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Neurolymphomatosis presenting as brachial plexopathy with involvement of cranial nerves

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Neurolymphomatosis (NL) is a rare disease characterized by lymphomatous invasion of the cranial or peripheral nerves by lymphoma. A high suspicion is important due to the various presenting symptoms mandating consideration of many differential diagnoses. We report a case of NL of the cranial nerves and plexus presenting as diplopia, facial palsy, and weakness of the upper and lower limbs in sequence.

Key words: Neurolymphomatosis; Cranial nerves; Plexus

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Neurolymphomatosis (NL) is defined as the infiltration of the peripheral nervous system including cranial nerves, peripheral nerves, roots, and plexus by non-Hodgkin's lymphoma and nontumorous lymphocytes.[1] NL can occur as a primary presentation of isolated nerve involvement by lymphoma cells, which is called primary NL, but it is more often seen when lymphoma disseminates neural structures from a site of relapse or the progression of a previously diagnosed lymphoma, which is termed secondary NL.[2] Most neoplasms of the nervous system are a systemic disease or a primary central nervous system lymphoma (PCNSL), with NL being a rare manifestation of lymphoma.[3–5]

Here we report a case of a 59-year-old female diagnosed as diffuse large-B-cell lymphoma (DLBCL) presenting sequentially as diplopia, facial palsy, and brachial and lumbosacral plexopathy.

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CASE

A 59-year-old female visited our clinic due to right abducens nerve palsy presenting with binocular horizontal diplopia. She denied a past medical history except for hypertension, and reported that the present symptom had started only 3 days previously. Left facial palsy occurred 17 days after the appearance of the first symptom, and brain magnetic resonance imaging (MRI) showed left facial neuritis (Fig. 1A). She was treated with oral corticosteroids, which improved the facial palsy. A month after the facial palsy she experienced mild weakness of left shoulder elevation (Medical Research Council grade 4), paresthesia, and pain in the left upper extremity. Electrophysiology showed reduced amplitudes of the compound motor action potentials in the left axillary nerve (4.2 mV) and musculocutaneous nerve (1.0 mV) compared with the right arm (29.3 mV and 10.2 mV, respectively). Needle electromyography revealed denervation of the left lateral deltoid and biceps brachii muscles (Table 1). These findings were compatible with left upper brachial plexopathy. Spine MRI also revealed left brachial plexus swelling and enhancement (Fig. 1B). Repeated cerebrospinal fluid (CSF) examinations were performed under suspicion of malignancy, but malignant cells were not detected. Positron emission tomography with fluorodexoyglucose integrated with computed tomography (FDGPET-CT) showed mild-to-moderate uptake along the left brachial plexus with no other systemic lesions (Fig. 1C).

She was transferred to another hospital for a further in-depth workup, which did not include a tissue biopsy. No

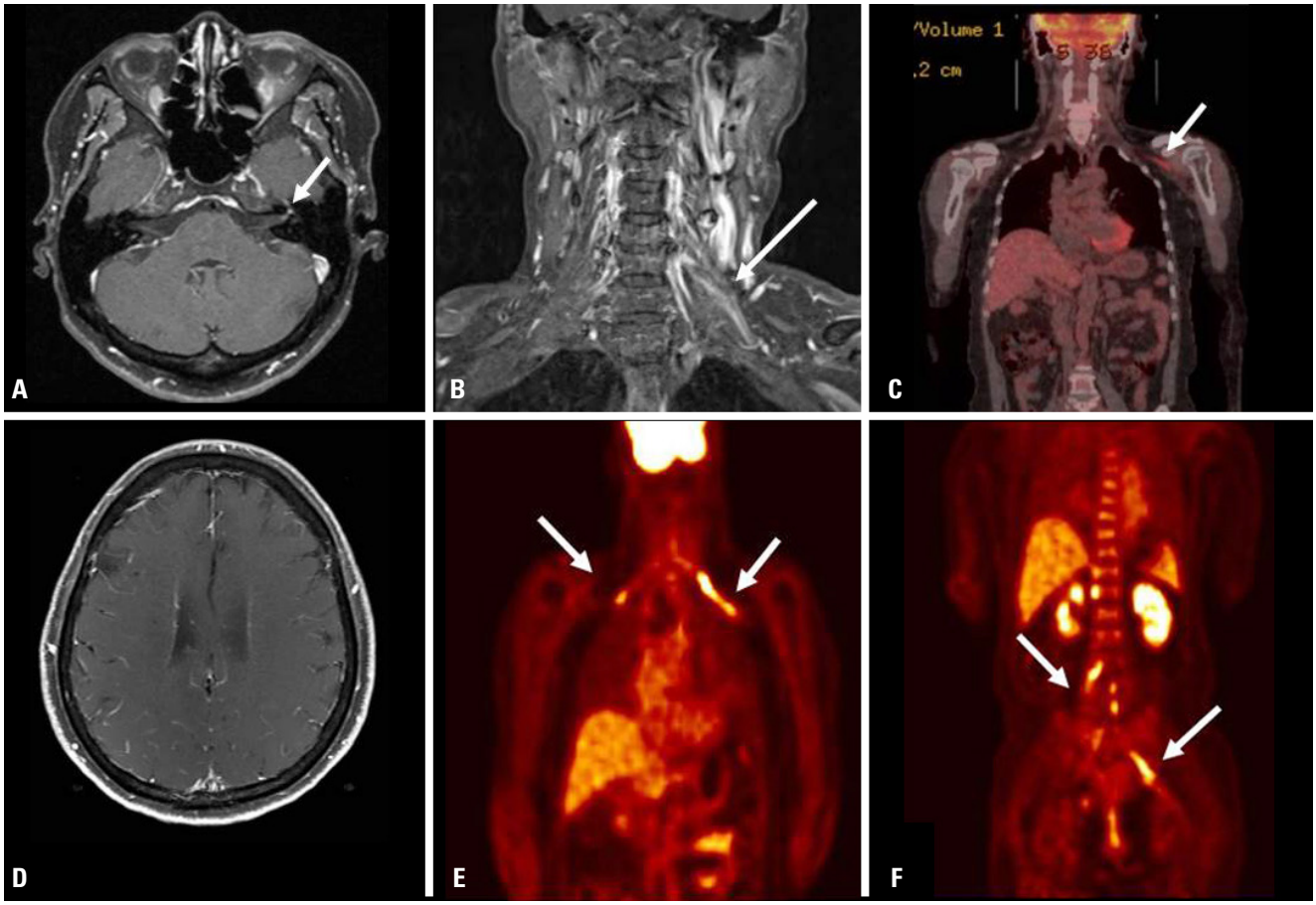

Fig. 1. Brain and spinal MRI showed thickening and enhancement on the left facial nerve (arrow) (A), and the left brachial plexus (arrow) (B). Initial PET-CT showed mild linear FDG uptake along the left brachial plexus (arrow) (C). Brain MRI revealed multifocal leptomeningeal enhancement of the systemic lymphoma or metastasis (D). FDG-PET revealed intense uptake in the brachial (arrows) (E) and lumbosacral (arrows) (F) plexus. MRI, magnetic resonance imaging; PET-CT, positron emission tomography–computed tomography; FDG, fluorodexoyglucose.

Table 1. Electrophysiological findings at the first symptoms of left upper limb weakness

Nerve (right/left)	Segments	Motor			Sensory	
		TL (msec)	NCV (m/sec)	Amp (mV)	NCV (m/sec)	Amp (μV)
Median	F-W	2.6/3.1		14.6/14.0	46/42	42/42
	W-E		53/56	14.1/13.4	55/58	54/58
	E-Ax		56/65	13.7/13.0	64/63	61/63
	F-latency	23.1/23.3				
Ulnar	F-W	2.0/2.4		18.7/15.6	48/42	32/42
	W-E		63/58	17.2/12.8	63/62	29/33
	E-Ax		64/58	16.7/12.1	72/65	47/27
	F-latency	23.7/23.7				
Axillary		3.1/4.0		29.3/4.2		
Musculocutaneous		4.4/10.1		10.2/1.0		
Peroneal	Fo-A	3.6/4.0		3.2/4.5		
	A-FH		46/44	2.9/3.1		
	K-PF					
	F-letency	46.6/44.2				
Tibial	Fo-A	3.5/3.7		23.5/17.0		
	A-K		45/48	18.0/12.8		
	F-latency	43.1/46.2				
	H-reflex			29.8/29.5		
Sural					39/38	27.9/24.9

TL, terminal latency; NCV, nerve conduction velocity; Amp, amplitude; F, finger; W, wrist; E, elbow; Ax, axilla; Fo, foot; A, ankle; FH, fibular head; K, knee; PF, popliteal fossa.

evidence of malignancy was found, and her symptoms improved with high-dose steroid treatment. Right leg weakness occurred 3 months later, at which time spine MRI revealed diffuse long segmental enhancements in the right lumbosacral plexus and both lumbar and sacral nerve roots. Brain MRI revealed multifocal leptomeningeal enhancement on the brain surface, indicating leptomeningeal enhancement of systemic lymphoma or leptomeningeal metastasis (Fig. 1D). FDG-PET showed diffuse hypermetabolism along the lumbosacral and brachial plexus (Fig. 1E, F). CSF cytology suggested a hematolymphoid malignancy with many atypical cells. The biopsy samples obtained in the C7 root were confirmed as DLBCL (Fig. 2).

DISCUSSION

NL is a rare clinical entity caused by nerve infiltration by hematological neoplastic cells, and is characterized clinically by painful polyneuropathy or polyradiculopathy, cranial neuropathy, painless polyneuropathy, and peripheral mononeuropathy.[6] NL is related to B-cell non-Hodgkin's lymphoma (90% of cases), especially DLBCL, and acute leukemia (10% of cases).[1,7] Secondary NL occurs in approximately 0.2% of all patients with non-Hodgkin's lymphoma.[7]

The diverse presenting symptoms vary with the involved sites. According to a previous report, the affected neural structures are peripheral nerves (60%), spinal nerve roots (48%), cranial nerves (46%), and plexus (40%), with multiple sites involved in 58% of cases.[1]

NL can be challenging to diagnose because not only may it mimic many conditions, but also requires histopathological proof. In addition, primary lymphomatosis of the cranial nerves and PCNSL are difficult to differentiate.[8] Thus, a nerve biopsy is the gold standard for diagnosing NL, but it is generally not performed due to its invasiveness; instead, ra-

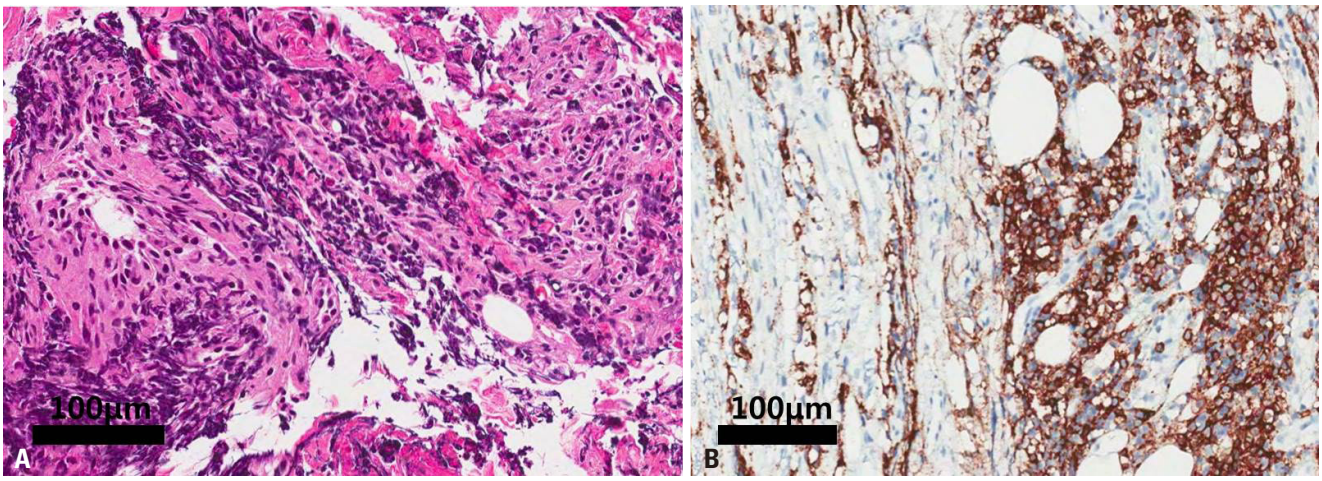

Fig. 2. Biopsy of the C7 root showed infiltration by predominantly small lymphocytes (hematoxylin-eosin stain, original magnification ×200) (A), and diffuse CD20-positive cells (immunohistochemical stain, original magnification ×200) (B).

diological evaluations are usually performed to evaluate NL. PET-CT has a sensitivity of 87.5–100%, and MRI has a sensitivity of 40%.[7] CSF cytology is not very helpful due to its low sensitivity of 21%.

We suspected NL during the early period in the present patient due to the successive occurrence of diplopia, facial palsy, and brachial plexopathy. Spinal MRI and PET-CT revealed enhanced or high-uptake lesion in the brachial plexus, but other systemic lesions were detected. In addition, repeated cytology revealed no malignant cells. The patient was treated with a steroid, which resulted in her symptoms improving. However, painful lumbosacral plexopathy developed shortly after the steroid treatment. Brain MRI showed leptomeningeal enhancement, suggesting systemic lymphoma or leptomeningeal metastasis. A biopsy of the C7 root was performed, for which the pathological finding was DLBCL.

No standard treatment for NL has been established, with chemotherapy predominating.[9] A steroid provides only short-term symptom control, and intravenous immunoglobulin elicits an initial response in secondary NL.[9] The prognosis in patients affected by NL is worse than in those affected by only systemic lymphoma.[9]

Since NL is extremely rare and its early diagnosis is important to the timely initiation of targeted therapy, a high suspicion of NL is necessary especially in the patients with pain and the rapid evolution of asymmetric neurological deficits. NL may precede systemic disease, and about 73% of cases eventually show evidence of systemic lymphoma.[4,10]

When there is stepwise progression of multiple focal neurological deficits, NL should be considered since its early diagnosis and treatment affect the prognosis. A radiological evaluation including MRI and PET-CT and an CSF examination have a role in the diagnosis, but their relatively low specificities mean that a tissue biopsy is the gold standard for diagnosing NL.

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