[Case Report]

Cervical Intramedullary Glioblastoma: A Report of a Long-Term Survival Case and a Review of the Literature

Taiki MATSUMOTO, Eiichirou URASAKI, Yoshiteru SOEJIMA, Yoshiteru NAKANO,
Akira YOKOTA and Shigeru NISHIZAWA

*Department of Neurosurgery, University of Occupational and Environmental Health, Japan.
Yahatanishi-ku, Kitakyushu 807-8555, Japan*

Abstract : Spinal intramedullary glioblastoma has rarely been reported. Among reported cases, the most characteristic features are rapid progression of the disease and very poor prognosis. The mean survival period is 12 months. We report a patient having cervical intramedullary glioblastoma with long-term survival (26 months after the onset). A 21-year-old man presented with weakness in bilateral hands, and the symptoms progressed rapidly. Magnetic resonance imaging (MRI) showed cervical intramedullary tumor. He underwent surgery of debulking of the cervical tumor, fractionated stereotactic irradiation, and repeated chemotherapy using nimustine hydrochloride (ACNU). Although dissemination of the tumor in the intracranial space deteriorated the patient, he survived for 26 months after the initial onset. It has been reported that no treatment is effective for this disease. However, it is also true that some patients respond well to the intensive treatment. It can be emphasized that scheduled intensive treatment for the disease under earlier histological confirmation should be performed.

Key words : cervical spinal cord, glioblastoma, differential diagnosis, stereotactic radiation, prognosis.

(Received 17 May 2008, accepted 11 August 2008)

Introduction

Spinal intramedullary glioblastoma is very rarely encountered, and the incidence of this pathology has been reported as 1.5% of all spinal tumors [4–7,12]. Among reported cases, the most characteristic point of spinal intramedullary glioblastoma is rapid progression even with intensive treatments, and the prognosis of the patients is very poor compared with cerebral glioblastoma [4,13]. Long-term survival of the patients with intramedullary glioblastoma can hardly be expected.

We present a patient with cervical intramedullary glioblastoma who underwent intensive treatments and survived for 26 months after initial presentation of the symptoms. Hereby, we report the case and discuss our treatment strategies in comparison with those in the literature.

Case presentation

A 21-year-old man noticed muscle weakness and clumsy finger movements in his right hand, and a numb feeling in the left hand in September, 2004. The patient also felt severe nuchal pain. He visited the Department of Neurology on October 2, 2004, and was admitted for further work-up. MRI on admission showed diffuse swelling of the cervical cord in a T1-weighted image, and intramedullary high signal in a T2-weighted image, although no obvious contrast enhance area was detected by intravenous administration of gadolinium (Fig. 1). No intracranial abnormal findings were detected in the MRI study. As those findings suggested spinal inflammatory disease, he received repeated steroid pulse treatments. However, his neurological condition deteriorated.

Fig.1. MRI on admission showing diffuse swelling of the cervical cord in enhanced T1-weighted image (A) and intramedullary high signal in T2-weighted image (B).

The patient was examined by MRI study again. Compared with the initial study, the repeated MRI showed further progressive swelling of the cervical spinal cord and ring-like enhancement from the C3 to C5 levels (Fig. 2). At the end of October in 2004, neurological examinations disclosed complete right hemiplegia, urinary incontinence and hypesthesia to pain below the C4 level. Soon after, the patient became tetraparetic. In addition, the respiration of the patient became irregular, and he was transferred to our department.

Fig.2. Preoperative enhanced cervical MRI with gadolinium.

A mass was located from the C3 to C5 levels, and showed irregular ring-like enhancement compared with the studies on admission.

As the neurological conditions of the patient were rapidly exacerbated, he underwent emergency surgery of subtotal removal of the lesion at the C4 and C5 level, C1 laminectomy and laminoplasty from the C2 to C5. The cervical intramedullary lesion was dark reddish and vascular-rich. The margin between the lesion and the normal cervical spinal cord was unclear. The surgical specimens were histologically composed of hypercellular glial cells with pleomorphism, many mitosis, necrosis and vascular endothelial proliferation. The cells were positive by glial fibrillary acidic protein (GFAP) staining and immunohistochemical staining for the proliferation-associated antigen Ki-67 (MIB-1) index was approximately 60% (Fig. 3). Those histological examinations were compatible with glioblastoma. As no intracranial lesion was detected, the lesion was diagnosed as primary spinal glioblastoma in the cervical cord.

After surgery, the tetraparetic condition still remained, and artificial respiratory support was mandatory, although a slight improvement of neck pain was obtained. Postoperatively, the patient received stereotactic radiotherapy up to 50 Gy with 25 fractionations from the C1 to C6

Fig.3. Photomicrographs of a surgical specimen of primary lesion showing pleomorphism, mitosis, necrosis and endothelial proliferation in H & E stain ($\times 40$, A). The MIB-1 index was approximately 60% ($\times 400$, B).

levels. Two months after surgery, his respiratory condition became better, and he could breathe by himself without any artificial respiratory support. Three months after surgery, movement of bilateral hands also improved, and he was able to grasp. At this moment, the patient received chemotherapy using nimustine hydrochloride (ACNU) for 4 months, and active physical rehabilitation allowed him to drive an electric wheelchair.

Despite general improvement after the treatment, his sphincter function deteriorated. Follow-up MRI revealed dissemination of the tumor at the Th12 and L1 levels. Irradiation to the total spinal axis except for the cervical region up to 30 Gy with 15 fractionations was performed. Even with the extensive treatments, the neurological conditions of the patient deteriorated, and consciousness disturbance appeared 22 months after the initial presentation of the symptoms. An MRI study revealed the spread of the disease throughout the whole spinal cord and the brain stem (Fig. 4). The patient died 26 months after the onset of the disease.

Fig.4. MRI when the patient showed consciousness disturbance.

They showed marked swelling of the cervical spinal cord. Diffuse dissemination of the disease in the cervical cord (A: postcontrast T1, B: T2), and metastases to the brain stem and skull base with compression to pons (C: postcontrast T1) were also observed.

Discussion

When the patients present with myelopathy due to an intramedullary lesion, especially when symptoms progress rapidly, the possibility of glioblastoma in the spinal cord should be considered. According to the literature, it is a very rare lesion, and the incidence is 1.5% of all spinal tumors [4–7,12]. However, the most characteristic point of spinal intramedullary glioblastoma is a significantly rapid clinical course, and the prognosis of the patients is very poor [4,13]. In this sense, it is extremely crucial for the patients to make a correct diagnosis and to start intensive treatments as soon as possible.

In the literature, it has been reported that spinal intramedullary glioblastoma most frequently affect the cervical and thoracic spinal cord [2,13]. Some lesions were found in the conus medullaris in children [3,10,11,14]. Clinical manifestations due to spinal intramedullary glioblastoma are not specific compared with other intramedullary lesions, such as other intramedullary tumors, or inflammatory disease based on various autoimmune diseases, i.e., progressive myelopathy [1,4]. The MRI findings of spinal intramedullary glioblastoma are not specific either. In the earlier stage, such findings are swelling of the spinal cord in T1/T2 images and T2-high intramedullary signal [5]. It is unexceptional that the lesion is not enhanced by intravenous administration of gadolinium, and it shows ring-like enhancement as it progresses. These findings are compatible with the present case.

As the earliest diagnosis is required, surgical exploration for the lesion is inevitable once spinal intramedullary glioblastoma is suspected. Biopsy associated with decompressive laminoplasty/laminectomy should be performed. The benefits of debulking of the tumor or extensive removal of the tumor have been controversial. Those procedures might postoperatively lead to severer neurological deficits compared with the preoperative state, and recovery from the serious myelopathy state can not be expected. It has been reported that obtaining a surgical specimen for the correct diagnosis as intramedullary glioblastoma is enough [4–7,12]. In our presented case, the patient underwent decompressive laminoplasty/laminectomy and debulking of the tumor, because the center of the tumor seemed to be more necrotic and it was expected that the spinal cord would not be further damaged by the surgical procedure.

Once a diagnosis of spinal intramedullary glioblastoma is obtained, irradiation followed by chemotherapy should be done intensively. Obvious evidence to compare the benefits between conventional irradiation to the whole spinal axis and fractionated stereotactic radiation method has not been clear. Ciappetta [4] reported that radiotherapy with 40 Gy to the entire spinal axis lengthened survival by 18 months compared with cases without irradiation. In contrast, Asano [2] reported a case of primary spinal cord glioblastoma with focal irradiation, and the patient survived for 26 months, which was almost as long as the present case. We selected fractionated stereotactic radiation treatment, because the lesion might have easily metastasized to the other levels of the spinal cord. Under these situations, fractionated radiation treatment can be repeated to such lesions. Moreover, the period of the treatment should be shortened under a very poor prognostic condition in the viewpoint of the patient's quality of life.

Following the radiation treatment, chemotherapy can be selected, although the therapeutic

efficacy of any chemotherapy has not been established [1 – 14]. We selected chemotherapy using ACNU based on our own experience in the chemotherapy for intracranial glioblastoma. It can be used with little adverse effect, which is also beneficial for a poor prognostic patient.

The poorest prognostic sign of this disease is dissemination not only into the total spinal canal but also into the intracranial subarachnoid space [2 – 4, 9,10,13,14]. In our reported patient, intracranial seeding induced him into the final stage. Consciousness disturbance, cranial nerve palsy or diabetes insipidus due to impaired hypothalamic function can be considered as the terminal stage of the patient.

In conclusion, total intensive treatment induced long-term survival for the patient. The survival period up to 26 months after the initial neurological onset in patients with spinal intramedullary glioblastoma is the longest that we could find in a search of the literature. It is clear that the progression of the disease is very rapid and the prognosis is very poor according to the literature. However, some patients like our presented patient might respond well to intensive therapy, and a better prognosis can be expected. In this viewpoint, such aggressive treatment for patients with spinal intramedullary glioblastoma should be selected.

In the future, chemotherapy using temozoromide, which is indicated for intracranial glioblastoma treatment, might be usable and beneficial even for spinal intramedullary glioblastoma.

References

1. Alatakis S, Malham GM & Thien C (2001): Spinal leptomeningeal metastasis from cerebral glioblastoma multiforme presenting with radicular pain. Case report and literature review. *Surg Neurol* 56: 33 – 38
2. Asano N, Kitamura K, Seo Y, Mukai K, Soga T, Hondo H & Matsumoto K (1990): Spinal cord glioblastoma multiforme with intracranial dissemination – case report. *Neurol Med Chir (Tokyo)* 30: 489 – 494
3. Caroli E, Salvati M & Ferrante L (2005): Spinal glioblastoma with brain relapse in a child: clinical considerations. *Spinal Cord* 43: 565 – 567
4. Ciappetta P, Salvati M, Capoccia G, Artico M, Raco A & Fortuna A (1991): Spinal glioblastomas: report of seven cases and review of the literature. *Neurosurgery* 28: 302 – 306
5. Cohen AR, Wisoff JH, Allen JC & Epstein F (1989): Malignant astrocytomas of the spinal cord. *J Neurosurg* 70: 50 – 54
6. Constantini S, Miller DC, Allen JC, Rorke LB, Freed D & Epstein FJ (2000): Radical excision of intramedullary spinal cord tumors: surgical morbidity and long-term follow up evaluation in 164 children and young adults. *J Neurosurg (Spine)* 93: 183 – 193
7. Helseth A & Mork SJ (1989): Primary intraspinal neoplasms in Norway, 1955 to 1986: a population-based survey of 467 patients. *J Neurosurg* 71: 842 – 845
8. Hoshimaru M (2001): Diagnosis and microsurgical treatment of intramedullary spinal cord tumors. *No Shinkei Geka* 29: 207 – 214
9. Kawashima A, Sasajima T, Sugawara T, Takahashi M, Suzuki A, Higashiyama N, Kinouchi

- H & Mizoi K (2004): Unusual MR appearance of intracranial dissemination from cervical glioblastoma. *No Shinkei Geka* 32: 937 – 944
10. Medhkour A & 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 – 583
 11. Mendonça R, Lima LG, Fernandes LN, Ferreira NP & Napoli G (2005): Primary conus medullaris glioblastoma: case report. *Arq Neuropsiquiatr* 63: 539 – 542
 12. Russell DS & Rubinstein LJ (1989): Glioblastoma multiforme. Tumours of central neuroepithelial origin. *Pathology of Tumors of the Nervous System*. Edward Arnold, London pp 219 – 247
 13. Santi M, Mena H, Wong K, Koeller K, Olsen C & Rushing EJ (2003): Spinal cord malignant astrocytomas: clinicopathologic features in 36 cases. *Cancer* 98: 554 – 561
 14. 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. *Am J Neuroradiol* 26: 2157 – 2160
-

長期生存が得られた頸髄膠芽腫の一例

松本 大樹, 浦崎 永一郎, 副島 慶輝, 中野 良昭, 横田 晃, 西澤 茂

産業医科大学 医学部 脳神経外科学講座

要 旨： 頸髄を原発巣とする膠芽腫は非常にまれな疾患であり，脊髄腫瘍に占める割合は約 1.5%とされ，その臨床的特徴は脳に発生する膠芽腫と比較し，急速進行性，予後不良であり，平均生存期間は12 ヶ月と報告され，髄腔内播種や水頭症を容易に合併することが知られている．そのため過去の報告では手術に加えて全脊髄照射による放射線治療が主体となっていた．今回われわれは，21 歳男性の頸髄膠芽腫に対し，手術，放射線治療，化学療法による積極的な集学的治療を施行し，発症から26 ヶ月間の長期生存が得られた症例を経験したが，その主たる要因は初回部分照射と再発時の追加照射による局所コントロールにより髄腔内播種の発生を遅延させたことであると考えられた．

キーワード： 頸髄, 膠芽腫, 鑑別診断, 定位放射線治療, 予後.

J UOEH (産業医大誌) 30 (4) : 413 - 420 (2008)