

Lumbosacral Plexopathy: Initial and Infrequent Manifestation of Relapsed Non-Hodgkin's Lymphoma

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Abstract

Lymphoma is a blood tumor, with an incidence of 11 cases per 100,000 inhabitants being 25% Hodgkin lymphoma (HL) and 75% non-Hodgkin's lymphoma (NHL). Peripheral neurological involvement is very uncommon (1-5% of lymphomas) and the most are due to NHL. The mechanisms described in peripheral neurological involvement are extrinsic tumor compression, direct infiltration, chemoradiotherapy, infection or paraneoplastic autoimmunity. We report the case of a patient of 69 years with a history of NHL in complete remission with progressive symptoms of pain, weakness, paresthesia and hypoesthesia in right lower limb. After complementary tests, infiltrative lumbosacral plexopathy as the initial manifestation of relapse NHL was diagnosed. For this reason the patient underwent hematological and rehabilitation treatment, without clinical improvement from the functional point of view. We highlight the case because of the uncommon of their presentation and the importance of diagnosis as to the prognosis for recovery.

Keywords: Neurorehabilitation; Lumbar plexopathy; Peripheral neuropathy; Hodgkin/Non-Hodgkin's lymphoma

Introduction

Lymphomas are hematopoietic neoplasms that originate in lymphocytes and expand to other lymphoid tissues, either by direct infiltration or by hematogenous spread. They are classified into Hodgkin's lymphoma (HL, 25% of cases) and Non-Hodgkin's lymphoma (NHL, in 75% of cases) [1]. The incidence is estimated between 3.5 to 11 new cases per 100,000 inhabitants [1,2]. Also NHL is divided into B or T cells type. The B cells type of NHL is the most frequent [1].

Peripheral neurological complications secondary to lymphoma are very rare and much less frequent than central ones [3]. Peripheral neurological complications are present only in 5% of patients with lymphoma, more frequent in the NHL, and within them, 90% of cases are the NHL B cells type [1]. The pathophysiological mechanisms described are due to tumor nerve compression, direct nerve infiltration, iatrogenic chemotherapy/radiotherapy or remote effects of the tumor (paraneoplastic syndromes) [1-9].

The clinical presentation is very variable. The onset can be acute or sub-acute. The course of the disease can be progressive or with remissions. The neuropathy can be sensitive, motor or a combination of both. Symmetric, asymmetric or multifocal neuropathy can be observed [4].

The confirmation of peripheral neuropathy requires exhaustive clinical evaluation [8]: pathological exams (biopsy, bone marrow aspiration), radiological imaging techniques (radiography, computed

tomography, magnetic resonance image and/or gammagraphy) [7], laboratory tests (blood count, biochemistry, bone marrow aspiration, lumbar puncture) and electrophysiological studies [6].

The electrophysiological studies allow to demonstrate the degree, type and extent of the lesion, and the probable differential diagnoses. They can also try to explain the underlying cause: metastatic infiltration, paraneoplastic effect, radiation or chemotherapy [6].

Similarly, paraneoplastic mechanisms, although highly infrequent (0.01%) [5] must be suspected in a patient with peripheral nerve disorder and malignant neoplasm [9].

In patients with Hodgkin's disease, the treatment of the underlying lymphoma is only rarely followed by recovery of the associated peripheral neuropathy [2].

Clinical case

A 69 year old woman with a history of NHL IV-B type treated in 2008 with chemotherapy and discharged with complete remission came to the emergency department referring buttock pain, radiating to the lower right leg. The course of symptoms was of one month evolution, accompanied by pain and numbness in her right foot, which does not subside with usual painkiller treatment. Progressive weakness also appeared with drop foot and incapability to walk properly.

Physical examination objectified inability to bend up the foot. The muscular balance of tibialis anterior, extensor digitorum brevis, extensor of the first toe and peroneal muscles was 0/5. All other muscles of the right leg were 4/5. Paresthesias were felt at the dorsum

of the foot and at the outer side of the right ankle. Right patellar tendon reflex was normal, Right Aquiles reflex was abolished. Positive right Bragard and Lasegue signs were observed. The patient walked with drop of her right foot. Under these circumstances rehabilitation treatment program began (Exercise Therapy and Ankle Foot Orthosis adaptation for facilitating gait and postural control). Later neuromuscular facilitation and electro stimulation was added.

Lumbar Spine Magnetic Resonance Image was performed. A small hernia was observed at foraminal disc in L4-L5 space. It reduced the caliber of the L4 right foramen obliterating partially the peri-radicular fat at its foraminal right path. There is no evidence of disc herniation or protrusion at L5-S1 space. Degenerative lumbar spine disc disease with disc protrusions at L1-L2, L2-L3 and L3-L4 were observed, but they do not originate clear root compromise. Besides, diffuse alteration on the intensity in the signal of the bone marrow is also shown, which may be secondary to infiltration of the lymphoma or effect of previous treatment (Figure 1).



Figure 1: Lumbar spine Magnetic Resonance Image: Sagittal view where suggestive medullar bone infiltration in L5 vertebral body is observed (left image). Axial view with dots in the medullar canal suggestive of tumoral infiltration in the raquis canal (right image)

The neurophysiological study showed acute denervation signs in tibialis anterior, tibialis posterior, peroneus longus, medial gastrocnemius, short head of biceps, semimembranous, gluteus medius and gluteus major muscles; no voluntary activity in tibial anterior or peroneal muscles; and the absence of motor response while stimulating the peroneal nerve (L5) at the fibular head. The electroneurography showed no sensitive surface potential of the right peroneal nerve (L5) and decreased amplitude of sensory potential at the right sural nerve (S1). The peroneal motor nerve (L5) was not evoked, and the latency and conduction velocity of tibial motor nerve (S1) was diminished (Table 1).

These findings show evidence of extended axonal degeneration and demyelination neuropathy at several root levels (L4, L5, S1) which support the final diagnosis of right lumbosacral plexopathy, probably by infiltrative etiology, given the rapid clinical course.

Pelvic Magnetic Resonance Image showed hyperintensity on T2 sequence of the gluteal, tensor of fascia lata, femoral, square, internal and external obturator muscles in the right side of the pelvis.

ENG: Nerve	Sensitive	SENSITIVE ACTION POTENTIAL		
		LATENCY	CONDUCTION VELOCITY	AMPLITUDE
Superficial Nerve (L5)	peroneal	Not evoked	Not evoked	Not evoked
Sural Nerve (S1)		NORMAL	NORMAL (46m/s)	Disminished 62%
ENG: Motor Nerve		MOTOR ACTION POTENTIAL		
		LATENCY	CONDUCTION VELOCITY	AMPLITUDE
Peroneal Nerve (L5)		Not evoked	Not evoked	Not evoked
Tibial Nerve (S1)		Disminished	Disminished (39m/s)	NORMAL
EMG: Muscles		SPONTANEOUS ACTIVITY		MAXIMAL EFFORT
		+ WAVES	FIBRILATIONS	
Tibial anterior (L4,L5)		+++	+++	Not evoked
Peroneal (L5,S1)		+++	+++	Not evoked
Medial Gemelous (L5,S1,S2)		+	+	INTERMEDIATE
Tibial posterior (L5,S1)		++	++	INTERMEDIATE
Biceps short head (L5,S1)		+++	+++	Not evoked
Semimembranous(L4, L5,S1,S2)		++	++	INTERMEDIATE
Medial Gluteous (L4,L5,S1)		+	+	INTERMEDIATE
Major Gluteous (L5,S1,S2)		+	+	INTERMEDIATE

Table 1: Neurophysiological studies of the right lower limb. EMG =Electromyography, ENG=Electroneurography

The right gluteus maximus muscle presented a marked decrease in volume compared to the contralateral. This data could translate denervation phenomena by lumbosacral plexus involvement (Figure 2).

Given these findings, it was decided to start reassessing lymphoma with extended studies, such as lumbar puncture, bone marrow biopsy and tomography of the thorax, abdomen and pelvis. Lymphoma relapse stage IV-A was confirmed, with involvement of the nasopharynx, gastrointestinal tract, and bone marrow.

Lumbosacral plexopathy was the first manifestation of relapse lymphoma and the most probable etiology was infiltrative, as suggested by the magnetic resonance images, although no nerve biopsy was performed. So a new cycle of chemotherapy began.

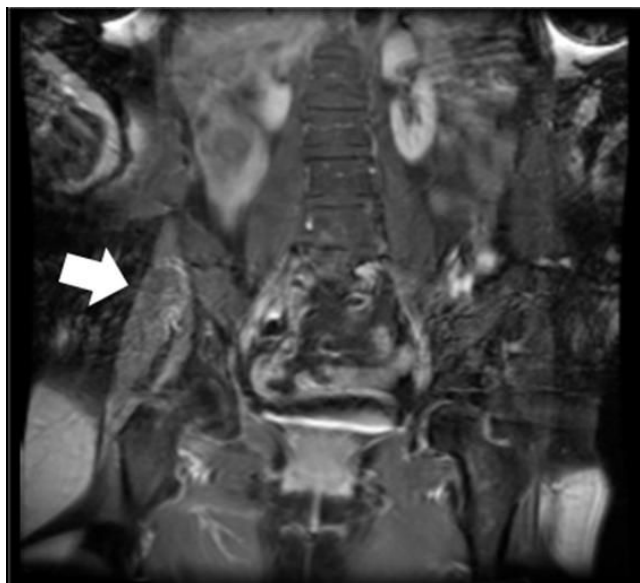


Figure 2: Pelvic Magnetic Resonance Image. Arrow showing hyperintensity in T2 sequence of the right pelvis muscles, which can be considered as a sign of denervation. Besides, atrophy is observed in the right pelvis muscles, compared to contralateral side

From the hematological point of view, the patient presented good evolution and was discharged after complete remission of NHL relapse. Regarding the peripheral neuropathy, after 6 months of treatment, the neurological deficits remained stable, without clinical improvement for ankle dorsiflexion (Figure 3). The patient was able to walk independently with the help of ankle foot orthosis and a cane.

Discussion

The presence of impaired peripheral nervous system (PNS) in lymphoma patients, are very rare (1-2% according to Amato, and 5% as Kelly states) [1,4]. There is great clinic heterogeneity (plexopathy, mononeuropathy or polyneuropathy), and the literature makes reference only to individual or small series of cases [3]. These peripheral neurological complications are rare and much less common than central neuropathies [1,3].

Lymphoma can affect the PNS, infiltrating the nerves, causing axonal or demyelinating damage. Walsh reported that while only 8% of patients with lymphoma presented clinical evidence of peripheral neuropathy, 35% already had neurophysiologic alterations [1,10].

Regarding the pathophysiologic mechanisms described [1-3,5-7,8,9], and outlined above, Herpes zoster infection is the most common cause. Infiltration or compression of the nerve roots by lymphoma is rare, but more common in advanced disease.

Radiation plexopathy occurs after 6 months of treatment and it is difficult to be distinguished from neoplastic infiltration. Malignant infiltration of the lumbosacral plexus is painful while radiation plexopathy is painless; both of them develop progressive paralysis, unilateral in infiltration (as it was in our case report) and bilateral in radiation [11].



Figure 3: No voluntary dorsiflexion of the right foot and atrophy of the right leg, compared to contralateral side (right picture is at rest and left picture is in active movement of the feet)

The multifocal infiltration of the nerves or the vasculitis may present as peripheral neuropathy. Sensory/motor sub-acute neuropathy appears as paraneoplastic syndrome, especially reported in HL [2], a fact that differs with the case report, a patient with NHL. Focal or multifocal cranial neuropathies, radiculopathies and plexopathies typically result from tumor infiltration (as our presented case report), Herpes Zoster infection or radiation-induced injury [12]. Toxic neuropathies occur with exposure to several chemotherapeutic agents, including vinca alkaloids, cisplatin, taxanes and suramine. These neuropathies are usually dose-related, sensory-predominant, and at least partially reversible, with an axonopathic or ganglionopathic mechanism. Suramine is unique in causing sub-acute, demyelinating polyradiculoneuropathy [12].

Depending on the type of lymphoma, NHL can cause neuronopathy by direct compression, by infiltration of nerves or remote paraneoplastic effects [1,4]. The HL can cause autoimmune, inflammatory neuropathies like Guillain Barre syndrome or chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) [1,2].

Paraneoplastic mechanisms, although highly infrequent (0.01%) must always be considered [5]. They should be suspected and included in the differential diagnosis in all patients with peripheral nerve impairment and malignant neoplasm [9], including lymphoproliferative cancer or small cell lung cancer [12].

Regarding the functional prognosis, as most of the researchers stated, our case report presented complete remission of lymphoma, without improvement of the neurological deficit; since the treatment of lymphoma hardly ever is associated with recovery of the neuropathy [2].

We conclude that the importance of the case report presented lies in the rarity and limited frequency of peripheral neurological complication of NHL (1 to 5% in lymphomas). A clinical, biochemical, neurophysiological and radiological study can help us characterize the degree, extent and type of the neurological lesion. Besides, it may explain the underlying mechanisms involved. On the other hand, we emphasize the importance of differential diagnosis of all neuropathies to rule out the presence of malignant disease, which as mentioned

above, it could compromise and/or interfere with the functional outcome.

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