett RJ, Haydon DH, Leonard JR, Phillips JJ, Perry A, Gutmann DH: BRAF V600 E mutation in pediatric and adult glioblastoma Neuro Oncol 16: 318-319, 2014