CLINICAL AND MOLECULAR NEUROIMAGING CHARACTERISTICS OF BRAZILIAN PATIENTS WITH PARKINSON'S DISEASE AND MUTATIONS IN PARK2 OR PARK8 GENES

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Abstract - Objective: To describe clinical and neuroimaging (SPECT) characteristics of Brazilian patients with Parkinson's disease (PD) and mutations in PARK2 or PARK8 genes. Method: A total of 119 patients meeting clinical criteria for PD were evaluated. Results: Of all patients studied, 13 had mutations in either PARK2 (n=9) or PARK8 genes (n=4). No statistically significant differences in clinical characteristics in both groups were seen. SPECT with [123I] TRODAT-1 showed significant differences between patient and control and the most remarkable difference was between PARK2 and control. Conclusion: The study found a frequency of mutation of 10.1% and it was most commonly seen in women. These patients had long disease course and high rates of dyskinesia after L-DOPA use. PARK8 patients did not have a relevant family history of PD.

KEY WORDS: Parkinson's disease, PARK2, PARK8, SPECT.

Características clínicas e de neuroimagem molecular de pacientes brasileiros com doença de Parkinson e mutações nos genes PARK2 ou PARK8

Resumo - Objetivo: Descrever as características clínicas e de neuroimagem (SPECT) de pacientes brasileiros com doença de Parkinson e mutações PARK2 e PARK8. Método: Foram avaliados 119 pacientes com critérios clínicos para a doença de Parkinson. Resultados: Entre os pacientes avaliados foram encontrados 13 pacientes com mutação nos genes PARK2 (n=9) ou PARK8 (n=4). Não houve diferença significativa na avaliação das características clínicas entre os dois grupos. Os resultados de SPECT mostraram diferenças significativas quanto ao potencial de ligação do [123I] TRODAT-1 entre pacientes vs. controle, sendo a diferença mais pronunciada entre PARK2 e controle. Conclusão: A frequência de mutação encontrada foi 10,1%, sendo mais comum em mulheres. Estes pacientes apresentavam longo tempo de doença e alta prevalência de discinesias associadas ao uso da levodopa. Nossos pacientes com PARK8 não apresentaram uma história familiar relevante de doença de Parkinson.

PALAVRAS-CHAVE: doença de Parkinson, PARK2, PARK8, SPECT.

Parkinson's disease (PD) is a chronic neurodegenerative disease affecting mostly patients over the age of 50 (late-onset PD or LOPD) and it has a prevalence of 1 to 3% in patients in their seventies or more. PD is characterized by motor and non-motor symptoms that first develop as a result of loss of dopaminergic neurons in the substantia nigra pars compacta in the mesencephalon. As for its etiology, it has been proposed a complex interaction between environmental and toxic factors, genetic predisposition and age. PD pathogenesis may involve dysfunction of protea-some-ubiquitin and mitochondrial system that triggers a cascade of events leading to dopaminergic loss, which is a distinctive trait of this disease. Environmental factors including well water drinking, living in rural areas, exposure to pesticides, herbicides and organic solvents have been implicated in the etiology of PD. We describe the main clinical findings of Brazilian patients with genetically defined PD with mutations in PARK2 or PARK8 genes as well as some molecular neuroimaging findings.

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HYPOGLOSSAL NERVE PALSY AS THE SOLE MANIFESTATION OF SPONTANEOUS INTERNAL CAROTID ARTERY DISSECTION

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Spontaneous internal carotid artery dissection (ICAD) is now recognized as an important cause of ischemic stroke in patients younger than 45 years of age, with annual incidence ranging from 2.5 to 3.0 per 10000013. The clinical presentation includes unilateral headache or neck pain ipsilateral to the affected carotid artery. Horner’s syndrome, transient or complete focal cerebral ischemic deficits, cranial nerve palsy, cervical bruit and tinnitus, which can be associated in various combinations12. Isolated cranial nerve palsy is an unusual manifestation of ICAD13.

We report a patient who presented with a twelfth-nerve involvement as the sole clinical sign of ICAD and discuss the mechanisms leading to this finding.

CASE

A 52-year-old white man was admitted to the emergency department of the Hospital São Camilo Pompeia, São Paulo, Brazil, with a 3-hour history of severe headache and facial pain near the angle of the left jaw associated with left-sided deviation of the protruded tongue. There was no history suggestive of head or cervical trauma, nor previous infection. At the emergency room he presented with heart rate=65bpm, blood pressure=140/80 mmHg, normal cardiorespiratory examination and no cervical bruits. The neurological examination disclosed only left hypoglossal nerve palsy (Fig 1). Laboratory work-up, including complete blood count, biochemical tests and glucose were normal. Brain computer tomography was promptly performed and no abnormality was found. Brain magnetic resonance imaging was normal but magnetic resonance angiography and four-veins cerebral digital subtraction angiography showed a left ICAD arising approximately 4 cm distal to the carotid artery bulb and extending to the cavernous segment of the artery (Fig 2). An asymptomatic 3 cm cavernous carotid artery aneurysm was also disclosed by the angiography. The patient was started on heparin in the Intensive Care Unit and maintained on oral anticoagulant (warfarin) after discharge from the hospital. Serological tests (HIV, syphilis, hepatitis B and C), rheumatological tests, vitamin B12, folic acid and homocy steine measurements were all normal. Outpatient follow-up 30 days after symptom onset disclosed an important improvement in tongue movement and there were no

Fig 1. Note the left-sided position of the tongue due to involvement of left hypoglossal nerve (arrow).

PARALISIA DO NERVÔ HIPÓGLOSSO COMO MANIFESTAÇÃO ISOLADA DE DISSECÇÃO DA ARTÉRIA CARÓTIDA INTERNA

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Neuroleptic-Induced Tardive Cervical Dystonia: Clinical Series of 20 Patients

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ABSTRACT: Background: Cervical dystonia (CD) may be classified according to the underlying cause into primary or secondary CD. Previous exposure to neuroleptics is one of the main causes of adult-onset secondary dystonia. There are few reports that characterize the clinical features of primary CD and secondary neuroleptic-induced CD. Here we investigated a series of patients with neuroleptic-induced tardive CD and compared clinical, demographic and therapeutic characteristics to another 77 patients with primary CD. All patients underwent Botulinum toxin type-A therapy. Results: We did not identify any relevant clinical and demographic characteristics in our group of patients that could be used to distinguish tardive and primary CD. Conclusion: Patients with tardive CD presented demographic characteristics and disease course similar to those with primary CD.

RÉSUMÉ: Dystonie cervicale tardive induite par les neuroleptiques : série clinique de 20 patients. Contexte : La dystonie cervicale (DC) peut être classifiée en DC primaire ou secondaire, selon la cause sous-jacente. Une exposition à des neuroleptiques est l'une des causes principales de dystonie secondaire survenant à l'âge adulte. Il existe peu de comptes rendus caractérisant les manifestations cliniques de la DC primaire et de la DC secondaire induite par les neuroleptiques. Notre but était d'évaluer une série de patients présentant une DC tardive induite par les neuroleptiques et de décrire leurs caractéristiques cliniques et démographiques. Patients et méthodes : Nous avons évalué rétrospectivement 20 patients présentant une DC tardive induite par les neuroleptiques et comparé leurs caractéristiques cliniques, démographiques et thérapeutiques à celles de 77 patients atteints d'une DC primaire. Tous les patients ont été traités au moyen de la toxine botulique de type A. Résultats : Nous n'avons pas identifié de caractéristiques cliniques et démographiques pertinentes chez notre groupe de patients qui pourraient être utilisées pour distinguer une DC tardive d'une DC primaire. Conclusion : Les patients atteints de DC tardive présentent des caractéristiques démographiques et une évolution de la maladie qui étaient semblables à celles des patients atteints de DC primaire.


Cervical dystonia (CD) is the most common presentation of primary adult-onset focal dystonia. Tardive dystonia, on the other hand, is a secondary movement disorder caused by exposure to dopamine-blocking medications, such as neuroleptics. Cranio-cervical type is the most common presentation form of tardive dystonia and may be clinically identical to primary CD. However, it has been postulated that the presence of extracervical involvement, retrocollis, and spasmodic head movements are more likely to occur in tardive CD.

In this paper we retrospectively evaluated a series of patients with neuroleptic-induced tardive CD and described their clinical and demographic features, comparing to a control group of patients with primary CD. Our aim was to investigate possible clinical patterns that could help to distinguish tardive and primary CD, besides documenting exposure to dopamine-blocking medications.

Patients and Methods

We retrospectively analyzed 184 medical charts of patients with CD who underwent Botulinum toxin type-A (BTX-A)
Bilateral Horizontal Gaze Palsy with Unilateral Peripheral Facial Paralysis Caused by Pontine Tegmentum Infarction

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Clinical features of pontine infarction depend on the topography of vascular lesion and most remarkably sometimes the same topographic region can lead to different clinical syndromes (e.g., dorsal pontine tegmentum). In this report we describe an elderly patient with acute dorsal pontine infarction leading to a unique syndrome of bilateral horizontal gaze palsy and unilateral peripheral facial paralysis. We propose that this syndrome could be included as a part of a continuum that involves one-and-a-half syndrome, eight-and-a-half syndrome, and other variants of pontine tegmentum infarction. Key Words: One-and-a-half syndrome—eight-and-a-half syndrome—bilateral horizontal gaze palsy—peripheral facial paralysis—pontine infarction. © 2009 by National Stroke Association

Tegmental pontine infarctions are unusual and may lead to a range of neuro-ophthalmologic findings such as gaze palsies, diplopia, internuclear ophthalmoplegia, nystagmus, and abducens palsy.1 Herein, we present a unique case of acute pontine infarction leading to a combination of bilateral horizontal gaze palsy and unilateral peripheral facial palsy. In addition, we also discuss the relationship between this case and the one-and-a-half and eight-and-a-half syndromes.

A 73-year-old white man was admitted with a 15-minute history of sudden-onset slurred speech and right facial weakness. He was on glaucocort (800 mg twice a day) and aspirin (200 mg/day) for diabetes and did not smoke cigarettes or drink alcohol. Family history was unremarkable. At the emergency department his heart rate was 100 beats/min, blood pressure was 178 × 96 mm Hg, and glucose was 250 mg/dL. The patient was alert, fully oriented, and collaborative. Pupils were symmetric (2 mm) and reactive to light. No ocular bobbing was found. There was a bilateral horizontal gaze palsy with preserved vertical saccades (Fig 1) associated to right peripheral facial paralysis. The oculocephalic reflexes were absent bilaterally. Despite his attentiveness and orientation, speech was compromised with a moderate dysarthria without aphasia. He scored 7 on the National Institutes of Health Stroke Scale. Brain computed tomography was performed and no abnormalities were found. The patient was excluded from venous thrombolytic recombinant tissue plasminogen activator because of recent leg bypass vascular surgery. Brain magnetic resonance imaging showed no alteration at 1.5 T with T1- T2, fluid-attenuated inversion recovery, and echocardiographic gradient-weighted images. Diffusion-weighted image showed a small but irregular restricted diffusion area on the midline pontine tegmentum with a corresponding hypointense lesion on the apparent diffusion coefficient map (Fig 2, A and B). Magnetic resonance angiography showed vascular irregularities on large vessels and a significant stenosis on the middle part of the left posterior cerebral artery (Fig 2, C). The patient was

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10.4 ARTIGOS CIENTÍFICOS PUBLICADOS COMO PRIMEIRO AUTOR OU CO-AUTOR DURANTE A TESE

ANO BASE – 2010
Semantic aphasia as a sole manifestation of acute stroke

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The concept of aphasia designates impairment in the symbolic domains of language (vocabulary, semantics, phonology, syntax and morphology) by one or more lesions in the dominant cerebral hemisphere, which may be manifest through spoken and written comprehension and production, but can not be explained by motor or sensory deficits in view of the preservation of phono-articulatory structures, and neither by generalized cognitive deficits (consciousness must be preserved)². Stroke is the leading cause of aphasia, which may be identified in more than 20% of stroke patients, reaching up to 40% in the acute phase²⁻⁵. These language disturbances may help forecast the vascular territories involved in brain injury⁶⁻⁷.

Errors in naming are more frequent when associated to grave mistakes in fluency and comprehension both for oral and written material⁸⁻¹⁰, such as in global aphasia, motor aphasia or sensory aphasia. The diagnosis of semantic aphasia may pass unnoticed if a specific assessment is not undertaken, particularly considering that semantic errors may be produced in naming, reading, spelling, copying or drawing from memory⁶. Prognosis is better than for other vascular aphasic syndromes, but may be related to the size of brain injury⁹⁻¹⁰ (including both the infarcted tissues and the hyperperfused areas) and to the presence of cortical involvement⁷, among other factors.

We report the case of a patient who presented with language impairment as the only symptom in the acute stroke phase, leading to a diagnosis of vascular semantic aphasia. The importance of accurate language evaluation for stroke diagnosis will be discussed.

CASE
A caucasian 81-year-old female patient was admitted to the Emergency Department of Hospital e Maternidade São Camilo (Pompeia) reporting a frequent reading practice, which included books and newspapers. She had a complete high school education. The day before her admittance, she woke up in the morning noticing that the letters of any texts she tried to read were "scrambled", making her reading very difficult. Since there were no other neurological deficits and her vision was allegedly unimpaired (no visual symptoms were acknowledged), she decided to wait for the next day to seek assistance. The patient reported a diagnosis of untreated systemic hypertension, and a 5-cigarette per day smoking habit.

At the Emergency Room, her blood pressure was 140/90 mmHg, along with a heart rate of 96 bpm, normal auscultation of the heart and lungs, and no cervical bruits. On neurological examination she was alert and oriented, with preserved fluency and repetition, and no paraparesis: she had some difficulty naming common objects (she could name a pen, not a clock, but was able to tell the purpose of each object) and recalling her accompanying son’s name, and could not tell the names of her daughters or of other 5 grandchildren, though she knew who they were; long-term memory was unimpaired; a hard difficulty for reading simple texts was presented, and
Progressive supranuclear palsy
New concepts

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Camila Catherine Henrique de Aquino, José Luiz Pedroso

ABSTRACT
Progressive supranuclear palsy (PSP) is a distinctive form of neurodegenerative
disease which affects the brainstem and basal ganglia. Patients present supranuclear
ophthalmoplegia, postural instability and mild dementia. PSP is defined neuropathologically
by the accumulation of neurofibrillary tangles in the subthalamic nucleus, pallidum, red
nucleus, substantia nigra, striatum, pontine tegmentum, oculomotor nucleus, medulla and
dentate nucleus. Over the last decade many lines of investigations have helped refine PSP
in many aspects and it is the purpose of this review to help neurologists identify PSP, to
better understand its pathophysiology and to provide a more focused, symptom-based
treatment approach.

Key words: progressive supranuclear palsy, atypical parkinsonism, tauopathy.

Paralisia supranuclear progressiva: conceitos atuais

RESUMO
A paralisia supranuclear progressiva (PSP) é uma doença neurodegenerativa, que afeta
principalmente o tronco cerebral e os núcleos da base. O quadro clínico se caracteriza
por oftalmoparesia supranuclear, instabilidade postural e demência. Do ponto de vista
anatômico-patológico, a PSP se caracteriza por acúmulo de emaranhados neurofibrilares no
núcleo subthalâmico, globo pálido, núcleo rubro, substância negra, estriado, tegmento da
ponte, núcleos oculomotores, bulbo e núcleo dentado. Nas últimas décadas, muitas linhas
de pesquisa têm colaborado para redefinir a PSP em muitos aspectos. Os objetivos dessa
revista são auxiliar o neurologista geral na identificação da doença, compreensão da sua
fisiopatologia, além de apresentar alternativas para seu tratamento sintomático.

Palavras-chave: paralisia supranuclear progressiva, parkinsonismo atípico, tauopatias.

Progressive supranuclear palsy (PSP), also called Steele-Richardson-Olszewski
syndrome, is a distinctive and probably under diagnosed neurodegenerative syn-
drome. It is the most common cause of degenerative parkinsonism after Parkinson's
disease (PD) in most series.1 The “classic” PSP syndrome is characterized by gait dis-
corder, ophthalmoparesis (down gaze palsy), cognitive dysfunction and parkinsonism,
but a number of PSP phenotypic variants have been described recently.2 The prev-
ance of PSP is age-dependent and estimated at 0% to 10% that of PD, or 6-7 cases
per 100,000. The disease has a peak onset at age 63 and no reported cases before
the age of 40. The correct diagnosis is usually made 3-6 to 4-9 years after the onset of
clinical signs.3

In the last few years, we have learned much about clinical, neuroimaging, mo-
lecular pathology and genetic of PSP. This syndrome is a tauopathy, with deposits of
neurofibrillary tangles in the brain, which are mainly composed of hyperphosphory-
lated microtubule-associated protein tau. Tauopathies refers generally to neurode-
generative disorders with prominent tau pathology in the neuronal or glial cells. Tau
is a microtubule-associated protein expressed in neurons, which in tauopathies
forms abnormal, fibrillar structures of age-
Heterozygous exon 3 deletion in the Parkin gene in a patient with clinical and radiological MSA-C phenotype

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1. Introduction

Parkin (PARK2) mutations on chromosome 6q25.2-27 are the most frequent cause of monogenic autosomal recessive forms of early-onset parkinsonism (EOPD), with good response to dopamine replacement therapy, dyskinesia at onset of symptoms, slow disease progression, and early complications from levodopa use [1]. However, the clinical presentation may be variable, including uncommon features like cervical dystonia, autonomic dysfunction, peripheral neuropathy, pyramidal tract dysfunction, psychiatric symptoms and cerebellar ataxia [2].

Multiple system atrophy (MSA), on the other hand, is a sporadic neurodegenerative disorder that usually presents in the sixth decade with autonomic failure, parkinsonism, cerebellar ataxia and pyramidal signs in any combination. In Caucasian populations the parkinsonism features predominate in 80% of patients (MSA-P subtype) and cerebellar features are the major motor disturbance in 20% of patients (MSA-C subtype)[3,4]. The definite diagnosis requires neuropathological demonstration of central nervous system alpha-synuclein-positive glial cytoplasmic inclusions with neurodegenerative changes in striatonigral or olivoponto cerebellar structures [3-5]. Herein, we describe an uncommon presentation of a Parkin heterozygous mutation carrier patient with a clinical phenotype resembling MSA-C.

2. Case

A 44-year-old woman developed bilateral bradykinesia and rigidity when she was 34 years. At age 37 she began walking with increasing difficulty, start hesitation, and cerebellar ataxia. She also presented autonomic dysfunction characterized by postural hypotension and urinary incontinence. Over the following years she developed increasing dysarthria, dysphagia, depressive symptoms and severe imbalance, with progressive locomotor ataxia. She did not have a family history of Parkinson's disease (PD) or other neuropsychiatric disorders. On neurological exam, at age 44, her cognition was normal on neuropsychological tests, including test of Mini Mental State Examination (MMSE), the were slow saccades with normal extraocular movements except for left gaze-evoked nystagmus and nasal speech. He had mild bilateral and symmetric rigidity and bradykinesia, an asymmetric bilateral upper extremity postural and kinetic tremor, severe bilateral upper extremity ataxia and dysdiadochokinesia and her gait was wide based and ataxic. Deep tendon reflexes are brisk and sensory examination was normal. Levodopa therapy up to 1 g/day produced only a mild
Tic Disorder: An Unusual Presentation of Neurotoxoplasmosis in a Patient with AIDS

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Key Words
AIDS - Movement disorders - Neurotoxoplasmosis - Tic disorder

Abstract
Movement disorders have been increasingly recognized in patients with HIV infection and may be due to distinct causes, as opportunistic infections or medication side effects for example. Parkinsonism, tremor and hemichorea have been more frequently noted in association with HIV and opportunistic infections. However, a variety of involuntary movements have already been described. We report a case of neurotoxoplasmosis in a patient with HIV infection who presented with a dystonic tic involving ocular, oral and cervical movements.

Introduction
In patients with human immunodeficiency virus (HIV) infection, neurological involvement is a common occurrence, possibly due to chronic immunosuppression and consequent opportunistic infections, direct neurotropic effects of HIV or even medication side effects [1].

Movement disorders have been increasingly recognized and may appear as first symptoms of HIV or opportunistic infections. Clinically relevant movement disorders were identified in 3% of the patients with acquired immunodeficiency syndrome (AIDS)
Olfactory Heterogeneity in LRRK2 Related Parkinsonism

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Abstract: LRRK2 mutations can cause familial and sporadic Parkinson's disease (PD) with Lewy-body pathology at post-mortem. Studies of olfaction in LRRK2 are sparse and incongruently. We applied a previously validated translation of the 16 item smell identification test from Sniffin' Sticks (SS-16) to 14 parkinsonian carriers of heterozygous G2019S LRRK2 mutation and compared with 106 PD patients and 118 healthy controls. The mean SS-16 score in LRRK2 was higher than in PD (p < 0.001, 95% CI for β = -0.47 to -1.7) and lower than in controls (p = 0.001, 95% CI for β = +0.6 to -3.6). In the LRRK2 group, subjects with low scores had significantly more dyskinesia. They also had younger age of onset, longer disease duration, and reported less frequently a family history of PD, but none of these other differences reached significance. Olfactory identification is diminished in LRRK2 parkinsonism but not to the same extent as in idiopathic PD. © 2010 Movement Disorder Society

Key words: olfaction; smell; LRRK2, PARK8, parkinsonism

A number of mutations in 12 different loci can cause familial parkinsonism. Of these, mutations in the α-synuclein and LRRK2 gene have been associated at post-mortem with Lewy bodies (LB) in the substantia nigra, which has been traditionally considered the hallmark of idiopathic Parkinson's disease (PD). Hypoosmia is as common as rest tremor in PD (about 85% of patients), and it is likely to be caused by the pathological alterations found in the olfactory bulb and primary olfactory cortex, which are believed to be invariable sites of pathology of LB disease. Concordantly, LB have also been found in the olfactory bulb in four LRRK2 cases examined post-mortem.

Previous reports of smell tests in LRRK2 mutation carriers are sparse, have varied methodology and showed mixed results (see Table 1, which contains references 7-12); only one performed statistical comparison with sporadic PD and controls adjusted for age and gender. We have analyzed the sense of smell in a series of LRRK2 carriers with levodopa (L-dopa)-responsive parkinsonism and compared to sporadic PD and control subjects.

PATIENTS AND METHODS

Genetic Testing

The LRRK2 mutation carriers were identified in previous screening studies as described by Munhoz et al.,13 Aguiar et al.,14 and Di Fonzo et al.,15

Smell Testing

A previously validated Brazilian-Portuguese translation of the 16 item smell identification test from Sniffin' Sticks (SS-16)16 was used.

Subjects

Sniffing was performed in 14 parkinsonian carriers of heterozygous G2019S LRRK2 mutation. Eleven (78.6%) were female and two (14.3%) were smokers. Clinical data of some of these patients is published elsewhere.13,14 Ten patients had at least one relative with PD, and seven had at least one affected first degree relative. All patients had bradykinesia, 12 had rest tremor, 12 had rigidity, but only 6 had gait impairment or postural instability. Twelve reported significant improvement with

Additional Supporting Information may be found in the online version of this article.

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Speech-induced lingual dystonia

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Dystonia can be classified according to its etiology as primary, dystonia-plus, secondary, heredodegenerative, and psychogenic. Pure lingual dystonia is rare but not uncommon in association with other cranial dystonias. However, in clinical practice, even after excluding the main secondary causes of dystonia, the differential diagnosis between primary versus psychogenic forms may be tricky. There are few cases in the literature describing speech-induced lingual dystonia and they were mostly classified as idiopathic. We report a case of a woman who presented with a speech-induced lingual dystonia and discuss the differential diagnosis and potential therapeutic options of this condition.

CASE

A 49-year-old woman was referred to our service with a six-year history of tongue protrusion when speaking. There was no relevant past or family history of neurological disorders. She did not take neuroleptics or other medications before the onset of symptoms and had no history of facial injury or infection. For six years she visited several physicians and no diagnosis was made. On her first appointment to our service she was taking clonazepam 2 mg/day without improvement. Her neurological examination showed speech-induced tongue protrusion associated with mild dysarthria. The movement disorder showed no improvement with chewing gum (sensory trick). The patient could eat, drink, whistle, sing, and whisper without any trouble. A trial with levodopa (750 mg/day) and then trihexyphenidyl (10 mg/day) did not ameliorate symptoms. A number of exams were ordered to rule out secondary dystonia. Drug-induced, dopa-responsive, post-traumatic and post-infectious dystonias had already been ruled out, and the absence of a family history suggested no heredodegenerative disorder. At this time the diagnosis considered were neuroanconehtosis, Wilson's disease, and pantetheine kinase-associated neurodegeneration. Routine hematological and biochemical evaluation were completely normal including copper levels and number of acanthocytes. Brain magnetic resonance imaging (MRI), electroencephalography (EEG), and electromyography (EMG) were within normal parameters.

A speech-therapist evaluated the tongue movement during several tasks: repeated words and sentences, reading a short text, automatic speech, singing, vowel and fricative phoneme prolongation, sequences of syllables, and spontaneous conversation. The tongue movement disorder was identified in all circumstances of speech and in all phonemes, except vowel and sound prolongations. Tongue protrusion occurred more often in alveolar and alveolar phonemes and less frequently in palatal and velar phonemes. Slower speech and low voice intensity improved tongue protrusion.

After the initial work-up ruling out many etiologies, we investigated non-organic causes and referred her to a psychiatric examination. In this evaluation the patient told that her symptoms started during a period she went through a serious moral dilemma while working in an illegal informal job she considered humiliating. She also told that these symptoms could...
Conjugal amyotrophic lateral sclerosis

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TO THE EDITOR

Sir,

With interest I read the paper of Godeiro C. et al. entitled "Conjugal Amyotrophic Lateral Sclerosis".

There are several reports, as mentioned by the authors, in the literature, describing the almost simultaneously appearance of sporadic amyotrophy lateral sclerosis (SALS) in a couple, no genetically related, living together for a long time.

Of course, this circumstance strongly suggests the existence of an environmental factor triggering the disease in people, perhaps genetically susceptible. The search for such factors has been, and it is, one of the main topics of research in SALS.

However, the particular description of Godeiro et al., as far as I can understand, does not follow the right clinical diagnostic concept of SALS, which requires the presence of lower and upper motor neurons clinical involvement. This happens neither with the husband of couple I, nor with the husband of family II. Both men seem to be affected by a denervatory condition involving, apparently, just the lower motor neurons.

According to "El Escorial" criteria (1991) the isolated compromise of the spinal motor neuron reaches the 4ª level of diagnostic certainty, called "suspected". The revised "El Escorial" criteria version, done later at Airlie House (1998), has positioned this criterion at the 5ª level, recommending to avoid this type of patients for SALS research and for therapeutic clinical trials.

I agree with this last notion, thinking that SALS is a unique and individualized entity, which needs, to be recognized, the simultaneous clinical involvement of the cortical and spinal motor neurons. Of course, I also agree with the concept that it is a disease inhabiting the spectrum of disorders known, as a group, as "motor neuron diseases" which encompasses other clinical entities such as progressive spinal atrophy, progressive bulbar atrophy and primary lateral sclerosis.

I think that, by the time being, the illnesses embraced under the name of "motor neuron diseases" should be considered as individual disorders. This theoretical position, actually, would allow researches to focus in one of them, when looking for its pathogenesis and etiology.

It is my opinion that mixing the diseases could introduce bias in such type of research, delaying the finding of the cause, whose achievement might lead to a rational treatment of those conditions, a goal which, right now, seems to be very far away.

Nevertheless, I do not deny the possibility that the authors are true and what they are showing are different steps of the same process, as most probably happens with the spectrum of disorders characterized by the presence of Lewy's bodies neuronal inclusions where the compromise of autonomic ganglia, basal nuclei and cerebral cortex seems to be different stages of the same process. Despite that this could be true as well regarding motor neuron diseases, I feel that before we can admit this notion as a hard scientific proposal, we should have a marker of these illnesses able to tell us whether they are different clinical phenotypes of the same condition, a tool that is lacking yet. In the meantime, I believe that it is advisable to concentrate in what we really have right now, which only is the clinical manifestations of these disorders, avoiding any other conception which might introduce just speculative thoughts about the nature of these diseases.

REFERENCES


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THE AUTHOR'S REPLY

We are grateful to Dr. Sica for his interest in our article and for the comments and questions he raised.

We agree that not all of our patients fulfilled the El Escorial clinical criteria for amyotrophic lateral sclerosis (ALS), therefore we would not be able to report their disease specifically as ALS, but only as a motor neuron disorder. In our paper, we considered as ALS those patients who had not only clinical, but also laboratory supported diagnosis of ALS.

This type of inclusion criteria may permit a misinterpretation of our data. Maybe, it would be more appropri-