Spinal Glioblastoma Multiforme: Unusual Cause of Post-Traumatic Tetraparesis

Pankaj Kumar Singh, MBBS, MS; Vinay K. Singh, MRCS; Juhi Tomar, MBBS; Amir Azam, MRCS; Sanjeev Gupta, MS, MCh (Neurosurg); Sushil Kumar, MCh (Neurosurg)

Royal Hallamshire Hospital, Sheffield, South Yorkshire, United Kingdom

Received August 17, 2008; accepted October 16, 2008

Abstract

Background/Objective: Glioblastoma multiforme (GBM) is the most common glial cell tumor of the adult brain. However, primary GBM of the spinal cord is a rare condition.

Methods: Case report.

Results: A young man presented with acute onset quadriparesis after a whiplash injury. A magnetic resonance scan showed the typical appearance of a high-grade intramedullary tumor with fusiform expansion of the entire cervical cord. Subtotal decompression and biopsy was done by posterior laminectomy, followed by external beam radiotherapy. Signs and symptoms improved after the completion of radiotherapy but did not resolve completely. Death caused by respiratory failure occurred 3 months later.

Conclusions: This presentation of GBM of the cervical cord is rare; an intramedullary tumor should be considered when minor cervical trauma results in disproportionate neurologic deficit. To the best of our knowledge, this is the first reported case of spinal GBM with extensive pan-cervical involvement.

J Spinal Cord Med. November 2009;32(5):583–586

Key Words: Tetraparesis; Intramedullary tumor; Glioblastoma multiforme; Spinal cord, cervical; Spine; Whiplash injury

INTRODUCTION

Glioblastoma multiforme (GBM) of the spine is rare, accounting for only 1.5% of all spinal cord tumors and 1% to 5% of all GBM cases (1). Whereas supratentorial GBM is common in middle-aged and elderly populations, the spinal variety is mostly seen during the second and third decades and shows a predilection for the thoracic region (2). However, although there are case reports of segmental GBM of the cervical cord (3–5), pan-cervical involvement extending from the lower medulla to the upper thoracic cord is exceedingly rare.

CASE REPORT

History and Examination

A 21-year-old man was admitted with a history of neck pain with mild weakness in all 4 limbs for the past 6 weeks. The neck pain and weakness was exacerbated after a low-velocity road traffic collision. He was traveling

20 to 30 mph and wearing a seatbelt when his car was rear-ended, and his head was thrown violently backward. Soon after the incident, he developed pain and stiffness in the neck with increased weakness in all 4 limbs. He also noticed electric-like sensations in both arms, with pins and needles sensation all over the body.

On admission, he was lying on a spinal board with his cervical spine immobilized. Strength was 3/5 in all 4 limbs, with slightly increased tone, brisk reflexes, and bilateral upgoing plantar reflexes. A patchy loss of touch and pinprick was noted without any sensory level. Bladder and bowel functions were intact, with preservation of perianal sensations. Hoffmann reflexes were elicited bilaterally. The radiographs taken in the emergency room were unremarkable. A provisional diagnosis of cervical cord injury caused by trauma was made, and the patient was admitted for further evaluation. A subsequent magnetic resonance imaging (MRI) scan showed the presence of an intramedullary lesion causing fusiform expansion of the entire cervical cord. The lesion was iso- to hypointense in T1-weighted images (Figure 1a) and hyperintense in T2-weighted sequences (Figure 1b), with inhomogeneous enhancement on gadolinium administration (Figure 1c). Rostrally, the lesion extended

Please address correspondence to Pankaj Kumar Singh, MBBS, MS, Royal Hallamshire Hospital, Glossop Road, Sheffield, South Yorkshire S10 2JF, UK; p: 0044 7757 669 448; f: 0044 1142 713 314 (e-mail: we.publish@googlegmail.com).

Figure 1. (a) T1-weighted image showing an iso- to hypointense mass in the cervical cord. (b) Lesion is better demarcated in the T2-weighted sequence showing enhancement on gadolinium injection. Tumor extends from the cervico-medullary junction to the first thoracic vertebra with fusiform expansion of the cervical cord. (c) Postcontrast T1-weighted coronal image at the level of the second cervical vertebra. An intrinsic tumor can be clearly visualized occupying most of the cervical cord with compression of normal parenchyma to the periphery and showing an inhomogeneous enhancement on contrast injection.

to the lower medulla, whereas caudally it extended to the lower border of the first thoracic vertebra.

Operation

Because of the symptomatic cervical cord compression, an extensive posterior laminectomy was performed from C1 to C7 for tissue diagnosis and maximal decompression. A midline myelotomy was done under an operating microscope. The cord was showing signs of expansion and neovascularization (Figure 2). An infiltrating tumor involved the entire length of the cord with no clear plane of cleavage between the tumor and the normal cord. The Cavitron ultrasonic-surgical aspirator (CUSA) (CUSA® Excel™, Integra Radionics, Burlington, MA) was used to aid the dissection with continuous physiologic monitoring throughout the operation. In the light of these findings, fixation of the spine was deemed unnecessary.

Postoperative Course

The patient was weaned from the ventilator on the second postoperative day. Strength testing remained

unchanged on immediate postoperative examination (MRC grade 3/5); however, the pins-and-needles sensations over the arms showed slight improvement. A postoperative MRI scan (not available) showed adequate decompression of the cord with evidence of excision of almost 80% of the tumor. Gadolinium administration, however, showed the presence of some enhancing tissue, especially surrounding a central cavity created by debulking. Histology was typical for GBM WHO grade 4 (Figure 2).

The patient underwent 6 cycles of fractionated spinal radiotherapy with prophylactic whole brain radiation. Steroid therapy was maintained during and after radiotherapy. The patient showed good response to the treatment with improvement in muscle strength from 3/5 to 4+/5. He was discharged and scheduled for outpatient follow-up. The patient was readmitted 10 weeks later complaining of difficulty in breathing. The steroid regimen was changed from the oral to intravenous route, but he quickly developed severe respiratory insufficiency that ultimately required ventilatory support.

Figure 2. Intraoperative photograph showing expansion of cervical cord and overlying aberrant vessels.

The patient died on the 18th day of admission because of ongoing respiratory complications.

DISCUSSION

Although it is the most common primary intrinsic brain tumor, GBM is surprisingly rare in the spinal cord (1). When we compared the histomorphologic and biological features of these 2 entities, we found some interesting similarities and differences. Histomorphologically, spinal and cerebral GBMs are identical and both show strong immunohistochemistry for p53⁶, which predicts their similar biological behavior. However, there are some important differences: the rarity of GBM in the spine and the high rate of leptomeningeal involvement by spinal GBM (5). Histologically, neuroglial cells outnumber neurons 5 to 10 times and comprise about one half the total volume of brain, as well as in the spinal cord. The relative ratio of glial to neuronal cells is constant in brain and spinal cord. However, because of the difference in the masses of the 2 organs, the absolute number of cells (including the glial cells) in the spinal cord may be 1/10th of the brain. This may be a contributory factor for the relative rarity of spinal involvement. The high rate of leptomeningeal spread has been attributed to the relatively thin parenchyma in the spinal cord, and hence, the short distance to the subarachnoid space (5).

Like cerebral GBM, the exact etiology of spinal GBM remains uncertain; however, radiation exposure may play a role (5). It is difficult to establish a causal relationship between whiplash injury and the spinal GBM. However, a spinal tumor may interfere with movement of the cervical spine. This could contribute to cord damage associated with hyperextension and hyperflexion movements in whiplash injury (6) as seen in this case. The resulting cord damage may increase the risk for neurologic deficit.

Figure 3. Photomicrograph showing the typical findings of GBM: marked cellularity with hyperchromatism and pleomorphism (hematoxylin and eosin stains, 600 × 452).

Because of the likelihood of early spread and poor prognosis in spinal GBM, we agree with the majority of authors who recommend aggressive multimodal therapy (7). Available modalities include surgery, radiotherapy, chemotherapy, and immunotherapy. In this case, the pan-cervical involvement and the close proximity of the tumor to the phrenic nerve nucleus made surgery difficult and challenging. Because of extensive infiltration of the normal cord, it is practically impossible to remove intramedullary GBMs completely without causing significant morbidity (8,9). However, in cases where the neurologic deficits are already permanent and the tumor occupies the lower lumbar or sacral segments, total resection can be attempted, as described by Marchan et al (10), in the form of a corpectomy.

Because of the difficulties inherent in treating spinal GBMs, outcome is very poor and survival time after onset is 6 to 16 months (1,11,12). The most important factor in deciding the prognosis is histologic grade (9); therefore, every attempt should be made to obtain a tissue diagnosis. Intracranial dissemination through cerebrospinal fluid channels is a common feature in spinal GBM, making the prognosis even worse (8). Spinal and whole brain irradiation was given to this patient because increased mean survival has been noted after postoperative radiotherapy (12). In fact, whole brain radiotherapy is recommended in addition to focal spinal radiation because of the high rate of spread to the brain (8,13). Temozolomide, an oral chemotherapeutic agent, has been shown beneficial in reducing tumor size (5). Asano et al (8) found that intrathecal administration of β -interferon can be a useful adjunct to irradiation and surgery in managing the primary spinal GBM. Yamazaki et al (14) reported promising results in a young woman treated with combination therapy including immunotherapy using lymphokine-activated killer cells given intrathecally. More recently, corpectomy in a patient

with paraplegia has been described as a means of delaying intracranial dissemination in spinal GBMs (10). However, for the tumor with widespread cervical cord involvement, this approach is not an option.

CONCLUSION

GBM of the cervical cord with such clinical findings is a rare condition that should be included in the differential diagnosis of disproportionate neurologic deficit after minor trauma. Survival rates for spinal GBM are short, and the major cause of death is leptomeningeal seeding and/or cerebral metastasis. Cervical GBM may have an even poorer outcome because of early involvement of phrenic nerve nucleus (C4–C6) and vasomotor centers. Because of the propensity for early brain metastasis, prophylactic whole brain radiation should be included with cranial screening as part of routine follow-up. Aggressive multimodal treatment may result in prolonged survival.

REFERENCES

1. Andrews AA, Enriques L, Renaudin J, Tomiyasu U. Spinal intramedullary glioblastoma with intracranial seeding. *Arch Neurol*. 1978;35(4):244–245.
2. Caroli E, Salvati M, Ferranate L. Spinal glioblastoma with brain relapse in a child: clinical considerations. *Spinal Cord*. 2005;43(9):565–567.
3. Chida K, Konno H, Sahara M, Takase S. Meningeal seeding of spinal cord glioblastoma multiforme without any signs of myelopathy [in Japanese]. *Rinsho Shinkeigaku*. 1995;35(11):1235–1240.
4. Russel DS, Rubinstein LJ. *Pathology of Tumors of the Nervous System*. 1st ed. London: Edward Arnold; 1959.
5. Yeung YF, Wong GK, Zhu XL, Ma BB, Hk NG, Poon WS. Radiation induced spinal glioblastoma multiforme. *Acta Oncologica*. 2006;45(1):87–90.
6. Ramamuthi B, Rao SB. Tumours of the spinal cord and the cauda equine. In: Ramamurthi B, Tandon PN, eds. *Textbook of Neurosurgery*. 2nd ed. New Delhi: BI Churchill Livingstone; 2001:708.
7. Al-Mefty O, Al-Rodhan NRF, Phillips RL. Factors affecting survival of children with malignant gliomas. *Neurosurgery*. 1987;20(3):416–420.
8. Asano N, Kitamura K, Seo Y, Mukai K, Soga T, Hondo H, Matsumoto K. Spinal cord glioblastoma multiforme with intracranial dissemination. Case report. *Neurol Med Chir (Tokyo)*. 1990;30(7):489–494.
9. Kopelson G, Linggood RM. Intramedullary spinal cord astrocytoma versus glioblastoma. The prognostic importance of histologic grade. *Cancer*. 1982;50(4):732–735.
10. Marchan EM, Sekula RF Jr, Jannetta PJ, Quigley MR. Long term survival enhanced by corpectomy in a patient with a spinal glioblastoma multiforme and paraplegia. Case report. *J Neurosurg Spine*. 2007;7(6):656–659.
11. Chigasaki H. Surgical treatment of malignant spinal tumors [in Japanese]. *Shinkei Shinpo*. 1978;20:90–99.
12. Takara E, Ide M, Yamamoto M, Imanaga H, Jimbo M, Imai M. A case of the intracranial and spinal dissemination of primary spinal glioma [in Japanese]. *No Shinkei Geka*. 1985;13:301–305.
13. Sagerman RH, Bagshow MA, Hanberg J. Considerations in the treatment of ependymoma. *Radiology*. 1979;84:401–408.
14. Yamazaki M, Ikota T, Okhata N, et al. A case of spinal cord glioblastoma multiforme [in Japanese]. *No Shinkei Geka*. 1992;20(1):85–89.