Intradural Spinal Metastases during Systemic Chemotherapy for Non-Hodgkin's Lymphoma: A Case Report

Taketoshi Kushida, Takashi Adachi, Yoichi Tani, Masaaki Paku, Shinichirou Taniguchi and Takanori Saito

Department of Orthopedic Surgery, Kansai Medical University, Osaka, Japan

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The blood-brain-barrier hampers the entry of chemotherapeutic drugs from systemic circulation into the central nervous system (CNS), preventing accumulation of the intradural concentrations required to eradicate tumor metastases[1]. We present a case of intradural spinal metastases that manifested during systemic chemotherapy for non-Hodgkin lymphoma (NHL). The case report was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from the patient's family.

A 62-year-old Japanese woman was referred to our hospital for severe back pain of two months' duration. She had no additional neurological disturbances. Computed tomography showed multiple osteolytic lesions in several vertebrae (Fig. 1A). Magnetic resonance imaging (MRI) showed deformities at several vertebrae, but did not show an obvious epidural or intradural infiltration (Fig. 1B). Fluorodeoxyglucose-positron emission tomography (FDG-PET) showed lesions in multiple lymph nodes and several vertebrae (Fig. 2 A).

Hemotoxylin and eosin (H & E) staining of her left groin lymph node biopsy showed large neoplastic cells with hyperchromatic nuclei in a background of small lymphocytes (Fig. 2B). Immunostaining revealed small $CD3^+/CD5^+$ lymphocytes and abnormally large $CD20^+/CD79a^+$ cells (Fig. 2 C, 2D). Based on these findings, she was diagnosed with NHL (diffuse large B-cell lymphoma, stage IV). She received systemic chemotherapy with eight cycles of R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone) in addition to fractionated radiotherapy. At the end of the final chemotherapy cycle, eight months after initial treatment, she complained of acute, progressive paraparesis. Her muscle strength had deteriorated to 2/5, and severe numbness in both lower extremities was apparent. FDG-PET confirmed successful resolution of the lesions identified on her initial examination. However, a new intradural uptake lesion, measuring 10.5 mm in diameter, was found at L2 (Fig. 3A). Gadolinium-enhanced MRI showed an enhanced lesion in the intradural space from T12 to L5 (Fig. 3B). Histological analysis of the cerebrospinal fluid (CSF) showed a number of atypical lymphocytes with irregular-shaped nuclei, leading to the diagnosis of intradural metastases (Fig. 3C). For management, she underwent intrathecal chemotherapy, which has been introduced in the treatment of CNS lymphoma[1,2], with nine cycles of methotrexate, cytarabine, and hydrocortisone.

Four months after the intrathecal chemotherapy, an MRI showed that the enhanced-intradural lesion had almost disappeared (Fig. 4A). Muscle strength in both lower extremities had improved to 3/5, and a rolling walking gait was possible. However, nine months after the intrathecal chemotherapy, FDG-PET showed lesions throughout her body (Fig. 4 B). Finally, despite treatment with several systemic chemotherapies, she died of recurrent NHL 20 months after the initial systemic chemotherapy course.

The occurrence rate of epidural metastases in patients with NHL has been reported as 7.4%[3,4], and the rate of CNS metastases, consisting of parenchyma and leptomeninges with NHL, is 4.2-4.8%[1,5,6]. The common pathway to metastatic involvement of the CNS is metastasis to the subarachnoid space, referred to as leptomeningeal spread[5]. The five-year survival rate of R-CHOP-treated patients with non-metastatic NHL is 87%[7]. On the other hand, the survival rate for patients with leptomeningeal meningitis is 2-6.5 months[1]. The most likely reason is that most systemically

Corresponding author: Taketoshi Kushida, kushidat@hirakata.kmu.ac.jp
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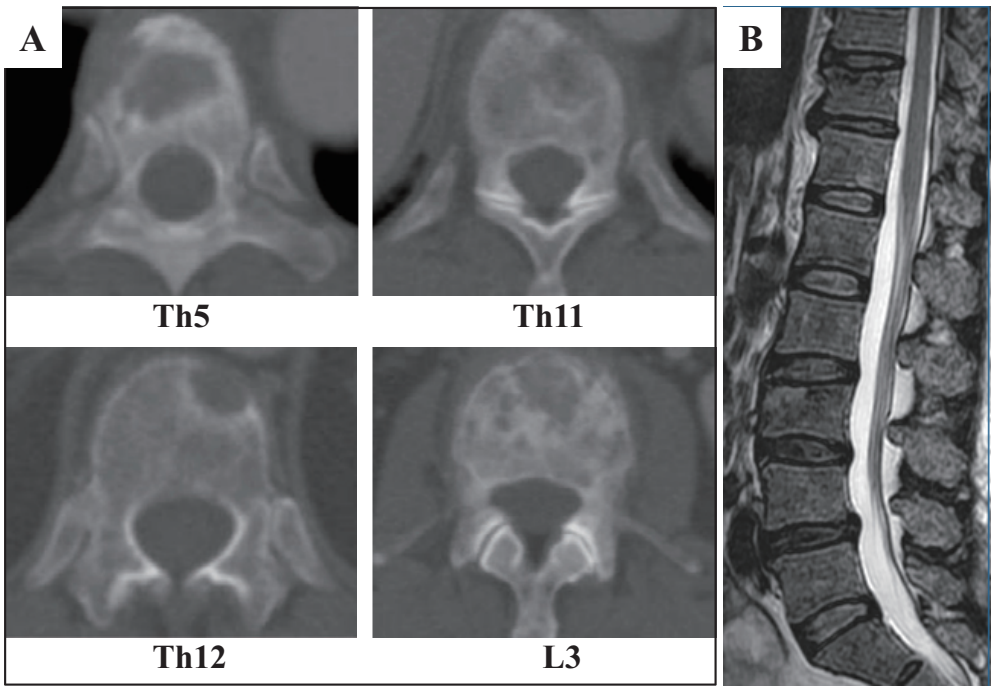

Figure 1. Pretreatment CT and MRI scan images.
A: Representative osteolytic vertebrae, such as Th5, Th11, Th12 and L3 by CT scan, were shown. B: A sagittal T2-weighted MRI scan of the lumbar spine showed deformities at T12 and L3 vertebrae, but did not show any obvious epidural or intradural infiltration. CT, Computed tomography MRI, magnetic resonance imaging.

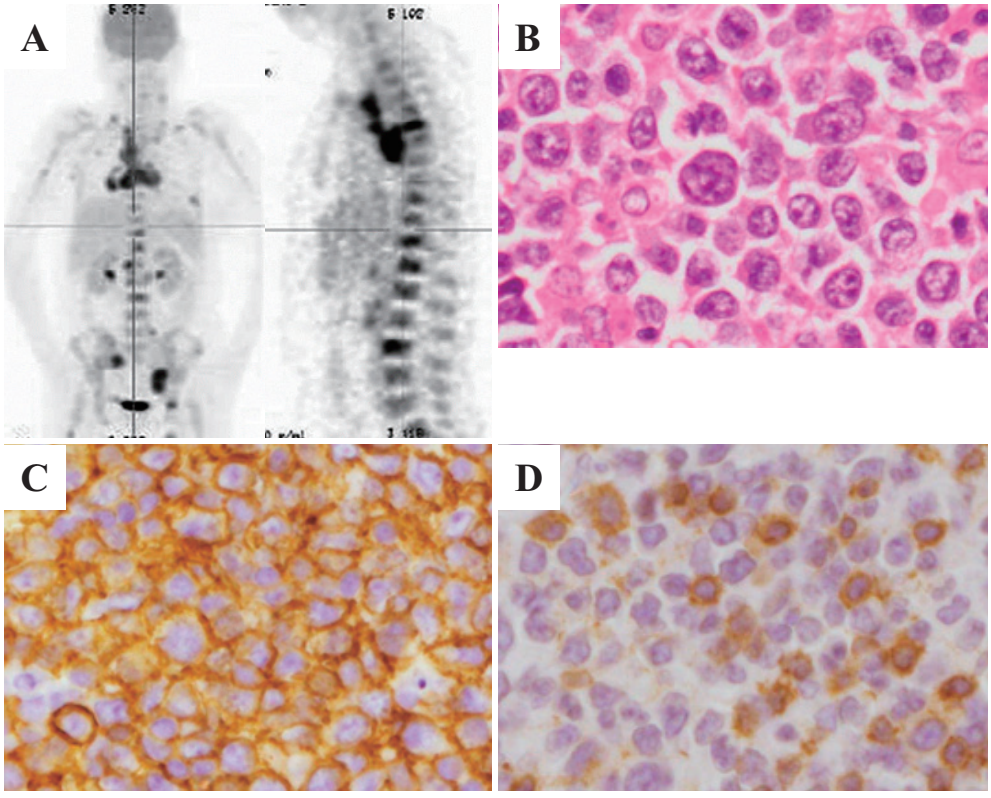

Figure 2. FDG-PET scan and histology before chemotherapy.
A: Pretreatment FDG-PET scan showing uptake in lesions in multiple lymph nodes and several vertebrae. B: H & E staining showed large neoplastic cells with hyperchromatic nuclei in the background of small lymphocytes (×100). C: Large neoplastic cells were stained by CD 20 (×100). D: Background- small lymphocytes were stained by CD3 (×100). FDG-PET, fluorodeoxyglucose-positron emission tomography. H & E, Hemotoxylin and eosin.

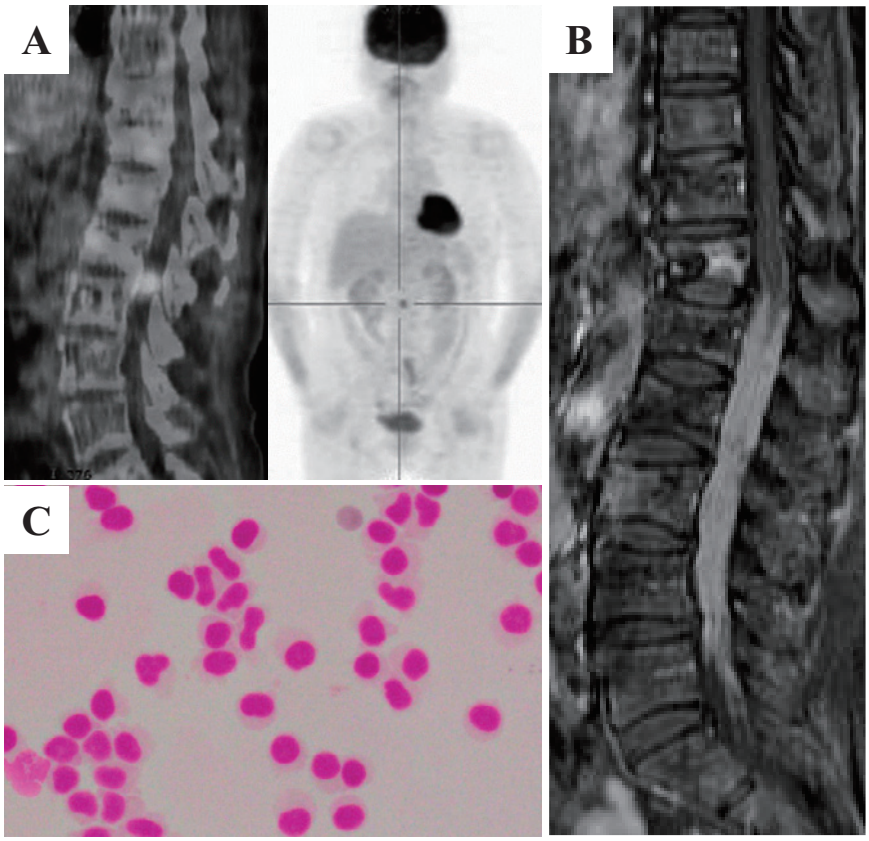

Figure 3. Images and CSF histology 8 months after systemic chemotherapy.
A: An FDG-PET scan eight months after systemic chemotherapy, showing absence of the previous uptake lesions in the lymph nodes and vertebrae, but new lesions in the intradural space. B: Sagittal and axial short-T1 inversion recovery images with gadolinium of the lumbar spine showing an enhanced lesion in the intradural space from T12 to L5. C: H & E staining showing a large number of atypical lymphocytes with irregular-shape nucleus (×100). FDG-PET, fluorodeoxyglucose-positron emission tomography. MRI, magnetic resonance imaging. CSF, cerebrospinal fluid.

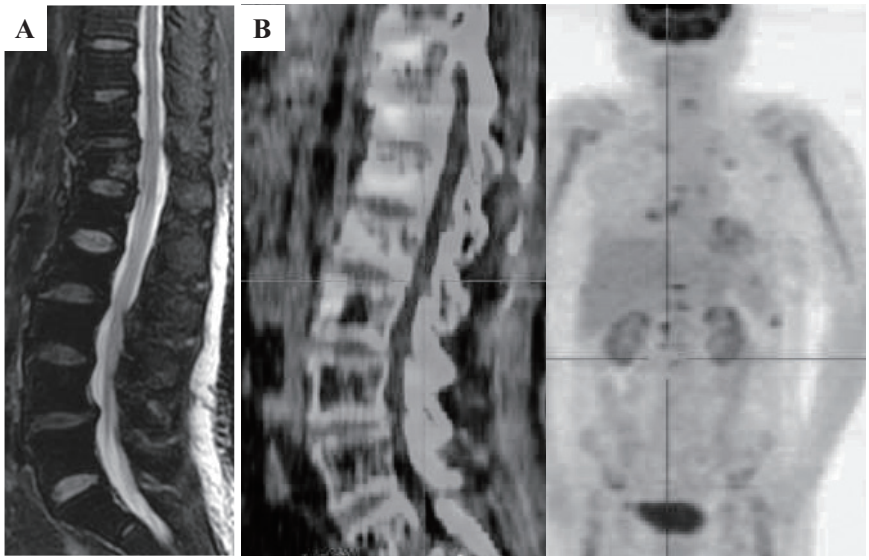

Figure 4. MRI and FDG-PET scan images after intrathecal chemotherapy.
A: Four months after the intrathecal chemotherapy, sagittal T2-weighted images (fat suppression) showed that the intradural enhanced lesion had almost disappeared. B: Nine months after the intrathecal chemotherapy, FDG-PET showed lesions throughout her body, with the exception of the intradural lesion (Fig. 4B). MRI, magnetic resonance imaging. FDG-PET, fluorodeoxyglucose-positron emission tomography.

administered cytotoxic drugs cannot penetrate the blood-brain barrier to achieve clinically relevant concentrations in the CSF[1]. In our case, intrathecal chemotherapy was temporarily effective for treating the intradural metastases; however, the patient eventually died of recurrent NHL.

In this patient, while minute intradural spinal metastatic lesions may have been present at the initial visit, they may have been too small to detect using the available imaging modalities. Therefore, treating physicians should collaborate with medical oncologists and carefully monitor for intradural metastases in patients with NHL during and after treatment with systemic chemotherapy.

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

Author Contributions: Taketoshi Kushida wrote and prepared the manuscript, and all of the authors participated in the study design. All authors have read, reviewed, and approved the article.

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