Clinical Case Report

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Primary spinal mucosa-associated lymphoid tissue lymphoma

A case report

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Abstract

Rationale: Mucosa-associated lymphoid tissue (MALT) lymphoma is an indolent B-cell lymphoma which occurs mainly in the organs having mucosal layer and owns a fairly good prognosis. To date, 7 cases of spinal primary MALT has been reported before. However, there is no consensus on the optimal adjuvant treatment modalities for primary spinal MALT. The aim of this study was to add a new case of MALT which responded well to systemic therapy to the literature and to review the current literature.

Patient concerns: A 68-year-old woman visited to our hospital due to back pain and progressive bilateral lower extremity weakness for 2 months. Magnetic resonance imaging (MRI) of the spine revealed a diffusely contrast-enhancing epidural mass extending from vertebral body T6 to T8 with compression of the spinal cord. Due to the spinal cord compression, patient underwent surgical resection. Histological examination indicated monocytoid small B-cells. Immunochemical study demonstrates that most tumor cells were positive for CD20, CD21, CD45, CD79a, CD43, bcl-2 with Ki-67 labing index was 15%, but were negative for CD3, CD5 cyclin D1, BCL6, and CD23. The positron emission tomography/computer tomography (PET/CT) revealed that right iliac wing and right liver were metastases for the standard uptake value (SUV) were 9.05 and 8.35, respectively.

Diagnoses: Based on these findings, final diagnosis of spinal MALT lymphoma was made.

Interventions: After the diagnosis, the patient received 6 cycles of immuno-chemotherapy and repeated intrathecal methotrexate and intrathecal cytarabine.

Outcomes: At 1 year follow up, no recurrence or other dissemination was detected.

Lessons: Chemotherapy and/or radiation have been employed in larger case series. While there is no defined treatment guideline for this rare disease entity, our reported case suggests a favorable prognosis when combining both surgical and adjuvant systemic approach.

Abbreviations: CNS = central nervous system, FDG = fluorodeoxyglucose, MALT = mucosa-associated lymphoid tissue, MRI = magnetic resonance imaging, PET/CT = positron emission tomography/computer tomography, SUV = standard uptake value.

Keywords: chemotherapy, dural MALT lymphoma, metastasis, mucosa-associated lymphoid tissue lymphoma, spinal MALT lymphoma

1. Introduction

Marginal zone B-cell malignant lymphoma refers to a low-grade malignant non-Hodgkin lymphoma that develops in mucosa-associated lymphoid tissue (MALT). The concept of MALT lymphoma for extranodal malignant lymphoma of marginal zone B-cell origin was proposed firstly by Isaacson and Wright in 1983.[1] MALT is closely associated with mucosal tissue and arises most commonly in the stomach which is associated with *Helicobacter pylori* infections.[2] Apart from stomach, MALT lymphoma may also present in organs and tissue sites without a mucosa, such as obit, thyroid, lungs, and urogenital tract; an excellent single-center study documenting 72 cases at various locations has been reported.[3,4]

Primary spinal epidural lymphoma is relatively rare among all lymphomas, with an incidence ranging from 0.8% to 2.8%.[5–7] The mid-thoracic spine is the most common site of involvement followed by the lumbar spine and the cervical spine.[5] Spinal MALT lymphoma is quite rare and little is known about its clinical course and optimal treatment. To the best of our knowledge, only 7 cases of primary MALT lymphoma involving the spine have been reported in the literature (Table 1).[8–14] In the reported cases, MALT lymphomas were confined to spine without distant destruction. Moreover, here we reported a rare case of primary spinal MALT lymphoma, which has distant metastases containing ilium and liver metastases.

2. Case report

A 68-year-old woman was admitted to our hospital in September 2016 because of a history of back pain and progressive bilateral

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Table 1

Primary spinal dural MALT lymphoma reported.

Study	Age (y)/Sex	Location	Clinical symptom	Pathology	Therapy	Outcome
Chahal et al[8]	77/Female	T2–T3	NA	NA	SC (R)	Survive for 8 y
Venkataraman et al[9]	36/Female	Thoracic	NA	NA	NA	NA
Ahmadi et al[10]	65/Male	T3–T7	Progressive paraparesis	Monomorphous lymphocytoid CD20+, CD45 +, bcl-2+, CD10-, bcl-6-	S R	NED after 11 y
Hojo et al[11]	58/Male	T11–L1	Symptoms of cord compression	Small lymphocytesr CD20+, CD79a+CD3-, CD5-, CD10-, λLCR	S R	Relapse after 3 y
Dey et al[12]	58/Female	Thoracic	Symptoms of cord compression	Atypical lymphocyte /plasmacytic CD19+, CD20+, bcl-2+, CD5-, CD10-, bcl-6-	S R	Relapse after 2 y
Alaya and Achour [13]	67/male	T6–T8	Progressive paralysis of the lower limbs	NA	C (8 RCHOP)	NA
Fleury et al[14]	NA	NA	NA	NA	NA	A&W
Current case	68/Female	T6–T8	Back pain, bilateral lower extremity weakness	Monocytoid small B-cells,CD20+, CD21+, CD45+, CD79a+, bcl-2+	S C	A&W after 9 mo

A&W = alive and well,C = chemotherapy, MALT = mucosa-associated lymphoid tissue, NA = not available, R-CHOP = rituximab-cyclophosphamide, adriamycin, vincristine, prednisone, R = radiotherapy, S = surgery.

lower extremity weakness for 2 months. The patient had no trauma history and her significant medical history included non-insulin-dependent diabetes mellitus and hypertension. On examination, tenderness in the thoracic spine region was positive. Neurologic examination demonstrated bilateral lower limb spasticity with an asymmetric pyramidal pattern of weakness (right > left, Medical Research Council grade 4 and 3, respectively). No reflex deficits were identified, and there was no evidence of bladder or bowel dysfunction. No further neurological deficits were found. Magnetic resonance imaging (MRI) of the spine revealed a diffusely contrast-enhancing epidural mass extending from vertebral body T6 to T8 with compression of the spinal cord (Fig. 1A, B, G). The epidural mass extended through the right intervertebral foramen of T6–7, forming a paravertebral tumor of similar size. No hemorrhage or infiltration of bony structures was noted. The possibility of inflammatory spondylitis with epidural abscess was considered while tumor should be excluded. Laboratory investigations including tumor markers did not show any abnormal findings.

To achieve early decompression of the spinal cord and establish a definite pathological diagnosis by samples from the epidural mass, a T6–8 laminectomy was performed. The dorsal mass was near-total resected with partial resection of the ventral and lateral tumor. The resected specimen appeared as a 4×2 cm, grayish, fleshy mass lesion of soft consistency. Complete resection was impossible because of significant adherence of the tumor to the dural sheath. After successful surgery procedure, the postoperative course was uneventful.

Pathological examination of the tumor samples revealed that the majority of the tumor cells were monocytoid small B-cells, which have small to medium sized nuclei and abundant pale cytoplasm, surrounding germinal centers. By immunochemical studies, most tumor cells were positive for CD20, CD21, CD45, CD79a, CD43, bcl-2 with Ki-67 labing index was 15%, but were negative for CD3, CD5, cyclin D1, BCL6, and CD23. Expression of CD3 and CD5 was restricted to reactive T lymphocytes. Given the nonspecific B-cell phenotype and the presence of reactive germinal centers, the pathology department reported that these findings were consistent with MALT lymphoma.

Four months later, the patient visited our hospital again for her progressive asymmetric weakness of both lower limbs and increasing back pain with bowel and bladder dysfunction. The PET/CT was performed which indicated that the thoracic spine of T6–8 level (SUVmax = 8.74), right iliac wing (SUVmax = 9.05), and right liver (SUVmax = 8.35) presented abnormal 18-fluorodeoxyglucose (18-FDG) uptake (Fig. 2). Taking together tumor and surgical destruction and distant metastases was considered. Unfortunately, the distant lesions did not undergo biopsy and surgical section. Then bone marrow biopsy and cerebrosppinal tapping were performed, which revealed no infiltration. Based on these findings, a diagnosis of stage IVE MALT lymphoma was made according to revised staging for primary nodal lymphoma and Lugano classification.[15] In combination with the patient's intention who refused to radiotherapy. Systemic therapy with rituximab, methotrexate, cyclophosphamide, vincristine, and prednisolone (R-MAX-COP protocol) every 3 weeks and central nervous system prophylaxis (intrathecal cytarabine and dexamethasone) were carried for the patient. After the first cycle of chemotherapy (Fig. 1C and D), her back pain, motor weakness, and urinary dysfunction showed remarkable improvement. After 4 cycles, her MRI of spine confirmed continuing clinical remission of the primary lesion and right iliac wing (Fig. 1E, F, H, I). No new disease manifestations development until recent fellow-up.

3. Discussion

MALT lymphomas are a subgroup of low-grade B-cell lymphomas that arise from extranodal sites normally devoid of lymphoid tissue. According to recent statistics, MALT lymphoma is among the more common lymphoma entities, accounting for 7% to 8% of newly diagnosed lymphomas; it is not as common as follicular and diffuse large B-cell lymphoma but is about equal in incidence to mantle cell lymphoma.[16] Although it initially was reported as a subtype of gastric,[1] any site of the body can be the original location of MALT. The most frequent localizations are salivary gland, skin, lung, and thyroid.[17]

Primary central nervous system (CNS) lymphomas are a rare type of extranodal non-Hodgkin lymphoma and account for approximately 4% of all primary cerebral tumors.[18] High-grade B-cell lymphomas of the diffuse large B-cell type are the classic primary CNS lymphomas.[19] These patients typically have poor

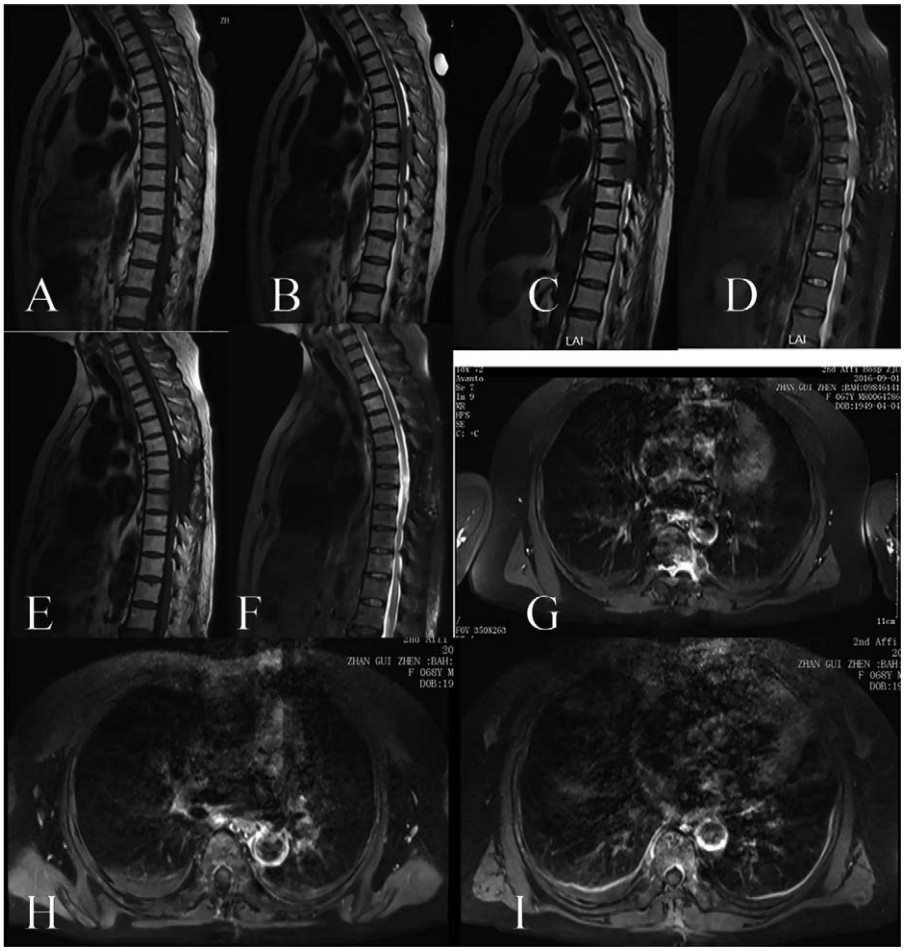

Figure 1. Magnetic resonance images at the initial visit (A, B, G), postoperation and after 1 cycle of chemotherapy (C, D), and at the latest follow-up (May 29, 2017) (E, F, H, I). (A, B) Sagittal plane at T6–7 showing abnormal lesion located in the epidural space of the thoracic spinal canal. (G) Axial planes note the mass extending through the foramen forming a paravertebral tumor (arrows). (C, D) Sagittal plane demonstrates the tumor at the thoracic spine, which had been partially resected and chemotherapy showed complete disappearance. (E, F, H, I) There was no recurrent tumor in the epidural space at the last follow-up.

outcome with a median survival time between 30 and 60 months when treated with radiation combination with chemotherapy.[18,19] Primary low-grade lymphomas, either primary at the time of initial presentation or secondary during the natural progression of the disease, by contrast, are exceptionally rare. Among the low-grade subset, marginal zone B-cell lymphomas are the most common.[20] MALT lymphomas involved the CNS are rare whenever they occur, the dura mater of the head is the most commonly involved site in comparison to other CNS compartments[21] and MALT lymphomas originating from the spine are extremely rare. Up to date, 7 cases of spinal MALT lymphoma are reported (Table 1). Monnard et al[5] reported the most common involved site of spinal lymphoma is the thoracic spine. Among the patients reviewed in the literature and reported here, the thoracic region was involved in patients.

Irrespective of the primary location, these types of tumor have much of the same clinical, pathological, and molecular features. They usually show a slow progression and often remain localized to their sites of origin for many years before dissemination. In contrast to nodal and splenic marginal zone B-lymphoma, CNS MALT lymphomas typically characterized as a non-aggressive lymphoma without bone marrow and lymph node involvement.[22] In the reported cases of spinal MALT lymphoma, the lesion remained localized to the spine. While our patient presented as spinal MALT lymphoma with involvement outside of the spine. It warrants further investigation to identify whether the spinal MALT transform to high-grade lymphoma. Since in most cases, MALT lymphomas have been reported to transform into diffuse large B-cell lymphoma, which has a much worse prognosis.[23,24] Moreover, indolent lymphomas transform into higher grade lymphomas at a rate of 3% per year.[25] While MALT lymphomas remain indolent, there is a potential life-long risk of recurrence. For the extragastric, the rate of recurrence after successful therapy appears to be high.[16] Moreover, Hojo et al[11] reported a case of primary spinal MALT relapse at a different spinal level after 3 years of primary lesion. Taken together, a routine long-term follow-up period is recommended.

In terms of its site of origin, there is no CNS-associated mucosa. Outside the CNS, MALT lymphomas are believed to result from chronic inflammation induced by infection microorganisms. However, some have indicated that dural-associated lymphoid tissue may arise from chronic inflammatory stimuli, similar to the MALT encountered in other organs.[16,26,27] It has been shown that MALT type tissue can be developed under inflammatory conditions within CNS, providing a location for the development

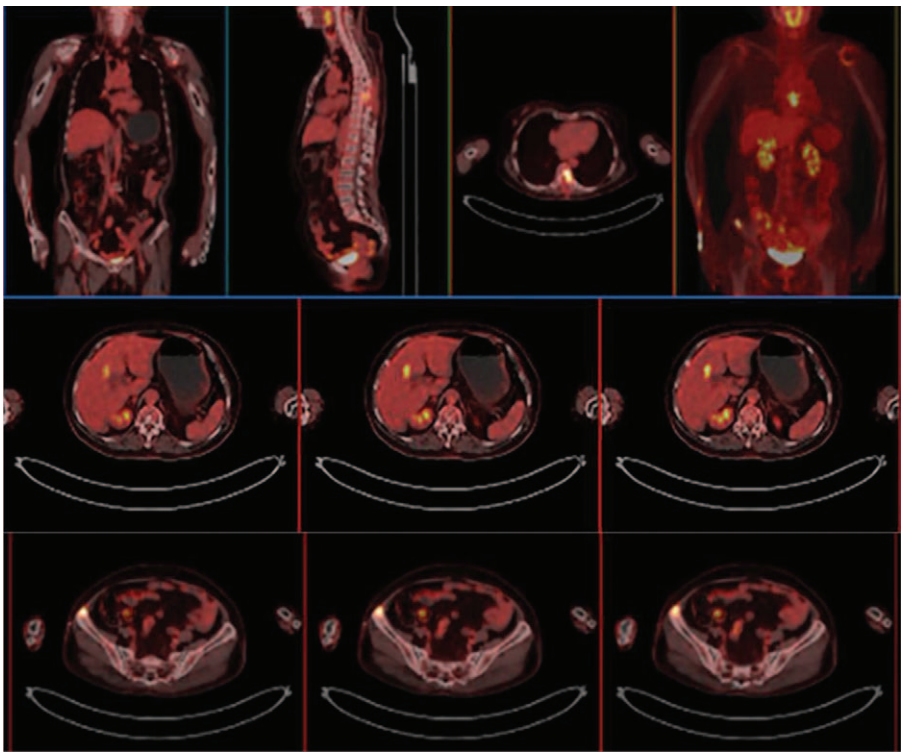

Figure 2. Positron-emission tomography (PET) was taken to classify the stage of the disease. Uptake in the spinal canal at T6–8, right iliac wing and right liver were clearly observed.

of MALT-lymphoma.[20] Another possible pathogenesis is that meningothelial cells or arachnoid cells play the role of epithelial cells in the development of marginal zone lymphomas at non-mucosal sites.[10] Additionally, IgG4 expression has been reported in a small subset of dural MALT lymphomas. In a recent histopathologic series of 32 MALT lymphomas, the authors found 1 patient with an IgG4 positive thoracic dural lesion without further elaboration, and concluded that there may be a strong association between marginal zone B-cell lymphoma of the dura and IgG4-related diseases.[9] Therefore, case reports including clinical and histopathological data should be accumulated for better understanding of this rare clinical entity.

Therapeutic management of MALT lymphomas is extremely heterogeneous, and universally accepted therapeutic guidelines for this rare clinical entity do not exist. Compared with parenchymal primary CNS lymphoma or systemic lymphoma with CNS metastasis, primary CNS MALT lymphoma originating from the dura matter is curable by surgical removal and radiation therapy. Stage of disease is the relevant parameter for therapeutic choice, because patients with limited-stage MALT lymphoma can achieve long-term complete remission, and probably a cure, with local treatments (i.e., surgery, radiotherapy), whereas patients with advanced disease. In some cases, chemotherapy might be suitable as the sole adjuvant treatment, as several case reports have shown long-term survival with methotrexate.[13,16,6] In a recent reported stage IV MALT lymphoma of spine who received 8 RCHOP cures. The patient's neurological signs were improved significantly with no lesion of evolutive suspicious nature at the thoracic and abdominopelvic stages at the end-of-treatment scan.[13] In our case high-dose methotrexate and rituximab intravenously and cytarabine intrathecally brought remission to the patient. Primary surgery was impressive in this particular case because of the patient with progressive neurologic deficits. We did not take radiotherapy immediately for patient' refusal and multiple involved sites of our patient.

4. Conclusion

In the present report, we described a case of primary spinal MALT lymphoma. The clinician encountering a patient with spinal lymphoma should be careful the type of the lymphoma. Since no curative treatment exists, the treatment should be "patient-tailored," taking into account the site, the stage, and the clinical characteristics of the individual patient. When systemic treatment is needed, chemotherapy (and/or immunotherapy with anti-CD20 monoclonal antibodies) can be considered.

5. Method

This was a case report. Ethics committee or institutional review board approval was not obtained. It was not necessary for the case report. The patient signed informed consent for the publication of this case report.

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