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Case Report

Intramedullary Glioblastoma Multiforme of Spine with Intracranial Supratentorial Metastasis: Progressive Disease with a Multifocal Picture

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Abstract

Primary spinal glioblastoma multiforme (GBM) is very uncommon while an intramedullary spinal GBM with intracranial metastasis is rarely heard of. A 23-year-old male presented with bilateral paraplegia associated with bowel and bladder incontinence. Craniospinal radiograph showed an intramedullary spinal mass lesion, for which he underwent laminectomy and histopathology revealed GBM. He received local radiotherapy (RT) with temozolomide (TMZ). While on adjuvant TMZ, he developed severe headache and recurrent episodes of vomiting. Brain and spine imaging showed intracranial mass lesions associated with expansion of the entire cord. Biopsy from the intracranial lesion was confirmed as GBM on immunohistopathology. He was treated with palliative RT to the brain and was put on metronomic TMZ; however, he succumbed to his illness. Review of literature reveals that our case may be the fourth such case in the world and probably the first case reported in India where the intracranial metastatic GBM again presented with a reverse spinal dissemination.

Keywords: *Glioblastoma multiforme, intracranial, intramedullary, spine, supratentorial*

Introduction

Glioblastoma multiforme (GBM) is the most common primary brain malignancy constituting 75% of cases[1] while primary GBM of the spine accounts for <3% of all intramedullary neoplasms[2] and only 1% of all central nervous system (CNS) malignancies.[3] Primary intracranial GBM with spinal seeding is known; however, metastatic intracranial GBM disseminating from a primary intramedullary spinal GBM is exceedingly uncommon and rarely reported in world literature till date. Radiotherapy (RT) with concurrent chemotherapy remains the cornerstone of adjuvant therapy due to the high probability of local recurrence after surgery while the treatment modality for the metastatic disease remains mainly palliative.

Case Report

A 23-year-old male with no known comorbidities or addiction presented with low back ache associated with progressive paraplegia and loss of bladder and bowel function of 2-month duration. Magnetic resonance imaging (MRI) of the spine showed a 1.2 cm × 1.4 cm × 6.4 cm intramedullary lesion spanning D8–D10 with evidence of lytic areas within [Figure 1]. MRI brain was normal. He underwent laminectomy with excision of the intramedullary lesion. Histopathology report (HPR) showed features of necrosis, endothelial proliferation, brisk mitosis, and nuclear atypia suggestive of GBM [Figure 2]. Immunohistochemistry (IHC) was positive for glial fibrillary acidic protein (GFAP) [Figure 3] with a Ki-67 of 60%, which confirmed the diagnosis. He received adjuvant RT to the spine to a dose of 5040 cGy in 28 fractions along with concurrent temozolomide (TMZ) which he tolerated well.

He was then started on adjuvant TMZ; however, during his fourth cycle, he developed headache and recurrent episodes of vomiting. MRI of the brain and spine revealed multiple, well-defined round-to-ovoid lesions attached to frontal, occipital horn and septum pellucidum of lateral ventricles, largest measuring 2.3 cm × 2.1 cm × 1.9 cm with resultant lateral ventricle, third ventricle dilatation with fourth ventricle obstruction with hydrocephalus [Figure 4]. Extensive areas of altered signal intensity with associated cord expansion were seen

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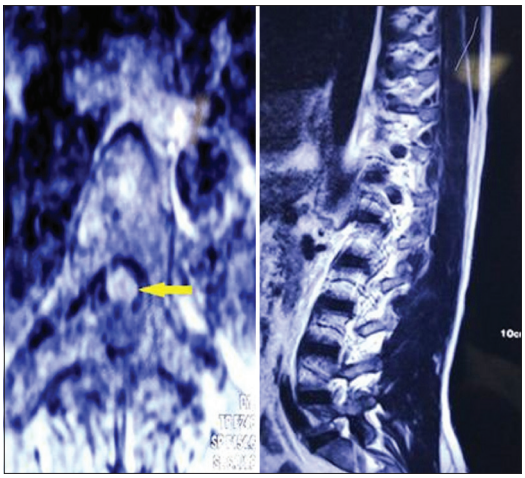

Figure 1: Magnetic resonance imaging of the spine (axial section) showing an intramedullary lesion (yellow pointer) spanning D8–D10 vertebrae (sagittal section)

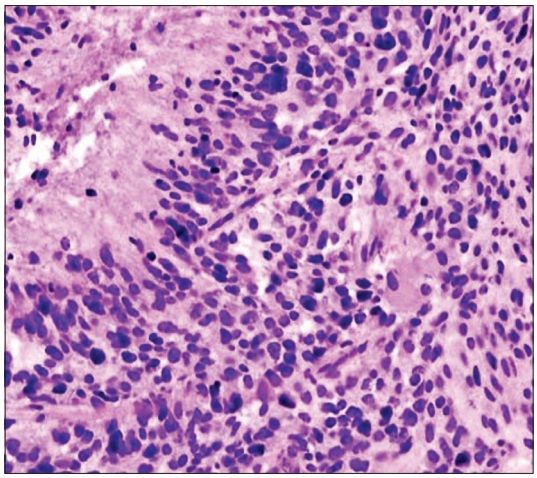

Figure 2: Postoperative histopathology report of spinal lesion showing features of necrosis, endothelial proliferation, brisk mitosis, and nuclear atypia suggestive of glioblastoma multiforme (H and E, ×100)

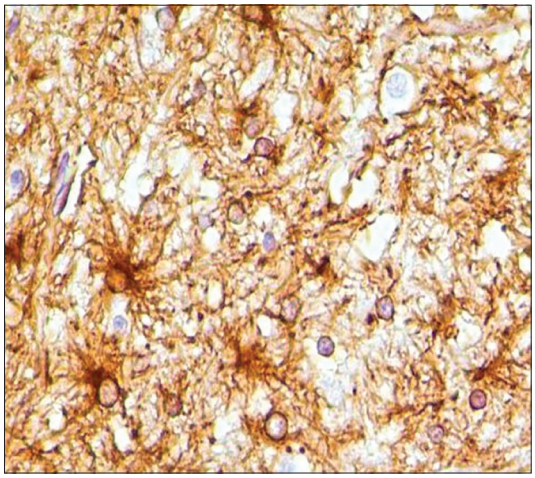

Figure 3: Immunohistochemistry positive for glial fibrillary acidic protein (×200)

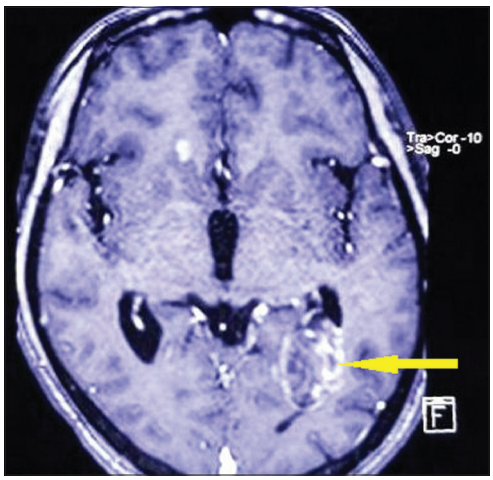

Figure 4: Magnetic resonance imaging of the brain (axial section) showing multiple, well-defined round-to-ovoid lesions attached to frontal, occipital horn and septum pellucidum of lateral ventricles (yellow pointer)

extending from cervicomedullary junction till cauda equina up to L1 vertebrae [Figure 5]. Whole-body and brain positron emission tomography scan showed multiple fluorodeoxyglucose (FDG) avid brain and spinal lesions without any FDG uptake in other parts of body. Craniospinal fluid (CSF) analysis was positive for tumor cells. The patient underwent craniotomy and ventriculoperitoneal shunt placement. Postoperative HPR [Figure 6] revealed large areas of necrosis with peripheral pseudopalisades, microvascular proliferation, mitosis, and high nuclear-cytoplasmic ratio which suggested a metastatic deposit from spinal GBM. IHC showed positivity for GFAP, synaptophysin, and Ki-67 of 70%, thus confirming the diagnosis. In view of his Karnofsky Performance Score of 50% and prior spinal RT, only palliative whole brain RT (WBRT) to a dose of 34 Gy in 10 fractions was given. He was then put on maintenance metronomic TMZ 50 mg Once a day (OD), but his general condition kept on deteriorating and he finally succumbed to his illness.

Discussion

Spinal cord malignancies can either be primary or metastatic, with the later constituting the majority. Primary spinal tumors are mainly intramedullary arising within the substance of the cord itself while metastatic deposits are mostly extradural though intramedullary metastatic deposits are being increasingly recognized. Approximately 70% of spinal intramedullary neoplasms are constituted by astrocytomas and ependymomas while GBM accounts for <3% intramedullary cases[2] and 1% of all primary CNS neoplasms,[3] thus depicting the rarity of the primary location of this entity itself. Primary intracranial malignancies such as medulloblastoma, ependymoma, germinoma, pinealoblastoma more commonly while anaplastic astrocytoma and GBM less commonly disseminate into the spinal cord. On the contrary, primary spinal cord tumor with intracranial dissemination is extremely rare.

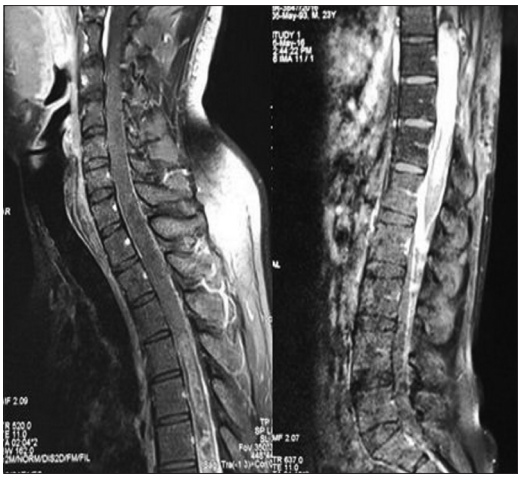

Figure 5: Magnetic resonance imaging of the spine (sagittal section) showing extensive areas of altered signal intensity with associated cord expansion extending from cervicomedullary junction to lumbar vertebrae

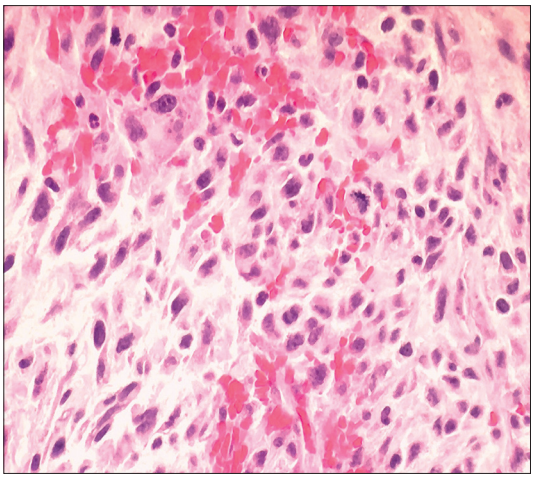

Figure 6: Postcraniotomy histopathology report showing large areas of necrosis with peripheral pseudopalisades (H and E, ×200)

Few cases of spinal anaplastic astrocytoma with brain metastasis[3,4] and spinal pilocytic astrocytoma with leptomeningeal dissemination[5,6] have been described. One case each of intramedullary spinal GBM with intracranial seeding has been reported by Andrews *et al*.[7] in 1978, Asano *et al*.[8] in 1990, and Morais *et al*.[9] in 2013. Intracranial spread has been mostly infratentorial; however, dissemination to supratentorial region is uncommon as it happened in our case. Route of spread of spinal malignancy to the brain may be either by direct leptomeningeal or CSF or rarely through hematogenous pathways. Tumor invasion of the subarachnoid space after meningeal breach may be the possible mechanism of leptomeningeal and intracranial dissemination. Eade and Urich[10] in 1971 postulated the risk factors for dissemination in CNS tumors such as younger age, higher grade, oligodendroglial component, and anaplasia. Overexpression of epidermal growth factor receptor and higher values of Ki-67 may also contribute to the disease process; however, no definitive evidence has been elucidated.

A primary spinal GBM generally occurs in young adults and presents with various features of cord compression such as pain, numbness, paresis, or paraplegia of lower limbs, and sphincter dysfunction. Those with features of raised intracranial tension are invariably aggressive with a dismal prognosis and a median survival of only 15–18 months.[11] Our patient developed metastasis during adjuvant treatment and survived for only 8 months' postdiagnosis. The peculiar feature of our case was the spinal dissemination of the supratentorial metastatic lesion, which gave a progressive and multifocal picture. Spinal GBM is identified based on radiological parameters such as its intracranial counterpart such as nuclear atypia, mitotic activity, vascular proliferation, and necrosis and immunohistochemical parameters such as GFAP and S-100 positivity with high Ki-67 leveling index, which was seen in both spinal and intracranial lesions in our case.

Surgery remains the treatment modality of choice for spinal GBM like intracranial lesion though intramedullary tumors generally present a surgical challenge of preserving the neurologic functions. Extent of surgery whether gross-total resection or piecemeal removal remains an important factor determining the addition of adjuvant therapy. Currently, there are no randomized controlled trials to guide the role of RT for primary spinal tumors due to the rarity of this lesion.[1] The role of RT has been associated with better outcomes as per various case reports or series. Radiation dose of 40 Gy or higher has been associated with significantly better local control and survival.[1] For high-grade gliomas with evidence of CSF dissemination, craniospinal irradiation (CSI) should be considered.[1] No CSI was given in our case as he had received full tolerance dose spinal RT and due to his poor general condition. The reported use chemotherapy for spinal GBM is limited and not well established. Kim *et al*.[12] in 2011 reported using concurrent TMZ with RT followed by adjuvant TMZ, with a median survival of 16 months as compared to 9 months in other reports.[1] We also exhibited concurrent and adjuvant TMZ, however, he progressed while on fourth TMZ cycle. As for the intracranial metastatic lesion with a multifocal scenario, palliative WBRT has a proven therapeutic role.

Conclusion

Spinal GBM with intracranial metastasis is exceedingly rare with surgery remaining the primary therapeutic modality aided by adjuvant RT. Advanced RT techniques such as intensity-modulated RT and stereotactic radiosurgery have shown promising potential in improving the therapeutic ratio. The role of chemotherapy is not clearly defined and is most often extrapolated from the intracranial GBM cases. Continued and diligent long-term follow-up of clinical outcomes and innovation of novel therapeutic approaches is essential for improving the management, overall survival, and quality of life of these sporadic cases.

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Conflicts of interest

There are no conflicts of interest.

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