Neurology Asia 2014; 19(2) : 203 – 206

Isolated peripheral neuropathy as an unusual presentation for an extramedullary relapse of acute leukemia

[1]Xiao-Ying Zhu *MD*, [2]Sheng-Han Kuo *MD*, [3]Li-Ping Wan *MD*, [1]Ye Liu *MD*, [1]Yun-Cheng Wu *MD PhD*

[1]Department of Neurology and [3]Hematology, Shanghai First People's Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, P.R. China; [2]Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, USA

Abstract

A 23-year-old man in remission from acute myeloblastic leukemia after allogeneic peripheral blood stem cell transplantation developed peripheral neuropathy presenting as sciatic and peroneal nerve deficits. Electrophysiological tests localized the lesions to the left sciatic and common peroneal nerve. Magnetic resonance imaging revealed nerve thickening and enhancement, while a positron emission tomography-computed tomography scan demonstrated increased fluorodeoxyglucose uptake tracking along the nerve, suggesting peripheral nerve infiltration. This report demonstrates an unusual presentation of acute leukemia relapse presenting as focal neuropathy.

INTRODUCTION

Acute leukemia can involve the central nervous system (CNS) and rarely, the peripheral nervous system (PNS). In PNS involvement, common sites include cranial nerves and nerve roots; but isolated peripheral nerves are seldom directly affected by infiltration without also involving the epidura or leptomeninges.[1-11]

Here we report a case with left sciatic and peroneal neuropathy as the only manifestation of an acute monocytic leukemia relapse following allogeneic peripheral blood stem cell transplantation (allo-PBSCT). Positron emission tomography (PET) and gadolinium (Gd) -enhanced magnetic resonance imaging (MRI) are invaluable in confirming nerve invasion by leukemia. Clinicians should always include the focal infiltration of leukemia in the differential diagnosis when encountering patients with a history of leukemia.

CASE REPORT

A 23-year-old man developed hematuria and was subsequently found to have pancytopenia. He was diagnosed with acute myeloblastic leukemia (AML) type M5 based on the bone marrow smear and immunophenotyping. He was treated with idamycin, cytarabine and a successful allo-PBSCT with complete remission. The post-transplanted course was complicated by acute graft-versus-host disease (GVHD) presenting as maculopapular rashes, hemorrhagic cystitis, and herpes zoster affecting his left arm, all of which resolved with appropriate treatment. Subsequent bone marrow examinations and PCR amplified short tandem repeat (STR-PCR) confirmed complete remission and full donor chimerism.

Eighteen months after his remission, he presented with left foot drop, persistent pins and needles over the dorsum of the left foot, and numbness over the lateral aspect of left calf, that had gradually progressed over the preceding two months. Neurological examination revealed diffuse muscular atrophy of the left lower extremity and decreased strength (MRC scale 3/5) of left ankle dorsiflexion, eversion (3/5), as well as dorsiflexion of all toe extensors. Power was preserved in the left iliopsoas, quadriceps, biceps femoris, and gastrocnemius. Ankle reflex was absent while knee reflex was normal. He had a positive Lasegue sign on the left and bilateral flexor plantar reflexes. Pinprick and light touch sensation was decreased over the lateral left lower leg and dorsal foot. Nerve conduction velocity (NCS) revealed left peroneal nerve involvement and electromyography (EMG) showed active and chronic denervation changes predominantly in

Address correspondence to: Yuncheng Wu, MD, PhD, Associate Professor of Neurology, Department of Neurology, Shanghai First People's Hospital, Shanghai Jiao Tong University School of Medicine, No. 100, Haining Road, Shanghai 200080, P.R. China. Tel: 86-21-37798581, Fax: 86-21-63240825, Email: yunchw@medmail.com.cn

Table 1: Nerve conduction studies

Nerve	Velocity (m/s)		Latency (ms)		Amplitude (μV for sensory, mV for motor)	
	L	R	L	R	L	R
Sural(S)	**42.6**	48.1	2.9	2.4	5.35	3.1
Superficial peroneal（S）	**NR**	38.7	**NR**	3.75	**NR**	1.85
Common peroneal（M）	**38.2**	54.4	**6**	5.05	**0.65**	10
Tibial (M)	52.3	48.2	3.75	3.70	17.1	14.7

Nerve conduction velocity (NCV) revealed a marked slow motor nerve conduction velocity (MNCV) with low compound muscle action potential (CMAP) amplitude as well as prolonged latency of left common peroneal nerve. Moderate slow sensory nerve conduction velocity (SNCV) was detected in left sural nerve. Sensory nerve action potential (SNAP) of left superficial peroneal nerve was absent. MNCV of tibial nerve was normal. *L, left; M, motor; NR, no response; R, right; S, sensory. Abnormal figures are in bold.*

the muscles innervated by the peroneal nerves (Table 1, 2). Bone marrow cytology did not show any malignant cells. Cerebrospinal fluid (CSF) analysis showed normal cell count, glucose, protein, and the cytology also did not show malignant cells. He was considered as idiopathic inflammatory focal neuropathy and was treated with pulse intravenous methylprednisolone, which worsened his symptoms as he developed severe sharp pain behind his left thigh and calf in the distribution of the sciatic nerve, with worsening numbness in the left calf, and further weakness in dorsiflexion. A tender, palpable tumor with the size of 5 cm × 1 cm developed in his left popliteal fossa. A left thigh MRI (Figure1) demonstrated T1 post Gd hyperintensity in left common peroneal and lower sciatic nerve, suggesting inflammation or leukemic infiltration (Figure 1A-C). A total body 18fluoro-deoxyglucose positron emission tomography-computed tomography (FDG- PET-CT) scan showed increased FDG tracking along the thickened sciatic and common peroneal nerve

Table 2: Electromyography

Muscle(L)	Ins	Fibs	Pos waves	MUP Dur	MUP Amp	Recruitment
Long head of biceps femoris	-	-	-	+	-	mixed phase
Short head of biceps femoris	+	-	+	-	-	simple phase
Tibials anterior	-	+++	++	++	+++	simple phase
Peroneus longus	-	++	++	++	-	simple phase
Gastrocnemius	-	-	-	-	-	mixed phase
Gluteus maximus	-	-	-	-	-	mixed phase
Vastus medialis	-	-	-	-	-	mixed phase
Extensor digitorum brevis	-	-	-	-	-	mixed phase

Needle electromyography (NE) recorded spontaneous fibrillations and positive shape waves with reduced recruitment of prolonged and polyphasic motor units especially in tibials anterior and peroneus longus muscles innervated by left common peroneal nerve. A prolonged insection potential was detected in left biceps femoris innervated by left sciatic nerve. NE recorded in gastrocnemius, gluteus maximus, vastus medialis and extensor digitorum brevis were almost normal. *Amp, amplitude; Dur, duration; Fibs, fibrillation potentials; Ins, insertional activity; L, left; M, motor; MUP, motor unit action potential; NR, no response; Pos, positive sharp waves; S, sensory. Amp, amplitude; Dur, duration; Fibs, fibrillation potentials; Ins, insertional activity; MUP, motor unit action potential; Pos, positive sharp waves.*

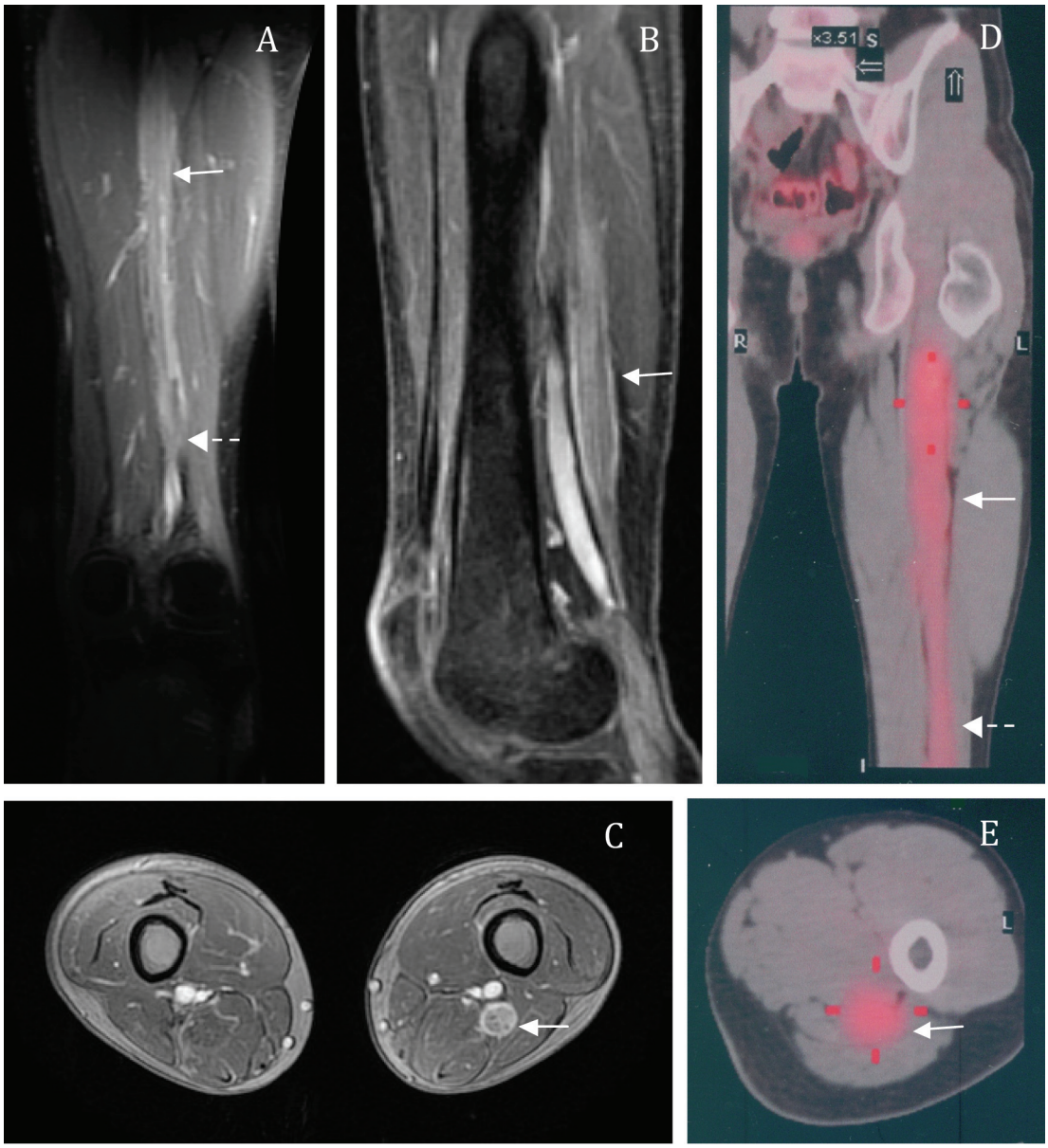

Figure 1. MRI and PET-CT scan imaging in the region of left thigh (A-E). Fat-saturated T1-weighted coronal (A) image shows hyperintense signals of the thickened left sciatic nerve (white arrow) and common peroneal nerve (white dotted arrow). Gd-DTPA enhanced MRI combined liver acquisition with volume acceleration (LAVA) sequence of sagittal (B) and axial (C) images show enhancement of the hyperintense signals of left lower sciatic nerve (white arrow). PET-CT coronal (D) and axial (E) images display increased FDG uptake along left sciatic (white arrow) and common peroneal nerve (white dotted arrow).

in the left thigh with maximum standardized uptake value (SUV_{max}) of 4.6 (Figure 1D, E), indicating focal peripheral nerve infiltration. There was also patchy abnormal FDG uptake in right upper femur and left apex pulmonis, which was considered eosinophilic granuloma and inflammatory focus respectively. Biopsy of left sural nerve indicated severe degeneration and axonal loss without inflammation or leukemia infiltration. He subsequently received teniposide (VM26) and pirarubicin (THP) treatment, which relieved his pain and dramatically decreased the size of the popliteal tumour. However, the left foot drop persisted possibly due to severe axonal damage of the affected nerves.

DISCUSSION

Peripheral neuropathy occurs frequently in cancer patients and the differential diagnoses include chemotherapy-induced neuropathy and paraneoplastic neuropathy. Other causes of neuropathies can also occur including neuropathies associated with systemic inflammatory or immune-mediated diseases or infectious diseases, malignancy infiltrations, and vasculitis. In the current case report, we describe an isolated nerve lesion. Both vasculitis and focal inflammation causes were excluded by the lack of supportive history (such as pain in vasculitis) and lack of response to corticosteroids along with unsupportive nerve biopsy. Imaging of the nerves along with the patient's dramatic clinical response after chemotherapy suggested the diagnosis of leukemia relapse.

Peripheral neuropathy due to direct leukemic infiltration in acute leukemia patients independent of epidural or leptomeningeal involvement is rare, with less than a dozen reported cases in literature.[1-11] Patients present with multiple mononeuropathies[6], symmetric[5,8-11] or asymmetric polyneuropathy[3], and isolated mononeuropathy. Isolated sciatic or common peroneal neuropathy due to direct leukemic infiltration is particularly rare as a presentation of an acute leukemia relapse. Mosch *et al*.[12] reported a case of sciatic pain due to spinal intradural granulocytic sarcoma within the Sl ganglion instead of direct sciatic nerve invasion. Stillman *et al*. reported an AML case developed sciatic neuropathy due to chloroma (granulocytic sarcoma) compression without nerve infiltration.[13] Aregawi *et al*.[1] and Liu *et al*.[4] reported two cases of acute lymphocytic leukemia (ALL) after allogeneic bone marrow transplantation (allo-BMT) with common peroneal and sciatic infiltrating neuropathy caused by leukemic relapse, but both cases had other extramedullary relapses (EMR) prior to the peripheral nerve involvement. In the current case, we describe an isolated sciatic and common peroneal neuropathy due to leukemic infiltration after allo-PBSCT. In leukemic patients presenting with peripheral nerve involvement, non-invasive PET-CT and MRI are helpful in demonstrating leukemic infiltration of nerves, especially when nerve biopsies are often not possible.

ACKNOWLEDGEMENT

This work was partially supported by the National Basic Research Program of China (973 Program) (2011CB707506) and Shanghai Pujiang Program (11PJD019).

DISCLOSURE

Conflicts of interest: None

REFERENCES

1. Aregawi DG, Sherman JH, Douvas MG, Burns TM, Schiff D. Neuroleukemiosis: case report of leukemic nerve infiltration in acute lymphoblastic leukemia. *Muscle Nerve* 2008; 38:1196-200.
2. Reddy CG, Mauermann ML, Solomon BM, *et al*. Neuroleukemiosis: an unusual cause of peripheral neuropathy. *Leuk Lymphoma* 2012; 53:2405-11.
3. Bakst R, Jakubowski A, Yahalom J. Recurrent neurotropic chloroma: report of a case and review of the literature. *Adv Hematol* 2011; 2011:854240.
4. Liu HC, Hung GY, Yen HJ, Hsieh MY, Chiou TJ. Acute sciatica: an unusual presentation of extramedullary relapse of acute lymphoblastic leukemia. *Int J Hematol* 2007; 86:163-5.
5. Platten M, Opitz CA, Kohlhof P, Hegenbart U, Ho AD, Wick W. Painful neuropathy due to intraneural leukemic spread in a patient with acute myeloid leukemia. Neurology 2007; 69:707.
6. Lekos A, Katirji MB, Cohen ML, Weisman R Jr, Harik SI. Mononeuritis multiplex. A harbinger of acute leukemia in relapse. *Arch Neurol* 1994; 51:618-22.
7. Vital A, Vital C, Ellie E, *et al*. Malignant infiltration of peripheral nerves in the course of acute myelomonoblastic leukaemia: neuropathological study of two cases. *Neuropathol Appl Neurobiol* 1993; 19:159-63.
8. Boiron JM, Ellie E, Vital A, *et al*. Isolated peripheral nerve relapse masquerading as Guillain-Barré syndrome in a patient with acute lymphoblastic leukemia. *Leuk Lymphoma* 1993; 10:489-91.
9. Billström R, Lundquist A. Acute myelomonocytic leukaemia with infiltrative peripheral neuropathy. *J Intern Med* 1992; 232:193-4.
10. Nishi Y, Yufu Y, Shinomiya S, *et al*. Polyneuropathy in acute megakaryoblastic leukemia. *Cancer* 1991; 68:2033-6.
11. Krendel DA, Albright RE, Graham DG. Infiltrative polyneuropathy due to acute monoblastic leukemia in hematologic remission. *Neurology* 1987;3 7:474-7.
12. Mosch A, Kuiters RR, Kazzaz BA. Intradural granulocytic sarcoma: a rare cause of sciatic pain. *Clin Neurol Neurosurg* 1991; 93:341-4.
13. Stillman MJ, Christensen W, Payne R, Foley KM. Leukemic relapse presenting as sciatic nerve involvement by chloroma (granulocytic sarcoma). *Cancer* 1988; 62:2047-50.