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Clinical Implication of Serial Neurophysiologic Study in Diagnosis of CIPN

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Objective

Taxane families are widely used in the management of patients with breast and ovarian cancers. Dose-limiting toxicity of taxanes is related to a distal sensory neuropathy, with symptoms of sensory loss and paresthesia in the extremities that can significantly impact quality of life in cancer survivors. However, the assessment of chemotherapy induced peripheral neuropathy (CIPN) is still based not on the objective findings of neurophysiologic study, but on clinical symptoms. Therefore, the aim of this retrospective study is to demonstrate neurophysiologic changes in symptomatic subjects early after and during chemotherapy and to suggest new criteria in diagnosing CIPN.

Methods

The medical charts of subjects with breast or ovarian cancers who visited university hospital between April 1, 2017 and January 1, 2018 were reviewed. Inclusion criteria were history of chemotherapy with taxane-containing regimen, sensory symptoms of glove and stocking distribution compatible with neuropathic pain (those with Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale ≥12), and those who had undergone nerve conduction study (NCS) twice during or after the chemotherapy. Subjects were excluded if they had predisposing condition for neuropathy, such as diabetes mellitus, thyroid disease, alcohol abuse history, and previous chemotherapy for other malignancies. Demographics and clinical features were acquired along with parameters of body mass index, body surface area, the regimen and the number of chemotherapy, LANSS Pain Scale, and the Sensory Nerve Action Potentials (SNAPs) recorded in the sural nerves.

Results

Data from 23 subjects were collected. Baseline characteristics are described in Table 1. All subjects scored over 12 in LANSS Pain Scale, subjectively having symptoms compatible with neuropathic pain. Follow-up NCS was performed after 2.2 months on average (Figure). Among the subjects who suffers from neuropathic pain after taxane-containing chemotherapy, only 10 out of 23 (43.5%) showed sural SNAP amplitude lower than 10uv in initial NCS. Additional five subjects developed sural SNAP amplitude lower than 10uv in the follow-up NCS (15 out of 23, 65.2%). Between the first and second NCS, 10 subjects showed more than 30% drop of sural SNAP amplitude (10 out of 23, 43.5%). The results are summarized in the Table 2.

Conclusion

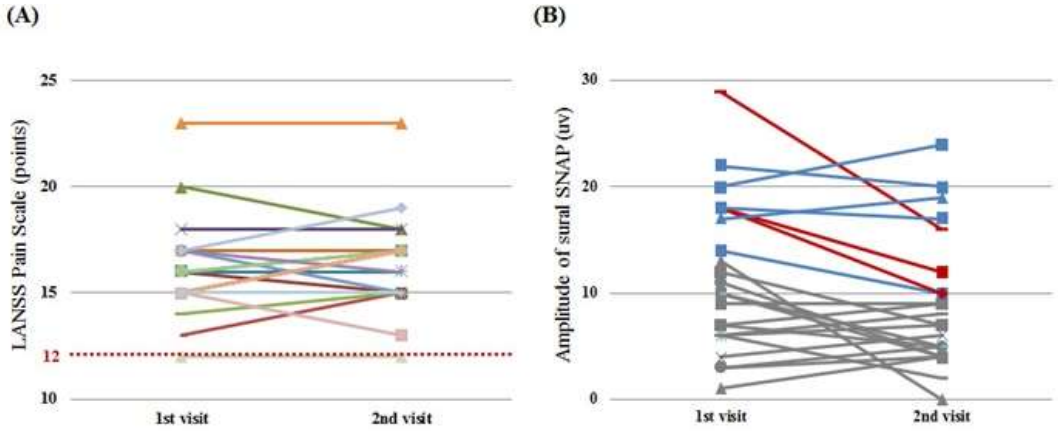
Considering the evidence of axonal injury in the sural nerve, maximum of 65.2% patients was determined as CIPN. However, including the subjects with more than 30% drop of

sural SNAP amplitude, serial NCS results could support as much as 78.2%.Therefore, serial NCS studies during chemotherapy may be helpful in assessing the chemotherapy induced nerve damage and to attain the objective evidence of CIPN. Evidence of axonal injury in sural nerve with more than 30% drop of SNAP amplitude in follow-up NCS can be used as a sensitive marker of early detection for CIPN.

Table 1. Baseline characteristics

Characteristics (*N*=23)	
Age (*years*), mean ± SD	53.6 ± 10.2
BMI (kg/m^2), mean ± SD	23.8 ± 3.4
BSA (m^2), mean ± SD	1.58 ± 0.13
Cancer type	
Breast cancer, *n*	13
Ovarian cancer, *n*	10
Additional chemotherapy regimen to Taxanes	
Cyclophosphamide, *n*	4
Cisplatin, *n*	10
Adriamycin+Cyclophosphamide, *n*	9

BMI, Body Mass Index; BSA, Body Surface Area



SNAP, Sensory Nerve Action Potential; LANSS, Leeds Assessment of Neuropathic Symptoms and Signs

(A) Subjective LANSS Pain Scale and (B) sural nerve SNAP amplitude from nerve conduction study was obtained from 23 subjects on two serial visits. (A) All subjects (*n*=23) showed subjective sensory symptoms compatible with neuropathic pain (LANSS Pain Scale ≥12). Red dashed line shows LANSS Pain Scale equivalent to 12. (B) Gray lines (*n*=15) show subjects with sural SNAP amplitude below 10uv in either study, implying axonal injury. Red lines (*n*=3) show subjects with sural SNAP amplitudes ≥10uv in both visits, however with SNAP amplitude drop of more than 30% in the follow-up study. Blue line (*n*=5) shows subjects with sural SNAP amplitudes ≥10uv and with less than 30% decrease in sural SNAP amplitude.

Fig. Clinical and neurophysiologic features in two serial visits

Table 2. Sensitvity of Neurophysiologic Criteria in Diagnosis of COPN

Criteria	Number of subjects	Sensitivity
1. Sural SNAP amp. < 10uv in initial NCS	**10/23**	**43.5%**
2. Sural SNAP amp. < 10uv in follow-up NCS	**15/23**	**65.2%**
3. Sural SNAP amp. < 10uv in either NCS	**15/23**	**65.2%**
4. Sural SNAP amp. drop > 30% in follow up studies	**10/23**	**43.5%**
5. 1) Sural SNAP amp. < 10uv in either NCS or 2) Sural SNAP amp. drop > 30% in serial studies	**18/23**	**78.2%**

CIPN, chemotherapy induced peripheral neuropathy; amp., amplitude; NCS, Nerve Conduction Study; SNAP, sensory nerve action potential