Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 9, Issue, 05, pp.50025-50028, May, 2017

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

SPINAL GLIOBLASTOMA MULTIFORME WITH BRAIN AND SPINAL SEEDING: TREATMENT APPROACH FROM VARIOUS VIEW POINTS

***Jagtap Vikas K., Bansal Shashank, Nayan Navin and Kalita Apurba K.**

Department of Radiotherapy, Dr. B. Borooah Cancer Institute, Gopinath Nagar, A K Azad Road, Guwahati (Assam) - 781016

ARTICLE INFO

Article History:
Received 22nd February, 2017
Received in revised form
16th March, 2017
Accepted 20th April, 2017
Published online 19th May, 2017

Key words:
Spinal glioblastoma, Glioblastoma, Brain and spinal seeding, Metastasis.

ABSTRACT

Primary spinal glioblastoma is a rare and aggressive entity with poor prognosis. With less than 200 reported cases the specific guidelines for the treatment of these cases are not yet formulated. Even with different treatments like radiotherapy, surgery and chemotherapy the survival is poor. We report a case of 10 year old female with spinal Glioblastoma Multiforme (sGBM) with cerebral and spinal deposits treated with radiotherapy and chemotherapy at our institute. Since this was a rare presentation we were keen on giving the best possible treatment to the patient. Literature review was done to assess the available treatment options. This review primarily focuses and gives insights in managing this rare entity with scientific approach.

Citation: Jagtap Vikas K., Bansal Shashank, Nayan Navin and Kalita Apurba K. 2017. "Spinal glioblastoma multiforme with brain and spinal seeding: treatment approach from various view points", *International Journal of Current Research*, 9, (05), 50025-50028.

INTRODUCTION

GBM (Glioblastoma) is extremely aggressive tumour with very poor prognosis. Astrocytoma is the most common primary tumour of the central nervous system (Cohen *et al*., 1989). Spinal cord astrocytomas comprise ~1% of all primary central nervous system tumours and 6 to 8% of all spinal cord tumours (Johnson *et al*., 1987), Spinal intramedullary tumours account for 5% of all spinal cord tumours (Balériaux *et al*., 1999), Of these, ~30% are tumours of low grade malignancy, including slow-growing astrocytomas and ependymomas. Glioblastomas (GBMs) represent ~7.5% of all intramedullary gliomas and 1 to 3% of all spinal cord tumours (Medhkour *et al*., 2005 and Ciappetta *et al*., 1991). It was seen that spinal GBM is most commonly found in cervical or cervicothoracic region in >60% of cases (Cohen *et al*., 1989; Asano *et al*., 1990; Grisold *et al*., 1981 and Guidetti *et al*., 1981). Even with aggressive management, these tumours are generally associated with a dismal outcome.

Case Report

A 10 year old female presented at our institute with pain in upper back and progressive weakness in both lower limbs since 2 month. She was initially evaluated at local private hospital. MRI of spine revealed moderately enhancing T2 hyper intense cervicodorsal fusiform cord enlargement from C6 to D3 level with associated widening of spinal canal and vertebral margins and hydromyelia extending up to D11 level with enhancing nodular T2 hyper intense deposits along the ependymal lining of central canal at D6-D7 level. Computed Tomography (non - contrast) scan of brain did not revealed any significant abnormality. Patient underwent C7-D3 laminectomy with tumour decompression under general anaesthesia at private hospital. Post-operative histopathology was conclusive of glioblastoma multiforme WHO grade IV and patient was referred to our hospital for further treatment. On initial examination she had paresis of both lower limbs, power 0/5, crude touch and pain sensation was present, soft touch sensation was absent and plantar extensor reflex with left sided facial palsy. Her bladder and bowel sensations were intact. In view of previous history and recent examination finding thorough metastatic work up was done at our institute. Post-operative contrast enhanced MRI of brain and whole spine was done. There was T2 hyper intense intramedullary lesion with iso to hyper intensity on T1 weighted images in cervicodorsal cord from the level of C5 up to D1 vertebra with posterior extrusion of the lesion through laminectomy defect Multiple T2 iso to slightly hyper intense nodular deposits were seen along the fibres of cauda equina with post contrast enhancement (Figure 1). MRI brain revealed mixed hypo and hyper intense lesion on T2 weighted images in right temporal lobe along the horn of lateral ventricle measuring 12 X 12 mm

****Corresponding author:*** **Jagtap Vikas K.**
Department of Radiotherapy, Dr. B. Borooah Cancer Institute, Gopinath Nagar, A K Azad Road, Guwahati (Assam) – 781016

with mild adjacent parenchymal edema. Another enhancing lesion is seen in frontal horn of left lateral ventricle with T2 hyper intense signal intensity in adjacent anterior corpus callosum. Meningeal enhancement was noted along the skull base with post contrast enhancement (Figure 2). Cerebrospinal fluid (CSF) analysis was negative for malignant cells. Chest radiograph and ultrasonography of the abdomen was normal. Histopathology review confirmed the diagnosis of spinal GBM. The patient was started on radiotherapy to the spinal primary lesion and also to deposits in cauda equina and brain (54Gy/30#). She also received concurrent chemotherapy with Temozolamide (75mg/m^2) daily with adequate supportive care. The patient improved significantly after the treatment.

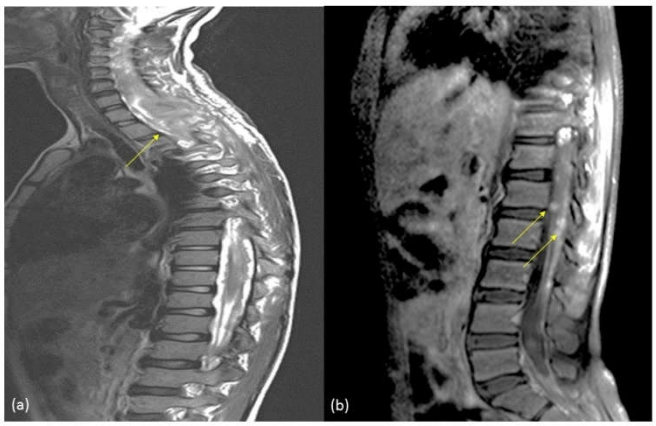

Figure 1. T1 Post Contrast image
a. Showing primary lesion in cervicodorsal spine (yellow arrow)
b. Showing deposits in cauda equine (yellow arrows)

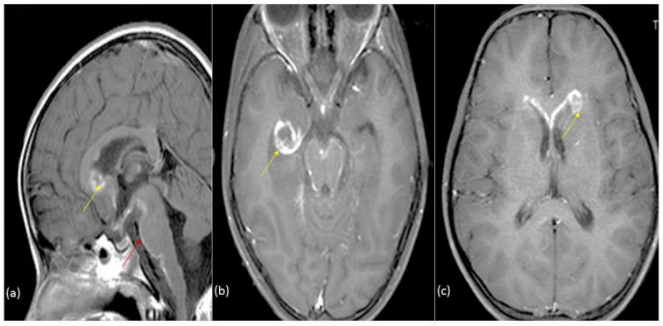

Figure 2. T1 Post Contrast image
a. Brain deposits in corpus callosum and ependyma and meningeal enhancement (red arrow)
b. Right temporal lobe (yellow arrow)
c. Left ventricle (yellow arrow)

DISCUSSION

Intramedullary GBM is an extremely rare entity. Most of the cases of Spinal GBM are from the drop metastasis from brain primary and in some cases it occurs as a primary lesion in spinal cord. Most of the cases reported in literature are below 30 years of age. Malignant astrocytomas spreads mostly via the leptomeningeal route (Cohen *et al*., 1989; Ciappetta *et al*., 1991). Metastasis from intracranial GBM along the spine occurs in approximately 25% of cases, but the reverse process is extremely rare (Cohen *et al*., 1989; Balériaux *et al*., 2005), The high rate of leptomeningeal spread has been attributed to the relatively thin parenchyma in the spinal cord, and hence, the shorter distance to the subarachnoid space (Reimer *et al*., 1985). MRI is considered the gold standard imaging modality to diagnose intramedullary tumors, and Gadolinium-enhanced MRI of the entire neuroaxis is advocated to rule out cranial metastasis, evaluate treatment efficiency, and detect local relapse. (Mori *et al*., 2012; Bonde *et al*., 2008; Stecco *et al*., 2005) Rarely the extra neuronal spread of the disease is noted most commonly involving the lungs, lymph nodes, bone, liver and pleura (Russell *et al*., 1998). With improvements in treatment of primary GBM including surgery, chemotherapy, radiation and standard of care the incidence of extraneural metastases has increased exponentially (Rory Goodwin *et al*., 2016). Direct access via dural vessels to extrameningeal tissue is considered the most likely path in the development of extraneural metastases (Beauchesne *et al*., 2000), which is potentially initiated by surgical intervention. Potential cause of spread is via direct invasion through the duramater and bone and cellular migration via ventricular drainage tubes (Maccauro *et al*., 2011; Rajagopalan *et al*., 2005). The presence of extraneural metastases is defined by criteria set forth by Weiss *et al*. (Weiss *et al*., 1995). Hence it is also recommended to do Computed Tomography (CT) scan of thorax and abdomen to detect extraneuronal metastasis at initial diagnosis and also in subsequent follow up as per clinical judgments.

The published literature shows the survival of 6 to 16 months in spite of the best available treatment options including surgery, radiotherapy and chemotherapy (Rajagopalan *et al*., 2005 and Kopelson *et al*., 1982). Posterior approach via laminectomy or laminoplasty is considered as standard surgical therapy (Bedjan Behmanesh *et al*., 2017). In some cases due to poor general condition surgery may not be possible and attempts to obtain a biopsy should be done before starting any other treatment. Some reports have shown that surgical manipulation of GBM does not increase the tumour seeding into the CSF (Bedjan Behmanesh *et al*., 2017). In a reported series median survival time from operation to death was 6.5 months with a range of 0.5 to 10 months. The median survival time from onset of symptoms until death was 10.94 months with a range of 2 to 26 (Péter Banczerowski *et al*., 2003). Unlike other tumors no association was seen between survival and degree of resection of malignant spinal gliomas (McGirt *et al*., 2008; Sandler *et al*., 1992 and Lam *et al*., 2012). In a population-based study, Wolff *et al*. (Wolff *et al*., 2012), published that Gross Total Resection (GTR) was associated with higher mortality. Subtotal resection followed by adjuvant therapy should be the empirical approach for spinal GBM as reported by some authors (Subhas *et al*., 2016). In some cases, especially in thoracic tumors with complete loss of neural function below that level, cordectomy can be planned which has shown to improve survival and in some reports postoperative recurrence free survival of upto 15 months has been reported (Merchant *et al*., 1999; Viljoen *et al*., 2014 and Subhas *et al*., 2017), Surgical total excision or debulking to obtain tissue samples of the tumor without much effect on preexisting neurodeficits or worsening of the condition most often remains the initial treatment of choice.

Adjuvant high-dose postoperative radiation that may exceed the radiation tolerance of the spinal cord is the standard of care after surgery (Scarrow *et al*., 2000). Most authors suggest focal spine radiotherapy and chemotherapy with TMZ. Others recommend a more aggressive course of whole-brain irradiation in addition to focal spine irradiation, even if there is no evidence of intracranial dissemination (Morais *et al*., 2013). RT with 40 Gy to the entire spinal axis lengthened patient survival from 4.5 to 22.7 months as shown by Ciappetta *et al*.

(1991). Minehan *et al*. (2009) reported that higher doses (59.4 Gy) was well tolerated by the spinal cord or could be given to a patient with near paraplegia (Lober *et al*., 2010). In general 50-54 Gy conventionally fractionated radiotherapy is advised. Lesions involving cauda or in patients with complete or irreversible myelopathy higher doses up to 60 Gy may be tried (Cancer, Principles and practice of oncology, 2014). Radiotherapy doses higher than the traditional tolerance dose for the spinal cord has been called "radiocordectomy" by Cohen *et al*. (1989), and patients surviving more than 4 years has been reported by some authors after radiocordectomy (Shirato *et al*., 1995). Adjuvant radiotherapy prolongs survival and it has shown to significantly improve median survival from 5.0 (95%CI 0.6 to 16.6) months to 12.0 (95% CI 1.0-72.0) months (P<0.0001) as reported by some centres (Zhang *et al*., 2014), RT is also recommended for unresectable and incompletely resected tumors of spine. In patients with very poor general condition hypofractionated radiotherapy (30Gy/10# or 20Gy/5#) may be a useful option to relieve pain and improve general condition of the patients. Chemotherapy agents like methotrexate and 1.3-bis (2-chloroethyl)-1-nitrosurea (BCNU) were given in some patients (PéterBanczerowski *et al*., 2003). Nowadays temozolamide has become the standard of care in treating cranial GBM and the same is being used by many authors to treat spinal GBM also despite the poor prognosis and lack of enough data to support (Morais *et al*., 2013; Thomas Linsenmannet *et al*., 2015). The chemotherapeutic agents can be given as a single modality but many of the patients ends up getting concurrent chemoradiation followed by adjuvant chemotherapy to achieve maximum benefit. Others suggest intrathecal administration of interferon-β via an Ommaya reservoir in conjunction with cranio-spinal irradiation (Johnson *et al*., 1987 and Asano *et al*., 1990). VEGF (Vascular Endothelial Growth Factors) is expressed in both entities, GBM and AVM, and may be the link for the simultaneous occurrence (Onishi *et al*., 2011). Therapies with antiangiogenic factors may be preferred in this special situation of a combined occurrence of both entities as reported in literature (Thomas Linsenmannet *et al*., 2015).

Conclusion

The spinal GBM has a poor overall survival despite multimodality therapy. A compassionate approach should be followed to achieve best outcome in these group of patients. We recommend doing a complete neuroaxis imaging and CT scan of thorax and abdomen for all the patients at diagnosis. Maximum safe resection of the tumor should be tried as early as possible. Adjuvant Radiotherapy should be given to all the patients irrespective of the extent of resection along with concurrent chemotherapy preferably Temozolamide. Radiotherapy doses from 54-60 Gy with conventional fractionation should be the standard approach. After radiotherapy further adjuvant chemotherapy should be offered to patients with good response and with good performance score. In patients with very poor general condition a hypofractionated radiotherapy course should be offered for symptomatic relief after biopsy confirmation. Whenever possible the patients should be taken up into clinical trials to help understand these tumors in a better way.

REFERENCES

Asano N, Kitamura K, Seo Y, *et al*. 1990. Spinal cord glioblastoma multiforme with intracranial dissemination - case report. *Neurol Med Chir* (Tokyo) 30: 489-494.

Balériaux DL. 1999. Spinal cordtumors. *EurRadiol*., 9: 1252-1258.

Beauchesne P, Soler C, Mosnier JF. 2000. Diffuse vertebral body metastasis from a glioblastoma multiforme: a technetium-99m Sestamibi single photon emission computerized tomography study. *J Neurosurg.,* 93:887-890.

Bedjan Behmanesh *et al*. 2017. Management of Patients with Primary Intramedullary Spinal Cord Glioblastoma World Neurosurg., 98:198-202.

Bonde V, Balasubramaniam S, Goel A. 2008. Glioblastoma multiforme of the conus medullaris with holocordal spread. *J ClinNeurosci*., 15(5):601–603.

Cancer, Principles and practice of oncology, Devita, Hellman and Rosenberg: 10th edition, p 1450.

Ciappetta P, Salvati M, Capoccia G, Artico M, Raco A and Fortuna A. 1991. Spinal glioblastoma: report of seven cases and review of the literature. *Neurosurgery*, 28: 302-306.

Cohen AR, Wisoff JH, Allen JC and Epstein F. 1989. Malignant astrocytomas of the spinal cord. *J Neurosurg*, 70: 50-54.

Grisold W, Pernetzky G and Jellinger K. 1981. Giant-cell glioblastoma of the thoracic cord. *ActaNeurochir* (Wien) 58: 121-126.

Guidetti B, Mercuri S and Vagnozzi R. 1981. Long-term results of the surgical treatment of 129 intramedullary spinal gliomas. *J Neurosurg*., 54: 323-330.

Johnson D and Schwarz S. 1987. Intracranial metastases from malignant spinal-cord astrocytoma. Case report. *J Neurosurg*., 66: 621-625.

Kopelson G and Linggood RM. 1982. Intramedullary spinal cord astrocytoma versus glioblastoma: the prognostic importance of histological grade. *Cancer*, 50: 732-735.

Lam S, Lin Y, Melkonian S. 2012. Analysis of risk factors and survival in pediatric high-grade spinal cord astrocytoma: a population-based study. *Pediatr Neurosurg*., 48:299-305.

Lober R, Sharma S, Bell B, Free A, Figueroa R, Sheils CW, *et al*. 2010. Pediatric primary intramedullary spinal cord glioblastoma. *Rare Tumors*., Sep 30; 2(3): e48.

Maccauro G, Spinelli MS, Mauro S, Perisano C, Graci C, Rosa MA. 2011. Physiopathology of spine metastasis. *Int J SurgOncol*., 107969.

McGirt MJ, Goldstein IM, Chaichana KL, Tobias ME, Kothbauer KF, Jallo GI. 2008. Extent of surgical resection of malignant astrocytomas of the spinal cord: outcome analysis of 35 patients. *Neurosurgery*, 63:55-60; discussion 60-61.

Medhkour A and Chan M. 2005. 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*., 63: 576-582.

Merchant TE, Nguyen D, Thompson SJ, Reardon DA, Kun LE, Sanford RA. 1999. High-grade pediatric spinal cord tumors. *Pediatr Neurosurg.,* 30:1-5.

Minehan, K.J., Brown, P.D., Scheithauer, B.W., Krauss, W.E., Wright, M.P. 2009. Prognosis and treatment of spinal cord astrocytoma. *Int J RadiatOncolBiol Phys*., 73:727-733.

Morais, N., Mascarenhas, L, Soares-Fernandes JP, Silva A, Magalhães Z, Costa JA. 2013. Primary spinal glioblastoma: a case report and review of the literature. *Oncol Lett.,* 5(3):992–996.

Mori K, Imai S, Shimizu J, Taga T, Ishida M, Matsusue Y. 2012. Spinal glioblastoma multiforme of the conus medullaris with holocordal and intracranial spread in a

child: a case report and review of the literature. *Spine J.,* 12(1):e1–e6.

Onishi M, Ichikawa T, Kurozumi K, Date I. 2011. Angiogenesis and invasion in glioma. *Brain Tumor Pathol*., 28(1):13–24.

Péter Banczerowski *et al*. 2003. Primary intramedullary glioblastoma multiforme of the spinal cord: report of eight cases. *ClinNeurosci*/*IdeggySzle*., 56(1–2):28–32.

Rajagopalan V, El Kamar FG, Thayaparan R, Grossbard ML. 2005. Bone marrow metastases from glioblastoma multiforme—A case report and review of the literature. *J Neurooncol*., 72: 157-161.

Reimer R, Onofrio BM. 1985. Astrocytomas of the spinal cord in children and adolescents. *J Neurosurg*., 63:669–675.

Rory Goodwin C. *et al*. 2016. Extraneural Glioblastoma Multiforme Vertebral Metastasis. *World Neurosurg*., 89:578-582.

Russell DS and Rubinstein LJ (eds): 1998. Glioblastoma. In: Pathology of Tumours of the Nervous System. 5th edition. Edward Arnold, London, pp 426-452.

Sandler HM, Papadopoulos SM, Thornton AF Jr, Ross DA. 1992. Spinal cord astrocytomas: results of therapy. *Neurosurgery*, 30:490-493.

Scarrow AM, Rajendran P, Welch WC. 2000. Glioblastoma multiforme of the conus medullaris. *ClinNeurolNeurosurg*., 102(3): 166–167.

Shirato, H., T. Kamada, K. Hida, I. Koyanagi, Y. Iwasaki, K. Miyasaka, *et al.* 1995. Therole of radiotherapy in the management of spinal cord glioma, *Int. J. Radiat.Oncol. Biol. Phys*, 33(2): 323–328.

Stecco A, Quirico C, Giampietro A, Sessa G, Boldorini R, Carriero A. 2005. Glioblastoma multiforme of the conus medullaris in a child: description of a case and literature review. *AJNR Am J Neuroradiol*., 26(8):2157–2160.

Subhas K. Konar *et al*. 2017. Spinal cordectomy: A new hope for morbid spinal conditions. *Clinical Neurology and Neurosurgery*, 152: 5–11.

Subhas K. Konar, *et al*. 2016 Predictive Factors Determining the Overall Outcome of Primary Spinal Glioblastoma Multiforme: An Integrative Survival Analysis. Citation: *World Neurosurg*., 86:341-348.

Thomas Linsenmannet *et al*. 2015. Primary Spinal Glioblastoma Multiforme with Secondary Manifestation as a Cerebral "Angioglioma." Literature Review and Case Report. *J NeurolSurg Rep*., 76:e128–e134.

Viljoen S, Hitchon PW, Ahmed R, Kirby PA. 2014. Cordectomy for intramedullary spinal cord glioblastoma with a 12-year survival. *SurgNeurolInt*., 5:101.

Weiss L. 1995. A metastasizing ependymoma of the cauda equina. *Cancer*, 8:161-171.

Wolff B, Ng A, Roth D, Parthey K, Warmuth Metz M, Eyrich M. *et al*. 2012. Pediatric high-grade glioma of the spinal cord: results of the HITGBM database. *J Neurooncol.,* 107:139-146.

Zhang, K. *et al.* Primary spinal cord glioblastoma: A systematic review, cjn2014.81 Suppl 2 – S14.

****