
Foot-drop due to involvement of lumbosacral plexus in diffuse large B-cell lymphoma

İrfan YAVAŞOĞLU¹, Gürhan KADIKÖYLÜ¹, Ayça ÖZKUL², Zahit BOLAMAN¹

¹ Department of Internal Medicine, Hematology, Adnan Menderes University School of Medicine,

² Department of Neurology, Adnan Menderes University School of Medicine, Aydın, TURKEY

Turk J Hematol 2006;23(1): 63-67

Received: 18.10.2005 **Accepted:** 09.11.2005

ABSTRACT

Extranodal nerve system involvement is seen in approximately 5% of the patients with non-Hodgkin's lymphomas. It causes as primary or secondary infiltration of brain, leptomeninges, or peripheral nerves and the signs of spinal cord compression. Here we present a 67-year-old woman with advanced stage diffuse large B-cell lymphoma who developed foot-drop due to lumbosacral plexus involvement.

Key Words: Diffuse large B-cell lymphoma, Lumbosacral plexus, Foot-drop.

ÖZET

Difüz büyük B-hücreli lenfomada lumbosakral pleksus tutulumuna bağlı düşük ayak

Ekstranodal sinir sistemi tutulumu Non-Hodgkin lenfomalı hastaların yaklaşık %5'inde görülmektedir. Primer ya da sekonder olarak beyin, leptomeninge, periferik sinir infiltrasyonuna ve bazen spinal kord bası bulgularına neden olabilir. Biz, ileri evre difüz büyük B-hücreli lenfomalı 67 yaşındaki kadında lumbosakral pleksus infiltrasyonu nedeniyle ortaya çıkan düşük ayak gelişimini sunuyoruz.

Anahtar Kelimeler: Difüz büyük B-hücreli lenfoma, Lumbosakral pleksus, Düşük ayak.

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL), which is the most common lymphoma worldwide, is responsible for about one-third of non-Hodgkin's lymphomas (NHL)^[1,2]. Thirty to 40% of the patients with DLBCL have extranodal involvement, with gastrointestinal tract and Waldeyer ring being the most commonly involved sites^[1-4]. Involvement of nervous system as an extranodal involvement is seen in approximately 5% of the patients with NHL. It usually takes the form of infiltration in the brain, leptomeninges or peripheral nerves and compression of the spinal cord^[5-7]. The compression of the spinal cord is rare in NHL and most commonly occurs in thoracic vertebrae^[6,8-10].

Here we present a case with DLBCL who developed foot-drop due to lumbosacral plexus infiltration.

A CASE REPORT

A 67-year-old woman presented with fatigue, cramps worsening with exercise on her entire right leg and weakness for three months. Her medical history, revealed cataract operation. Her father, brother and sister died from liver cirrhosis, NHL and brain tumor, respectively. On her physical examination, blood pressure was 100/70 mmHg, heart rate 78 beats per minute, respiratory rate 16 per minute, and body temperature 36.7°C and conjunctivae were pale. Lymphadenopathy (diameter 2 x 2 cm) on the right axillary area, 4 cm splenomegaly and 6 cm hepatomegaly were detected. On the neurological examination, flexion, adduction and eversion of the hip and extension of the knee were restricted and muscle strength was 4/5. There were sensory losses in the genital area, lateral, anterior and medial hip regions and medial side of the lower legs. The reflexes of cremaster and patellar on right side were diminished. On the follow-up, Achilles reflex on right side was hypoactive and urinary incontinence occurred. The hematological parameters were hemoglobin 9.5 g/dL,

hematocrit 27.8%, white blood cell count 2500 cell/mm³ and platelet count 19.1000/mm³. Peripheral smear was normal. Erythrocyte sedimentation rate was 63 mm/hour, lactate dehydrogenase 935 IU/L, ferritin 718 ng/mL, and D-dimer 1289 mg/mL. Protein electrophoresis, immune globulin values, vitamin B₁₂ levels, and thyroid function tests were in normal limits. PPD, HBsAg, anti-hepatitis C virus (HCV), anti-human immunodeficiency virus (HIV), and cytomegalovirus (CMV)-IgM tests were negative. The aspiration and biopsy of bone marrow revealed minimal dysplastic changes in the erythroid cells and lymphoma infiltration. Chest X-ray, electrocardiography, and venous Doppler ultrasonography of lower extremities were normal. On thoracic tomography, there were multiple lymphadenopathies, infiltration areas of widespread reticular view in the parenchyma and pleural effusion on the right side. Abdominal tomography showed hepatosplenomegaly, multiple conglomerated lymphadenopathies (diameter of 5 x 4 cm) surrounding the aorta and inferior vena cava in the retroperitoneal area and mass lesion in the right adductor lodge. CD20 (+) DLBCL was found in the biopsy specimen of the right axillary lymphadenopathy. On the electromyography (EMG), mild degeneration in the muscles innervated by L₂₋₅ and S₁ on the right side and severe degeneration in the muscles innervated by L₅ (peroneal neuropathy due to involvement of sacral plexus) were detected. Malignant soft tissue infiltration involving the lumbosacral plexus and obturator area on the right side of the pelvis and the paravertebral area, lumbar spondylosis, and disc protrusions of L₁₋₂, L₂₋₃, L₄₋₅ and L₅-S₁ intervertebral discs were observed on magnetic resonance imaging (MRI) of the lumbar plexus (Figure 1). Cranial MRI was normal.

According to Ann-Arbor classification, Stage IVA DLBCL with 5 IPI (International Prognostic Index) was diagnosed. Six regimens of R-CHOP (rituximab and cyclophosphamide, adriamycin, oncovin and prednisolone) were given. Foot-drop and gait difficulty partially regressed. The

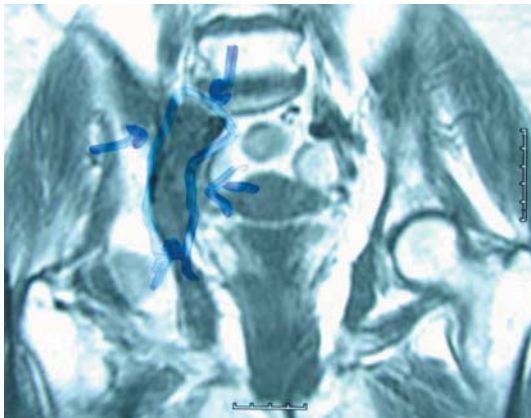


Figure 1. Pre-treatment MRI.

patient then received radiotherapy (RT) of 45 Gy on para-aortic region including the right sacroiliac area. After RT and chemotherapy, while thoracic tomography was normal, increase in soft tissue was observed in the retroperitoneal area surrounding the aorta and inferior vena cava. MRI of the lumbosacral plexus revealed a mass of soft tissue extending from the mid-line distally along the paracaval side of the anterior aspect of the spinal aorta and to the piriformis and obturator internus muscles by surrounding the internal iliac vein. Increase in soft tissue as observed on the tomography and MRI, was considered as fibrosis secondary to the RT (Figure 2). Positron emission tomography (PET) supported this appearance (Figure 3). On the follow-up, bone marrow involvement disappeared. On the EMG, there were neurological motor unit potential changes in the muscles innervated by L₂₋₅ and S₁ on the right side. The patient has been followed in remission for six months.

DISCUSSION

After the examinations of lymph node and bone marrow, the patient was diagnosed as advanced stage DLBCL. Additionally, she had polyradiculopathy and foot-drop. In the patients with lymphoma, peripheral neuropathy may appear due to direct peripheral nerve invasion, spinal cord compression, monoclonal gammopathy, anti-neoplastic drugs, and autoimmunity. Guillain-Barré



Figure 2. Post-treatment MRI.

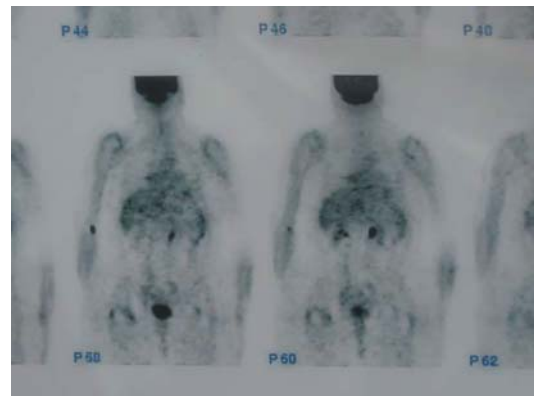


Figure 3. Post-treatment PET.

syndrome, hypothyroidism, megaloblastic anemia, HIV and CMV infections should also be considered in the differential diagnosis of peripheral neuropathy^[11-13].

We excluded the other causes of neuropathy in our patient because there were negative viral markers, normal thyroid function and normal serum level of vitamin B₁₂. Moreover, spinal disc compression was considered as the findings related to peroneal neuropathy on the EMG and mass lesions on MRI of the lumbosacral area. Hematological and neurological findings disappeared following R-CHOP chemotherapy and RT. These lesions detected radiologically were considered to be related to fibrosis.

Lymphomas cause spinal cord compressions in 6.8 to 10% of the patients. Spinal cord, dura mater, meninx or vertebra may be infiltrated. The infiltration of the lumbosacral region is rare. In polyradiculopathies due to infiltrations of the lumbosacral region, back pain, weakness, sensory loss, paresthesia and such findings as urinary frequency and constipation related to autonomic dysfunction as well as spasticity, ataxia, increased or decreased deep tendon reflexes, pathological reflexes or cauda equina syndrome may develop^[7-10]. CT, MRI and PET are the most useful diagnostic tools in the diagnosis of lumbosacral infiltration^[7,9,14].

Hollender et al.^[15] reported the involvement of central nervous system in 170 (6.6%) of 2561 patients with NHL. While 85% of these patients had advanced stage, 140 patients were secondary NHL. The overall median survival was 2.6 months and seven of the patients had spinal cord infiltration.

Sciatic nerve infiltration of NHL may be rarely seen^[6,16]. In these patients, paresthesia, numbness, weakness and pain in the lower extremity occurred, but no foot-drop. According to the working classification, these patients were in intermediate or high grade NHL. Cauda equina syndrome due to spinal cord involvement may result in paraplegia in NHL. These patients were reported as advanced stage DLBCL. Their median survival was short^[17,18]. Patients with DLBCL with progressive neuropathy leading to spinal cord compression and sensory and motor losses have been reported. Although triceps palsy occurred in a patient related to brachial plexus compression, foot-drop was not seen in these patients^[9,19].

In conclusion, foot-drop may develop due to lumbosacral cord compression as an extranodal involvement in the patients with advanced stage DLBCL. Thus, lymphoma should be considered in the patients with peripheral neuropathy and spinal cord compression.

REFERENCES

1. Pugh WC, McBride JA. The pathologic basis for the classification of non-Hodgkin's lymphomas. In: Hoffman R, Brnz Jr EJ, Shattil SJ, Furie B, Cohen HJ, Silberstein LE, McGlave P, eds. Hematology Basic Principles and Practice. 3rd ed. Philadelphia: Churchill Livingstone, 2000:1263-93.
2. Moller MB, Pedersen NT, Christensen BE. Diffuse large B-cell lymphoma: clinical implications of extranodal versus nodal presentation—a population-based study of 1575 cases. *Br J Haematol* 2004;124:151-9.
3. Isikdogan A, Ayyildiz O, Buyukcelik A, Arslan A, Tiftik N, Buyukbayram H, Muftuoglu E. Non-Hodgkin's lymphoma in southeast Turkey: clinicopathologic features of 490 cases. *Ann Hematol* 2004;83:265-9.
4. Morabito F, Gallamini A, Stelitano C, Callea V, Guglielmi C, Neri S, Lazzaro A, Orsucci L, Ilariucci F, Sacchi S, Vitolo U, Federico M. Clinical relevance of immunophenotype in a retrospective comparative study of 297 peripheral T-cell lymphomas, unspecified, and 496 diffuse large B-cell lymphomas: experience of the Intergruppo Italiano Linfomi. *Cancer* 2004;101:1601-8.
5. Feugier P, Virion JM, Tilly H, Haioun C, Marit G, Macro M, Bordessoule D, Recher C, Blanc M, Molina T, Lederlin P, Coiffier B. Incidence and risk factors for central nervous system occurrence in elderly patients with diffuse large-B-cell lymphoma: influence of rituximab. *Ann Oncol* 2004;15:129-33.
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 literature. *Neurosurgery* 1997;40:618-22.
7. Arrowsmith ER, Jagasia MH. Complications of hematopoietic neoplasms. In: Greer JP, Foerster J, Lukens JN, Rodgers GM, Paraskevas F, Glader B, eds. *Wintrobe's Clinical Hematology*. 11th ed. Philadelphia: Lippincott Williams-Wilkins, 2004:1919-43.
8. Vallat JM, De Mascarel HA, Bordessoule D, Jauberteau MO, Tabaraud F, Gelot A, Vallat VA. Non-Hodgkin malignant lymphomas and peripheral neuropathies-13 cases. *Brain* 1995;118:1233-45.
9. Kanter P, Zeidman A, Streifler J, Marmelstein V, Even-Sapir E, Metser U, Stein GY, Cohen AM. PET-CT imaging of combined brachial and lumbosacral neurolymphomatosis. *Eur J Haematol* 2005;74:66-9.
10. Raval SN, Yahalom J, DeAngelis LM. Management of central nervous system lymphoma. In: Mauch PM, Armitage JO, Coiffier B, Dalla-Favera R, Harris NL, eds. *Non-Hodgkin's Lymphomas*. 1st ed. Philadelphia: Lippincott Williams-Wilkins, 2004:643-55.
11. Walk D, Handelsman A, Beckmann E, Kozloff M, Shapiro C. Mononeuropathy multiplex due to infiltration of lymphoma in hematologic remission. *Muscle Nerve* 1998; 21:823-6.

12. Vital C, Vital A, Julien J, Rivel J, deMascarel A, Vergier B, Henry P, Barat M, Reiffers J, Broustet A. Peripheral neuropathies and lymphoma without monoclonal gammopathy: a new classification. *J Neurol* 1990;237:177-85.
13. Jordan JE, Donaldson SS, Enzmann DR. Cost effectiveness and outcome assessment of magnetic resonance imaging in diagnosing cord compression. *Cancer* 1995;75:2579-86.
14. Hollender A, Kvaloy S, Lote K, Nome O, Holte H. Prognostic factors in 140 adult patients with non-Hodgkin's lymphoma with systemic central nervous system involvement. A single center analysis. *Eur J Cancer* 2000;36:1762-8.
15. Kanamori M, Matsui H, Yudoh K. Solitary T-cell lymphoma of the sciatic nerve. *Neurosurgery* 1995;36:1203-5.
16. Miyata E, Koga H, Yamamoto H, Okamoto M, Hirano M. Cauda equina syndrome due to recurrent malignant lymphoma of the spinal cord. A case report. *Rinsho Shinkeigaku* 1999;39:1071-4 (abstract).
17. Zagami AS, Granot R. Non-Hodgkin's lymphoma involving the cauda equina and ocular cranial nerves: case reports and literature review. *J Clin Neurosci* 2003;10:696-9.
18. Liu JK, Kan P, Schmidt MH. Diffuse large B-cell lymphoma presenting as a sacral tumor. Report of two cases. *Neurosurg Focus* 2003;15:10.

Address for Correspondence:

İrfan YAVAŐOđLU, MD
Department of Hematology
Adnan Menderes University
School of Medicine
Aydın, TURKEY
e-mail: dryavas@hotmail.com