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CASE REPORT

A case of neurolymphomatosis caused by follicular lymphoma successfully treated with bendamustine

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Key Clinical Message

Currently, there is no standard treatment for neurolymphomatosis because of the scarcity of clinical studies. Here, we report the successful treatment of neurolymphomatosis caused by follicular lymphoma with bendamustine, which could be an effective treatment option for this condition.

Keywords

Bendamustine, blood-nerve barrier, follicular lymphoma, neurolymphomatosis.

Introduction

Neurolymphomatosis, the direct infiltration of lymphoma cells into the peripheral or cranial nerves, occurs very rarely in lymphoma patients [1]. It manifests chiefly in aggressive B-cell or T-cell lymphomas and is not normally diagnosed in patients with low-grade lymphomas such as follicular lymphoma [2]. There is no standard treatment for neurolymphomatosis because of the scarcity of clinical studies. We report the successful treatment of neurolymphomatosis caused by follicular lymphoma with bendamustine.

Case history

A 47-year-old woman with a history of follicular lymphoma presented with severe pain in her left leg. She had been diagnosed with follicular lymphoma Grade I at age 30 years, and she had been assigned a low-risk classification according to the follicular lymphoma international prognostic index(FLIPI) score. Complete remission was achieved after eight courses of the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisolone). After the first complete remission, the patient experienced multiple relapses, and she was treated with a combination of chemotherapy and focal radiotherapy (Table 1), achieving complete remission each time.

On admission, the patient had difficulty walking because of the pain intensity. However, she did not report sensory loss in either leg or the presence of symptoms of bladder and bowel disturbances. Physical examination did not reveal peripheral lymphadenopathy or hepatosplenomegaly. Findings of neurologic examination of the cranial nerves were unremarkable. Upper and lower limb examination did not show motor dysfunction or sensory loss, and tendon reflexes were normal. Gadolinium-enhanced magnetic resonance imaging (MRI) revealed enlargement and strong postgadolinium enhancement of the left sacral nerve root, findings consistent with neurolymphomatosis (Fig. 1A). Positron emission tomography did not show uptake around the sacral nerve root or signs of lymphoma recurrence at other sites. Cytological examination and flow cytometric analysis of cerebrospinal fluid did not show any lymphoma infiltration. Because of the difficulty in performing a biopsy of the nerve, we diagnosed the patient with neurolymphomatosis clinically, and initiated a BR regimen (90 mg/m^2

Table 1. Treatments provided from the onset of neurolymphomatosis.

	Age	Radiation	Regimen	Agent				
Primary lymphoma	30		CHOP	Doxorubicin	Cyclophosphamide	Vincristine	Prednisolone	
1st relapse	32	40 Gy on cervical region	MECP	Mitoxantrone	Etoposide	Carboplatine	Prednisolone	
2nd relapse	40		R+mitoxantrone	Rituximab	Mitoxantrone			
3rd relapse	43	36 Gy on left femur	Rituxiamab monotherapy	Rituximab				
4th relapse	44							
5th relapse	45		R-CHASE	Rituximab	Cyclophosphamide	Etoposide	Cytarabine	Dexamethasone
			R-MEAM and autologous stem cell transplantation	Rituximab	Ranimustine	Etoposide	Cytarabine	Melphalan

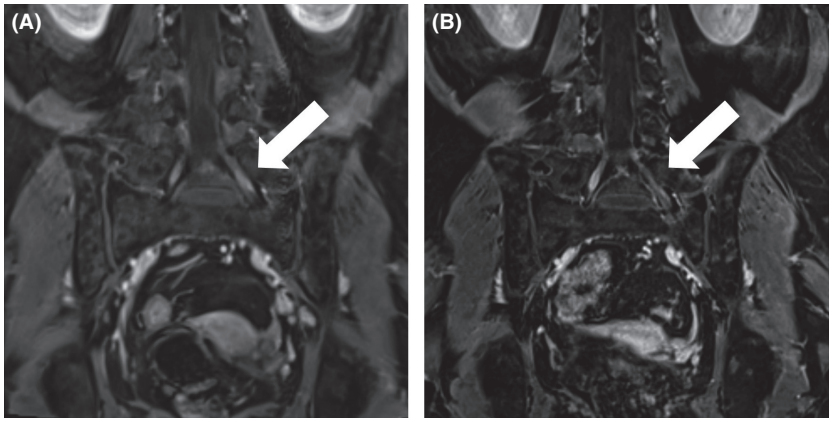

Figure 1. Coronal images from gadolinium-enhanced magnetic resonance imaging at initial diagnosis of neurolymphomatosis (Panel A), and after treatment with bendamustine (Panel B). Enlargement and strong postgadolinium enhancement of the left sacral nerve that was observed at diagnosis (Panel A, arrow) disappeared after six courses of treatment with bendamustine and rituximab (Panel B, arrow).

bendamustine on days 1 and 2 with 375 mg/m^2 rituximab on day 1). The pain began to resolve 4 days later and disappeared completely by 2 weeks. MRI performed 3 weeks after chemotherapy revealed shrinkage of the lesion. The patient received six courses of BR, after which MRI showed no sign of the lesion (Fig. 1B). No recurrence was observed 14 months postchemotherapy.

Discussion

Systemic chemotherapy, including methotrexate, and intrathecal chemotherapy as well as radiotherapy have traditionally been used for treating neurolymphomatosis. However, their effectiveness is unclear because there are no standardized criteria to measure treatment response [1]. Methotrexate, which penetrates the blood–brain and blood–nerve barriers, can cause renal impairment and mucositis, especially when administered in a high dose. Bendamustine is effective for treating relapsed or refractory indolent lymphoma [3]. However, there are no reports of bendamustine penetrating the human blood–brain or blood–nerve barriers, although another investigation showed that bendamustine does cross the murine blood–brain barrier [4]. Retrospective studies also showed the efficacy of bendamustine for recurrent primary central nervous system lymphoma [5, 6] and brain metastasis of breast cancer [7]. To the best of our knowledge, this is the first report indicating that bendamustine can cross the human blood–nerve barrier, and evidence suggests that bendamustine may be effective not only for CNS lymphoma, but also for neurolymphomatosis caused by follicular lymphoma.

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