

Glimpse into Routine EMG Findings of Patients with Malign Neoplasms

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ABSTRACT

Neurological complications in cancer patients may arise due to direct tumor effects, treatment-related toxicity, or paraneoplastic syndromes. Neurological complications in patients with neoplasms can affect all structures of the peripheral nervous system, either alone or in combination. We reviewed the electrodiagnostic test database of our EMG unit between 2017 and 2024. The clinical and electrophysiological data from 322 patients with cancer were collected. Descriptive statistics were reported and electrophysiological findings were compared between the two groups with the largest number of patients (gynecological and breast cancer groups). Among 322 patients, 189 (58.6%) had polyneuropathy, 21 (6.5%) had myopathy, 63 (19.5%) exhibited spinal root/anterior horn involvement, and 4 (1.2%) had plexopathy. Additionally, 19 patients developed nerve damage postoperatively, with spinal accessory nerve injury being the most common (63%). Electrophysiological findings related to anticancer drugs were detected in 57 patients (17.7%). Significant differences were found between gynecological and breast cancer groups regarding peroneal compound muscle action potential amplitude ($p=0.007$) and sural sensory nerve action potential amplitude ($p=0.03$). To the best of our knowledge, this study is the first to report the routine EMG findings of patients with oncological and hematological diseases with a broad approach design. Patients with plexopathy, neuropathy, and myopathy were examined in combination. Therefore, our findings will provide valuable insights into the electrophysiological findings of patients with oncological and hematological diseases.

Keywords: Cancer, Chemotherapy, EMG, Myopathy-Polyneuropathy, Neurotoxicity

INTRODUCTION

Neurological complications are frequent in patients with neoplasms, and both the central and peripheral nervous systems may be affected by malignant diseases. Malignant diseases can lead to neuromuscular complications, affecting various structures of the peripheral nervous system, including the anterior horn, nerve roots, dorsal root ganglion, plexus, axons, myelin, neuromuscular junction, and muscle.¹

Regarding malignant diseases, neurological complications may occur due to treatments^{2,3}, direct ef-

fects of the cancer itself, or indirect complications, namely, remote effects.^{1,4} Distinguishing between these entities, demonstrating the type and degree of the lesion and delineating the extent of neuromuscular involvement is particularly important for proper patient care and treatment strategies. Furthermore, several interrelated structures may be affected by the disease course, such as secondary axonal loss in demyelinating neuropathy and involvement of both the anterior horn and motor axons. Therefore, electroneuromyography (EMG) is indispensable for these patients.

This retrospective study reports the routine EMG findings of patients with oncological and hematological diseases with a broad approach design, that is, patient groups such as patients with plexopathy, neuropathy, and myopathy were examined in combination.

PATIENTS AND METHODS

The electrodiagnostic (EDx) test database of our laboratory was reviewed from July 2017 to January 2024, and the clinical and electrophysiological data of 322 patients with cancer were collected. Additionally, clinical information was obtained from the medical recording system.

All electrodiagnostic tests were performed and interpreted by three experienced neurologists specialized in clinical neurophysiology (CMT, FGY, HUU). To ensure consistency, standardized protocols were followed throughout the study period. Routine nerve conduction studies (NCSs) included median and ulnar sensory/motor studies in the upper extremities and tibial, peroneal motor, and sural sensory studies in the lower extremities were analyzed. The compound muscle action potential (CMAP) amplitude, sensory nerve action potential (SNAP) amplitude, distal motor latency, and motor and sensory nerve conduction velocities were evaluated. NCSs were considered abnormal when these parameters exceeded the normal range in the corresponding age groups. A Keypoint Denmark EMG scanner was used to record, filter, and sort all patient data during the EDx tests. The filter settings were set at 20 Hz - 10 kHz for the motor and 20 Hz–2 kHz for the sensory nerve studies.

Electrodiagnostic terminology was used in accordance with standard guidelines. CMAP amplitude is defined as the size of the electrical response recorded from a muscle after stimulating its motor nerve. It reflects how many muscle fibers are activated. SNAP amplitude reflects the integrity and number of functioning sensory axons by measuring the size of the electrical signal recorded from a sensory nerve after stimulation. Distal motor latency is the time interval between nerve stimulation and the onset of muscle response at the distal segment. Motor and sensory nerve conduction velocities measure the speed of electrical impulses travel

along the motor and sensory nerves. Polyneuropathy was classified as axonal, demyelinating, or mixed type (with both demyelinating and axonal features) based on above NCS parameters. Demyelinating involvement is a condition where the myelin sheath is damaged and this causes prominent prolonged latencies, slowing of nerve conduction velocities, and reduced CMAP and SNAP amplitudes. Axonal involvement is a condition in which the axons themselves are damaged, in turn, CMAP and SNAP amplitudes are reduced and conduction velocities and latencies may be relatively preserved or mildly affected. Myopathy refers to a disorder of the muscles themselves, where the muscle fibers do not function properly may lead to reduced CMAP amplitude. Sensory ganglionopathy (SG) is a disorder in which dorsal root ganglia are damaged. SG is characterized by severe reduction or absence of SNAPs, often in a patchy or asymmetric pattern.

Patients were categorized based on their symptoms, electrophysiological diagnosis, malignancy type, metastasis presence, EMG unit-referral department, antineoplastic treatments received, treatment-related neurological complications. Patients were also classified into two main groups based on their malignancy type: the oncology group that included patients with solid tumors such as gynecological, breast, gastrointestinal, and lung cancers, and the hematology group consisting of patients with hematological malignancies including leukemia, lymphoma, and myeloma/plasmacytoma. Patients with nerve injury resulting from any tumor surgery or biopsy were also noted.

This study was approved by the Ethics Committee of Hacettepe University (February 06, 2024, No: SBA 24/197) .

Statistical Analysis

Data analyses were conducted using the Statistical Package for the Social Sciences (SPSS) version 25 for Windows (IBM, Armonk, NY, USA). For categorical variables, numbers and percentages were used; and for continuous variable data, mean \pm standard deviation, median, and range (minimum and maximum) values were used. The normality of continuous variables was assessed using the

Kolmogorov-Smirnov and Shapiro-Wilk tests. Student's t-test and Mann-Whitney U test were used to compare continuous variables between the two groups. A p value < 0.05 was considered statistically significant.

RESULTS

Results in the Context of Demographic and Clinical features

Overall, most patients were female (59.3%), with a median patient age of 61 (range: 18-84); 80 patients were below 50 years of age, of which, 65% (n= 52) were female. The departments that most frequently referred patients to the EMG unit were neurology (n= 162), oncology (n= 49), physical therapy and rehabilitation (n= 26), and hematology (n= 23).

Gynecological cancer (ca) was the most common malignancy group (n= 53), followed by breast ca (n= 38), myeloma/plasmacytoma (n= 34), lymphoma (n= 33), gastrointestinal malignancy (n= 33), leukemia (n= 26), lung ca (n= 25), and the "other malignancies" (n= 64) groups. Upon closer examination of the "other malignancies" group, the gastrointestinal cancer subgroup had the highest number of cases (n= 44). To detail the distribution of gastrointestinal cancers, 21 patients were diagnosed with colorectal cancer, 12 with esophageal/gastric ca, and 11 with liver/gallbladder/pancreas ca. Less common "other malignancies" groups included 8 patients diagnosed with renal/bladder ca, 5 with larynx ca, 4 patients each diagnosed with brain tumors, malignant bone tumors, and skin ca, and 2 each with prostate, testicular, and thyroid ca. Additionally, two primary cancers were observed in 16 patients.

Specifically, 38 (11.8%) patients had metastatic carcinomas, 62 (19.2%), 20 (6.2%), and 17 (5.2%) patients had diabetes mellitus (DM), rheumatic disease, and renal disease as a comorbidity, respectively.

The most common symptom among referred patients was "stocking-and-glove pattern hypoaesthesia/paresthesia" (52.1%), followed by "lower extremity weakness" (11.1%) and "generalized weakness" (10.8%). In contrast, the less common

symptoms include "difficulty walking", "loss of strength in the upper extremities", "extremity pain", "imbalance", "facial asymmetry", "orthostatism", and "cramps."

Demographic and clinical features above-mentioned for all patients are presented in Table 1 along with malignancy grouping.

Results in the Context of Electrophysiological Diagnosis

No electrophysiological abnormalities were observed in 57 patients (17.7%). However, 189 patients were documented with axonal, demyelinating, or mixed type polyneuropathy (58.6%), 15 of whom had the demyelinating features. Of which, 10 had more prominent demyelinating features compared to the axonal features. Two patients had pure demyelinating polyneuropathy (DP). These were cases with acute inflammatory demyelinating polyneuropathy (AIDP) associated with anti-neoplastic therapy. Among patients with hematological diseases whose polyneuropathy included demyelinating features, five were diagnosed with POEMS, three with Castleman disease, one with plasmacytoma, and one with multiple myeloma.

Twenty-eight (8.6%) patients had myopathy; however, critical illness myopathy (CIM) was not included in this group. Separately, seven patients with CIM were documented.

Sixty-three patients (19.5%) had cervical, lumbosacral, or diffuse spinal root/anterior horn involvement. Of which, 52 patients (82.5%) had cervical and lumbosacral disc pathologies that were unrelated to malignancy and four (1.2%) had plexopathy. When we reviewed the EMG findings related to spinal root/anterior horn-plexus-nerve metastases, we observed bilateral cervical and lumbosacral spinal root/anterior horn involvement in a patient with lung cancer with long-segment spinal metastasis; multiple lumbosacral root/anterior horn involvement in a patient with non-Hodgkin lymphoma; right lumbosacral root/anterior horn involvement in a patient diagnosed with vertebral metastatic prostate cancer and drop foot on the right; and sciatic nerve axonal involvement in a patient diagnosed with metastatic prostate cancer.

Table 1. Results of demographic and clinical features

	Patients with gynecological cancer	Patients with breast cancer	Patients with myeloma /plasmacytoma	Patients with gastrointes-tinal tract malignancy	Patients with lymphoma	Patients with leukemia	Patients with lung cancer	Patients with other malignan-cies-	Patients with two primary cancers
n	53	38	34	33	33	26	25	64	16
Female (n)	53	38	15	16	14	14	5	26	11
Mean of age (SD)	61.5(11.6)	58.5(10.3)	59.02(11.7)	59.06(12.7)	57.3(16.07)	41.6(18.1)	62.6(11.3)	54.6(15.7)	65.2(12.5)
Most frequently referred department	Neurology	Neurology	Neurology	Neurology	Neurology	Hematology	Neurology	Neurology	Neurology
Presence of metastasis(n)	1	11	-	9	2	-	5	9	1
DM (n)	16	5	2	7	5	1	6	14	6
Renal disease (n)	1	2	6	1	-	2	1	2	2
Rheumatic disease (n)	6	-	4	2	3	1	1	2	1
HT (n)	15	4	6	3	5	3	2	9	6
Stocking and glove pattern hypoesthesia-paresthesia (n)	37	21	18	18	15	5	6	21	7
Loss of strength in the lower extremities (n)	4	4	3	4	6	4	7	5	1
Generalized weakness (n)		3	2	8	3	5	7	3	5 -
Difficulty walking (n)	1	3	2	1	1	1	2	9	1
Loss of strength in the upper extremities (n)		-	1	1	1	1	3	2	6 -
Extremity pain (n)	1	2	2	1	2	-	2	2	3
Imbalance (n)	1	-	-	-	-	3	1	-	-
Facial asymmetry (n)	-	1	-	1	-	-	-	2	-
Orthostatism (n)	-	-	-	-	-	-	1	-	-
Cramps (n)	-	-	-	-	-	-	-	3	-

* n: Number; DM: Diabetes mellitus; HT: Hypertension; SD: Standard deviation

Of the 76 patients with entrapment neuropathy (23.6%), 11 were diagnosed with breast, 10 with lymphoma, 5 with leukemia, 8 with ovarian cancer, 7 with endometrial cancer, 6 with colorectal cancer, and 6 with multiple myeloma. Furthermore, EMG was performed in five patients with foot drop syndrome and one patient with wrist drop syndrome. The causes were peroneal entrapment syndrome associated with capecitabine detected in one patient, DP detected in one, and segmental spinal root/anterior horn involvement detected in the other four patients, with vincristine being a facilitating factor in one patient.

Patients with axonal nerve injuries resulting from surgery can be listed as follows: ten with pure spinal accessory nerve injury, four with facial nerve injury, two with femoral nerve injury, one with

brachial plexopathy and spinal accessory nerve injury together, one with brachial plexopathy alone, one with spinal accessory nerve and hypoglossal nerve injuries together. Additionally, one with chemotherapy-induced facial neuropathy and one with sciatic neuropathy due to tumor invasion were included in the mononeuropathy group.

Polyneuropathy, 2 of which was demyelinating, was detected in 43 (69.3%) of 62 patients with DM. Regarding less frequently detected electrophysiological diagnoses, eight patients had sensory ganglionopathy. The electrophysiological diagnoses are detailed in the Table 2.

Herein, gynecological cancers were the most common malignancies (n= 53), followed by breast cancer (n= 38). In the comparative analyses of the ulnar, median, tibial, peroneal motor, and ulnar,

median, and sural sensory nerve conduction findings of these two entities, significant differences were detected in terms of the peroneal CMAP ($p=0.007$) (Cohen's $d=0.273$) and sural SNAP amplitudes ($p=0.03$) (Cohen's $d=0.445$).

Results in the Context of Antineoplastic Therapy

In 78 patients (24.2%), their symptoms were due to the anticancer regimen. Of which, 57 (17.7%) patients were observed to have electrophysiological findings. Of whom, 47 patients were evaluated as chemotherapy-induced peripheral neuropathy (CIPN), which is mostly axonal. From another perspective, CIPN was detected in 47 of 189 patients with polyneuropathy. In the CIPN etiology, in 18 patients paclitaxel-carboplatin regimen (38.2%), in 8 patients doxorubicin (17%), in 7 patients vincristine (14.8%), in 7 patients oxaliplatin (14.8%), in 5 patients capecitabine (10.6%), in 4 patients cisplatin (8.5%), in 3 patients bortezomib (6.3%), in 3 patients gemcitabine (6.3%), in 2 patients docetaxel (3.5%), and in 2 patients lenalidomide (4.2%) were observed.

A patient diagnosed with pure DP was evaluated as having oxaliplatin-associated AIDP, and another patient was evaluated as having brentuximab-associated AIDP.

The database was checked for the presence of anticancer drug-induced myopathy (CHIM). In seven non-CIM myopathy, the culprit regimens were as follows: RT and gemcitabine together in three patients, tislelizumab in one patient, gemcitabine alone in one patient, bortezomib in one patient, and hydroxyurea in one patient.

Three patients diagnosed with SG were treated with bortezomib, two with oxaliplatin, one with paclitaxel-carboplatin, one with cisplatin, and one with sunitinib.

DISCUSSION

Our study provides a comprehensive overview of routine EMG findings in patients with different types of malignancies and treatments highlighting the prevalence and characteristics of peripheral nerve involvements in this population. These findings also emphasize the importance of electrophysiological monitoring during cancer treatment.

Neurological toxicity from treatments and direct or indirect cancer effects; it was difficult to tell the two apart.⁴ Therefore, we were able to definitively classify 14.5% of our patients within the CIPN group. In literature, it is reported that 15-20% of patients with cancer have neurological symptoms.¹ Neuropathy is the most common type of neurotoxicity and may be the first symptom of malignancy in some patients.⁵ CIPN has been reported with variable incidence, ranging from 19% to >85%^{6,7}, and the prevalence of polyneuropathy in patients receiving chemotherapy was found to be 68%.⁶

DP can manifest either alone or in combination with axonal polyneuropathy, and is a complication of many types of cancer treatments.^{1,8-12} Immune check point inhibitor (ICI)-associated Guillain-Barre syndrome was previously reported at a rate of 0.1-0.2%.¹³ Herein, two AIDP cases were determined, one associated with an alkylating agent and the other with a monoclonal antibody, not with ICIs.

Excluding CIM, myopathy/myositis in patients with cancer may occur due to direct muscle infiltration of tumors and paraneoplastic conditions such as dermatomyositis-polymyositis, radiotherapy (RT), graft-vs-host disease, and CHIM.¹⁴⁻¹⁹ However, these involvements are relatively rare.²⁰ As expected, a causal link was established in only seven patients with myopathy, in whom a diagnosis of CHIM was made in our study.

Spinal metastases of tumors or primary malignant spinal tumors may cause root/anterior horn involvement.²⁰ Three of our patients with spinal root/anterior horn involvement presented in this manner. The risk of radiation-induced brachial plexopathy (RIBP) is dose-dependent, and rates have been described at 1-2% when associated with lower doses.¹³ In our cohort, two of our four patients with brachial plexopathy had RIBP.

Surgeries such as head-neck surgery, mastectomy, and pelvic surgery may cause morbidity by damaging peripheral nerves.^{13,21,22} Overall, nineteen patients had nerve injury secondary to the surgery, with the most common being spinal accessory nerve injury.

The peripheral nerve is vulnerable to toxic damage because it has an enormous surface area and the

Table 2. Detailed electrophysiological diagnoses

			Oncology patients (n)	Hematology patients (n)	Anticancer drug-related (n)	Radiation induced (n)
Polyneuropathy	Axonal	Pure sensory	60	16	14	-
		Pure motor	-	4	1	-
		Sensorimotor	60	37	29	-
	Demyelinating		1	1	2	-
	Mixed (axonal + demyelinating)		2	10	3	-
Myopathy	CIM		4	3	-	-
	Non-CIM		19	9	7	3
Spinal radix/anterior horn involvement			44	23	-	-
Plexopathy			4	-	-	2
Sensory ganglionopathy			5	3	3	-
Mononeuropathy			53	24	1	-
(inclusive entrapment neuropathy; except post-operative axonal injury)						
Postoperative axonal injury			17	2	-	-
CIM: Critically illness myopathy						

distance between the cell body and axon terminal is vast. Combinations of high single, or cumulative doses of antineoplastic agents may result in more severe presentations. CIPN was first implicated in the vincristine.¹³ The most frequent neurotoxicity-inducing treatments are platinum-based compounds (carboplatin, cisplatin, and oxaliplatin), taxanes (paclitaxel and docetaxel), vinca alkaloids (vincristine and vinblastine), bortezomib and thalidomide.²³⁻²⁷ In a multicenter study, CIPN rates were documented as 48.9% for paclitaxel, 58.5% for oxaliplatin, 50.5% for docetaxel, and 43.7% for bortezomib.²⁴ In our study, consistent with the literature, the most common chemotherapy agents associated with electrophysiological findings were paclitaxel, carboplatin, doxorubicin, vincristine, and oxaliplatin, either individually or in combination. Supporting the notion that neurotoxicity risk increases with age 17, 80.7% of affected patients were over fifty. Platinum-based compounds such as cisplatin, carboplatin, and oxaliplatin, particularly at large cumulative doses, cause SG.^{1,28} Among the eight patients with SG in our cohort, three had previously been treated with platinum-based compounds. As an additional inference from our study, based on patients whose complete records were accessible and who had not previously

received any other chemotherapy regimen, we can conclude that peripheral involvement is more frequent after the second or third cycle of the chemotherapy regimens.

The two malignancy groups that we encountered most frequently in our EMG unit were gynecological and breast cancers. In comparative analyses of the electrophysiological parameters of these two patient groups, significant differences were detected in terms of peroneal CMAP and sural SNAP amplitudes. The anticancer drugs most commonly associated with CIPN are the platinum and taxane groups, which are relatively more frequently used in the treatment of gynecological cancers. Therefore, the presence of lower sural SNAP and peroneal CMAP amplitudes might be expected to be more pronounced in the gynecological cancer group than in the breast cancer group. Moreover, it may be useful to keep in mind discussions regarding genetic differences in treatment-related neurotoxicity.²³ In this context, when it is necessary to use CIPN-related agents, baseline EMG values before treatment and periodic EMG monitoring during treatment can be performed. If necessary, changes of treatment cycles or regimen changes can be planned by the clinician.

Limitations of the study: This observational study has a number of limitations, starting with its own retrospective nature. The main limitation is that since the anticancer treatment cycle numbers, cumulative doses and radiotherapy information of most patients could not be obtained from the existing records, the information we presented regarding anticancer drug and radiotherapy-related EMG findings was limited to what we could obtain. Another limitation of this study is the absence of a healthy control group, which restricts the ability to definitively attribute electrophysiological findings solely to malignancy or its treatment.

Conclusion

In the literature, studies reporting the electrophysiological findings of peripheral neurological complications in patients with oncological-hematological diseases are presented as specific studies wherein patient groups, such as plexopathy, neuropathy, and myopathy, are examined separately. Our findings offer valuable insights into the electrophysiological characteristics of malignancy-associated routine EMG findings, highlighting the importance of routine EMG in oncology-hematology care.

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