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PRIMARY SPINAL GLIOBLASTOMA MULTIFORME INVOLVING CONUS MEDULLARIS- A RARE CASE REPORT

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Introduction

Malignant astrocytomas are known for their grim prognosis owing to short survival and rapid neurological deterioration [1]. Their occurrence in the brain is quite common in fact making them the most common primary tumor of the central nervous system [2]. But as far as spinal cord is considered, primary neoplasms are rare. Astrocytomas account for 30% of gliomas and low to high grade ratio of astrocytomas are approximately 1:3. Thus Glioblastoma multiformes are a rare primary malignancy of the spinal cord. Till date less than 200 cases are reported in literature [2], making any statistical study on this disease exceptionally difficult. Thus no established treatment protocol or guideline has been postulated making treatment of this disease even more challenging and thus contributing to poor prognosis of the disease.

This case study is aimed at adding to the limited pool of literature about primary spinal GBM and that too involving conus medullaris which is further rare, having a known frequency of about 5.5%[3]. Also this case report intends to acknowledge its readers to the treatment protocol used by us to treat this condition which was based on our experience from brain primary GBM and the available literature. Patient was offered concurrent chemoradiation in the form of oral Temozolomide and Radiation by IMRT technique; the details have been included in the report. Authors want the readers to understand the rarity of the disease, thus carefully diagnosing the disease and cautiously choose the treatment protocol from meagre available data.

CASE REPORT

26 years old male patient presented with chief complaints of backache since 6 months and weakness in both lower limbs (Left > Right) since 3-4months. Symptoms were progressively increasing without any episode of relief. On examination there was loss of lumbar lordosis, with no scoliosis. There was no local tenderness in spine. Both lower limb muscles showed wasting more on left side. Patient had grade II power in left lower limb while grade III to IV in right lower limb. His Mc Cormick score was IV. Deep tendon reflexes were diminished in both lower limbs. Bladder & bowel control were normal.

Patient underwent a screening MRI of the spine which showed a lesion in conus medullaris at the level of T12. Further contrast imaging was done. Lesion was isointense on T1 weighted and hyper intense on T2 weighted imaging with poor and irregular uptake of contrast. Owing to the rarity of primary spinal lesion MRI brain was performed . An provisional radiological diagnosis of ependymoma was made and the patient was referred to the department of neurosurgery. Underwent surgical excision of the tumor.

Histopathology showed highly cellular tumor with indistinct cell borders having pleomorphic hyper chromatic nuclei, with few tumor giant cells. Vascular proliferation with vessels having plump endothelial cell linings seen. Few foci of necrosis were also seen. IHC was done to further characterize the tumor and came strongly positive for GFAP (Glial Fibrillary Acid Protein). Diagnosis of Glioblastoma – small cell type WHO grade IV was made.

After discussion in the multidisciplinary tumor board, the patient was post operatively considered for adjuvant treatment. He received concurrent chemo radiation. Radiotherapy was given by Intensity modulated Radiotherapy (IMRT) technique focally to dorso lumbar spine between spinal levels T10 to L1. A total of 45Gy of 6MV of photon beam was given in 25 fractions(Fig 1a&b). Portal imaging (EPID) was taken every alternate day to match the set up errors. Chemotherapy was given in the form of per oral Cap. Temozolomide 105 mg(75mg/m^2) that he was supposed to take 35- 40 minutes before radiation every day and was asked to continue medicine even on weekends when radiation was not given. Throughout the course of radiation patient's complete blood counts were monitored weekly (on Saturday). After he finished his radiation Temozolamide was continued in a dose of 210mg (150mg/m^2) for five days a month planned to be given for a year after confirming normal complete blood counts, liver and renal profile post radiotherapy.

Patient followed upto one and half years and was in good health. His symptoms improved. Backache reduced after irradiation and went off round the clock analgesic. His power in both the lower limbs improved to grade IV. His initial arrival in OPD was on a wheelchair but post treatment follow ups he used to walk with support. Didn't develop any major

complication during therapy. Just once he developed hemoptysis which was due to thrombocytopenia secondary to Temozolomide which was managed conservatively without altering the dosage of chemotherapy.

After around one and half year post radiation he had headache with projectile vomiting. MRI brain with spine showed cranio spinal deposits.Patient deteriorated within a week and succumbed to disease.

DISCUSSION

Primary spinal cord GBM is a rare tumor and has a dishearteningly bad prognosis. It is seen most commonly in younger age groups(<30 years) [1]. It has a predilection for cervical and thoracic region accounting for combined 28.5%, followed by cervicothoracic 14.5%, lumbar 9.5% and rarest being conus medullaris accounting 5.5%. Also there is slight male predominance(57.1%)[4]. This disease also shows a tendency to metastasize within or outside CNS, contributing to its poor prognosis. Although metastasis is rare and most commonly occurs in parts of CNS and neuraxis. Extra neural metastasis is rare;in a series it was 6% , being reported at sites like liver and spleen[5]. Usually presenting symptoms are motor related but could be mixed or even purely sensory. In a series studied by *Ononiwu* 100% had motor symptoms while 50% had additional sensory symptoms (n=8)[6]. Even the patient in this case presented with motor symptoms but no sensory deficit.

Preliminary diagnosis is based on radiological imaging. Gadolinium enhanced MRI is the radiological investigation of choice. High grade lesions especially if located in the conus medullaris region have poor uptake of contrast. MRI, although a sensitive modality, lacks specificity, and GBM can be confused with fibrillary astrocytoma and ependymoma, two more common intramedullary neoplasms[7]. Another useful imaging modality is FDG-PET but its use is limited owing to lack of specificity and risk of enhancing glycolysis in tumor cells[8]. Final diagnosis is based on histopathological findings. Dense cellular arrangement with high mitotic figures and nuclear pleomorphism is common to all anaplastic astrocytomas. Presence of necrosis with tumor cells palisading along the margin or microvascular proliferation are specific to Glioblastoma. On IHC presence of GFAP(Glial Fibrillary Acidic Protein) points to astrocytoma [9].

Treatment of primary spinal GBM is the major challenge due to absence of statistically significant study to determine the standard treatment protocols for primary spinal GBM. Surgery plays a major role not only by providing tissue for diagnosis but also by debulking the disease. A series by McGirt on eight spinal GBM patients showed improved survival in those who had complete resection compared with those with subtotal resection[10]. Thus establishing the role of surgery from a mere biopsy procedure to an important part of multimodality treatment. The wonderful work of *Stupp* et al has established concurrent chemoradiation using oral Temozolomide a chemotherapy as standard treatment for brain

GBM, where concurrent chemoradiation has longer disease free and overall survival compared to only radiation[11]. But does this apply for spinal GBM is a question? Although many authors have used focal Radiotherapy as modality some have favoured cranio spinal irradiation even in absence of dissemination, since CSF cytology as well as contrast enhanced imaging both had failed to prove sensitive modality to detect dissemination[12]. Another emerging treatment modality is intrathecal interferon-β. It was studied ASANO et al at Tokushima, Japan where interferon- β was administered via the Ommaya reservoir placed in the left lateral ventricle along with craniospinal irradiation. He found interferon to be stable in CSF, its uptake in tumor tissue and improvement in survival compared with controls of other studies[13]. Kaley et al have reported the role of bevacizumab in prolonging survival after recurrence in those who received surgery and only radiation as treatment[14]. Although these novel therapies hold a promise of improved prognosis in future, they all lack statistically significant results owing to the small number of cases that can be included in study owing to the rare nature of the disease.

CONCLUSION

Since no standard treatment protocols are available authors advise to judicially use the available treatment modalities considering patient factors, to use the novel treatment modalities wherever feasible. Owing to the rarity of this disease, readers are encouraged to report this disease. Since most of our understanding of the disease is from GBM of the brain similar treatment protocols can be applied but biologically primary spinal cord GBM is a different disease and needs to be studied zealously so as to improve its prognosis.

ABBREVIATIONS

CNS: Central Nervous System

CSF : Cerebrospinal Fluid

EPID: Electronic Portal Imaging Device

FDG-PET: Fluorodeoxyglucose Positron Emission Tomography

GFAP: Glial Fibrillary Acidic Protein

GBM: Glioblastoma Multiforme

IHC: Immunohistochemistry

IMRT: Intensity modulated Radiotherapy

MRI: Magnetic Resonance Imaging

OPD: Outpatient Department

WHO: World Health Organisation

Key words

1. Spinal
2. Glioblastoma Multiformae
3. Conus medullaris
4. Temozolomide
5. IMRT
6. Paraplegia

REFRENCES

1. Alan R. Cohen M.D., Jeffrey H. Wisoff M.D., Jeffrey C. Allen M.D. and Fred Epstein M.D. Malignant astrocytomas of the spinal cord.jns. Volume 70: Issue 1 (Jan 1989).pages: 50-54. Available from (DOI): https://doi.org/10.3171/jns.1989.70.1.0050

2. Nuno Morais,Lino Mascarenhas,J. P. Soares-Fernandes,Ana Silva,Zita Magalhães,J. A. Moreira Da Costa. Primary spinal glioblastoma: A case report and review of the literature. Published online on: December14,2012 Pages: 992-996
Available from: https://doi.org/10.3892/ol.2012.1076

3. Azedine MedhkourMD,Michael ChanMSc .Extremely rare glioblastoma multiforme of the conus medullaris with holocord and brain stem metastases, leading to cranial nerve deficit and respiratory failure: a case report and review of the literature.Surg Neurol.Volume 63, Issue 6, June 2005, Pages 576-582;discussion 582-3. doi: https://doi.org/10.1016/j.surneu.2004.08.044. https://www.ncbi.nlm.nih.gov/pubmed/15936395

4. Shen, Chao-Xiong MD; Wu, Jian-Feng MD; Zhao, Wei MD; Cai, Zhao-Wen MD; Cai, Ran-Ze MD; Chen, Chun-Mei PhD*, Primary spinal glioblastoma multiforme: A case report and review of the literature. Medicine (Baltimore),April 2017 - Volume 96 - Issue 16 - p e6634

Published online 2017 Apr 21.doi: 10.1097/MD.0000000000006634

5. Mariarita Santi M.D.,Hernando Mena M.D. ,Kondi Wong M.D.,Kelly Koeller M.D.,Cara Olsen M.S. ,Elisabeth J. Rushing M.D.Spinal cord malignant astrocytomas.Cncr. Volume98, Issue3,1 August 2003,Pages 554-561
Available from (Doi):https://doi.org/10.1002/cncr.11514

6. Ononiwu, C., Mehta, V., Bettegowda, C. et al..Childs Nerv Syst (2012). 28: 715. https://doi.org/10.1007/s00381-012-1705-0

7. Igor Faria, MD; Renata Bertanha, MD; Marcio Ricardo Taveira Garcia, MD . SPINAL CORD GLIOBLASTOMA MULTIFORME.Case of the Week.ajnr .July 9, 2015 available from: (http://www.ajnr.org/content/cow/07092015)

8. Won, Kyoung Sook, MD; Kim, Jae Seung, MD; Ra, Young Shin, MD; Sohn, Cheol Ho, MD; Zeon, Seok Kil, MD.FDG PET of Primary Spinal Glioblastoma Initially Mimicking a Transverse Myelitis on MR..Clinical Nuclear Medicine: September 2006 - Volume 31 - Issue 9 - p 556-557
doi: 10.1097/01.rlu.0000233030.35986.5f
https://journals.lww.com/nuclearmed/Abstract/2006/09000/FDG_PET_of_Primary_Spinal_Glioblastoma_Initially.13.aspx

9. Kumar V,Abbas AK, Aster JC.Robbins basic pathology.10th edition. Pennsylavania: ELSEVIER. CHAPTER 23 CENTRAL NERVOUS SYSTEM , page 881

10. McGirt MJ[1], Goldstein IM, Chaichana KL, Tobias ME, Kothbauer KF, Jallo GI.
Extent of surgical resection of malignant astrocytomas of the spinal cord: outcome analysis of 35 patients. Neurosurgery. 2008 Jul;63(1):55-60; discussion 60-1.
doi: 10.1227/01.NEU.0000335070.37943.09.

11. Roger Stupp, M.D., Warren P. Mason, M.D.,Martin J. van den Bent, M.D., et al. Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma.
N Engl J Med March 10, 2005; 352:987-996
DOI: 10.1056/NEJMoa043330

12. Johnson DL, Schwarz S. Intracranial metastases from malignant spinal-cord astrocytoma. Case report.J Neurosurg. 1987 Apr;66(4):621-5.
Doi: https://doi.org/10.3171/jns.1987.66.4.0621

13. Noboru ASANO, Katsushi KITAMURA, Yoshinobu SEO, Kanji MUKAI, Tetsuro SOGA, Hideki HONDO, Keizo MATSUMOTO.Spinal Cord Glioblastoma

Multiforme with Intracranial Dissemination.Neurologia medico-chirurgica.1990 Volume 30 Issue 7 Pages 489-494 Doi: https://doi.org/10.2176/nmc.30.489

14. Thomas J. Kaley. Kaley TJ , Mondesire-Crump I , Gavrilovic IT Temozolomide or bevacizumab for spinal cord high-grade gliomas.Journal of Neuro-Oncology.September 2012, Volume 109, Issue 2, pp 385–389

Doi: 10.1007/s11060-012-0905-5

STATEMENT AND DECLARATION

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