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Gliosarcoma: A Rare Variant of Glioblastoma Multiforme: Case Report

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Abstract: ***Introduction: Gliosarcoma is rare central nervous system tumour and a variant of glioblastoma multiforme with bimorphic histological pattern of glial and sarcomatous differentiation. It occurs in elderly between 5th and 6th decades of life and extremely rare in children. It is highly aggressive tumour and managed like glioblastoma multiforme. Case report: A 48 years old female patient presented to neurosurgery department with chief complaints of altered sensoriumX 1 days. Magnetic resonance imaging of brain shows s/o Aggressive Oligodendroglioma /Glioblastoma Multiforme, Frozen section shows histology of highgrade glioma-Glioblastoma with small cell component and pleomorphic spindle cell component WHO Grade-IV with complete excision of mass revealed a primary glioblastoma with sarcomatoid differentiation on histopathological investigation which is confirm by Immuno-Histochemistry. Methods: Multiple sections are taken from given biopsy and stain by H&E stain and For Immuno-histochemistry stain done by P53, G-FAP, Vimentin and EMA. Result: Final diagnosis is High Grade CNS tumor-suggestive of Glioblastoma with predominant sarcomatoid differentiation-WHO Grade IV confirmed by Histological and Immuno-histochemistry.***

Keywords: Gliosarcoma, Glioblastoma multiforme, Microvascular proliferation, Mixed tumor, Radiotherapy

1. Introduction

Gliosarcoma is a rare primary malignant tumor of central nervous system with reported incidence being 0.59-0.76% of all adult brain tumors. It has a biphasic morphological pattern with both glial and malignant mesenchymal components. It is considered as a variant of glioblastoma multiforme (GBM) representing only 2% of all GBM cases [1]. It usually affects fifth and sixth decade of life (average age of onset is 54 years) with slight male preponderance (males being affected twice as often as females) [2]. Therapeutic modalities are surgical resection, external beam radiotherapy and chemotherapy but prognosis remains poor in terms of survival [3]. Localized mostly in subcortical white matter and deeper grey matter of cerebral hemisphere, affecting all cerebral lobes. High-grade gliomas occurring in a midline structure. In Microscopy, Mixed tumor of biphasic differentiation with glial and sarcomatous component seen.

- Glial component shows typical features of glioblastoma, including pleomorphic astrocytic cells with nuclear atypia, mitosis, pseudopalisading necrosis and microvascular proliferation
- **MVP (**microvascular proliferation**) is a qualitative feature** whichissimple to recognize in its two forms. One form-increase in the number of nuclei within the vascular wall, other form-formation of multiple lumina within the vascular structure so that it resembles a renal glomerulus
- Sarcomatous component shows spindle shaped cells with nuclear atypia.
- Immunohistochemistry: GFAP is positive for Glial component only and negative or focal positive for sarcomatous component. Vimentin positive in sarcomatoid component, EMA negative and Reticulin, P53 positivity
- Molecular abnormalities: Mutations in TP53, PTEN, TERT, CDKN2A deletion, MDM2 and CDK4 co-amplification
- Prognosis: Poor [(4), (5), (6)]

2. Case Report

A 48 years old female patient presented to neurosurgery department with chief complaints of altered sensoriumX 1 days and P/H/O headache and giddiness x 2 months. On MRI-Brain, Heterogenous lesion measuring 9x8x8 cm3 in right basi frontal region. s/o Aggressive Oligodendroglioma /Glioblastoma Multiforme. On Frozen section, Histology of high grade glioma-Glioblastoma with small cell component and pleomorphic spindle cell component WHO Grade – IV

2.1 Gross Examination:

Three grayish brown soft tissue structure total measuring 2.8x2.6x1.5 cm3 and largest measuring 2.4x2.2x0.8 cm3 (Image 1)

Image 1: Gross examination

2.2 Method

Multiple sections are taken from given biopsy and stain by H&E stain and For Immuno-histochemistry stain done by P53, G-FAP, Vimentin and EMA.

2.3 Microscopic Examination

The final diagnosis wasHigh Grade CNS tumor-suggestive of Glioblastoma with predominant sarcomatoid differentiation-WHO Grade IV. Advice immunochemistry for exact Histogentic typing of lesion

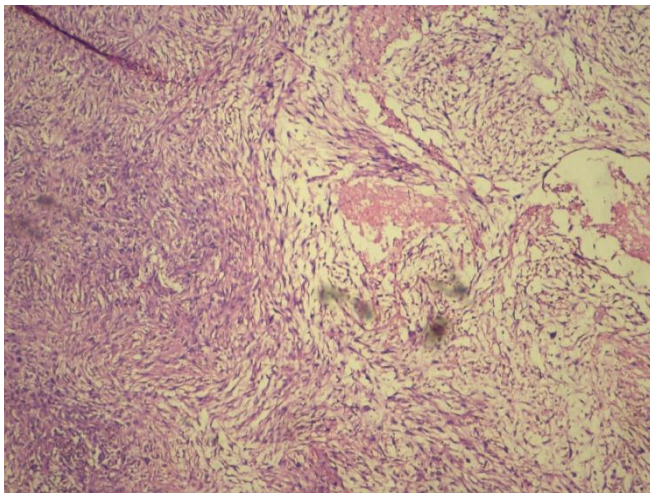

Image 2: Dark pink sarcomatoid and Light pink Glial tissue in scanner view

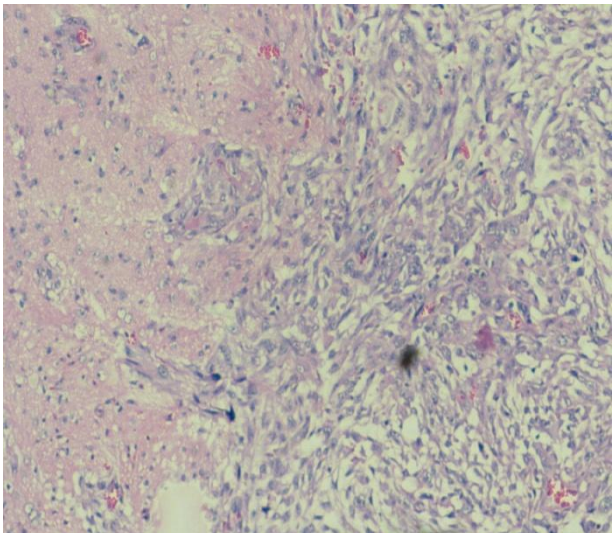

Image 3: Microvascular proliferation in low power view

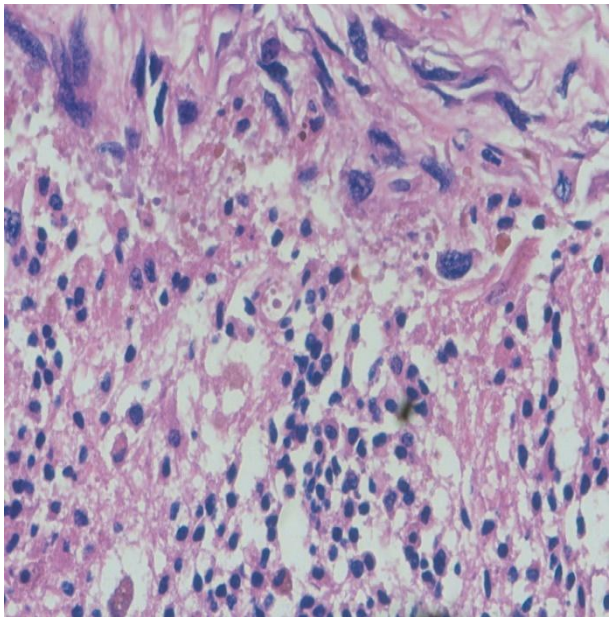

Image 4: Small cell and spindle cell component in High power view

2.4 Immuno-Histochemistry

Here used stains wereP53, Vimetin, GFAP, EMA. We found P53 immunoreactivity (Image 5), GFAPnegative (Image 6) and Vimentin positive (Image 7) in areas with sarcomatoid differentiation, EMA negative (Image 8) which confirm biopsy result.

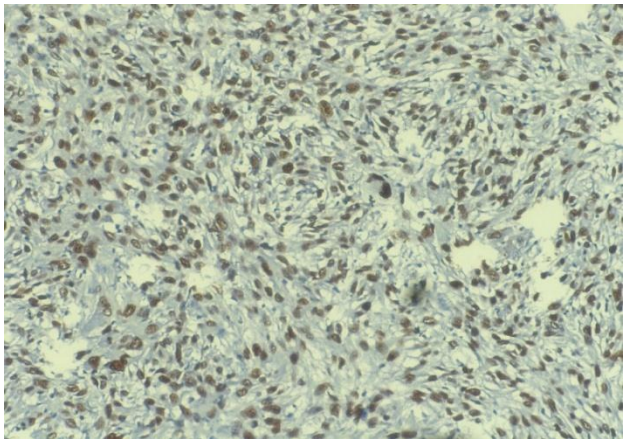

Image 5: P53 immunoreactivity

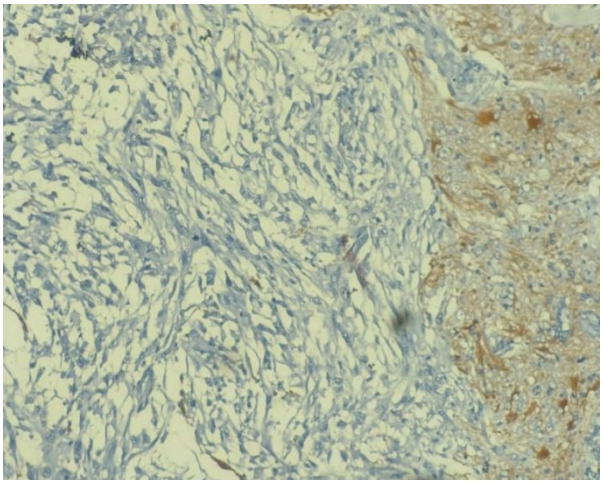

Image 6: GFAP-negative in areas with sarcomatoid differentiation

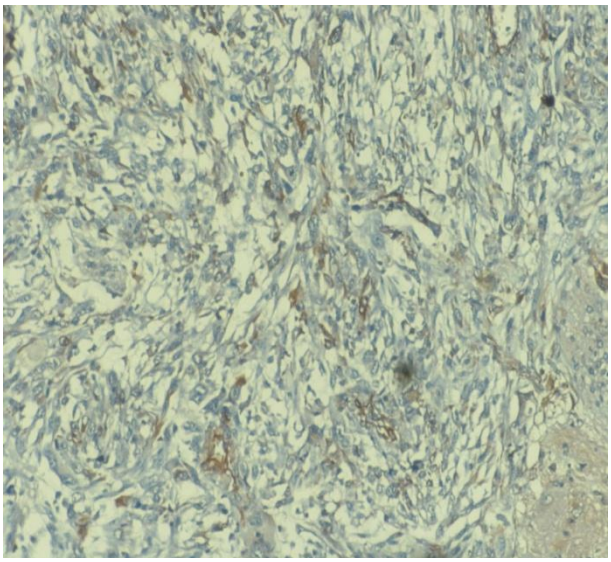

Image 7: Vimentine-Positive in areas with sarcomatoid differentiation

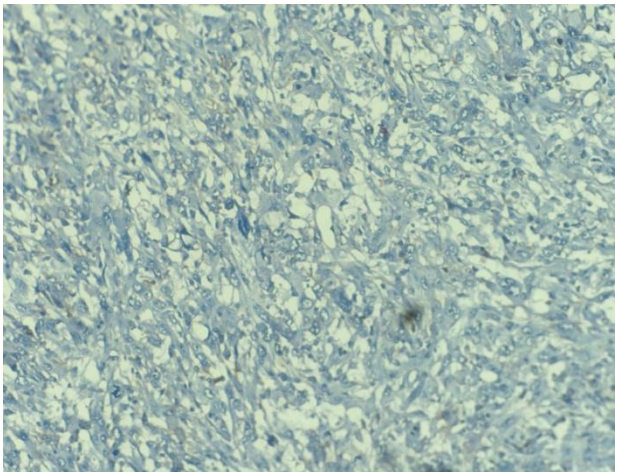

Image 8: EMA negative

3. Discussion

Gliosarcoma (GS) was first defined in 1895 as a highly malignant brain tumor that resembles glioblastoma (GBM) based on the typical age of onset, location, and overall prognosis [7]. The term GS was subsequently reintroduced as referring to a subtype of GBM with a biphasic histological pattern consisting of both glial and malignant mesenchymal components [8]. The latter component of GS was first believed to originate from neoplastic transformation and proliferation of endothelial cells lining intra-tumoral vessels within malignant astrocytoma [9]. However, further studies did not seem to be able find conclusive evidence that could confirm the consistent presence of endothelial markers in such tumors. Later studies instead suggested a monoclonal origin of glial and sarcomatous components of GS, as both neoplastic tissues seemed to comprise cells with identical genetic aberrations (mutations in p53 and PTEN), homozygous p16 co-deletion, and co-amplification of MDM2 and CDK4 [10, 11].

Studies have also reported varying patient symptomatology upon clinical presentation. Singh et al. (2015) studied 16 cases of histologically-proven gliosarcoma (14 primary, 2 secondary) that were operated on over a 5-year period from 2009 to 2014. Of these patients, 11 (69%) had features of raised intracranial pressure, and 3 (20%) presented in an obtunded state. Five (31%) of these patients had a history of 1 or more episodes of seizures [12]. In a retrospective review by Cachia et al. (2015) of 34 cases of pathologically-diagnosed gliosarcoma (24 pri- mary, 10 secondary), 20 (59%) patients initially presented with symptoms of headaches, while hemiparesis, seizures, and hemihypoesthesia were less common [13]. In Kakkar et al. ’s (2017) review of 4 cases of gliosarcoma in younger adults, the predominant presentation in all 4 patients was headaches [14]

Management of gliosarcoma continues to be based on the therapeutic approach to conven- tional glioblastoma – a maximal safe surgical resection followed by adjuvant radiotherapy and concurrent temozolomide chemotherapy [15].

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