



Recurrent Diffuse Large B-Cell Lymphoma Involving the Sciatic Nerve: A Rare Case Report and Review of the Literature

Chun-Yi Lee¹, Tsung-Yen Ho¹, Yung-Tsan Wu^{1,2}, Liang-Cheng Chen^{1,2}, Tsung-Ying Lee^{1,2}

¹Department of Physical Medicine and Rehabilitation, National Defense Medical Center, Tri-Service General Hospital,

²National Defense Medical Center, School of Medicine, Taipei, Taiwan

Neurolymphomatosis (NL) is an uncommon condition involving lymphomatous invasion of the cranial or spinal nerve roots. Sciatic nerve neuropathy and dysfunction represent a common cause of lower extremity symptoms in clinical practice. However, cases of recurrent lymphoma infiltrating a single peripheral nerve, such as the sciatic nerve, are rare. To date, only one case has been reported in the literature. Isolated lymphomatosis may occur sporadically in patients with lymphoma relapse. Nevertheless, the precise mechanisms underlying such cases remain unclear. The present report describes a patient with recurrent lymphoma who presented with drop foot due to sciatic nerve involvement. In this report, we highlight the importance of ultrasound for diagnosing peripheral neuropathy based on the characteristic nerve enlargement and loss of echogenicity. Our findings, together with existing evidence from the literature, support that ultrasonography, which is relatively rapid, easy, and low risk, can aid in the differential diagnosis of NL.

Key words: Neurolymphomatosis, lymphoma relapse, isolated sciatic neuropathy, sciatic nerve tumor, peripheral nervous system diseases

INTRODUCTION

Neurolymphomatosis (NL) involves the lymphomatous invasion of the cranial or spinal nerve roots. Along with primary NL, secondary cases may occur in patients experiencing relapse following systemic or primary central nervous system lymphoma. Symptoms of NL include sensation or motor function loss in the extremities.¹ When initially evaluating suspected NL patients, the disease's site and extent should be established. Several methods exist for diagnosing NL based on nerve swelling or enlargement, including ultrasound, magnetic resonance imaging (MRI), and positron-emission tomography/computed tomography (PET/CT). Furthermore, biopsy specimens can help identify infiltrative lymphoma. Although the treatment approach and prognosis depend on the above information, few cases of mononeuropathy involving the sciatic nerve have been reported, and the underlying mechanisms remain unclear. Herein, we describe the case of a patient who exhibited recurrent lymphoma with sciatic nerve involvement and discuss the role of ultrasound plays in

diagnosing peripheral neuropathy. The study is approved by Institutional Review Board of Tri-Service General Hospital, National Defense Medical Center, TSGHIRB. The approval number is 2-108-05-157.

CASE REPORT

A 64-year-old Taiwanese female was diagnosed with diffuse large B-cell lymphoma of the left breast through sonogram and core-needle biopsy in February 2016. She underwent six chemotherapy cycles using the regimen rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone. On protocol completion in July 2016, she exhibited good therapeutic response on PET/CT and demonstrated only mild fluorodeoxyglucose uptake in the left breast. However, beginning in October 2016, she underwent 6 months of outpatient rehabilitation for left lower leg

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Lee CY, Ho TY, Wu YT, Chen LC, Lee TY. Recurrent diffuse large B-cell lymphoma involving the sciatic nerve: A rare case report and review of the literature. J Med Sci 2020;40:236-40.

Received: October 02, 2019; Revised: November 06, 2019; Accepted: January 31, 2020; Published: February 21, 2020
Corresponding Author: Dr. Tsung-Ying Lee, No. 161, Section 6, Minquan E. Road, Neihu District, Taipei City 114, Taiwan. Tel: +886-2-87923311; Fax: +886-2-87927162. E-mail: doc31141@gmail.com

dysfunction, tingling sensations over the left plantar foot upon compression of the posterior knee and nerves, stiffness/numbness of the left calcaneus region, drop foot, and limping gait. Physical examinations revealed reduced muscle power during dorsiflexion and plantar flexion (0/5) and reduced sensation in the left S1 dermatome. Straight leg raise test results were positive for the left side, and the test exacerbated her symptoms. Electrodiagnostic examinations [Figure 1] revealed high amplitude (mostly higher than 5000 UV) of voluntary motor unit action potentials with acute denervation signal such as positive sharp wave of spontaneous activity in paraspinal muscles and lumbosacral plexopathy innervated muscles. A mixed echotexture and clear borderline mass was observed in the left deep posterior thigh on sonographic images [Figure 2]. PET/CT [Figure 2] revealed newly developed intense fluorodeoxyglucose uptake over the posterior aspect of the left lower thigh suggestive of lymphoma relapse. Following three chemotherapy rounds with the R-ICE regimen (rituximab, ifosfamide, carboplatin, and etoposide), she underwent high-dose chemotherapy with the BEAM regimen (carmustine [BiCNU®], etoposide, cytarabine, and melphalan), followed by autologous peripheral blood stem-cell transplantation. She experienced clinical remission following

the treatment, although brain metastases were observed on MR images at 10 months after the first relapse.

DISCUSSION

Non-Hodgkin lymphoma (NHL) is a diverse group of malignant neoplasms derived several cell types. The clinical presentation of NHL varies, depending on the lymphoma

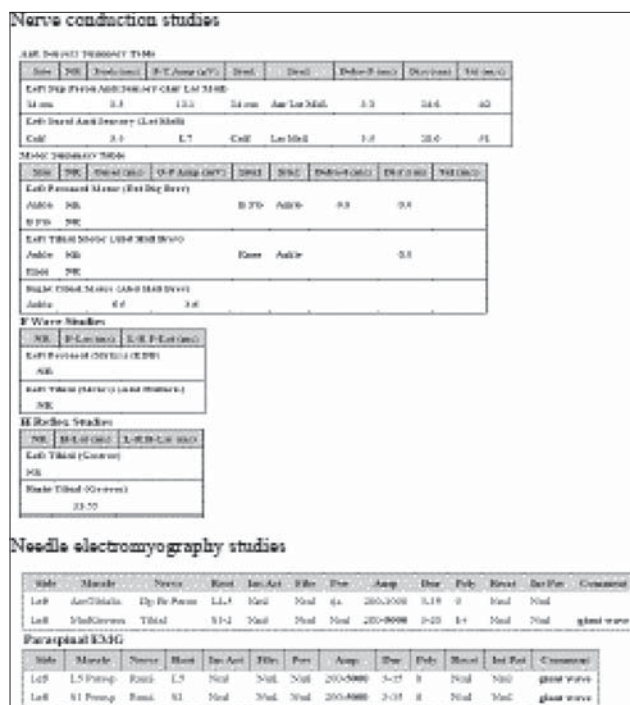


Figure 1: Electrodiagnostic examinations (Nerve conduction studies and Needle electromyography studies) from the case. The studies revealed high amplitude (mostly higher than 5000 UV) of voluntary motor unit action potentials with acute denervation signal such as positive sharp wave of spontaneous activity in paraspinal muscles and lumbosacral plexopathy innervated muscles

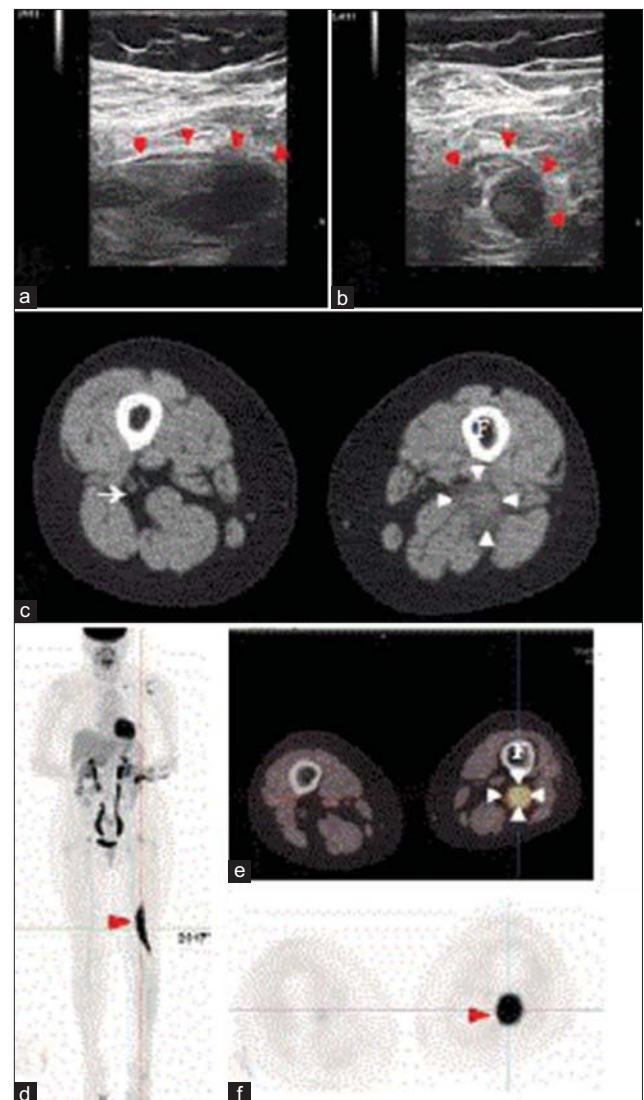


Figure 2: Images from a 64-year-old female with recurrent diffuse large B-cell lymphoma involving sciatic nerve mononeuropathy. Transverse (a) and longitudinal (b) sonographic images presented as a large heterogeneous fusiform mass (arrowheads) in the deep posterior thigh. (c-f) Positron-emission tomography/computed tomography images [(d) coronal view; (c, e, f) axial view] showing intense fluorodeoxyglucose uptake in a mass (arrowheads) infiltrating and compressing the sciatic nerve, corresponding to a swollen muscle (likely the biceps femoris muscle). Findings for the right thigh were normal (arrow). F: Femur

Table 1: Published cases of neurolymphomatosis involving the sciatic nerve

Case report	Age	Sex	Pathology	Type	Side	Radiology	Therapy	Response
Purohit <i>et al.</i> ¹⁰	64	Female	B-cell lymphoma	Primary	Right	CT	Surgery + radiotherapy	Evidence of metastasis at 36 months after incidence
Pillay <i>et al.</i> ¹¹	61	Male	B-cell lymphoma	Primary	Left	CT, MRI	Radiotherapy	No evidence of disease at 12 months after incidence
Eusebi <i>et al.</i> ¹²	72	Male	B-cell lymphoma	Primary	Right	CT	Surgery + chemotherapy	Died of systemic disease at 16 months after incidence
Kanamori <i>et al.</i> ¹³	34	Male	T-cell NHL	Primary	Left	MRI	Chemotherapy + radiotherapy	No evidence of disease at 30 months after incidence
Roncaroli <i>et al.</i> ⁶	44	Male	B-cell lymphoma	Primary	Left	CT, MRI	Chemotherapy + radiotherapy	Died of CNS disease at 50 months after incidence
Quiñones-Hinojosa <i>et al.</i> ⁸	52	Male	B-cell lymphoma	Primary	Right	MRI	Chemotherapy	Died of respiratory failure after 4 months of chemotherapy
Misdraji <i>et al.</i> ⁴	62	Female	B-cell lymphoma	Primary	Left	MRI	Chemotherapy + radiotherapy	Survival with local residual disease at 57 months after incidence
	49	Male	B-cell lymphoma	Primary	Right	MRI	Chemotherapy	NL relapse at 4 months Died of CNS disease at 50 months after incidence
Descamps <i>et al.</i> ¹⁴	55	Male	-	Primary	Left	MRI	Chemotherapy	No evidence of disease at 48 months after incidence
Strobel <i>et al.</i> ¹⁵	59	-	B-cell lymphoma	Primary	Left	PET/CT	Chemotherapy	Remission after six cycles of chemotherapy
Teng <i>et al.</i> ¹⁶	58	Male	B-cell lymphoma	Primary	Right	MRI	Surgery + chemotherapy	Died of infectious disease during the first cycle of chemotherapy
Kahraman <i>et al.</i> ⁷	63	Female	B-cell lymphoma	Primary	Left	MRI	Chemotherapy	No evidence of disease at 10 months after incidence
Deivaraju <i>et al.</i> ⁹	24	Female	B-cell lymphoma	Relapse (4 months after first CR)	Left	PET/CT Ultrasound (biopsy)	Primary: Chemotherapy - Relapse: Unclear	-
Advani <i>et al.</i> ¹⁷	72	Male	B-cell lymphoma	Primary	Left	MRI, PET/CT	Chemotherapy	No evidence of disease at 18 months after chemotherapy
He <i>et al.</i> ¹⁸	65	Male	B-cell lymphoma	Primary	Right	MRI	Chemotherapy	Lost to follow-up
Present case	64	Female	B-cell lymphoma	Relapse (3 months after first CR)	Left	Ultrasound, PET/CT	Primary: Chemotherapy Relapse: Chemotherapy + PBSCT	Survival with brain metastasis after chemotherapy + PBSCT at 12 months
Mean: Male/female: 56.13 10/5 B-cell lymphoma in 15 patients (total 16) Relapse in only 2 patients Left/right: 10/6								

CNS=Central nervous system; CR=Complete remission; CT=Computed tomography; MRI=Magnetic resonance imaging; NHL=Non-Hodgkin lymphoma; NL=Neurolymphomatosis; PBSCT=Peripheral blood stem cell transplantation; PET/CT=Positron-emission tomography/CT

type and involved areas. Approximately 50% of NHL patients develop secondary extranodal disease, whereas 10%–35% present with primary extranodal lymphoma at initial diagnosis.² The gastrointestinal tract is the most common site of primary extranodal disease, followed by the skin.

NL refers to a form of systemic lymphoma (primary or relapse-related) that is associated with peripheral nervous system involvement. Few cases of mononeuropathy due to isolated primary or recurrent lymphoma involving the sciatic, axillary, sympathetic chain, radial, median, or ulnar nerves have been reported.^{3–5} In sciatic nerve lymphoma patients, diffuse lymphoma cells have been observed in the endoneurium and perineurium, rather than in the epineurium or adjacent tissue.⁶ In such cases, lymphoma is thought to originate from B cells in the sciatic nerve, rather than from surrounding or remote tissues.^{7,8} According to the literature review in [Table 1],^{4,6–18} our case is the second case of “relapsed” lymphoma involving the sciatic nerve in the previously published article. However, the mechanisms underlying sciatic nerve involvement remain unclear; in the only published report describing lymphoma recurrence, the authors observed peripheral nerve involvement, arguing that lymphoma cells can penetrate the blood–nerve barrier, whereas chemotherapy cannot, which may explain lymphoma relapse cases.⁹ In our case, the recurrent lymphoma penetrated the blood–nerve barrier and blood–brain barrier, as observed during follow-up.

Confirming an NL diagnosis can be difficult given that the disease’s clinical presentation is similar to that of lumbar disc pathology and peripheral nervous system diseases. Moreover, the clinical presentation varies depending on the nerves involved. In previously reported cases of isolated sciatic neuropathy [Table 1], signs and symptoms of peripheral nerve tumors were caused by direct nerve invasion, infiltration of the surrounding tissues, or mass effects. The most common clinical findings included progressively worsening pain and numbness and weakness in the affected lower limb. Foot drop was observed in three of these previous cases,^{7,11,18} which was consistent with the sign observed in our patient. Large toe numbness was observed in only one other patient. In previously published cases of NL involving the sciatic nerve, the ages of them are between about 40 and 60 years (mean, 56 years). Most of them are B-cell lymphoma (15 cases), and one case is T-cell NHL. Otherwise, there are only two patients presented in relapsed lymphoma. Collectively, these findings indicate that progressive sciatic neuropathy should be suspected in patients previously diagnosed with lymphoma.

Currently, there is no gold-standard diagnostic tool for NL, although imaging may prove invaluable for evaluating

patients with suspected NL. Many tumors are first identified through imaging performed to assess causes of pain, sensory loss, or weakness. In most forms of compressive and hereditary demyelinating neuropathy, nerve enlargement and loss of echogenicity are commonly observed through ultrasonography.^{19,20} Moreover, diagnostic ultrasound can help exclude musculoskeletal diseases, which exhibit symptoms similar to those of NL. Accordingly, as our patient presented with foot drop, we performed diagnostic ultrasound. Along with providing qualitative and quantitative information regarding nerve and muscle diseases, ultrasonography is a convenient, cost-effective, fast, safe, and real-time image tool. With advancements such as Doppler blood flow imaging and high-frequency linear-array transducer, it appears providing more detailed assessment of vascularity and disease activity of neuromuscular disorders (NL).²¹ However, both contrast MRI and fluorodeoxyglucose-PET/CT are generally used in NL diagnosis and staging and in the evaluation of treatment responses.¹⁵ Electrophysiological studies should be utilized to differentiate atypical sciatica from other neuropathy types with similar etiology.¹⁴ In addition, lumbar puncture may aid in the differential diagnosis of NL, particularly in patients exhibiting acute neurological deterioration.²²

CONCLUSION

We described a patient who exhibited recurrent diffuse large B-cell lymphoma involving sciatic nerve mononeuropathy. Based on the accumulated evidence, we recommend that electrophysiological studies, contrast MRI, and fluorodeoxyglucose-PET/CT be used together to ensure timely and accurate diagnosis. Because most compressive neuropathies are associated with nerve enlargement and loss of echogenicity, ultrasound is a relatively rapid, easy, and low-risk method that can facilitate differential diagnosis.

Acknowledgments

This manuscript was edited by Editage.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Tomita M, Koike H, Kawagashira Y, Iijima M, Adachi H, Taguchi J, *et al*. Clinicopathological features of neuropathy associated with lymphoma. *Brain* 2013;136:2563-78.
2. Anderson T, Chabner BA, Young RC, Berard CW, Garvin AJ, Simon RM, *et al*. Malignant lymphoma. 1. The histology and staging of 473 patients at the National Cancer Institute. *Cancer* 1982;50:2699-707.
3. van den Bent MJ, de Bruin HG, Beun GD, Vecht CJ. Neurolymphomatosis of the median nerve. *Neurology* 1995;45:1403-5.
4. Misdraji J, Ino Y, Louis DN, Rosenberg AE, Chiocca EA, Harris NL. Primary lymphoma of peripheral nerve: Report of four cases. *Am J Surg Pathol* 2000;24:1257-65.
5. Kim J, Kim YS, Lee EJ, Kang CS, Shim SI. Primary CD56-positive NK/T-cell lymphoma of median nerve: A case report. *J Korean Med Sci* 1998;13:331-3.
6. Roncaroli F, Poppi M, Riccioni L, Frank F. Primary non-Hodgkin's lymphoma of the sciatic nerve followed by localization in the central nervous system: Case report and review of the literature. *Neurosurgery* 1997;40:618-21.
7. Kahraman S, Sabuncuoglu H, Gunhan O, Gurses MA, Sirin S. A rare reason of foot drop caused by primary diffuse large b-cell lymphoma of the sciatic nerve: Case report. *Acta Neurochir (Wien)* 2010;152:125-8.
8. Quiñones-Hinojosa A, Friedlander RM, Boyer PJ, Batchelor TT, Chiocca EA. Solitary sciatic nerve lymphoma as an initial manifestation of diffuse neurolymphomatosis. Case report and review of the literature. *J Neurosurg* 2000;92:165-9.
9. Deivaraju C, Inzunza JF, Hammel N, Conway SA. Isolated recurrence of diffuse large B-cell lymphoma in sciatic nerve. *World J Oncol* 2014;5:126-8.
10. Purohit DP, Dick DJ, Perry RH, Lyons PR, Schofield IS, Foster JB. Solitary extranodal lymphoma of sciatic nerve. *J Neurol Sci* 1986;74:23-34.
11. Pillay PK, Hardy RW Jr, Wilbourn AJ, Tubbs RR, Lederman RJ. Solitary primary lymphoma of the sciatic nerve: Case report. *Neurosurgery* 1988;23:370-1.
12. Eusebi V, Bondi A, Cancellieri A, Canedi L, Frizzera G. Primary malignant lymphoma of sciatic nerve. Report of a case. *Am J Surg Pathol* 1990;14:881-5.
13. Kanamori M, Matsui H, Yudoh K. Solitary T-cell lymphoma of the sciatic nerve: Case report. *Neurosurgery* 1995;36:1203-5.
14. Descamps MJ, Barrett L, Groves M, Yung L, Birch R, Murray NM, *et al*. Primary sciatic nerve lymphoma: A case report and review of the literature. *J Neurol Neurosurg Psychiatry* 2006;77:1087-9.
15. Strobel K, Fischer K, Hany TF, Poryazova R, Jung HH. Sciatic nerve neurolymphomatosis – Extent and therapy response assessment with PET/CT. *Clin Nucl Med* 2007;32:646-8.
16. Teng LH, Lu DH, Xu QZ. Tumor arising in the right sciatic nerve of a 58-year-old man. *Neuropathology* 2009;29:637-9.
17. Advani P, Paulus A, Murray P, Jiang L, Goff R, Pooley R, *et al*. A rare case of primary high-grade large B-cell lymphoma of the sciatic nerve. *Clin Lymphoma Myeloma Leuk* 2015;15:e117-20.
18. He W, Wang W, Gustas C, Malysz J, Kaur D. Isolated sciatic neuropathy as an initial manifestation of a high grade B-cell lymphoma: A case report and literature review. *Clin Neurol Neurosurg* 2016;149:147-53.
19. Zaidman CM, Al-Lozi M, Pestronk A. Peripheral nerve size in normals and patients with polyneuropathy: An ultrasound study. *Muscle Nerve* 2009;40:960-6.
20. Cartwright MS, Walker FO. Neuromuscular ultrasound in common entrapment neuropathies. *Muscle Nerve* 2013;48:696-704.
21. Walker FO, Cartwright MS. Ultrasound in neurolymphomatosis: The rise of the machines. *Neurology* 2015;85:746-7.
22. Pham M, Awad M. Lymphoma relapse presenting as neurolymphomatosis. *Asian J Neurosurg* 2016;11:73.