CASE REPORT

Thalidomide-induced sensory polyneuropathy and electrophysiological study of the sural nerve as a screening diagnosis: a case report

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ABSTRACT

Polyneuropathy is a common clinical condition with debilitating symptoms whose treatment depends on etiology. There are numerous possible causes of this type of disorder and the etiological diagnosis is not always easy. In this case report we describe a case of a patient with multiple myeloma who developed purely sensory polyneuropathy, confirmed by electrophysiological study, induced by thalidomide.

Keywords: electrophysiological processes, polyneuropathies, rehabilitation, sural nerve, thalidomide

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INTRODUCTION

Polyneuropathies pose a common and challenging clinical condition with a debilitating symptomology fundamentally dependent on the etiology. The possible causes of this type of disturbance are innumerable and the etiological diagnosis is not always easy. Up to 25% of the cases are labeled "idiopathic."[1]

Polyneuropathy can present sensory disturbances, motor disturbances, alterations of reflexes, and autonomic disturbances.[1]

They are classified according to electromyography into: (1) uniform demyelination associated with sensory-motor polyneuropathy; (2) segmental demyelination, predominantly motor; (3) axonal loss, predominantly motor; (4) axonal loss, with neuropathy and sensory neuronopathy; (5) axonal loss, with mixed sensory-motor peripheral neuropathy; (6) combined with axonal loss and sensory-motor demyelination.[1]

CASE PRESENTATION

Patient C.A.R. is a male, 60 years of age, white, born and raised in São Paulo, SP and complained of paresthesia in both hands and feet, but with greater intensity in the lower limbs, accompanied by hypoesthesia in these areas and moderate proximal muscular weakness. He denied using tobacco or alcohol.

He was diagnosed with multiple myelomas in May of 2007, which was treated with Thalidomide and Dexamethasone. There were no comorbidities or the use of other medications.

He was submitted to a bone marrow transplant in November of 2009 and chemotherapy medicines were then suspended until March of 2010.

A physical examination revealed no reflex alterations, overall muscular strength grade 5, diminution of sensitivity to touch and pain in the distal regions of the lower limbs.

In February of 2010, electromyography was performed which showed action potentials with latency and amplitude absent in the sensitive neuroconduction of the lower limbs, of the upper left limb, and of the right medial and radial nerves. The right ulnar nerve showed action potentials with latency increase and reduced amplitude. The neuroconduction was normal in the upper and lower members and the H reflex of the posterior tibial nerve was absent. Surveyed bilaterally in the myography were the roots from C5 to T1 and from L2 to S3, which appeared normal except for presenting polyphasic potentials in the right deltoid muscle and the presence of positive waves and polyphasic potentials in both first dorsal interossei of the feet.

The examination was interpreted as predominantly sensory axonal polyneuropathy, diffusely affecting the four limbs to an accentuated degree.

DISCUSSION

The main causes of neuropathy and neuronopathy are Friedreich's Ataxia, cerebro-spinal degeneration, vitamin E deficiency, abetalipoproteinemia, secondary to lymphoma and carcinoma, hereditary sensory autonomic neuropathy, gluten-induced enteropathy, paraproteinemias, primary biliary cirrhosis, idiopathic sensory neuropathy and neuronopathy, and the use of drugs such as chemo-therapeutic (thalidomide, vincristine, paclitaxel), microbial (nitrofurantoin, metronidazole, isoniazid, ethambutol, dapsone), anticonvulsives (diphenylhydantoin), oral hypoglycemics (chlorpropamide, carbutamide, tolbutamide), antiarrhythmics (amiodarone), in addition to statins, ergotamine, chloroquine, colchicine, and others.[1,2] In this reported case, the probable cause of the sensory alterations is the use of thalidomide or dexamethasone.

Chronic users of corticoids present lower neuroconduction readings. The use of corticoids can cause demyelinating segmental peripheral neuropathy and myopathy presenting neurophysiological findings similar to polymyositis, however with less cellular hyperexcitability.[1]

Lilienfeld-Toal et al.[3] made a systematic review of the literature on phase-II studies on the combined use of thalidomide and dexamethasone for the treatment of refractory multiple myeloma. Twelve studies were chosen, with a total of 451 patients, and showed better responses to the treatment of multiple myeloma with a treatment involving thalidomide and dexamethasone as compared with monotherapy with thalidomide alone; there was no difference in the incidence of collateral effects such as somnolence, constipation, and peripheral neuropathy, however there was a higher incidence of thromboembolic events in the group with combined therapy.

Based on this study, the use of corticoids is less likely as a cause of reported sensory neuropathy.

Plasmati et al.[4] made clinical and electrophysiological examinations on 31 patients with recently-diagnosed multiple myeloma before and after four months of therapy with thalidomide (200 mg/day, total dosage: 21 gm) before the autologous transplant. After the transplant, the patients used thalidomide at 200 mg/day for three more months (total dosage over the three months: 18 gm). At the beginning of the study they observed that four patients showed signs of slight peripheral sensory-motor neuropathy, combined with multiple myeloma, which tends to worsen slightly during the course of treatment with thalidomide. At the end of the treatment, 83% of the patients showed clinical and electrophysiological evidence of slight sensory axonal polyneuropathy, with no motor alterations, while 100% of them showed a basic pathological improvement.

Fleming et al.[5] reported four cases of axonal sensory-motor neuropathy in children 10-15 years of age, treated with thalidomide for myxopapillary ependymoma, Crohn's disease, and major recurrent canker sores. Neuropathy from thalidomide is frequently associated with proximal weakness and can progress by "coasting" even after discontinuing the treatment

Bastuji-Garin et al.[6] made a study with 135 patients treated with thalidomide for different types of dermatological diseases. Electrophysiological signals were defined by the presence of a 50% reduction in the sensory action potential of the sural nerve in comparison with previous electrophysiological readings, with a relative conservation of the sensory nerve conduction speed. They observed a neuropathy prevalence rate of 25.2% when considering only those cases defined, and 55.6% when all potential cases were considered. The annual incidence rate was greatest during the first year of treatment. Neuropathy was discovered by a systematic electrophysiological examination in almost one quarter of the patients with this kind of adverse event.

In the case reported, the patient presented electroneuromyography with action potentials showing absent latency and sensory neuroconduction amplitude from the lower limbs.

Precise diagnosis of sensory polyneuropathy is not easy. Taking into account the great number of patients with possible causes of sensory polyneuropathy and the clinical presentation frequently imprecise, the possibility of a screening method would

be very useful. Burke et al.[7] made a study with 300 patients with symptoms suggesting sensory polyneuropathy; they showed that an electrophysiological study of the sural nerve is the most useful and reproducible method of screening patients suspected of sensory polyneuropathy, with significant sensitivity of the method.

CONCLUSION

Thalomide, currently a popular chemotherapy drug, is a frequent cause of polyneuropathy. Its detection is important in order to prevent irreversible neurological damage and to improve both the rehabilitation process and the quality of life of these patients. An electrophysiological study using electroneuromyography is as useful in the diagnosis as in the clinical follow-up. Using an electrophysiological study of the sural nerve in these patients could be a fast method of screening.

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