



A case of sustained neurological improvement in a metastatic intramedullary spinal cord tumor from lung cancer treated with immune checkpoint inhibitor therapy

Ron Fujii¹ · Masayoshi Morozumi² · Akio Muramoto² · Yuji Matsubara²

Received: 25 January 2025 / Revised: 30 March 2025 / Accepted: 13 April 2025 / Published online: 22 April 2025
© The Author(s) 2025

Abstract

Purpose Metastatic intramedullary spinal cord tumors generally have poor prognosis, with chemotherapy often deemed ineffective. We report about a patient who achieved a favorable outcome with an immune checkpoint inhibitor following the resection of the extramedullary component of a metastatic intramedullary tumor.

Method A 74-year-old man underwent upper lobectomy for lung cancer. Seven months after surgery, he developed urinary retention and walking difficulty. Contrast-enhanced magnetic resonance imaging (MRI) revealed an intradural extramedullary tumor with homogeneous enhancement at the C7/Th1 level. Emergent tumor resection was performed.

Results Intraoperatively, a part of the tumor was found to be firmly adhered to the spinal cord. The tumor was resected, and the adhered portion was cauterized. Postoperatively, the patient's paraparesis improved, enabling him to walk with a cane. Histopathological analysis confirmed the tumor as a metastasis of lung cancer. Postoperative MRI revealed residual intramedullary lesions, leading to a metastatic intramedullary tumor diagnosis. Given the high PD-L1 expression in the tumor cells, treatment with an immune checkpoint inhibitor was initiated. This resulted in the resolution of spinal cord edema and residual tumor disappearance on follow-up MRI. The patient maintained ambulatory function for 2 years.

Conclusion Recent studies have demonstrated the efficacy of immune checkpoint inhibitors for brain metastases of lung cancer with high PD-L1 expression. In our case, spinal cord edema resolved, and the residual tumor regressed, with good neurological function sustained over 2 years. These findings suggest that immune checkpoint inhibitors may also be effective for metastatic intramedullary spinal cord tumors.

Keywords Metastatic intramedullary spinal cord tumor · Immune checkpoint inhibitor · Lung cancer · PD-L1

Introduction

Metastatic intramedullary spinal cord tumors (MISCTs) are exceedingly rare, with an incidence of 0.1–0.4% among patients with cancers [1]. MISCTs' prognosis remains poor, with median survival times reported at 6.5 months following surgical resection and 4.0 months with radiotherapy [2, 3]. Standard chemotherapy efficacy is limited, primarily due to the blood–spinal cord barrier (BSCB) protective role, which hinders drug delivery to the tumor site [2, 3].

Although immune checkpoint inhibitors (ICIs) have shown efficacy in managing brain metastases [4], their application in spinal cord metastases has not been extensively studied. Here, we present a case in which ICI treatment resulted in significant tumor regression and preserved neurological function in a patient with a metastatic

✉ Ron Fujii
ronionion.322@gmail.com

Masayoshi Morozumi
musa_uffizi_1207@yahoo.co.jp

Akio Muramoto
akiomuramoto@gmail.com

Yuji Matsubara
magic@mc.ccnw.ne.jp

¹ Toyota Kosei Hospital, Toyota, Japan

² Kariya Toyota General Hospital, Kariya, Japan

intramedullary tumor. Given the current lack of literature and data regarding the application of ICI in MISCT, this case highlights a previously unexplored therapeutic avenue and provides novel insights into potential treatment strategies for this rare and challenging condition.

Case presentation

A 74-year-old man was experiencing pain in the right back and anterior chest for 1 year and 5 months. One year ago, he visited a local physician and was referred to the pulmonology department due to an abnormal shadow on chest imaging. Bronchoscopy was performed, leading to a diagnosis of right upper lobe non-small cell lung cancer (NSCLC). The clinical TNM classification was T4N2Mx. Eleven months ago, he received chemotherapy with paclitaxel and carboplatin for 6 weeks. Concurrently, radiotherapy (66 Gy/33 fractions) was administered to the right lung for 8 weeks. As the tumor size reduced, 7 months ago, he underwent right upper lobectomy combined with resection of the second, third, and fourth ribs along with the associated chest wall, as well as ND2a-1 lymph node dissection in the thoracic surgery department. Since no residual tumor was identified, adjuvant chemotherapy was not administered, and the patient was followed up without recurrence. Later, he developed

urinary retention and gait disturbances, which raised suspicion of spinal involvement, and he subsequently presented to our department for further evaluation.

On examination, he exhibited paraparesis predominantly affecting the right lower extremity, with a lower limb muscle strength score (MMT) of 2–3. Cysto-rectal dysfunction was also noted. Contrast-enhanced magnetic resonance imaging (MRI) revealed an intradural extramedullary lesion extending from C7 to the upper T1 level, with homogeneous internal enhancement. On T1- and T2-weighted images, the lesion appeared isointense to the spinal cord. Computed tomography (CT) showed no calcifications, initially indicating meningioma (Fig. 1).

Emergency tumor resection was performed the same day. Intraoperatively, the lesion was predominantly extramedullary. The tumor was excised using an ultrasonic surgical aspirator with simultaneous cauterization. Although the extramedullary portion was completely removed, part of the tumor adhered tightly to the ventral spinal cord. During dissection, a reduction in compound muscle action potential amplitude was observed, prompting cauterization of the adhered portion to be limited to prevent further neurological deficits.

Histopathological examination of the resected tissue revealed tumor cells with pale, foamy cytoplasm, consistent with metastatic lung adenocarcinoma. Immunohistochemical

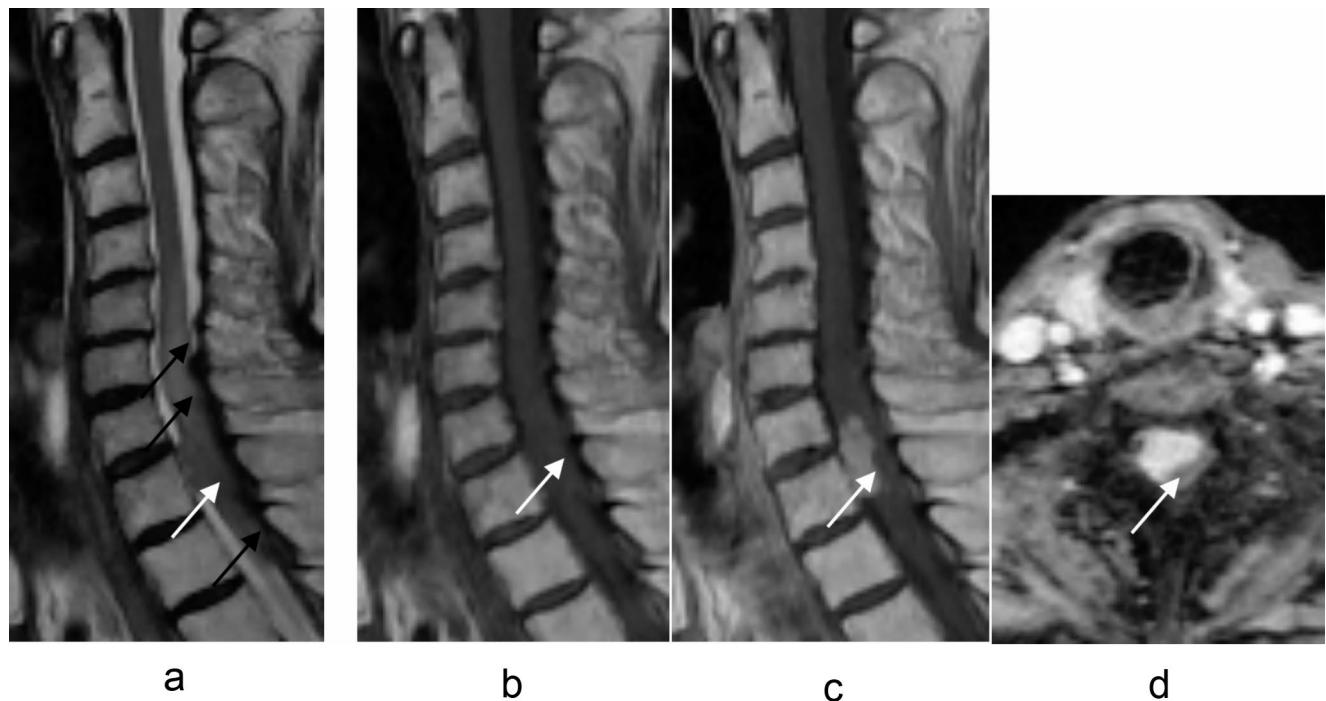


Fig. 1 (a-d) Preoperative MR images (a) T2-weighted image, (b) T1-weighted image, and (c, d) contrast-enhanced MRI. (d) Axial image at the C7/Th1 level. Contrast-enhanced MRI revealed an intradural extramedullary lesion with homogeneous internal enhancement

extending from C7 to Th1. The white arrow indicates the tumor and the black arrow indicates spinal cord edema MRI, magnetic resonance imaging

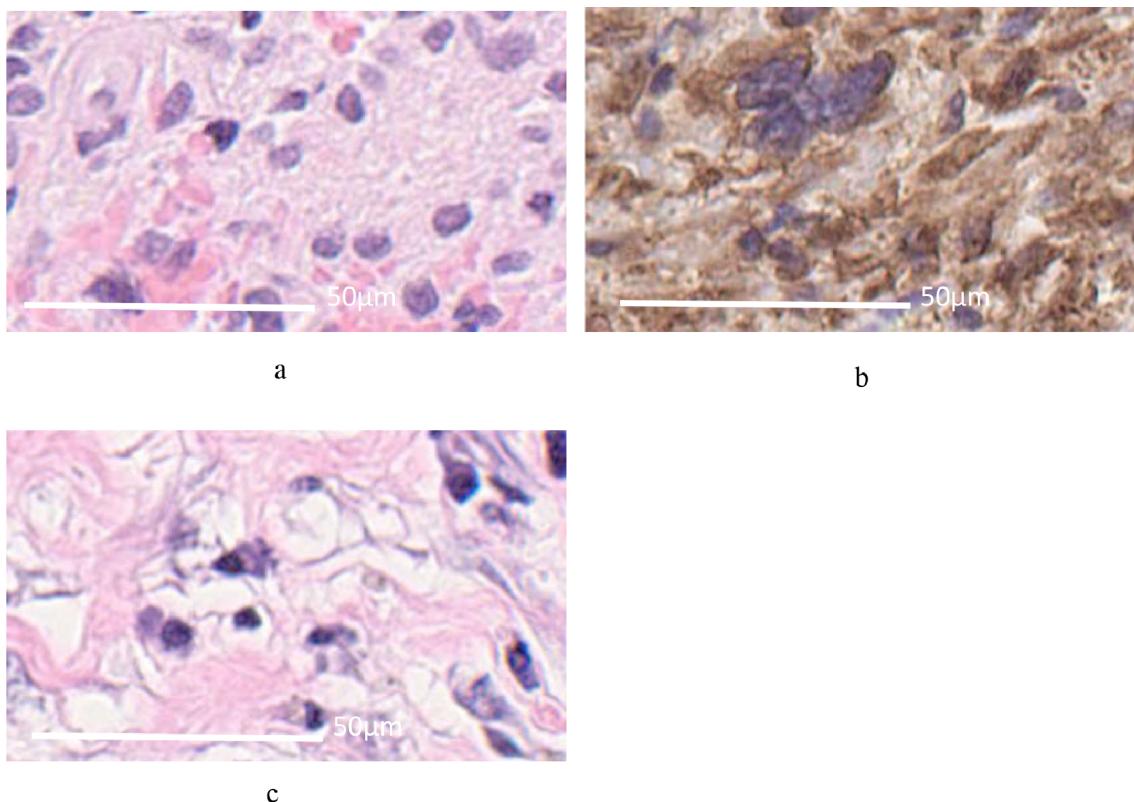


Fig. 2 (a–c) Pathological analysis of the excised tumor. (a) Histopathology with hematoxylin and eosin staining shows tumor morphology. (b) Immunohistochemical staining for cytokeratin-7 confirms

tumor origin. (c) Pathology of the lung cancer excised 7 months prior demonstrates similar staining patterns, consistent with metastatic lung adenocarcinoma

Table 1 Molecular profiling results of lung cancer

Gene	Mutation/Fusion	Result
BRAF	V600E	Negative
EGFR	L858R	Negative
EGFR	Exon 19 deletions	Negative
EGFR	E709X	Negative
EGFR	G719X	Negative
EGFR	S768I	Negative
EGFR	L861X	Negative
EGFR	T790M	Negative
EGFR	Fusion Gene	Negative
ALK	Fusion Gene	Negative
ROS1	Fusion Gene	Negative

Results of molecular profiling for lung cancer using the Oncomine Dx Target Test Multi-CDx System (FFPE) are presented. The analysis includes key genetic mutations and fusion genes associated with targeted therapy

staining for cytokeratin-7 confirmed the lung as the primary site of the tumor (Fig. 2).

Tumor proportion score was reported as 80%. Tumor sections were sent to SRL for PD-L1 testing using the PD-L1 IHC 22C3 pharmDx kit for PD-L1 staining. Tumor proportion score was calculated as the number of PD-L1-positive tumor cells divided by the total number of all tumor cells multiplied by 100. A molecular profiling test using the

Oncomine Dx Target Test Multi-CDx System (FFPE) was performed for lung cancer. No mutations or rearrangements were detected in BRAF, EGFR, ALK, or ROS1 (Table 1). Postoperatively, the patient showed marked improvement in paraplegia and regained the ability to ambulate with a cane within 2 weeks. Lower limb MMT improved to the 4–5 level. The thoracic surgery department was consulted, and it was decided that postoperative adjuvant therapy would be initiated once the patient's general condition allowed for outpatient treatment.

However, follow-up MRI 2 months after surgery revealed progressive spinal cord edema despite no clinical deterioration. Contrast-enhanced imaging confirmed an intramedullary neoplastic lesion, leading to metastatic intramedullary spinal cord tumor diagnosis (Fig. 3). Given the tumor's high PD-L1 expression (80%), pembrolizumab (200 mg intravenously every 3 weeks), an ICI targeting the PD-1/PD-L1 pathway, was initiated. Treatment was carefully monitored to manage immune-related adverse events (irAEs). Radiation therapy was considered since it involved direct irradiation to the spinal cord and carried a risk of radiation myelitis. The risks were explained to the patient; however, based on the patient's preference, radiation therapy was not initiated.

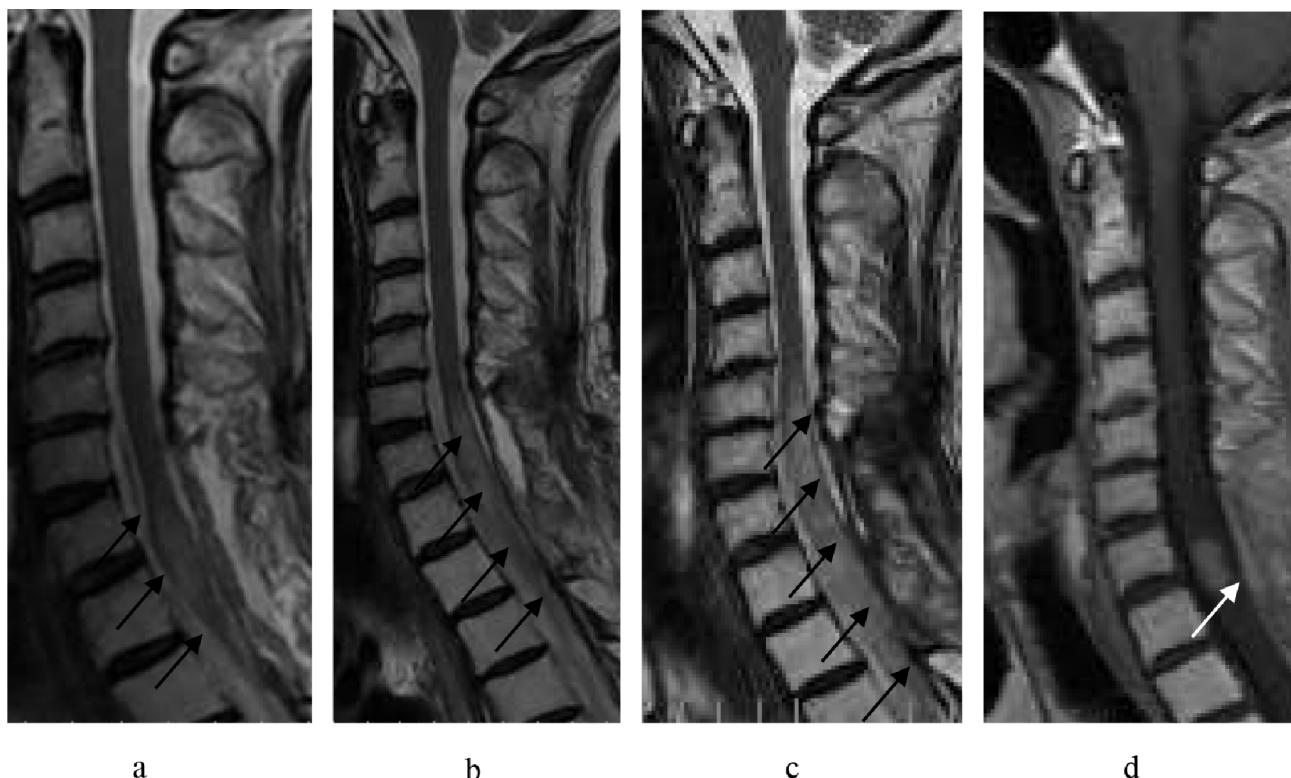


Fig. 3 (a–d) Postoperative MRI findings (a) MRI on postoperative day 7, (b) MRI on postoperative day 25, and (c, d) MRI on postoperative day 57. (d) Contrast-enhanced MRI. Progressive spinal cord edema

Over the subsequent 5 months, MRI demonstrated a significant reduction in spinal cord edema (Fig. 4).

To detect irAE, KL6 and simple chest XP were performed once a month. Chest CT was also performed every 3 months. After 28 cycles of pembrolizumab, the patient was asymptomatic; however, periodic chest CT revealed interstitial pneumonia, and the KL6 level was elevated to 991 U/ml. Pembrolizumab was discontinued due to the development of interstitial pneumonia. Oral steroids (prednisolone) were initiated at 30 mg/day as an outpatient. The dose was gradually tapered off for 6 months after administration. Despite therapy discontinuation for 8 months, the patient retained mobility with a cane, and a follow-up MRI confirmed the complete disappearance of the residual tumor (Fig. 5). Cervical spine MRI was performed once a year, and thoracic CT every 6 months for careful follow-up to determine local recurrence.

Discussion

MISCTs are exceedingly rare, with lung cancer being the most common primary source, accounting for 54% of cases, followed by breast cancer and malignant melanoma [5]. These tumors can cause severe symptoms, including acute

and intramedullary neoplastic lesions were observed over time MRI, magnetic resonance imaging

paraplegia, that markedly impact the quality of life, making prompt diagnosis and intervention critical [6]. MRI plays a pivotal role in diagnosis, typically showing homogeneous contrast enhancement, extensive high-signal regions on T2-weighted images, and the absence of cysts or hemorrhage [7]. Although no recurrence was observed herein, the patient had a history of lung cancer, and the rapid progression of muscle weakness in both lower limbs was characteristic of metastatic spinal intramedullary tumors. Yet, the isointense signal on the T2-weighted MRI was atypical for such tumors, highlighting the unique imaging presentation.

Despite treatment advancements, MISCT prognosis remains poor even after surgical resection and radiotherapy [2, 3]. Chemotherapy is often ineffective due to limited BSCB permeability. While radiation therapy offers benefits, especially for radiosensitive tumors, it is constrained by the spinal cord's fixed radiation tolerance, posing challenges for long-term management [8]. Furthermore, radiation therapy carries radiation myelopathy risk, which can result in severe neurological deficits if it occurs [9]. Surgical intervention carries risks of neurological deficits, and outcomes vary depending on tumor histology and location [10].

Recent evidence suggests that ICIs, including pembrolizumab, can cross the blood-brain barrier (BBB) in metastatic brain tumors with high PD-L1 expression [4]. ICIs

Fig. 4 (a, b) MRI findings 5 months after initiating chemotherapy. (a) Plain MRI and (b) contrast-enhanced MRI demonstrate significant tumor shrinkage and improvement in spinal cord edema MRI, magnetic resonance imaging

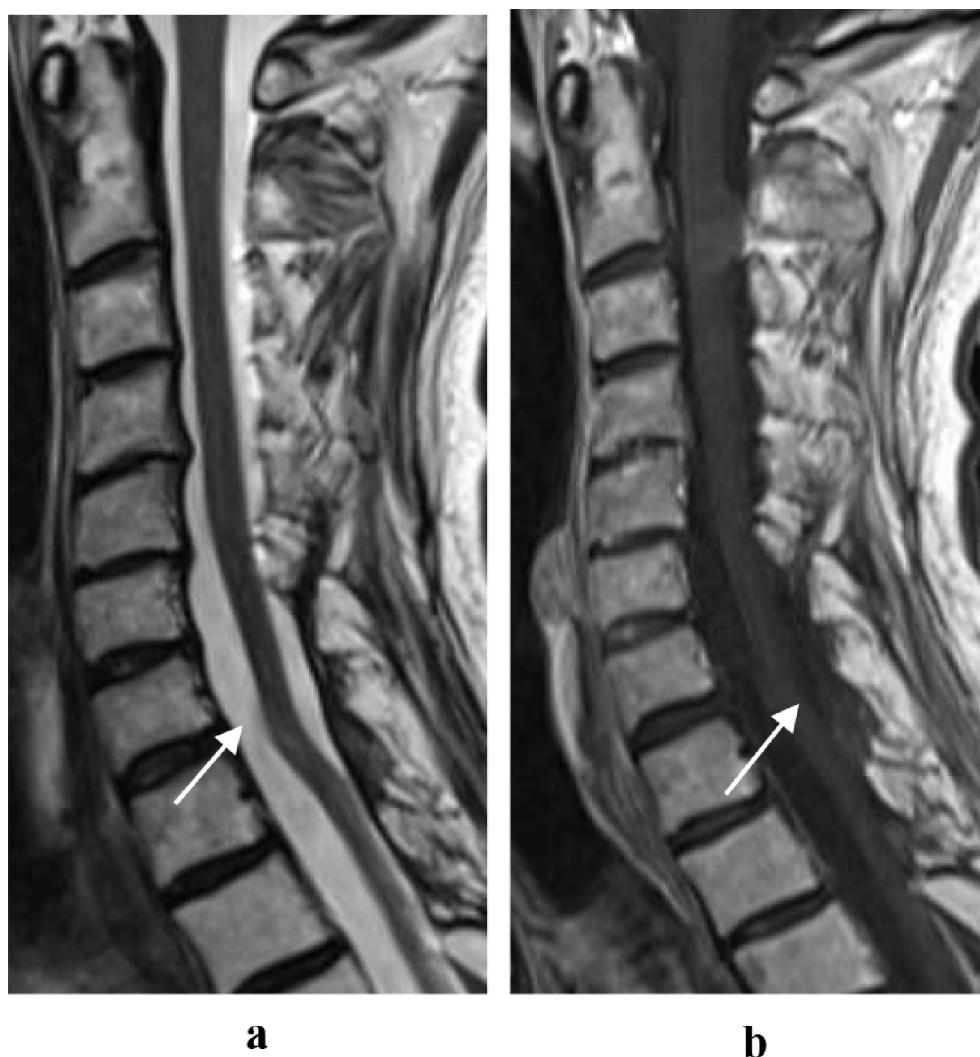


work by binding directly to PD-L1 on tumor cells, reactivating suppressed T-lymphocytes, and enhancing vascular permeability via interferon-gamma production. Additionally, activated lymphocytes outside the tumor can migrate to the lesion, amplifying the antitumor response. Currently, there are no reports elucidating the mechanism by which ICIs traverse the BSCB. Similar to the BBB, the BSCB comprises endothelial cells with tight junctions, a basal membrane, pericytes, and astrocyte endfeet, collectively regulating the penetration of bloodborne molecules into spinal cord tissue. The BSCB exhibits lower expression levels of tight junction proteins, including ZO-1 and occludin, and contains fewer pericytes than the BBB, which contributes to its increased permeability [11]. Given that ICIs have demonstrated efficacy in metastatic brain tumors, protected by the relatively impermeable BBB, these inhibitors may possibly be effective in metastatic spinal cord tumors, where the more permeable BSCB may facilitate their activity.

However, ICIs are associated with irAEs due to heightened immune activation. These irAEs can affect various systems, presenting as skin disorders, hepatitis, nephritis, interstitial pneumonia, encephalitis, or endocrine dysfunctions, including thyroiditis and diabetes [12]. irAEs severity is graded from 1 to 4. For grade 1 interstitial pneumonia, ICIs may be resumed after radiological improvement. In cases with grade 2, reintroduction is possible if symptoms resolve to grade 1 or lower and corticosteroid doses are tapered to ≤ 10 mg/day within 12 weeks. However, ICIs should not be reintroduced for grade 3 or higher irAEs [13]. In this case, although the patient did not experience significant oxygenation impairment, the interstitial pneumonia was classified as grade 2, requiring steroid treatment.

In this patient, pembrolizumab effectively reduced spinal cord edema and tumor burden. Despite ICI therapy discontinuation due to interstitial pneumonia, the patient maintained ambulatory function. This case highlights the potential of ICIs as a promising therapeutic option for

Fig. 5 (a, b) MRI findings 8 months after discontinuation of chemotherapy due to the onset of immune-related adverse events (irAEs). (a) Plain MRI and (b) contrast-enhanced MRI show no evidence of tumor regrowth MRI, magnetic resonance imaging



MISCTs with high PD-L1 expression. Moreover, the exacerbation of spinal cord edema observed post-surgery underscores the importance of initiating ICI treatment early in this aggressive disease. Although postoperative radiotherapy has been employed as adjuvant therapy in a previous report [14], it was not introduced in our case because of the potential risk of radiation myelopathy and the favorable clinical course achieved with ICI therapy alone. Nevertheless, irAE risk necessitates vigilant monitoring and prompt management to balance therapeutic efficacy with patient safety.

This study is limited by its single-case design, which inherently restricts the generalizability of the findings. While pembrolizumab demonstrated promising results in reducing tumor burden and preserving neurological function in this patient with MISCTs, the lack of a control group or comparative analysis with alternative treatments, including radiotherapy or chemotherapy, limits the contextualization of the observed efficacy. Additionally, the single-patient nature of this study may not account for variability in tumor biology, clinical presentation, or individual responses to ICIs.

Further, spinal cord edema progression following surgery, which later improved with pembrolizumab, could involve multiple confounding factors, including surgical trauma or natural disease progression. These factors may influence the interpretation of the treatment's efficacy. Finally, the follow-up duration may not be sufficient to capture long-term outcomes, including late tumor recurrence or delayed irAEs.

Future research is required to evaluate the efficacy and safety of ICIs in MISCTs. Larger case series with standardized treatment protocols and outcome measures will enhance the reliability of findings.

Conclusion

This case underscores the potential efficacy of ICIs in treating MISCTs. Pembrolizumab showed notable clinical benefits, including tumor burden reduction and sustained neurological function. However, irAEs remain a major concern. Further studies are necessary to validate the

effectiveness of ICIs in this rare tumor type and to develop guidelines that balance therapeutic efficacy with the management of adverse effects.

Author contributions R.F. and M.M. wrote the main manuscript, and R.F. prepared Figs. 1, 2, 3, 4 and 5; Table 1. All authors reviewed the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

References

1. Kalayci M, Çağavi F, Gül S, Yenidünya S, Açıkgöz B (2004) Intramedullary spinal cord metastases: diagnosis and treatment – an illustrated review. *Acta Neurochir (Wien)* 146(12):1347–1354. <https://doi.org/10.1007/s00701-004-0386-1>
2. Strickland BA, McCutcheon IE, Chakrabarti I, Rhines LD, Weinberg JS (2018) The surgical treatment of metastatic spine tumors within the intramedullary compartment. *J Neurosurg Spine* 28:79–87. <https://doi.org/10.3171/2017.5.SPINE161161>
3. Hashii H, Mizumoto M, Kanemoto A, Harada H, Asakura H, Hashimoto T, Furutani K, Katagiri H, Nakasu Y, Nishimura T (2011) Radiotherapy for patients with symptomatic intramedullary spinal cord metastasis. *J Radiat Res* 52:641–645. <https://doi.org/10.1269/jrr.10187>
4. Eguren-Santamaria I, Sanmamed MF, Goldberg SB, Kluger HM, Idoate MA, Lu BY, Corral J, Schalper KA, Herbst RS, Gil-Bazo I (2020) PD-1/PD-L1 blockers in NSCLC brain metastases: challenging paradigms and clinical practice. *Clin Cancer Res* 26:4186–4197. <https://doi.org/10.1158/1078-0432.CCR-20-0798>
5. Schiff D, O'Neill BP (1996) Intramedullary spinal cord metastases: clinical features and treatment outcome. *Neurology* 47:906–912. <https://doi.org/10.1212/WNL.47.4.906>
6. Tobin MK, Geraghty JR, Engelhard HH, Linninger AA, Mehta AI (2015) Intramedullary spinal cord tumors: a review of current and future treatment strategies. *Neurosurg Focus* 39:E14. <https://doi.org/10.3171/2015.5.FOCUS15158>
7. Rykken JB, Diehn FE, Hunt CH, Schwartz KM, Eckel LJ, Wood CP, Kaufmann TJ, Lingineni RK, Carter RE, Wald JT (2013) Intramedullary spinal cord metastases: MRI and relevant clinical features from a 13-year institutional case series. *AJNR Am J Neuroradiol* 34:2043–2049. <https://doi.org/10.3174/ajnr.A3526>
8. Winkelman MD, Adelstein DJ, Karlins NL (1987) Intramedullary spinal cord metastasis. Diagnostic and therapeutic considerations. *Arch Neurol* 44:526–531. <https://doi.org/10.1001/archneur.1987.00520170054022>
9. Wong CS, Fehlings MG, Sahgal A (2015) Pathobiology of radiation myopathy and strategies to mitigate injury. *Spinal Cord* 53:574–580. <https://doi.org/10.1038/sc.2015.43>
10. Gasser T, Sandalcioglu IE, El Hamalawi B, van de Nes JA, Stolke D, Wiedemayer H (2005) Surgical treatment of intramedullary spinal cord metastases of systemic cancer: functional outcome and prognosis. *J Neurooncol* 73:163–168. <https://doi.org/10.1007/s11060-004-4275-5>
11. Chopra N, Menounos S, Choi JP, Hansbro PM, Diwan AD, Das A (2021) Blood-spinal cord barrier: its role in spinal disorders and emerging therapeutic strategies. *NeuroSci* 3:1–27. <https://doi.org/10.3390/neurosci3010001>
12. Wang M, Ma X, Guo L, Xia F (2017) Safety and efficacy profile of pembrolizumab in solid cancer: pooled reanalysis based on randomized controlled trials. *Drug Des Devel Thers* 11:2851–2860. <https://doi.org/10.2147/DDDT.S146286>
13. Brahmer JR, Lacchetti C, Schneider BJ, Atkins MB, Brassil KJ, Caterino JM, Chau I, Ernstoff MS, Gardner JM, Ginex P, Hallmeyer S, Holter Chakrabarty J, Leighl NB, Mammen JS, McDermott DF, Naing A, Nastoupil LJ, Phillips T, Porter LD, Puzanov I, Reichner CA, Santomaso BD, Seigel C, Spira A, Suarez-Almazor ME, Wang Y, Weber JS, Wolchok JD, Thompson JA, National Comprehensive Cancer Network (2018) Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American society of clinical oncology clinical practice guideline. *J Clin Oncol* 36:1714–1768. <https://doi.org/10.1200/JCO.2017.77.6385>
14. Gazzeri R, Telera S, Galarza M, Callovini GM, Isabella S, Alfieri A (2021) Surgical treatment of intramedullary spinal cord metastases: functional outcome and complications—a multicenter study. *Neurosurg Rev* 44:3267–3275. <https://doi.org/10.1007/s10143-021-01491-8>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.