Patients Treated with Antitumor Drugs Displaying Neurological Deficits Are Characterized by a Low Circulating Level of Nerve Growth Factor

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INTRODUCTION

Patients with malignancy exposed to chemotherapeutic agents such as Vinca alkaloids, suramin, taxanes, and cisplatin can develop PN.\(^1\) Neurological observations published in recent years indicate that administration of taxanes and cisplatin in patients affected by neoplasm induces nerve deficits in a dose- and time-dependent manner (1–6). Moreover, when platinum compounds and taxanes are used in combination, the patients develop more severe PNs (7). The pathophysiology of chemotherapeutic agent-induced neuropathy is still not clear, although a variety of studies have shown that taxanes interfere with axonal transport, causing axonal distal sensory-motor lesions (4), whereas platinum compounds induce sensory neuronopathy acting mainly on the neuronal cell bodies of the spinal ganglion (3). Pathological and electrophysiological studies have also indicated that neurons of the dorsal root ganglion are selectively damaged after cisplatin treatment (1, 3). It has been reported that the development of this PN can induce clinicians to interrupt therapy to prevent more severe neurological deficits (1). Because of the neurotoxic effects, much effort has been devoted to the identification of potential neuroprotective agents (8–10). It is reasonable, therefore, to hypothesize that identification of molecules, which can prevent neurotoxicity and/or promote peripheral innervation after chemotherapy, would be clinically useful. One molecule that seems to display these properties is NGF. NGF is known to play a crucial role in growth and differentiation of specific neuronal population of the peripheral nervous system (11, 12) and is able to reduce the neuronal damage induced by surgical, chemical, and physical injuries both in animal models and humans (8, 13–18). The development of neuropathies induced by antitumor drugs might be the result of impaired synthesis and/or release of endogenous NGF. As a first approach to test the validity of this hypothesis, we investigated whether there is a correlation between the PNs induced by antineoplastic chemotherapy and circulating NGF. To further understand the role of NGF, we studied the relationship between serum levels of NGF and severity of neurotoxicity in patients treated with neurotoxic drugs.

MATERIALS AND METHODS

This study (Table 1) was performed on 23 cancer patients (10 males and 13 females) hospitalized at the Regina Elena Cancer Institute (Rome, Italy) and at the S. Carlo Hospital (Potenza, Italy). Eligibility criteria for entry in this study were as follows: (a) adult patients older than 50 years but not exceeding 70 years; (b) cytologically and/or hystologically proven cancer; (c) Karnofsky performance score between 60 and 100; (d) adequate hepatic, renal, bone marrow, and cardiac function; (e) no previous cytotoxic or radiation therapy; (f) no brain metastasis, neurological disorders (including PNs), diabetes, or systemic diseases affecting the nervous system.

**Study Design.** This study was approved by local intramural ethics committees and was carried out following Italian law for biomedical research. An authorized blood sample was required as baseline sample before the beginning of the first