

THE ESSENTIAL ROLE OF TOTAL NEURO-AXIS SURVEY IN A MEDULLOBLASTOMA PATIENT WITH POSTOPERATIVE QUADRIPLÉGIA: A CASE REPORT

Liang Cheng Chen¹, Shih-Kai Hung^{1,2}, Moon-Sing Lee^{1,2}, Wen-Yen Chiou^{1,2,3}, Bing-Jie Shen¹,
Wei-Ta Tsai¹, Yi-An Lin¹, Hui-Ling Hsieh¹, Po-Hao Lin¹, Hsin-Yu Kuo¹, Hon-Yi Lin^{1,2,4*}

*Departments of Radiation Oncology¹, Dalin Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation
School of Medicine², Tzu Chi University, Hualien*

Department of Public Health³, College of Medicine, National Cheng Kung University

Institute of Molecular Biology⁴, National Chung Cheng University, Min-Hsiung, Chia-Yi

Medulloblastoma, mainly arising from the posterior cranial fossa, accounts for 15%-20% of pediatric central nerve system (CNS) tumors. Surgical resection is the major treatment modality used to manage medulloblastoma. Clinically, very few patients develop quadriplegia after surgery. We report a case of medulloblastoma patient developing quadriplegia postoperatively which was initially thought to be secondary to surgery but was later found to due to leptomeningeal carcinomatosis of the cervical spine. Postoperative radiotherapy significantly improved the patient's symptoms. The positive outcome in this patient is a reminder of the pivotal role radiotherapy plays in the management of cancer-related neurologic dysfunction in medulloblastoma patients.

[Therapeut Radiol Oncol 2016; 23(2): 137-144] DOI: 10.6316/TRO/201623(2)137

Key words: Medulloblastoma, Quadriplegia, Radiotherapy

INTRODUCTION

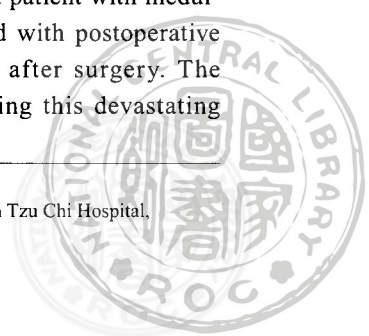
Medulloblastoma, arising primarily from the posterior cranial fossa, accounts for 15%-20% of pediatric central nerve system (CNS) tumors and occurs in children with a median age of 6 years [11]. Clinically, medulloblastoma can present with both intra- and extra-axial neurological involvement and/or metastasis including supratentorial (14.6%), intraspinal (12.5%), and systemic involvement

(9.7%) [33]. Surgical resection is the major treatment modality. Very few patients sustain postoperative quadriplegia after surgery [14]. Many etiologies have been reported to contribute to postoperative quadriplegia, such as infection [9], infarction [3], and surgical positioning [1, 6, 13, 18, 20, 23].

We report a case of a patient with medulloblastoma who presented with postoperative quadriplegia one month after surgery. The pathophysiology underlying this devastating

Received: 2015, 11, 10. Accepted: 2016, 1, 19.

Address reprint request to: Dr. Hon-Yi Lin., Address: Department of Radiation Oncology, Buddhist Dalin Tzu Chi Hospital,
No. 2, Min-Sheng Road, Dalin, Chiayi, Taiwan, R.O.C.



complication is discussed and the clinical effect of radiotherapy in restoring neurologic function is highlighted.

CASE REPORT

An 8-year-old boy was admitted to our hospital with symptoms of headache, vomiting, gait disturbance, and personality change which developed over a one month period. His neurological exam showed mildly increased deep tendon reflexes of the right knee. Gait disturbance with left-sided deviation was also observed. On the other hand, Kernig's and Brudzinski's signs were negative. Brain MRI disclosed a large mass measuring 6 cm x 4.5 cm x 4 cm occupying the fourth ventricle and protruding down through the foramen magnum. Marked hydrocephalus and perifocal interstitial edema were also observed. Spinal MRI reported no definite lesions (Fig. 1).

After review of the patient's neuro-axis survey and discussion with the family, his parents requested a transfer to another hospital for further management, where craniotomy with tumor removal was carried out via a prone

surgical position. Pathology reported medulloblastoma, WHO grade 4. After craniotomy, however, he developed hydrocephalus and a CNS infection with methicillin-resistant staphylococcus aureus (MRSA). Therefore, a ventricular-peritoneal (VP) shunt was inserted, and antibiotics were administered. Cytology from the cerebrospinal fluid was negative for malignant cells. Postoperative complications gradually improved, however, one month after craniotomy, quadriplegia developed. Muscle power score 1 was observed in all four extremities. Therefore, the patient was returned to our hospital for further management.

At our hospital, postoperative brain MRI showed no evidence of hemorrhage, stroke, or recurrent tumor in the posterior fossa; instead, only postoperative changes within the fourth ventricle were demonstrated (i.e., periventricular increased signal on the T2-flare sequence; Fig. 2). At our CNS tumor board combined conference, most physicians recommended that no radiotherapy be given. Two reasons supported their recommendation: (1) as already mentioned, postoperative brain MRI reported no evidence of intracranial residual tumor;

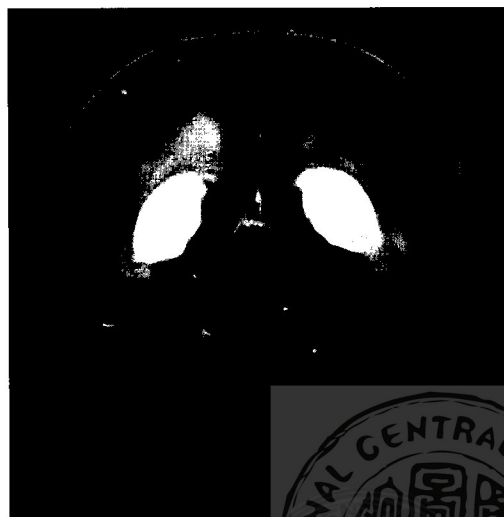
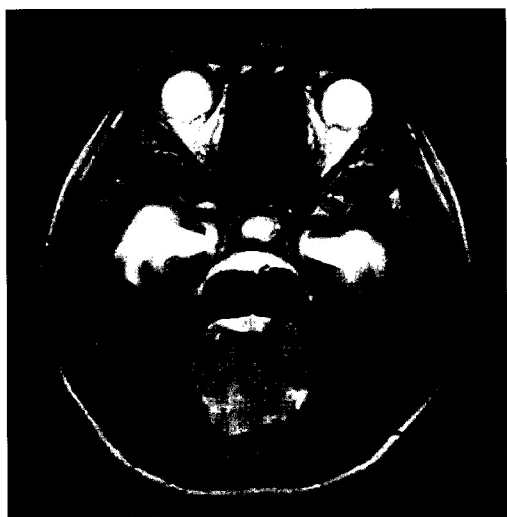


Fig 1. Preoperative T2-weighted, fast recovery and fast spin-echo MRI images show a large, lobulated mass lesion within the fourth ventricle, measuring approximately 60 mm x 45 mm x 40 mm, with heterogeneous enhancement. Note that the mass extends downward through the foramen magnum.

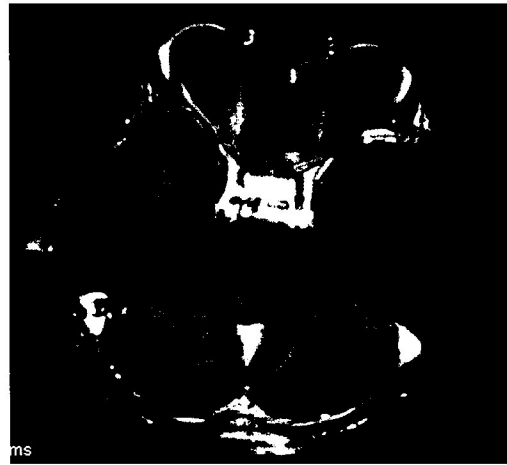
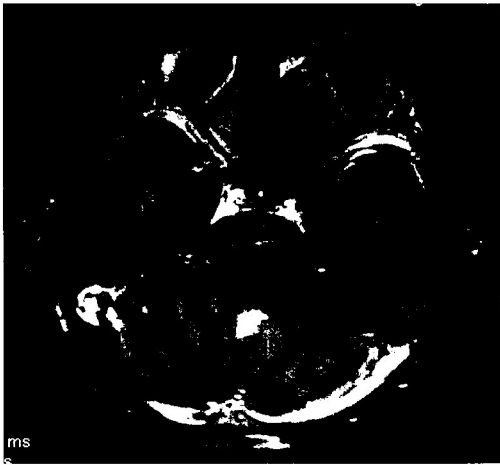


Fig 2. Postoperative T1-weighted brain MRI images with gadolinium enhancement show postoperative changes within the fourth ventricle (i.e., intense periventricular increased signal). However, there is no evidence of recurrent tumor within the posterior fossa.

and (2) as a result, the observed postoperative quadriplegia was highly suspicious for a surgery-related morbidity, which would not be reversed by radiotherapy. Thus, postoperative best supportive care was suggested as management for this patient.

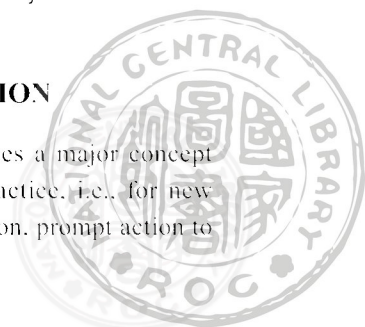
However, after detailed imaging review, mild enhancement over the peri-C6 spinal cord region was observed, and tumor seeding could not be totally excluded (Fig. 3). In addition, several lines of evidence supported postoperative adjuvant RT to prolong both progression-free and overall survival in standard-risk medulloblastoma patients [5, 11, 17, 25, 30, 33]. Thus, after discussion with the patient's families, we recommended postoperative radiotherapy for the patient. Volumetric-Modulated Arc Therapy (VMAT), i.e., Rapid Arc[®], was used for radiation delivery, with the following dose levels: 30.6 Gy in 17 fractions to the whole brain; 54 Gy in 30 fractions to the posterior fossa; and, 19.8 Gy in 11 fractions to the whole spine. Two months after irradiation, the patient's quadriplegia significantly improved and muscle power recovered from score 1 up to 4+ in all four limbs.



Fig 3. Spine MRI shows no definite spinal mass. However, after a detailed imaging review, a lesion with mildly increased signal was noticed over the peri-C6 spinal cord region on T1-weighted images with gadolinium enhancement and leptomeningeal carcinomatosis could not be totally excluded.

DISCUSSION

This case demonstrates a major concept in oncological clinical practice, i.e., for new onset neurologic dysfunction, prompt action to



seek potentially reversible etiologies is crucial. For patients with cancer-associated neurologic dysfunction, prompt radiotherapy is highly recommended to ensure full functional restoration [28].

Clinically, postoperative quadriplegia may result from many etiologies [3, 4, 8, 9, 19, 22, 24, 26, 29, 31, 32] such as hypokalemia [22], drug overdose [31], streptococcal vertebral osteomyelitis [9], stroke [3], hemorrhage from tumor [12, 20], and surgical positioning [1, 6, 13, 18, 20, 23]. In our case, most of the above mentioned etiologies were excluded after extensive history taking, physical examination, and laboratory studies. Although MRSA was identified in the patient's blood stream, no other specific sign supported the diagnosis of streptococcal osteomyelitis. In addition, postoperative brain MRI further excluded stroke, hemorrhage, and residual intracranial medulloblastoma that might induce quadriplegia.

At the CNS tumor board, most team members suggested that the observed postoperative quadriplegia could be an irreversible surgery-related morbidity, which could not be rescued through the use of radiotherapy. However, there were two points against this suggestion. First, cervical quadriplegia is a rare postoperative surgically-related complication in brain tumor patients. In addition, in the literature, it is usually associated with a sitting position or extended-neck surgical position, rather than a prone position (as in our case) [1, 6, 13, 18, 20, 23]. Second, leptomeningeal spread is sometimes found in medulloblastoma. After detailed MRI imaging review, we observed a subtle high-signal lesion adjacent to the C6 cervical spinal cord on the T2-flare sequence, which could not be totally excluded as a leptomeningeal involvement from medulloblastoma. Based on the imaging finding, radiotherapy appeared reasonable and suitable, especially when cancer treatment outcomes were considered [5, 11, 17, 25, 30, 33].

In addition to the surgical position, several other factors have been associated with postoperative cervical quadriplegia, including excessive spinal cord traction, canal stenosis, systemic arterial hypotension, brain tumor extending down through the foramen magnum with resulting cord swelling (especially after surgical manipulation), and tumor bleeding from the surgical bed into the spinal canal [12, 20]. However, all of these etiologies induce primarily acute cervical quadriplegia during or immediately after surgery. On the other hand, our case demonstrated delayed quadriplegia one month after surgery. This clinical picture was difficult to explain based on these etiologies.

Leptomeningeal spread has been described as a major metastatic pattern in many pediatric brain tumors such as supratentorial primitive neuroectodermal tumor (up to 40%), atypical teratoid/rhabdoid tumor (25% - 33%), ependymoma (5% - 10%), pineoblastoma (up to 50%), and medulloblastoma (30% - 35% at diagnosis) [11]. In these tumors, surgical procedures have been observed to correlate with an increased rate of CSF cancer spread [2, 7, 10, 15]. Risk factors for surgery-associated leptomeningeal tumor seeding include tumor location (adjacent to a CSF pathway or exposure to the CSF space), tumor-resection method (piecemeal or en bloc), and the use of the Cavitron Ultrasonic Surgical Aspirator (CUSA) [2]. In our case, the primary bulky tumor was located within the posterior fossa and the fourth ventricle was involved at presentation. As a result, leptomeningeal metastasis was reasonably high on our list of possible causes. In clinical practice, a new neurological pathological sign should be excluded as a cancer-associated neuropathy.

For medulloblastoma patients, leptomeningeal metastasis is an independent prognostic factor [11, 27]. In terms of timing, two types of leptomeningeal metastasis have been reported including early and late drop metastasis.

Generally, “early drop metastasis” is defined as a drop metastasis found on preoperative or immediate postoperative (i.e., less than 1 month) MRI images. On the other hand, “late drop metastasis” is defined as new radiologic evidence of leptomeningeal involvement found one month after CNS surgery. Clinically, patients with “late drop metastasis” showed a significantly shorter survival when compared with those patients with “early drop metastasis” [15]. Late drop leptomeningeal metastasis reflects a relative resistance to adjuvant therapy and is considered a poor prognostic sign [15].

In patients with delayed quadriplegia, late drop leptomeningeal metastasis should be considered, especially when the tumor location involves (or is adjacent to) the bridge apertures of the CSF circulation system, such as foramina of Luschka, the foramen of Magendie, or the foramen magnum. In our case, the patient’s brain tumor extended downward through the foramen magnum, consistent with a high risk for late drop leptomeningeal metastasis. Although delayed quadriplegia developed, clinical symptoms were significantly improved after radiotherapy, reminding us that radiotherapy is essential for restoring cancer-associated pathological neuropathy [28].

This case had one major limitation in terms of cancer management. Although we informed the patient’s families that chemotherapy was an essential treatment modality in managing medulloblastoma [16, 17, 21], they still refused postoperative chemotherapy. Lacking co-treatment with postoperative chemotherapy might ultimately compromise the patient’s clinical outcome.

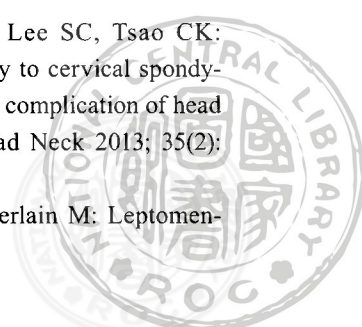
CONCLUSION

Medulloblastoma patients with leptomeningeal metastasis involving the cervical spinal

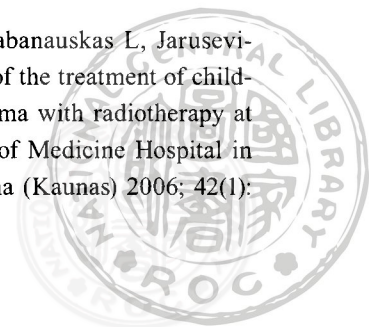
cord may incur rapid clinical deterioration and cardiorespiratory instability. Thus, in patients with unexplained postoperative quadriplegia, cancer-associated cervical quadriplegia should be ruled out aggressively. Prompt action, by delivering RT to the tumor-involved sites, is critical for restoring neurological function.

REFERENCES

1. Agarwal J, Tandon MS, Singh D, Ganjoo P: Quadriplegia in a child following adenotonsillectomy. *Anaesthesia* 2013; 68(5): 523-526.
2. Ahn JH, Lee SH, Kim S, et al.: Risk for leptomeningeal seeding after resection for brain metastases: implication of tumor location with mode of resection. *J Neurosurg* 2012; 116(5): 984-993.
3. Amoudi AS, Merdad AA, Makhdoom AQ, Jamjoom RA: Development of stroke-induced quadriplegia after endovascular repair of blunt aortic injury pseudoaneurysm. *Neurosciences (Riyadh)* 2015; 20(1): 52-54.
4. Beavers CT, Parker JJ, Flinchum DA, Weakley-Jones BA, Jortani SA: Pesticide-induced quadriplegia in a 55-year-old woman. *Am J Forensic Med Pathol* 2014; 35(4): 239-241.
5. Carrie C, Muracciole X, Gomez F, et al.: Conformal radiotherapy, reduced boost volume, hyperfractionated radiotherapy, and online quality control in standard-risk medulloblastoma without chemotherapy: results of the French M-SFOP 98 protocol. *Int J Radiat Oncol Biol Phys* 2005; 63(3): 711-716.
6. Chen WF, Kang CJ, Lee SC, Tsao CK: Quadriplegia secondary to cervical spondylotic myelopathy—a rare complication of head and neck surgery. *Head Neck* 2013; 35(2): E49-51.
7. Chowdhary S, Chamberlain M: Leptomen-



- ingeal metastases: current concepts and management guidelines. *J Natl Compr Canc Netw* 2005; 3(5): 693-703.
8. Couillard P, Wijdicks EF: Flaccid quadriplegia due to thyrotoxic myopathy. *Neurocrit Care* 2014; 20(2): 296-297.
 9. Furitsch M, Trager K, van der Linden M, Spellerberg B: Group A streptococcal vertebral osteomyelitis presenting with acute quadriplegia. *Infection* 2011; 39(4): 389-391.
 10. Grabb PA, Albright AL, Pang D: Dissemination of supratentorial malignant gliomas via the cerebrospinal fluid in children. *Neurosurgery* 1992; 30(1): 64-71.
 11. Halperin EC, Brady LW, Wazer DE, Perez CA: *Perez and Brady's principles and practice of radiation oncology* 2013. Philadelphia, PA 19103 USA.
 12. Hicdonmez T, Kilincer C, Hamamcioglu MK, Cobanoglu S: Paraplegia due to spinal subdural hematoma as a complication of posterior fossa surgery: Case report and review of the literature. *Clin Neurol Neurosurg* 2006; 108(6): 590-594.
 13. Hitselberger WE, House WF: A warning regarding the sitting position for acoustic tumor surgery. *Arch Otolaryngol* 1980; 106(2): 69.
 14. Hongo K, Nakagawa H, Tamai K, Kobayashi S: Paraplegia following surgery for medulloblastoma in the posterior fossa. *J Clin Neurosci* 1999; 6(6): 522-524.
 15. Hsieh PC, Wu CT, Lin KL, et al.: The clinical experience of medulloblastoma treatment and the significance of time sequence for development of leptomeningeal metastasis. *Childs Nerv Syst* 2008; 24(12): 1463-1467.
 16. Jakacki RI, Burger PC, Zhou T, et al.: Outcome of children with metastatic medulloblastoma treated with carboplatin during craniospinal radiotherapy: a Children's Oncology Group Phase I/II study. *J Clin Oncol* 2012; 30(21): 2648-2653.
 17. Lannering B, Rutkowski S, Doz F, et al.: Hyperfractionated versus conventional radiotherapy followed by chemotherapy in standard-risk medulloblastoma: results from the randomized multicenter HIT-SIOP PNET 4 trial. *J Clin Oncol* 2012; 30(26): 3187-3193.
 18. Li CC, Yie JC, Lai CH, Hung MH: Quadriplegia after off-pump coronary artery bypass surgery: look before you place the neck in an extended position. *J Cardiothorac Vasc Anesth* 2013; 27(2): e16-17.
 19. Martindale JL, Hwang JQ, Nadel ES, Brown DF: Acute atraumatic quadriplegia. *J Emerg Med* 2012; 43(2): 335-338.
 20. Martinez-Lage JF, Almagro MJ, Izura V, Serrano C, Ruiz-Espejo AM, Sanchez-Del-Rincon I: Cervical spinal cord infarction after posterior fossa surgery: a case-based update. *Childs Nerv Syst* 2009; 25(12): 1541-1546.
 21. Massimino M, Cefalo G, Riva D, et al.: Long-term results of combined preradiation chemotherapy and age-tailored radiotherapy doses for childhood medulloblastoma. *J Neurooncol* 2012; 108(1): 163-171.
 22. Mirijello A, Rinninella E, De Leva F, et al.: Hypokalemia-induced pseudoischemic electrocardiographic changes and quadriplegia. *Am J Emerg Med* 2014; 32(3): 286 e281-284.
 23. Mostafa RM, Mejadi A: Quadriplegia after interscalene block for shoulder surgery in sitting position. *Br J Anaesth* 2013; 111(5): 846-847.
 24. Raeymaeckers S, Nieboer K, De Mey J: Progressive quadriplegia resulting from septic facet joint arthritis. *JBR-BTR* 2015; 98(1): 58.
 25. Rutkauskiene G, Labanauskas L, Jarusevicius L: The results of the treatment of childhood medulloblastoma with radiotherapy at Kaunas University of Medicine Hospital in 1994-2000. *Medicina (Kaunas)* 2006; 42(1): 22-32.



26. Safadi W, Srour S, Waksman I: Infarction of the cervical spinal cord in a 20-year-old healthy man resulting in complete quadriplegia. *BMJ Case Rep* 2013;2013. pii: bcr2013009359.
27. Salunke P, Gupta K, Kovai P, Sura S, Aggarwal A: Preoperative diffuse leptomeningeal spread in a medulloblastoma: Paraplegia following surgery for posterior fossa and call for newer management protocols. *J Pediatr Neurosci* 2011; 6(2): 152-154.
28. Shapiro RH, Chang AL: Urgent radiotherapy is effective in the treatment of metastatic medulloblastoma causing symptomatic brainstem edema. *Pediatr Blood Cancer* 2011; 57(6): 1077-1080.
29. Taub AL, Keune JD, Kodner IJ, Schwarze ML: Respecting autonomy in the setting of acute traumatic quadriplegia. *Surgery* 2014; 155(2): 355-360.
30. Taylor RE: United Kingdom Children's Cancer Study Group (UKCCSG) radiotherapy and brain tumour groups: medulloblastoma/PNET and craniospinal radiotherapy (CSRT): report of a workshop held in Leeds, 30 June 1999. *Clin Oncol (R Coll Radiol)* 2001; 13(1): 58-64.
31. Wang TS, Grunch BH, Moreno JR, Bagley CA, Gottfried ON: Drug overdose resulting in quadriplegia. *Eur Spine J* 2012; 21 Suppl 4: S521-524.
32. Wang YC, Huang SY, Lin HT, Hu JS, Chan KH, Tsou MY: Quadriplegia after parathyroidectomy in a hemodialysis patient. *Acta Anaesthesiol Taiwan* 2011; 49(1): 32-34.
33. Winn HR, Youmans JR. ed. *Youmans neurological surgery*. Philadelphia, Pa. W. B. Saunders. 2004.

詳細神經軸評估於髓母細胞瘤術後四肢癱瘓病人之重要性：一個病例報告

陳良政¹ 洪世凱^{1,2} 李文星^{1,2} 邱文彥^{1,2,3} 沈秉杰¹ 蔡維達¹
林怡安¹ 謝慧苓¹ 林柏豪¹ 郭心語¹ 林宏益^{1,2,4*}

佛教大林慈濟醫院 放射腫瘤科¹

花蓮慈濟大學 醫學院²

成功大學醫學院 公共衛生研究所³

中正大學 分子生物研究所⁴

髓母細胞瘤大部分長自顱後窩，約佔 15%-20% 的兒童中樞性神經腫瘤。手術是髓母細胞瘤的主要治療方式。臨床上，手術後發生四肢癱瘓的情況非常少見。本文報告一位於術後發生四肢癱瘓的髓母細胞瘤病患，一開始此情況被認為是無法治癒的術後病發症。然而在詳細的影像判讀後，我們於 T2W 核磁共振影像上看到第 6 節頸椎有部分的訊號增加，無法完全排除腫瘤浸潤的可能性。在與病人的家屬詳細討論治療的好處及壞處後，病人接受了術後放射治療，並在治療後臨床症狀得到顯著地改善。此病例提醒我們在合併有腫瘤相關神經學症狀的髓母細胞瘤病人身上，放射治療扮演了重要的角色。

[放射治療與腫瘤學 2016; 23(2): 137-143]

關鍵詞：髓母細胞瘤、四肢癱瘓、放射治療

