Arq Neuropsiquiatr 2008;66(4):800-804

CLINICAL FEATURES OF DYSTONIA IN ATYPICAL PARKINSONISM

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Abstract – Background: The association between Dystonia and Parkinson's disease (PD) has been well described especially for foot and hand dystonia. There is however few data on dystonic postures in patients with atypical parkinsonism. **Objective:** To evaluate the frequency and pattern of dystonia in a group of patients with atypical parkinsonism (multiple system atrophy – MSA, progressive supranuclear palsy – PSP, and corticobasal degeneration – CBD) and to investigate whether dystonia could be the first presenting symptom at disease onset in those patients. **Method:** A total of 38 medical charts were reviewed (n=23/MSA group; n=7/CBD group; n=8/PSP group) and data values were described as means/standard deviations. The variables evaluated were sex, age at onset, disease duration, first symptom, clinical features of dystonia and other neurological signs, response to levodopatherapy, Hoehn&Yahr scale >3 after three years of disease, and magnetic resonance imaging findings. **Results:** The overall frequency of dystonia in our sample was 50% with 30.4% (n=7) in the MSA group, 62.5% (n=5) in the PSP group, and 100% (n=8) in the CBD group. In none of these patients, dystonia was the first complaint. Several types of dystonia were found: camptocormia, retrocollis, anterocollis, blepharoespasm, oromandibular, and foot/hand dystonia. **Conclusion:** In our series, dystonia was a common feature in atypical parkinsonism (overall frequency of 50%) and it was part of the natural history although not the first symptom at disease onset. Neuroimaging abnormalities are not necessarily related to focal dystonia, and levodopa therapy did not influence the pattern of dystonia in our group of patients.

KEY WORDS: dystonia, atypical parkinsonism, multiple system atrophy, progressive supranuclear palsy, corticobasal degeneration, Parkinson's disease.

Características clínicas da distonia no parkinsonismo atípico

Resumo – Introdução: A associação de distonia e doença de Parkinson (DP) já foi bem estabelecida, principalmente para distonia focal em pé ou mão. Entretanto, há poucos dados quanto a distonia em pacientes com parkinsonismo atípico. **Objetivo:** Avaliar a freqüência e o padrão da distonia em um grupo de pacientes com parkisnonismo atípico (atrofia de múltiplos sistemas – AMS; paralisia supranuclear progressiva – PSP; degeneração corticobasal – DCB) e investigar se a distonia pode ser a manifestação inicial neste grupo. **Método:** Um total de 38 prontuários médicos foi revisado (n=23/grupo AMS; n=8/grupo PSP; n=7/grupo PSP) e os dados foram apresentados em médias/desvios padrões. As variaveis avaliadas foram: sexo, idade de início, duração da doença, primeiro sintoma, características clínicas da distonia e outros sinais neurológicos, resposta ao tratamento com levodopa, escala de Hoehn & Yahr >3 em 3 anos de doença, e achados de ressonância magnética. **Resultados:** A frequência total de distonia em nosso grupo foi 50%, sendo 30,4% (n=7) no grupo AMS, 62.5% (n=5) no grupo PSP e 100% (n=8) no grupo DCB. Em nenhum dos pacientes, distonia foi o primeiro sintoma. Várias apresentações de distonia foram observadas: camptocormia, anterocólis, retrocólis, distonia oromandibular, em pé e mão. **Conclusão:** Em nossa série, distonia foi uma característica comum em pacientes com parkinsonismo atípico (freqüência de 50%) e fez parte da história natural em todos os grupos, embora não tenha sido o sintoma inicial em nenhum deles. Anormalidades no exame de neuroimagem não necessariamente estão relacionadas a distonia focal, e o tratamento com levodopa não influenciou o padrão da distonia em nosso grupo de pacientes.

PALAVRAS-CHAVE: distonia, parkinsonismo atípico, atrofia de múltiplos sistemas, paralisia supranuclear progressiva, degeneração corticobasal, doença de Parkinson.

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Received 29 July 2008. Accepted 26 September 2008.

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Most patients who are referred to specialized movement disorders clinics with akinetic-rigid forms of parkinsonism are generally diagnosed as having Parkinson's disease (PD). The second most common group of parkinsonian patients is clinically categorized as having parkinsonism-plus disorders or atypical parkinsonism, such as multiple system atrophy (MSA) and progressive supranuclear palsy (PSP)[1]. Parkinsonism is considered atypical when the condition evolves rapidly, responds poorly or transiently to levodopa therapy or has other clinical and neuroimaging-associated features[2]. A previous series of parkinsonian patients in Brazil found a lower frequency of MSA (1.8%) and PSP (2%) that could reflect a short follow-up period, since it is known that many patients initially diagnosed with PD later are found to have parkinsonism-plus disorders[3].

Postmortem studies reveal that a substantial proportion of patients thought to have PD in life were, in fact, afflicted with other sporadic degenerative conditions such as MSA and PSP[4]. Dystonia, most often in the form of foot and hand posturing, occurs in untreated patients with clinical diagnosis of PD[5]. However, there is few data on the occurrence of the typical intermittent dystonic spasms that characterize idiopathic dystonia in MSA and PSP. Anterocollis certainly occurs in MSA, but may not be a true dystonia and more likely represents a special imbalance of rigidity in neck muscles producing a sustained posturing. Frequently, the MSA patients exhibit orofacial dystonia associated with a characteristic high-pitched dysarthria In patients with PSP, late dystonic posturing of the limbs could represent contractures, and eye-lid elevator inhibition may have been confused with blepharoespasm[5]. On the other hand, asymmetrical limb dystonia is a typical feature of patients with Corticobasal degeneration (CBD). Although uncommon at presentation, 60–70% of patients with CBD develop limb dystonia during the clinical course[6]. Other study found a high prevalence of joint and skeletal deformities in PD, MSA, and PSPincluding "striatal" hand, foot deformities, involuntary trunk flexion, anterocollis and scoliosis[7].

Our aim was to retrospectively investigate the frequency and clinical features of dystonia in a group of patients with atypical parkinsonism (MSA, PSP and CBD), and also highlights the clinical presentation of each group at first neurological visit.

METHOD

We reviewed the medical charts of twenty-three patients with probable MSA, eight patients with probable PSP and seven patients with probable CBD, according to the criteria of Gilman et al.[8], Litvan et al.[9], and Gibb et al.[10], respectively.

We searched for the presence of dystonia and its clinical pattern in all patients. We also described demographic and clinical features of all groups: sex, age at onset, disease duration before first neurological visit, first symptom, clinical signs at the neurological exam, response to levodopatherapy, Hoehn&Yahr scale >3 after three years of disease, and brain magnetic resonance imaging (MRI) abnormalities.

Data were described as mean±standard deviation, and whenever possible percentages.

This protocol was submitted to and approved by the local ethical committee.

RESULTS

On Table 1, we present the clinical features of the patients evaluated in the three groups: MSA, PSP, and CBD. On Tables 2, 3 and 4 we detailed the specific findings on dystonia in those groups aforementioned.

The frequency of dystonia in our group of patients with atypical parkinsonism was: 30.4% (7 patients) in the MSA group, 62.5% (5 patients) in the PSP group, and 100% (8 patients) in the CBD group. Overall, the frequency of dystonia in our series was 50%. In none of these patients, dystonia was their first complaint. We did not find among the patients with dystonia and brain MRI abnormalities a topographic correlation between brain lesions and dystonia.

DISCUSSION

In this retrospective study of patients with atypical parkinsonism the overall frequency of dystonia found was high (50%) if we compare to the frequency of patients with PD. Another interesting finding was that dystonia was not the first symptom at onset disease in any patient with atypical parkinsonism.

A common form of dystonia in patients with MSA is a severe, isolated anterocollis[5,11]. In our group of patients with MSA, only three subjects presented cervical dystonia (2 anterocollis and 1 retrocollis). Cervical dystonia, contralateral arm, hand and foot dystonias, occurring alone or in various combinations, may be the manifestation of a structural lesion involving the head of the caudate nucleus[12]. In only one of our patients (patient 7 in MSA group) we were able to find an MRI abnormality that could justify dystonia. In fact, MRI is a useful diagnostic tool in the early course of MSA and it can be used to differentiate parkinsonian disorders[13,14], but there is no clinical radiological correlation to dystonia phenomenom.

Since PSP was first characterized in 1964[15], dystonic manifestations have been reported only sporadically. Retrocollis or "axial dystonia in extension" is the only such manifestation, which has been disclosed; however, the pathogenesis of this tonic, rigid extended posture is probably distinct from other forms of dystonia and is more correlated with interstitial nucleus of Cajal lesions than lesions of the basal ganglia[16]. The neck positioning

Table 1. Clinical profile of patients with atypical parkinsonism and dystonia.

	Multiple system atrophy (MSA) N=23	Progressive supranuclear palsy (PSP) N=8	Corticobasal degeneration (CBD) N=7
Male/Female	13/10	3/5	3/4
Onset age (year–old)	57.1±9.3	64.7±10.3	62.7±6.8
Disease duration before diagnosis (months)	30.4±12.6	36.3±26.2	52.3±26.1
Dystonia	7 (30.4%)	5/8 (62.5%)	7 (100%)
First symptom			
Gait disorder	11	2	1
Falls	4	5	0
Rigidity	1	0	4
Bradikynesia	6	0	2
Tremor	1	1	0
Dystonia	0	0	0
Asymmetric parkinsonism	2 (8.6%)	3 (37.5%)	7 (100%)
H&Y ≥3 in 3 years	20 (86.9%)	8 (100%)	6 (85.7%)
Response to levodopa	4 (17.3%)	0	1 (14.3%)
Bradikinesia	23 (100%)	8 (100%)	6
Rigidity	22 (95.6%)	8 (100%)	7 (100%)
Tremor	4 (17.3%)	2 (25%)	1 (14.3%)
Postural unsteadiness	22 (95.6%)	7 (87.5%)	2 (28.5%)
Ocular movement abnormalities	8 (34.7%)	8 (100%)	3 (42.8%)
Postural hypotension	20 (86.9%)	1 (12.5%)	1 (14.3%)
Sphincters disorders	15 (65.2%)	1 (12.5%)	0
Erectile dysfunction	11 (47.8%)	0	0
Cold blue hands	6 (26%)	0	1 (14.3%)
Pyramidal signs	12 (52.1%)	3 (37.5%)	4 (57.1%)
Cerebellar signs	5 (21.7%)	0	0
DSM-IV dementia	3 (13%)	0	1 (14.3%)
Dysphagia	14 (60.8%)	7 (85.5%)	3 (42.8%)
Dysartria	16 (69.5%)	8 (100%)	3 (42.8%)
Alien hand	0	0	4 (57.1%)

Table 2. Patients with MSA and dystonia.

	Sex	Onset age (years)	Disease duration (months)	First symptom	Pattern of dystonia	Levodopa response	Brain MRI
1	F	54	36	Falls	Anterocollis	No	Pons and cerebellum atrophy
2	F	64	12	Gait disorder	Camptocormia	No	Normal
3	F	62	36	Rigidity	Left foot	No	Normal
4	M	50	24	Bradikinesia	Left foot	No	Normal
5	F	76	36	Falls	Anterocollis	No	Normal
6	M	64	36	Gait disorder	Retrocollis	Yes	Mesencephalum atrophy
7	M	43	24	Gait disorder	Left arm	No	Putamen atrophy and putaminal rim

Table 3. Patients with PSP and dystonia.

	Sex	Onset age (years)	Disease duration (months)	First symptom	Pattern of dystonia	Levodopa response	Brain MRI
1	F	74	72	Falls	Oromandibular	No	Mild Microangipathy
2	F	64	30	Falls	Right arm	No	"Hummingbird" sign
3	M	69	48	Falls	Retrocollis	No	Generalized cerebral atrophy
4	F	60	36	Falls	Left arm	No	"Hummingbird" sign
5	F	42	9	Gait disorder	Retrocollis	No	"Hummingbird" and "Morning Glory" signs

Table 4. Patients with CBD and dystonia.

	Sex	Onset age (years)	Disease duration (months)	First symptom	Pattern of dystonia	Myoclonic jerks	Levodopa response	Brain MRI
1	F	65	60	Gait disorder	Left arm	Yes	No	Right frontal lobe atrophy
2	M	50	84	Rigidity	Right arm	Yes	No	Normal
3	F	60	24	Rigidity	Left arm	No	No	Right parietal and tempotal lobes atrophy
4	F	62	72	Bradikinesia	Right arm	Yes	No	Normal
5	F	71	72	Bradikinesia	Right arm and retrocollis	Yes	No	Left frontal lobe atrophy
6	M	62	36	Rigidity	Left arm and blepharoespasm	No	No	Global cortical atrophy (right > left)
7	M	69	18	Rigidity	Left arm	Yes	No	Normal

in PSP tends to be fixed and does not alter with posture or activity as idiopathic dystonia does. Patients fail to show sensory tricks for improving the posturing, diurnal variation is absent ("morning benefit"), and painful neck spasms and hypertrophic muscles are not seen[17]. Two of our patients (patients 3 and 5) presented retrocollis and MRI abnormalities in brainstem. The MRI findings in patients with atypical parkinsonism reflect the involvement of many structures. The midbrain atrophy is particularly well demonstrated on midline sagittal images ("Hummingbird sign"), showing reduced midbrain diameter, enlarged cerebral aqueduct and thinned quadrigeminal plate. Signal abnormalities are mild and consist of hyperintensity in the periaqueductal region on T_2-weighted sequences ("Morning Glory sign")[18,19]. The most widely reported dystonic manifestation on PSP is blepharospasm[20], but none of our patients presented such manifestation. Two of our patients (patients 2 and 4) presented limb dystonia. It is possible that limb dystonia in PSP is an indicator of concomitant cortical and basal ganglia neuropathological changes. It is becoming increasingly recognized that such cortical pathology does occur in PSP[17]. Interestingly, oromandibular dystonia was observed in one of our patients and it was not related to levodopa therapy. The potential role of medication, especially levodopa, must be considered when dealing with dystonia in patients with PSP[17]. A Brazilian series of PSP patients observed that 13% had transiently good response to levodopa, but it did not point out whether these patients also presented dystonia[21]. None of our patients with PSP responded to levodopa, including those who presented dystonia.

Classically, typical features of CBD can be categorized into movement disorders (akinesia, rigidity, postural instability, limb dystonia, cortical myoclonus and postural/intention tremor) and cortical signs such as cortical sensory loss, apraxia and Alien hand phenomenon[22]. A rigid, dystonic posture arm with some fingers extended and others forcibly flexed into the palm causing skin maceration characteristically develops early in the course of the illness in a substantial minority of patients[5,22]. Jerking of the affected limb due to action-induced and stimulus sensitive focal reflex myoclonus commonly precedes or accompanies the development of such dystonic postures and, if rhythmic, may mimic tremor[23]. In our series, all patients with CBD presented limb dystonia, and five of them also had associated myoclonus. The brain MRI was abnormal in four patients, all presenting asymmetrical brain atrophy (Table 4). In these patients the side with

more prominent atrophy was opposite to the side of limb dystonia. MRI findings of atrophy in the perirolandic gyri, atrophy of the basal ganglia, and T_2 prolongation in the posterolateral putamen are useful evidence supporting the clinical diagnosis of corticobasal degeneration[24]. As expected, dystonia was not the chief complaint in any patient and did not respond to levodopa therapy.

Clinico-pathologic studies are needed to disclose the relationship between these dystonic manifestations and the pathological substrates of these atypical parkinsonisms. We did not have a longer follow-up that could allow the observation of dystonia progression, and of those patients who initially did not have dystonic features but later developed these signs correlating to levodopa therapy.

In conclusion, in our series dystonia was a common feature in atypical parkinsonism (overall frequency 50%) and it was part of the natural history although not the first symptom at disease onset. Moreover, neuroimaging abnormalities are not necessarily related to focal dystonia, and levodopa therapy did not influence the pattern of dystonia in our group of patients. Prospective studies of natural history and post-mortem brain pathological analysis are necessary to disclosure a better comprehension of dystonia phenomenology in atypical parkinsonism.

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