

Malignant Peripheral Nerve Sheath Tumor of the Cervical Spine Treated with Surgical Resection Followed by X-ray Radiotherapy or Carbon Ion Radiotherapy: A Report of Three Cases

Akira Honda¹⁾, Yoichi Iizuka¹⁾, Masahiko Okamoto²⁾, Shintaro Shiba³⁾, Hiromi Koshi⁴⁾, Tokue Mieda¹⁾, Sho Ishiwata¹⁾, Yohei Kakuta¹⁾, Tsuyoshi Tajika¹⁾, Tatsuya Ohno³⁾ and Hiroataka Chikuda¹⁾

1) Department of Orthopaedic Surgery, Gunma University Graduate School of Medicine, Maebashi, Japan

2) Department of Radiation Oncology, Gunma University Graduate School of Medicine, Maebashi, Japan

3) Gunma University Heavy Ion Medical Center, Maebashi, Japan

4) Clinical Department of Pathology, Gunma University Hospital, Maebashi, Japan

Abstract:

Introduction: Spinal malignant peripheral nerve sheath tumors (MPNSTs) are extremely rare. Because of vital surroundings, en bloc resection can be difficult in MPNSTs of the cervical spine. Herein, we report three cases of MPNST followed by radiotherapy or carbon ion radiotherapy (CIRT) after surgery.

Technical Note: In case 1, the patient underwent subtotal resection from both a posterior and anterior approach following by adjuvant X-ray radiotherapy. The patient died 13 years after surgery due to liver cancer unrelated to MPNST. In case 2, recurrence spread to the spinal canal in 10 months after primary CIRT. The patient underwent resection of the spinal canal lesion with the residual lesion treated by additional CIRT. Recurrence could be controlled for at least 1 year. In case 3, the patient underwent partial resection for the spinal canal lesion with the residual lesion treated by CIRT. Intradural and extradural recurrences from outside of the CIRT field were observed at 3 years after surgery.

Conclusions: Complete resection and adjuvant X-ray radiotherapy would be an effective treatment for MPNST of the cervical spine, even if en bloc resection with a wide margin is impossible. CIRT for the residual tumor after incomplete resection may have the potential to be an additional treatment option; however, further investigation is warranted.

Keywords:

malignant peripheral nerve sheath tumor, cervical spine, conventional radiotherapy, carbon ion radiotherapy

Spine Surg Relat Res 2020; 4(3): 269-273

dx.doi.org/10.22603/ssrr.2019-0100

Introduction

Malignant peripheral nerve sheath tumors (MPNSTs) are rare sarcomas, accounting for 3-10% of all soft tissue sarcomas with an incidence of 0.0001% in general population and 3-5% in patients with neurofibromatosis type 1 (NF1)^{1,2)}. Spinal MPNSTs are extremely rare, accounting for 2-3% of all MPNSTs³⁾. Although resection followed by radiation therapy is the standard treatment strategy for MPNSTs of the extremities and the achievement of en bloc resection with wide margins is a prognostic factor, en bloc resection of spinal MPNSTs, especially MPNSTs of the cervical spine, can be difficult due to the surrounding vital structures, including critical nerves and blood vessels^{4,5)}. Herein,

we report three cases of MPNST of the cervical spine.

Technical Note

Three patients with MPNST of the cervical spine were treated with adjuvant or salvage therapy, including surgical resection and conventional radiotherapy or carbon ion radiotherapy (CIRT). The ethics committee of Gunma University Graduate School of Medicine approved this study.

Case 1

A 68-year-old woman presented with a palpable mass in the neck. She had no medical history of NF1. She underwent resection for a dumbbell tumor at the C6/7 level. A

Corresponding author: Akira Honda, m1820046@gunma-u.ac.jp

Received: November 3, 2019, Accepted: December 22, 2019, Advance Publication: February 10, 2020

Copyright © 2020 The Japanese Society for Spine Surgery and Related Research

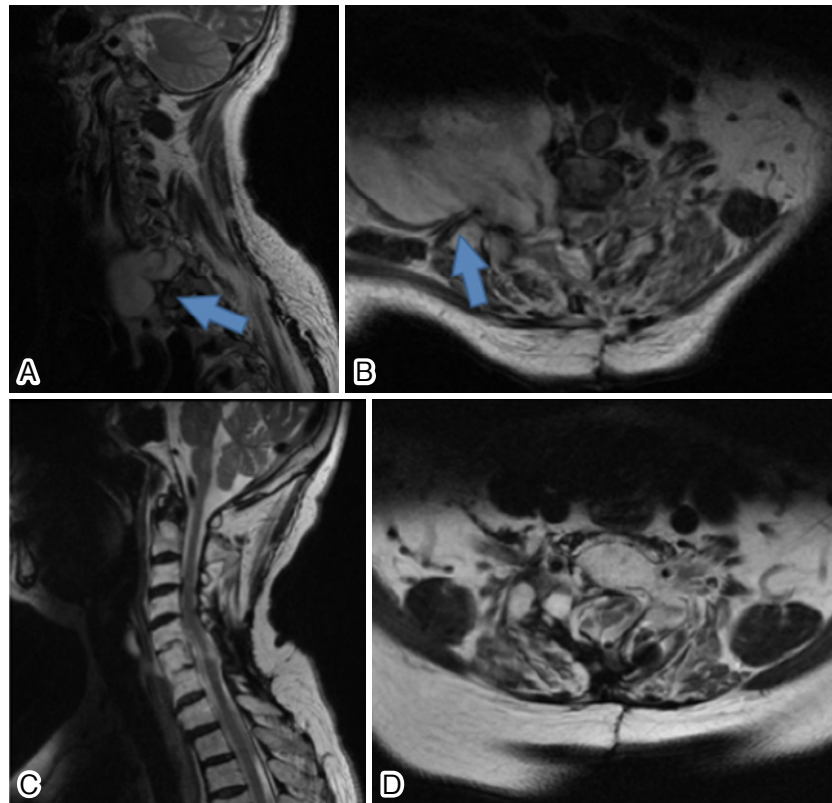


Figure 1. A 78-year-old woman (case 1, Eden type III dumbbell tumor). At 10 years after primary surgery, T2-weighted sagittal MRI of the cervical spine (A) showed local recurrence of a dumbbell tumor at the C6/7 level (arrow). T1-weighted axial MRI of the C6/7 level (B) showed that the tumor extended from foramen to the paravertebral area. At 8 years after surgery, follow-up T2-weighted sagittal (C) and axial (D) MRI of the cervical spine showed no signs of recurrence or distal metastasis.

pathological examination of the resected tumor revealed schwannoma. At 10 years after surgery, she noticed a mass lesion in her neck, and right-side upper extremity pain and weakness occurred. Magnetic resonance imaging (MRI) revealed local recurrence of the dumbbell tumor (Eden type III) at the C6/7 level (Fig. 1A, B). She underwent subtotal resection for the extradural and foraminal tumor via a posterior approach. The pathological findings of the tumor were consistent with benign schwannoma. She also underwent gross total resection of the residual tumor via an anterior approach, and a pathological examination revealed MPNST. After these surgeries, she received X-ray radiotherapy (50 Gy in 25 fractions) as adjuvant therapy. Follow-up examinations revealed no recurrence or distal metastasis (Fig. 1C, D). She died of liver cancer (osteoclast-like giant cell-rich sarcoma) unrelated to MPNST 13 years after the second surgery.

Case 2

A 35-year-old man presented with left-side cervical pain. He had a medical history of resection for NF1-associated benign tumors, including cervical spinal cord tumors. At 12 years after surgery for the cervical spinal cord tumors, left-side cervical pain occurred. MRI of the cervical spine

showed a huge C6 nerve root tumor on the left side (Fig. 2 A, B). The diagnosis, based on a CT-guided biopsy, was MPNST. He received CIRT (70.4 Gy [relative biological effectiveness, RBE] in 16 fractions) as a definitive treatment. Although we selected CIRT for the MPNST, the tumor recurred at the marginal site on the spinal canal side of the radiation field and spread to the spinal canal, resulting in an Eden type III dumbbell tumor after 10 months, and the symptom of myelopathy worsened (Fig. 2C, D). He underwent resection for the spinal canal lesion, and then he received additional CIRT (57.6 Gy [RBE] in 12 fractions) for the residual tumor (Fig. 2E, F). His symptoms improved after those treatments, and no apparent recurrence or distal metastasis was detected for at least 12 months after surgery.

Case 3

A 56-year-old woman presented with left-side upper extremity weakness and numbness. She had no medical history of NF1. MRI showed an Eden type II dumbbell tumor at the C5/6 level (Fig. 3A, B). She underwent partial resection for the intradural and extradural components of tumor. The pathological findings of the resected tumor were consistent with MPNST. She received 64.0 Gy (RBE) in 16 fractions with CIRT for the residual disease. Although follow-up MRI

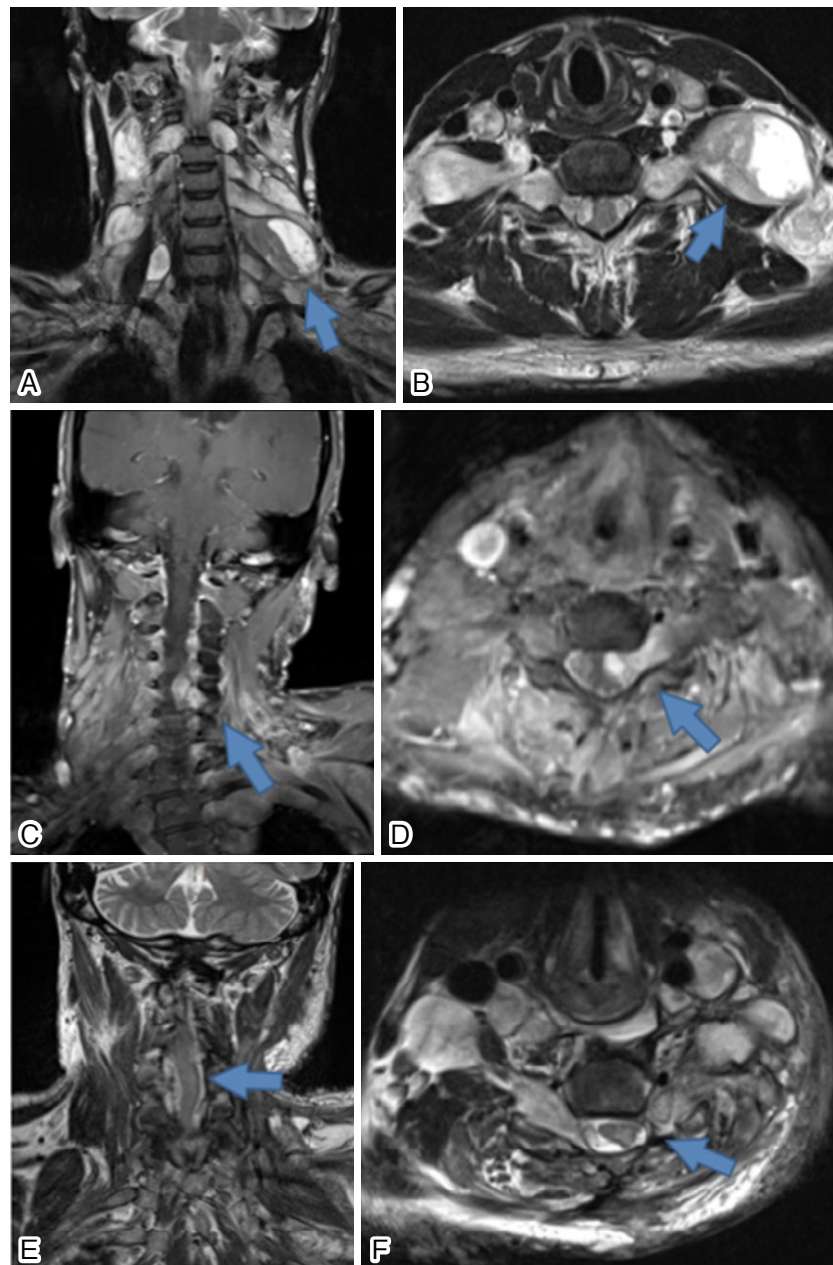


Figure 2. A 35-year-old man (case 2, Eden type III dumbbell tumor). T2-weighted coronal (A) and axial (B) MRI of the cervical spine showed a huge C6 nerve root tumor on the left side (arrow). At 10 months after primary CIRT, T2-weighted coronal (C) and Gd-enhanced axial (D) MRI showed that the tumor extended to the spinal canal (arrow) and resulted in an Eden type III dumbbell tumor. At 1 year after combined treatment with resection and CIRT, T2-weighted coronal (E) and axial (F) MRI of the C5/6 level showed that the spinal canal lesion was removed with no signs of recurrence.

showed intradural and extradural recurrence from outside the CIRT field at 3 years after surgery, she declined additional therapy, and her neurological symptoms gradually worsened (Fig. 3C, D).

Discussion

Spinal MPNSTs are extremely rare pathologies and have also been reported to have a poorer outcome in comparison

to non-spinal MPNSTs^{1,3,6}. Although en bloc resection with a wide margin is the optimal surgical procedure for the treatment of non-spinal MPNSTs, it is often difficult to perform for spinal MPNSTs-especially MPNSTs of the cervical spine-due to vital structure invasion. Thus, adjuvant radiotherapy is critical in the management of spinal MPNSTs⁴. In this report of three cases, a patient treated with two-stage gross total resection without a wide margin and conventional fractionated X-ray radiotherapy achieved long-term survival

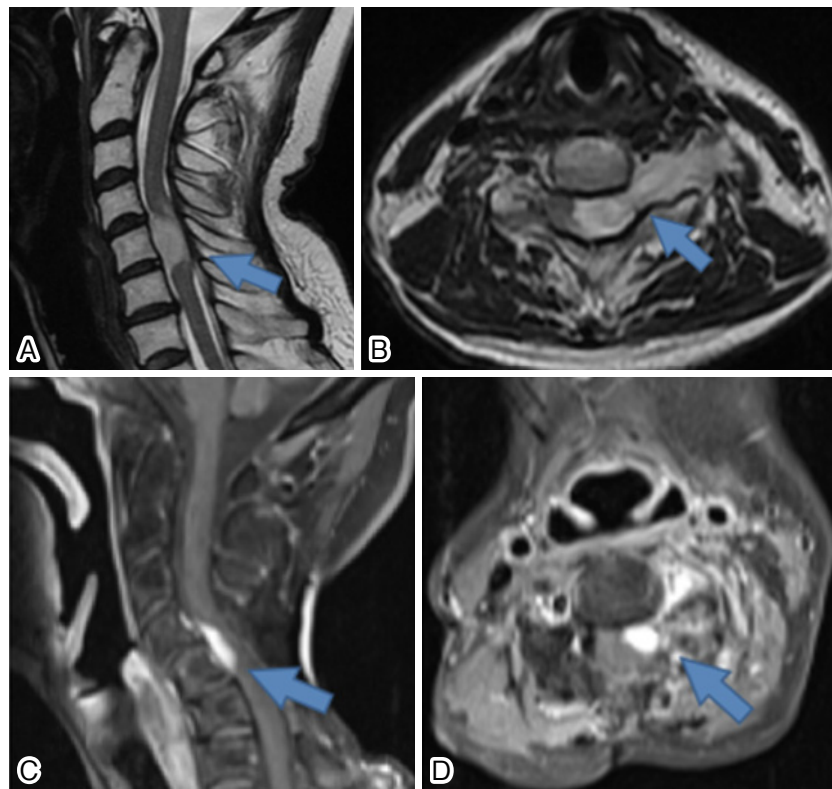


Figure 3. A 56-year-old woman (case 3, Eden type II dumbbell tumor). T2-weighted sagittal (A) and axial (B) MRI showed an intradural and extradural tumor in the spinal canal extending to the paravertebral body at the C5/6 level. Follow-up T1-weighted Gd-enhanced sagittal (C) and axial (D) MRI 3 years after surgery showed intraspinal recurrence (arrow).

for more than 10 years. This may imply that gross total resection followed by radiotherapy can provide long-term control or a cure of MPNSTs of the cervical spine, even if en bloc resection with a wide margin is impossible.

X-ray radiotherapy for the spinal cord is associated with several possible complications, including radiation-induced myelopathy. These complications appear to be associated with the radiation dose schedule, including the dose per fraction, the total dose, and the inter-fraction interval⁷. Spinal MPNSTs are located close to the spinal cord, and irradiation of spinal MPNSTs is a risk associated with a risk of serious radiation myelopathy. Thus, it is difficult to administer X-ray radiotherapy at a radiation dose that is sufficient to control the gross tumor. Recently, high precision radiotherapy, such as stereotactic body radiotherapy and intensity-modulated radiotherapy, has been used to deliver high doses of radiation for spinal MPNSTs^{8,9}. Furthermore, CIRT has been used to treat MPNSTs because CIRT has higher dose localization and a superior cell-killing effect against radioresistant tumor cells compared to X-ray radiotherapy¹⁰⁻¹⁴. In this report, a case with recurrent MPNST after CIRT could be controlled for at least 1 year after combined surgical resection and additional CIRT. However, marginal recurrence on the side of the spinal cord after CIRT was observed in the case. Another case with gross residual disease after the resection of the intradural and extradural components also

developed recurrence following additional CIRT after surgery. Although CIRT is an attractive treatment option for spinal MPNSTs in terms of increased efficacy, as shown in other radioresistant tumors, there is little information regarding the management of spinal MPNSTs using CIRT. Additionally, it is difficult to determine the radiation dose fractionation schedule and to obtain a margin on the side of the spinal cord because the spinal cord is an adjacent radiosensitive organ and because the risk of recurrence on the side of the spinal cord is considered to be high. In contrast, the tumor on the non-spinal cord side was controlled by CIRT. Thus, if a margin between the tumor and spinal cord can be obtained by surgery before CIRT, and a sufficient radiation dose can be delivered, then the recurrence risk will be reduced. In cases of spinal MPNST that cannot be completely resected, such as cases 2 and 3, combined treatment of surgery for the tumor on the side of the spinal cord followed by CIRT for the residual tumor would improve the treatment outcome. However, there is no consolidated report of CIRT for spinal MPNSTs. Further investigations are warranted to elucidate the efficacy of CIRT in the treatment of MPNSTs of the cervical spine.

Conclusion

We performed surgical resection followed by X-ray radio-

therapy or CIRT for MPNSTs of the cervical spine. Complete resection and adjuvant X-ray radiotherapy would be an effective treatment for MPNSTs of the cervical spine, even if en bloc resection with a wide margin is impossible. Additionally, CIRT may be a potential treatment for the residual tumor after incomplete resection.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

Author Contributions: AH designed and executed the experiments and wrote the manuscript. YI was a major contributor in writing the manuscript. MO, SS, and TO contributed to introduce the concept of radiology and helped to write the manuscript. HK contributed to introduce the concept of pathology. TM, DT, SI, YK, and TT contributed to introduce the concept of orthopedic surgery and helped to write the manuscript. HC is a supervisor and edited the manuscript. All authors reviewed and approved the final manuscript.

Informed Consent: Informed consent was obtained from all participants in this study.

References

- Gupta G, Maniker A. Malignant peripheral nerve sheath tumors. *Neurosurg Focus*. 2007;22(6):E12.
- Zhu B, Liu X, Liu Z, et al. Malignant peripheral nerve sheath tumours of the spine: clinical manifestations, classification, treatment, and prognostic factors. *Eur Spine J*. 2012;21(5):897-904.
- Kourea HP, Bilsky MH, Leung DH, et al. Subdiaphragmatic and intrathoracic paraspinal malignant peripheral nerve sheath tumors: a clinicopathologic study of 25 patients and 26 tumors. *Cancer*. 1998;82(11):2191-203.
- Gupta G, Mammis A, Maniker A. Malignant peripheral nerve sheath tumors. *Neurosurg Clin N Am*. 2008;19(4):533-43.
- Vauthey JN, Woodruff JM, Brennan MF. Extremity malignant peripheral nerve sheath tumors (neurogenic sarcomas): a 10-year experience. *Ann Surg Oncol*. 1995;2(2):126-31.
- Anghileri M, Miceli R, Fiore M, et al. Malignant peripheral nerve sheath tumors: prognostic factors and survival in a series of patients treated at a single institution. *Cancer*. 2006;107(5):1065-74.
- Rampling R, Symonds P. Radiation myelopathy. *Cure Opin Neurol*. 1998;11(6):627-32.
- Chang UK, Cho WI, Lee DH, et al. Stereotactic radiosurgery for primary and metastatic sarcomas involving the spine. *J Neurooncol*. 2012;107(3):551-7.
- Terezakis SA, Lovelock DM, Bilsky MH, et al. Image-guided intensity-modulated photon radiotherapy using multifractionated regimen to paraspinal chordomas and rare sarcomas. *Int J Radiat Oncol Biol Phys* 2007;69(5):1502-8.
- Jensen AD, Uhl M, Chaudhri N, et al. Carbon ion irradiation in the treatment of grossly incomplete or unresectable malignant peripheral nerve sheath tumors: acute toxicity and preliminary outcome. *Radiat Oncol*. 2015;10(1):109.
- Hagi T, Nakamura T, Yokoji A, et al. Medullary metastasis of a malignant peripheral nerve sheath tumor: A case report. *Oncol Lett*. 2016;12(3):1906-8.
- Kanai T, Endo M, Minohara S, et al. Biophysical characteristics of himac clinical irradiation system for heavy-ion radiation therapy. *Int J Radiat Oncol Biol Phys*. 1999;44(1):201-10.
- Nakano T, Suzuki Y, Ohno T, et al. Carbon beam therapy overcomes the radiation resistance of uterine cervical cancer originating from hypoxia. *Clin Cancer Res*. 2006;12(7 Pt 1):2185-90.
- Tsujii H, Kamada T, Shirai T, et al. Carbon-ion radiotherapy. Tokyo: Springer Science & Business Media, 2013. 127-309 p.

Spine Surgery and Related Research is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).