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CASE REPORT

Charcot-Marie-Tooth hereditary neuropathy revealed after administration of docetaxel in advanced breast cancer

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Abstract

Charcot-Marie-Tooth (CMT) neuropathy is the most common hereditary cause of neuropathy. Diagnosis is usually not made during the childhood but in adolescence or late adulthood. It is reported in the literature that some neurotoxic chemotherapeutical agents can reveal an asymptomatic CMT IA hereditary neuropathy. To our knowledge, we report here the first case of CMT IA revealed in a 55-year-old woman after the administration of docetaxel/trastuzumab/pertuzumab for metastatic breast cancer. This case stresses again the necessity to obtain a complete personal and familial anamnesis and to perform a neurologic examination before the administration of neurotoxic chemotherapeutical agents to prevent the clinical expression of these hereditary neuropathies.

Key words: Charcot-Marie-Tooth IA; Docetaxel; Breast cancer; Neurotoxicity; Peripheral neuropathy

Core tip: This case report represents the first case of Charcot-Marie-Tooth IA revealed after the administration of docetaxel/trastuzumab/pertuzumab for metastatic breast cancer. This paper will help to focus on the revelation of rare hereditary neuropathies after the administration of chemotherapies.

Kourie HR, Mavroudakis N, Aftimos P, Piccart M. Charcot-Marie-Tooth hereditary neuropathy revealed after administration of

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INTRODUCTION

Charcot-Marie-Tooth (CMT) type Ⅰ neuropathy is the most common hereditary cause of neuropathy. Seventy percent to 80% of these patients present the subtype IA. This disease involves the motor and sensory peripheral nerves. Age of onset is variable; diagnosis is usually made between the age of 5 and 25 years. The diagnosis of CMT IA is confirmed with genetic testing and electro-diagnostic studies. There is no approved medical therapy to prevent the progression of CMT[1].

To our knowledge, we report here the first case of CMT IA revealed in a patient after receiving docetaxel/trastuzumab/pertuzumab for metastatic breast cancer. We first discuss the originality of our case and the potential role of chemotherapies in revealing or accentuating these syndromes. Then, we review the reported cases in the literature describing the relationship between these diseases and different chemotherapeutical agents.

CASE REPROT

We present the case of a 55-year-old patient, with unremarkable past medical history, who was diagnosed with HER2-positive and hormonal receptor positive stage Ⅳ metastatic breast cancer in 2014 with a primary tumor of 2.7 cm and one liver metastasis. Her first-line therapy consisted of the standard of care regimen docetaxel combined to trastuzumab and pertuzumab followed by surgery of the primary breast tumor and radiofrequency ablation of the unique metastatic hepatic lesion given an excellent response and the presence of oligometastatic disease.

Chemotherapy was stopped after 6 cycles of docetaxel and the patient was kept on maintenance therapy with trastuzumab and pertuzumab. Three months after the last cycle of chemotherapy, the patient developed numbness in the extremities, generalized depressed tendon reflexes, and hypoesthesia in the lower third of legs. At the clinical examination, pes cavus foot deformity, bilateral foot drop and generalized depressed tendon reflexes were detected.

After a complete anamnesis, the patient mentioned that many members of her family (her sister, her niece and her grand-father) were diagnosed with the CMT type IA disease. A genetic analysis of *PMP22* gene confirmed the diagnosis in our patient and conduction velocity studies demonstrated demyelinating abnormalities concordant with the diagnosis. In fact, multiple ligation-dependent probe amplification of the exons 1-5 of the *PMP22* gene located at 17p11.2 showed genomic duplication comprising the *PMP22* gene.

The patient continued her treatment for breast cancer based on targeted therapies (pertuzumab and trastuzumab) and hormonal therapy (letrozole) and is currently in complete remission. For her stable persistent neurologic deficits physiotherapy was prescribed for maintaining posture and balance, genetic counseling for the family members, namely her two sons, and avoidance of neurotoxic drugs.

DISCUSSION

Neurologic toxicities represent the second most frequent chemotherapy-induced side effect after hematologic toxicities. Vinca-alkaloids, taxanes and platinum-based agents are the most frequent drugs inducing peripheral neurotoxicity. These drugs are used in the treatment of ovarian, breast, lung, prostate, colon and hematological malignancies. Chemotherapy-induced neuropathy is usually dose-dependent. Patients with pre-existing neuropathic symptoms due to diabetes, hereditary neuropathies or earlier treatment with neurotoxic chemotherapy are probably more vulnerable to further development of chemotherapy-induced peripheral neuropathy[2,3].

We report, here, an interesting case of a hereditary CMT IA disease revealed after the administration of docetaxel in combination with anti-HER2 antibodies, in an advanced HER2-positive breast cancer. Our case represents the first case of CMT IA revealed after the administration of docetaxel. It is less likely that this disease was revealed by trastuzumab or pertuzumab, because it was not reported in the literature any CMT related to biologic agents.

A case of an aggravation of CMT after the administration of carboplatin and paclitaxel for ovarian cancer was reported before; the symptomatology resolved after the replacement of paclitaxel by docetaxel, considered as less neurotoxic 4. Thus, our case demonstrates that even less neurotoxic taxanes, as docetaxel, can sometimes reveal or worsen CMT neuropathies.

In some cases, CMT IA has been diagnosed after the administration of neurotoxic drugs including chemotherapeutical agents, mainly vincristine. The cases reported in the literature are summarized in Table 1.

A retrospective case series, in three families with known hereditary neuropathies treated with vincristine, concluded that vincristine in patients with 17p11.2-12 may lead to severe neurotoxicity from vincristine and that this drug should not be administered in patients with CMT1A[5]. On the other hand, a recent study of the Mayo Clinic investigated the association of non-CMT polyneuropathy with *CMT* genes in patients treated with paclitaxel. The results demonstrated a relationship between the *CMT* gene allelic variability and the susceptibility to chemotherapy-induced peripheral neuropathy[6].

This case stresses again the importance for on-

Table 1 Summary of all the reported cases in the literature of Charcot-Marie-Tooth revealed after administration of chemotherapy

Ref.	Patient characteristics	Drug	Malignancy	Signs and symptoms	Diagnosis
Uno *et al*[7], 1999	44 M	Vincristine	NHL	Rapid and marked weakening progressing to quadriplegia and bulbar palsy pes cavus (hollow foot)	Slower nerve conduction velocity 17p11.2-12 duplication
Martino *et al*[4], 2005	F	Paclitaxel/ Carboplatine	Ovarian cancer	Distal sensory and motor neuropathy; Unable to walk, write, or drive	Already diagnosed
Hildebrandt *et al*[8], 2000	52 F	Vincristine	NHL	Dysphagia, dysarthria, muscular weakness of both lower and upper extremities, areflexia, paraesthesia of the fingertips and bilateral sensory impairment of feet and lower legs	Peripheral axonal and demyelinating sensorimotor neuropathy 17p11.2 duplication
Graf *et al*[5], 1996	9 F	Vincristine	Acute lymphoblastic leukemia	Severe acquired weakness, areflexia and distal muscle atrophy	17p duplication
	18 F		Burkitt lymphoma	Pes cavus, distal muscle atrophy and weakness, stocking glove sensory deficits	17p duplication Slower nerve conducting velocity
	46 M		Testicular embryonal cell carcinoma	Foot drop, per cavus and areflexia, marked weakness	Slow motor nerve conduction velocity

NHL: Non-Hodgkin lymphoma; M: Male; F: Female.

cologists to perform a complete anamnesis on past personal and familial history, before the administration of a neurotoxic chemotherapeutical regimen. It is also crucial to perform a complete neurological examination before administrating neurotoxic chemotherapies to avoid the worsening of non-diagnosed peripheral neuropathies.

COMMENTS

Case characteristics

The patient presented numbness in the extremities, generalized depressed tendon reflexes, and hypoesthesia in the lower third of legs, 3 mo after the last cycle of chemotherapy.

Clinical findings

The clinical examination of the patient revealed pes cavus foot deformity, bilateral foot drop and generalized depressed tendon reflexes.

Differential diagnosis

Acute myelitis or Guillain-Barré syndrome are possible differential diagnosis.

Laboratory findings

A multiple ligation-dependant probe amplification of the exons 1-5 of the *PMP22* gene located at 17p11.2 showed genomic duplication comprising the *PMP22* gene.

Pathological diagnosis

Pathological diagnosis was not necessary.

Treatment

Physiotherapy was prescribed for maintaining posture and balance, genetic counseling for the family members, namely her two sons, and avoidance of neurotoxic drugs.

Experiences and lessons

Perform a complete anamnesis on past personal and familial history, before the administration of a neurotoxic chemotherapeutical regimen. Perform a complete neurological examination before administrating neurotoxic chemotherapies to avoid the worsening of non-diagnosed hereditary peripheral neuropathies.

Peer-review

This manuscript presents the first case of Charcot-Marie-Tooth disease identified after the administration of docetaxel in combination with anti-HER2 antibodies. This is an important and interesting report of a rare case.

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