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Case Report

Bilateral Thalamic Glioblastoma Multiforme with Synchronous Asymptomatic Bone Metastasis- A Rare Case Report

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Abstract

Bilateral Glioblastoma multiforme (GBM) at the thalamus is an extremely rare condition accounting for 1-2% of brain tumors. Extra-cranial metastases of GBM are rare due to the absence of lymphatics in the brain and the difficulty of tumors penetrating blood vessels. Moreover, these metastatic lesions remain asymptomatic and are often identified during autopsy. Hereby, a case of a rare presentation of bilateral thalamic GBM with synchronous asymptomatic bone metastasis to the humerus treated using Radiation therapy to both bilateral thalamic lesions and humerus bone metastasis with concurrent and adjuvant temozolomide-based chemotherapy is reported.

Keywords: Glioblastoma multiforme; Brain tumor; Radiotherapy; Metastasis.

Introduction

Glioblastoma multiforme (GBM) is an aggressive, lethal form of neural tumor accounting for 10-15% of all intracranial tumors [1]. Bilateral thalamic gliomas are a rare subset of primary thalamic glioma which constitutes 1-2% of brain tumors [2]. Despite advances in neurosciences average survival rate is 12.1-14.6 months [3]. They rarely metastasize with a five-year survival rate of less than 10% [4]. Treatment consists of a multidisciplinary approach to surgical resection, radiation, chemotherapy, palliative care, and psychological support [5].

Radiotherapy is the main mode of treatment of thalamic glioma since surgical intervention is limited to the role of biopsy and management of secondary effects, due to the deep brain location of the lesion and the complexity of the involved structures [2]. A rare case of Bilateral thalamic glioblastoma multiforme with synchronous asymptomatic

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bone metastasis to the humerus treated using radiation therapy to both bilateral thalamic lesions and humerus bone metastasis with concurrent and adjuvant Temozolomide based chemotherapy is reported.

Case report

A 66-year-old male patient presented with a 15- 20 days history of rapidly progressing left hemiparesis. The patient was a known case of ischaemic heart disease, Type 2 diabetes mellitus, and hypertension on medications for 10-15 years. T2 weighted Magnetic Resonance Imaging (MRI) brain with gadolinium showed a well-defined rounded hyperintense lesion in the right thalamus and focal hyperintensity in the left pulvinar nucleus of the thalamus.

Post-contrast T1 weighted MRI revealed the right thalamic lesion shows enhancement with a central unenhanced area suggestive of necrosis, however, the left pulvinar lesion did not show enhancement.

On MR spectroscopy, the right-sided lesion showed central lipid lactate peak and a large choline peak in the wall while the left-sided lesion showed a choline peak. The multiplicity of lesions and choline peaks was suggestive of metastatic lesions or high-grade glioma (Figure 1 A-D).

On a whole body 18FDG PETCT, FDG uptake on the right thalamic lesion was greater than white matter and lesser than grey matter. Additionally, a metabolically active soft tissue density lesion in the mid-shaft of the right humerus measuring 1.5 × 1.3 × 1.1 cm with SUV max of 5.3 was noted as suggestive of bone deposit (Figure 2). Following this, a stereotactic biopsy of the right thalamic lesion was done under local anesthesia and monitored Anesthesia care. Microscopically, a Hematoxylin and Eosin-stained cellular smear with pleomorphic hyperchromic cells in a fibrillary background was noted (Figure 3 A-D).

A tumor with moderate cellularity showing hyperchromatic and mildly pleomorphic cells in a fibrillary background with areas of necrosis along with endothelial proliferation suggestive of Glioblastoma multiformae, Additionally, the biopsy of humerus bone lesion showed many islands of tissues in marrow spaces resembling CNS tissue with fibrillary background and having glial cells within.

Immunohistochemistry showed glial cells to be positive with thin glial fibers projecting out from the cells. These features were consistent with metastatic deposits from a cerebral glioblastoma multiformae in the shaft of the humeral bone.

Based on the above findings, a diagnosis of Bilateral Thalamic Glioblastoma multiformae with synchronous humerus shaft metastasis was established. The patient was treated with external beam radiotherapy to both the lesions of the brain to a total dose of 60Gy in 30 fractions concurrent with temozolomide 75 mg/m^2 over 6 weeks and 45Gy in 15 fractions to the right humerus mid-shaft lesion. This was followed by 6 cycles of four weekly adjuvant temozolomide 200mg/m^2 × 5 days. At the last follow up there was persistent left hemiparesis without any progression.

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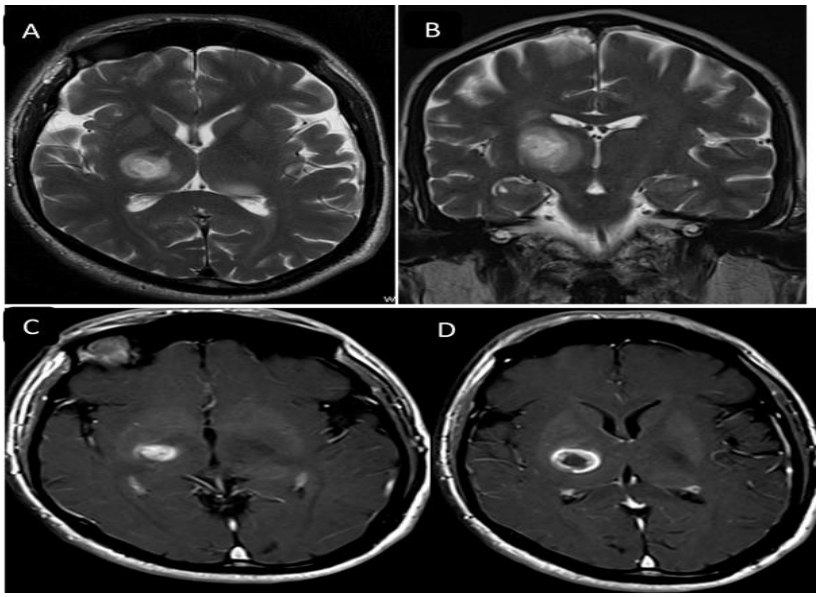

Figure 1 A and B: T2WI showing well-defined rounded hyperintense lesion in the right thalamus and focal hyperintensity in the left pulvinar nucleus of the thalamus. **C and D:** Post-contrast T1W1 showing enhancement of the right thalamic lesion with central unenhanced area suggestive of necrosis with no enhancement in the left pulvinar lesion.

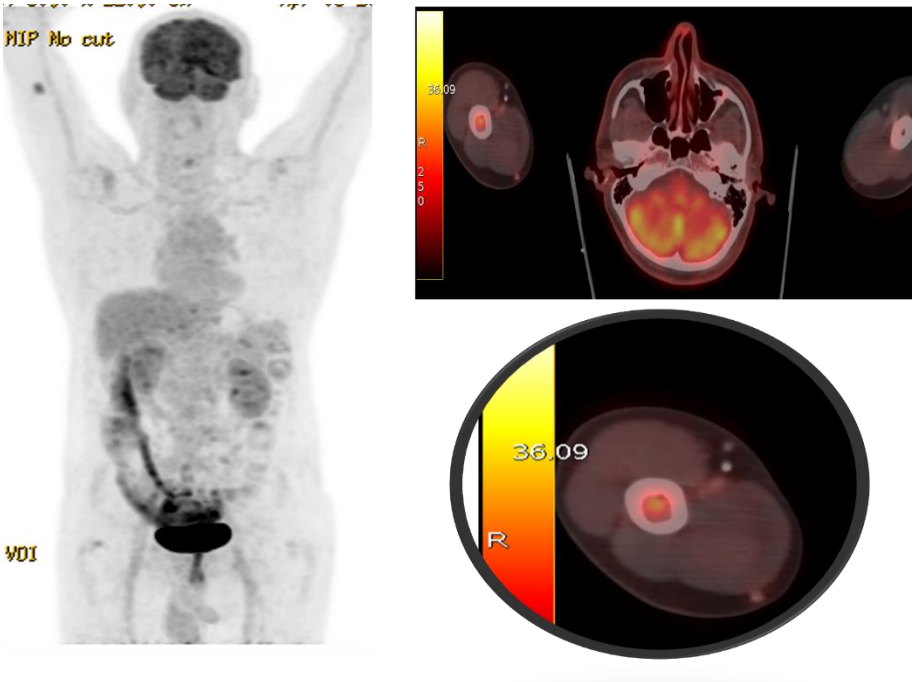

Figure 2: Whole body 18FDG PETCT showing right thalamic lesion noted in MRI showed FDG uptake greater than white matter and lesser than grey matter and metabolically active soft tissue density lesion in mid shaft of right humerus suggestive of bone deposit (1.5x1.3x1.1cm with SUV max of 5.3).

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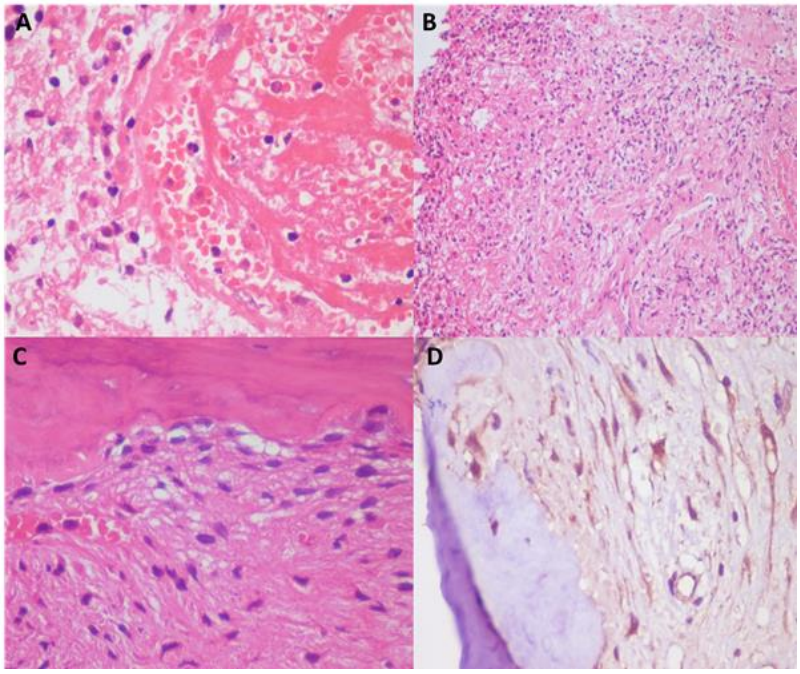

Figure 3A: Hematoxylin and Eosin stains of the right thalamic lesion show cellular smear with pleomorphic hyperchromic cells in a fibrillary background along with the endothelial proliferation of vessels. **B:** Tumor with moderate cellularity showing hyperchromatic and mildly pleomorphic cells in a fibrillary background with areas of necrosis. **C:** Hematoxylin and Eosin stains from the biopsy of the humerus bone lesion show many islands of tissues in marrow spaces resembling CNS tissue with fibrillary background and having glial cells within. **D:** Immunohistochemistry shows glial cells to be positive with thin glial fibers projecting out from the cells.

Discussion

Gliomas were first reported in 1800 by Berns and in 1804 by Abernethy. In 1865 Rudolf Virchow gave a histomorphological description [6]. Recently GBM has been classified into two types isocitrate dehydrogenase (IDH) wild type (90%) and IDH mutant type (10%) [7]. Bilateral thalamic GBM presentation is extremely rare with less than 75 cases reported in the literature. They can occur in both adults and pediatric populations with a median age of diagnosis of 64 years [8]. The common risk factors include prior therapeutic radiation, susceptibility to allergy, immune factors and immune genes as well as tall height, high socioeconomic status and genetic mutation have also contributed to GBM. There is no evidence of an association of GBM with smoking, alcohol consumption, or dietary exposure to N-nitroso compounds [8]. The incidence rate for extraneural metastases is 0.2% [4,7]. The most common location is supratentorial followed by the cerebellum. Other metastatic sites include lung, lymph nodes, bone, and liver.

This is the first time that the GBM metastasizing to humerus bone was diagnosed at initial presentation. The rarity of metastasis is explained by the absence of

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lymphatics and the difficulty of brain tumors penetrating blood vessels. The median time of presentation of metastasis is 4-12 months after the initial diagnosis of GBM [4]. Interestingly, in this case, the metastasis to the humerus was asymptomatic and was diagnosed concurrently during primary diagnosis.

The presence of primary GBM, a morphologically identical lesion in the humerus which was histologically identified as a CNS tumor confirmed the bone metastasis. Previous studies lacked an explanation for metastatic spread due to its short survival time however recently the existence of a glymphatic system explained the pathogenesis for metastatic spread due to its drainage to cervical and meningeal lymphatics [7].

Other explained theories include iatrogenic procedures- craniotomy/ biopsy leading to breakage of blood-brain barrier leading to migration of cells into the circulatory system. The bone metastases with the genetic study are explained by the mutation of BRCA1, ARID1A, C8A-R30W, and overexpression of IGFBP2 [7,8]. To date, no satisfactory results of treatment outcomes have been published. The available therapeutic options include surgical excision with an aim to remove the lesion, prolong survival and relieve compression thereby alleviating pain and improving the quality of life; radiation and chemotherapy to delay the progression of the disease. Palliative care is of utmost importance in locoregionally advanced cancer [4-6]. More recently immunotherapies and nanoformulations have been used for the treatment of GBM [9]. Radiotherapy is the main mode of treatment of thalamic glioma since surgical intervention is limited to the role of biopsy and management of secondary effects, due to the deep brain location of the lesion and the complexity of the involved structures [2]. In this case, due to bilateral thalamic presentation, surgical intervention was limited to stereotactic biopsy to confirm the diagnosis. The patient subsequently received a curative dose of external beam radiotherapy to both primary brain lesions and distant bone metastases with concurrent temozolomide and adjuvant chemotherapy which was considered the preferred choice to improve symptoms and prevent further progression of lesions. The overall survival rate is poor with GBM. The cohort studies have reported a 10-year survival rate of 0.71% however the factors affecting long-term survival are still unknown [10,11]. Recently methylation of the O6-methylguanine methyltransferase gene has led to prolong survival [11]. In this case, following the chemoradiotherapy, at the last follow-up, despite the presence of left hemiparesis, there was no sign of disease progression.

Conclusion

This case report underlines the significance of keeping in mind the possibility of bilateral thalamic GBM and the possibility of asymptomatic synchronous distant metastasis of GBM. In general, earlier diagnosis of dissemination can lead to improvement in prognosis as well as the quality of life. Future fields of research in such cases include the development of new radio surgical, chemotherapeutic, and immunotherapeutic treatments.

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References

1. Zhang K, Yang Y, Zhuang J, Guo G, Chao X, Zhang Z. Intracranial Dissemination of Glioblastoma Multiforme: A Case Report and Literature Review. J Int Med Res. 2022;50(7):3000605221112047. PubMed | CrossRef
2. Ganewatte E, Al-Zahrani Y, Purohit B, Kollias S. A Case Report on 1-Year Follow-Up of Bilateral Thalamic Glioma. Neuroradiol J. 2015;28(6):584-6. PubMed | CrossRef
3. Wańkowicz P, Nowacki P. Glioblastoma Multiforme–the Progress of Knowledge on the Pathogenesis of C. Pomeranian J Life Sci. 2014;60(2):40-3. PubMed
4. Blume C, von Lehe M, van Landeghem F, Greschus S, Boström J. Extracranial Glioblastoma with Synchronous Metastases in the Lung, Pulmonary Lymph Nodes, Vertebrae, Cervical Muscles, and Epidural Space in a Young Patient - Case Report and Review of the Literature. BMC Res Notes. 2013;6:290. PubMed | CrossRef
5. McMahon DJ, Gleeson JP, O'Reilly S, Bambury RM. Management of Newly Diagnosed Glioblastoma Multiforme: Current State of the Art and Emerging Therapeutic Approaches. Med Oncol. 2022;39(9):129. PubMed | CrossRef
6. Stoyanov GS, Dzhenkov DL. On the Concepts and History of Glioblastoma Multiforme - Morphology, Genetics, and Epigenetics. Folia Med (Plovdiv). 2018;60(1):48-66. PubMed | CrossRef
7. Liu H, Chen C, Li F, Zheng Y, Liu J, Yu X, Chen L. Glioblastoma Multiforme with Vertebral Metastases: A Case Report. CNS Neurosci Ther. 2022;28(2):310-313. PubMed | CrossRef
8. Thakkar JP, Dolecek TA, Horbinski C, Ostrom QT, Lightner DD, Barnholtz-Sloan JS.,et al. Epidemiologic and Molecular Prognostic Review of Glioblastoma. Cancer Epidemiol Biomarkers Prev. 2014;23(10):1985-96. PubMed | CrossRef
9. Alifieris C, Trafalis DT. Glioblastoma Multiforme: Pathogenesis and treatment. Pharmacol Ther. 2015;152:63-82. PubMed | CrossRef
10. Tykocki T, Eltayeb M. Ten-year Survival in Glioblastoma. A Systematic Review. J Clin Neurosci. 2018;54:7-13. PubMed | CrossRef
11. Krex D, Klink B, Hartmann C, von Deimling A, Pietsch T, Simon M., et al; German Glioma Network. Long-term Survival with Glioblastoma Multiforme. Brain. 2007;130(Pt 10):2596-606. PubMed | CrossRef

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