# Intramedullary spinal cord metastasis of malignant melanoma:Two cases with rim signs in contrast-enhanced magnetic resonance imaging: A case report

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**Abstract.** Spinal cord metastasis of malignant melanoma is mostly caused by the invasion of the spinal cord by malignant melanoma. However, direct metastasis in the spinal cord is rare and difficult to diagnose accurately. A few diagnostically valuable findings of intramedullary spinal cord metastases (ISCMs) have been published. However, a highly specific finding of ISCMs of all carcinomas is the 'rim sign', which signifies the enhancement of the edge-dominant effect of the lesion in contrast-enhanced MRI. The objective of this case series was to examine the ratio of ISCMs of malignant melanoma with an indication of rim signs in contrast-enhanced MRI. The present report describes two cases of ISCMs of malignant melanoma in which the rim sign in contrast-enhanced MRI was useful for diagnosis.

## Introduction

Most metastatic spinal cord tumors are epidural metastases caused by the direct invasion of vertebral metastatic tumors. Intramedullary spinal cord metastasis (ISCM) of malignant tumors is rare, accounting for 0.9-2.1% of all cases of spinal cord metastasis. Malignant melanoma accounts for approximately 9% of all cases of ISCM (1). A literature review was performed to include studies published in English on this topic, including our two cases. To the best of our knowledge, 27 cases of ISCMs associated with malignant melanoma have been reported; 12 cases were examined and 15 cases had no description of contrast MRI and were excepted. The rim sign was recognized in 33.3% (4/12) of these cases. However, none of the five cases of ISCMs of malignant melanoma identified in this series showed a rim sign. This study revealed that the rim sign is observed in ISCMs of malignant melanoma and in those of other cancers. We believe that the rim sign in an MRI is a clue for the diagnosis of ISCM of malignant melanoma.

## Case report

*Case 1.* A 35-year-old woman with no significant medical history presented with malignant melanoma over the left clavicle. The tumor was 1.3 mm thick and had ulceration. Therefore, she was treated by resection of the primary lesion and axillary dissection. Metastases were detected in two of the 18 lymph nodes.

Four years later, she developed metastasis in the right lung, subcutaneous metastasis in the scalp, and multiple metastases in the bone. The tumors were positive for v-Raf murine sarcoma viral oncogene homolog B1 (BRAF) V600E mutation determined via a biopsy of metastasis in the scalp. Oral dabrafenib plus trametinib was initiated. Thereafter, all metastases reduced and her status was maintained. However, 5 years and 1 month after surgery, she developed multiple brain metastases and pleural dissemination and was treated with nivolumab and whole-brain irradiation. Bone metastases also progressed; therefore, the sternum and lumbar spine 5 were also irradiated. Four days after radiation therapy, she developed severe back pain. In addition, she experienced sensory disturbances caudal to the costal arch. She had no sensory disturbances or movement disorders in the upper limbs but had severe movement disorders in both lower limbs.

Contrast-enhanced magnetic resonance imaging (MRI) revealed a low-density mass with gadolinium-based contrast media at the peripheral ridge of T4-T6 (Fig. 1). Hence, an emergency evacuation was performed on the same day. Only a hematoma was intraoperatively visualized (Fig. 2A). However, although melanoma cells were not visualized, histopathological examination revealed that they were present, as evidenced

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*Abbreviations:* CT, computed tomography; ISCM, intramedullary spinal cord metastasis; MRI, magnetic resonance imaging

*Key words:* intramedullary spinal cord metastasis, malignant melanoma, rim sign, contrast-enhanced magnetic resonance imaging, immune-checkpoint inhibitor

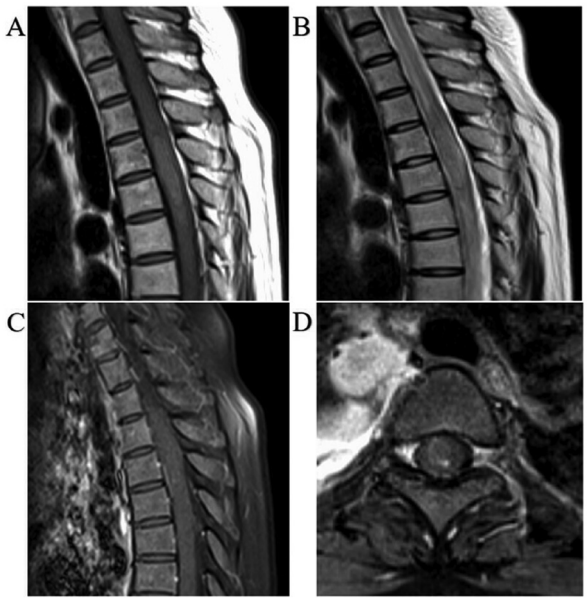


Figure 1. Magnetic resonance imaging of case 1 demonstrating the intramedullary spinal cord metastasis at the T6-T7 level. Rim signs were revealed after the administration of Gd-based contrast media. (A) Sagittal T2-weighted images. (B) Sagittal T1-weighted images. (C) Sagittal contrast-enhanced T1-weighted images. (D) Axial contrast-enhanced T1-weighted images.

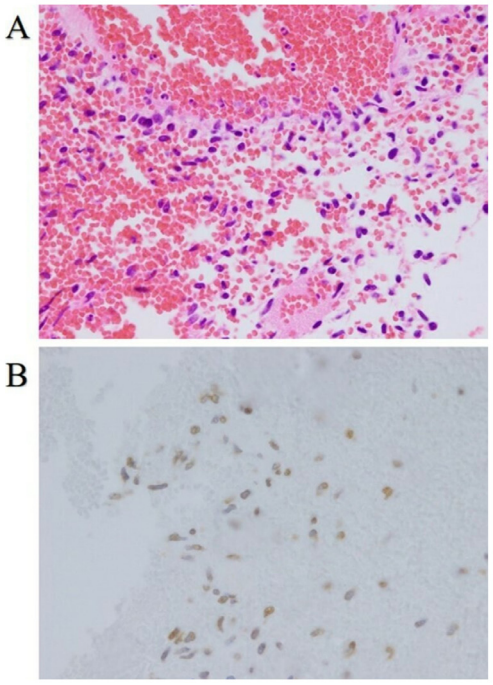


Figure 2. Histopathology. H&E staining and IHC. (A) H&E staining (magnification, x400). Melanoma cells could not be recognized. (B) IHC staining (magnification, x400). Tumor cells were positive for SOX-10. H&E, hematoxylin and eosin; IHC, immunohistochemistry.

by SOX-10, S-100, and BRAF-V600E positive staining and the metastasis in the scalp (Fig. 2B). The patient was diagnosed with micro-metastases of malignant melanoma.

The day after surgery, a marked improvement in back pain was reported; however, movement disorders in both her lower limbs persisted. Fourteen days after surgery, computed tomography (CT) revealed exacerbation of pleural

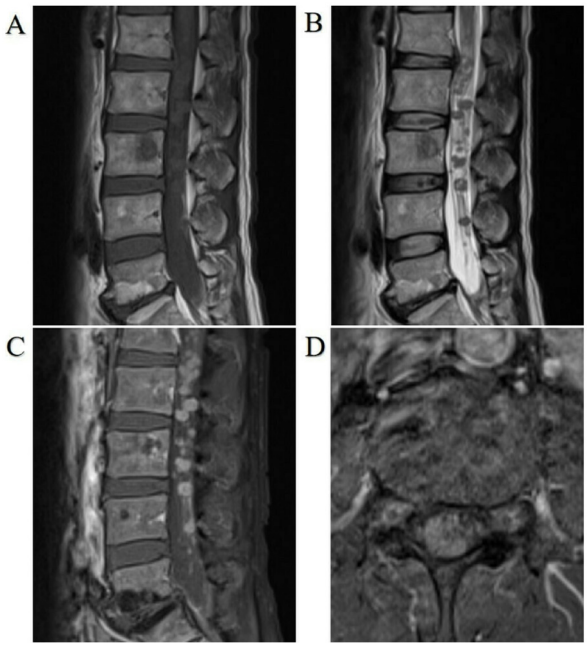


Figure 3. Magnetic resonance imaging of case 2 demonstrating the intramedullary spinal cord metastasis broadly at the lumbar level. Rim signs of multiple masses were revealed after the administration of Gd-based contrast media. (A) Sagittal T2-weighted images. (B) Sagittal T1-weighted images. (C) Sagittal contrast-enhanced T1-weighted images. (D) Axial contrast-enhanced T1-weighted images.

dissemination. Thereafter, oral dabrafenib (300 mg per day) plus oral trametinib (2 mg per day) was resumed; it was highly effective in treating pleural dissemination. She developed fever; therefore, oral dabrafenib plus trametinib was continued subsequently. Because the antitumor effects of the treatment were apparent, cycles of treatment withdrawal and resumption were intermittently repeated. Six months after surgery, pleural dissemination increased in size. Therefore, nivolumab plus ipilimumab combination therapy was initiated. However, she died soon after.

*Case 2*. A 48-year-old man with a local recurrence of malignant melanoma of the left conjunctiva without BRAF mutation was treated by wide excision and reconstruction by a free flap. Because the stumps were partially positive, proton therapy was performed. Two months after the proton therapy, CT revealed right adrenal and retroperitoneal metastases. Therefore, nivolumab plus ipilimumab combination therapy was initiated. However, after 1 month, cervical spine and right upper humerus metastases were detected; thus, radiation therapy was performed. The dose was 20 Gy at 5 Gy/fraction. Eight months after the combination therapy, he experienced numbness and weakness in the right upper and lower limbs. Contrast-enhanced MRI revealed multiple masses with a contrast effect at the peripheral ridge of C2, Th1, and most of the lumbar spine (Fig. 3).

## Discussion

Palliative radiation or conservative treatment is often selected for ISCM because the disease is associated with a poor prognosis. The main purpose of palliative radiation therapy is to

Table I. Contrast-enhanced MRI findings of intramedullary spinal cord metastasis of malignant melanoma reported previously.

| First author, year | Age, years/sex | Primary tumor | Metastatic location of spinal cord | Brain metastases | Rim sign | Flame sign | Both signs | Either sign | Neither signs | (Refs.) |
|---|---|---|---|---|---|---|---|---|---|---|
| Connolly *et al*, 1996 | 39/F | Left forehead | T8-T9 | - | - | - | - | - | + | (1) |
| Rykken *et al*, 2013 | NR | NR | NR | NR | - | + | - | + | - | (4) |
| | NR | NR | NR | NR | + | + | + | - | - | |
| | NR | NR | NR | NR | - | - | - | - | + | |
| | NR | NR | NR | NR | - | - | - | - | + | |
| | NR | NR | NR | NR | - | - | - | - | + | |
| Sun *et al*, 2013 | 67/F | Vulvar | L3-L4 | - | + | - | - | + | - | (5) |
| O'Reilly *et al*, 2017 | 30s/M | NR | Multiple (T5/6, T9 and T12–L3, intramedullary and intradural extramedullary) | + | - | - | - | - | + | (6) |
| Śniegocki *et al*, 2018 | 49/F | Left forearm | T11 | + | - | - | - | - | + | (3) |
| Ruschel *et al*, 2018 | 36/M | Left upper limb | C6-C7 | + | - | - | - | - | + | (7) |
| Present study, 2020 | 35/F | Left clavicle | T4-T6 | + | + | - | - | + | - | - |
| Present study, 2020 | 48/M | Left conjunctiva | Multiple (C2, T1, lumber level broadly) | + | + | - | - | + | - | - |

NR, not reported.

reduce the pain; therefore, radical cure cannot be achieved with only radiation therapy.

Patients expected to respond well to therapeutic intervention are considered candidates for surgical treatment, which can improve the overall survival and neurological functions (2). A few patients with ISCMs of malignant melanoma undergo surgical resection because melanoma tends to be highly resistant to radiation (3). Therefore, the dose of radiation for melanoma is often 4 Gy or more/fraction. In case 1, surgical resection considerably reduced the patient's pain.

Considering the MRI findings, two unique characteristics of ISCMs, rim and flame signs, have been reported (4). Rim signs indicate a more intense thin rim with peripheral enhancement than other tumor areas and flame signs indicate flame-shaped enhancements at the edge of the lesion (above or below). These findings have been reported to be highly specific for ISCMs.

For all ISCMs, the rim sign was detected in 47% cases and the flame sign in 40% cases. Both signs were found in 27% cases and neither sign in 40% cases. Either sign was recognized in 60% cases. Melanoma was detected in five cases in this series but the rim sign was not detected in any (0/5), whereas neither sign was observed in 60% cases (3/5) (4). The authors of the respective studies did not mention these results because of the small number of cases of malignant melanoma.

According to a previous literature review, MRI could not reveal a specific pattern within the tumor owing to a mixture of melanin, intra-tumoral hemorrhage, and fat deposition (5). As a result, no characteristics have been reported so far to aid the diagnosis of ISCM of malignant melanoma.

To the best of our knowledge, 27 cases of ISCM of malignant melanoma (including our two cases) have been reported. In the literature, ISCM of malignant melanoma is described as a small percentage of the ISCMs of all cancer types; thus, it is sometimes not reported in detail.

We examined 12 cases, as the 15 other cases were excepted because there was no description of contrast-enhanced MRI findings (Table I) (5-7). One patient underwent MRI without using a contrast agent, but the characteristics of the lesion was described nonetheless (8).

Moreover, 83.3% (10/12) of these cases showed a single mass by MRI and multiple masses in only two cases (including our case 2). Another case was noted to have intramedullary and intradural extramedullary lesions.

Besides these two cases, a case with multiple masses discovered at autopsy has been reported (9). However, the lesions were not identified by an MRI in this case. Therefore, our case 2 is the first case of ISCM of malignant melanoma with multiple masses localized within the intramedullary area that was detected by MRI.

The rim sign was detected in 33.3% (4/12) and the flame sign was detected in 16.6% patients (2/12). Both signs were found in 8.3% (1/12), either sign in 33.3% (4/12), and neither in 58.3% of patients (7/12). Although the ISCM of malignant melanoma was found in 33.3% patients, the rim sign frequency was slightly lower than that observed in the ISCM of other cancers. Conversely, the flame sign in ISCMs of malignant melanoma was less than that in ISCMs of other cancers.

In the cases of ISCMs of malignant melanoma, the incidence of brain metastasis was as high as 76.4% (13/17). The response rate of intracranial metastases of BRAF V600 mutation-positive malignant melanoma to combination therapy with dabrafenib plus trametinib was 58% and that of extracranial metastases was 55% (10). The response rate of intracranial lesions to the nivolumab plus ipilimumab combination therapy for BRAF V600 mutation-negative malignant melanoma was 57%. Conversely, the response rate of intracranial metastases to immune-checkpoint inhibitor monotherapy was almost 22% (11). Hence, combination therapy was established to be significantly effective. Our cases are unique as patients with ISCMs of malignant melanoma are treated by immune-checkpoint inhibitors or molecule-targeted agents.

In conclusion, the rim sign is detected in some ISCMs of malignant melanoma and in ISCMs of other cancers. We believe that the rim sign in MRI is a useful diagnostic clue of ISCM of malignant melanoma. Although ISCM of malignant melanoma is difficult to diagnose accurately and is associated with poor prognosis owing to complications of brain metastases, the prognosis of malignant melanoma has substantially improved because of treatment advances. Therefore, more accurate diagnoses and the development of therapeutic strategies will help improve patients' quality of life in the future.

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**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Authors' contributions**

HM analyzed and interpreted the patient data and was a major contributor in writing the manuscript. NY and KNam offered valuable feedback regarding the study. KNak assisted in the early stages of this work. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

Not applicable.

**Patient consent for publication**

A waiver of informed consent requirement was obtained from the National Cancer Center Hospital Institutional Review Board.

**Competing interests**

The authors declare that they have no competing interests.

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