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The role of cerebellum in patients with late onset cervical/segmental dystonia?—Evidence from the clinic

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ABSTRACT

Background: There is evidence from animal studies, post-mortem pathology, functional imaging and neurophysiological studies to suggest that the cerebellum may be involved in the pathophysiology of dystonia. We sought to explore further the association of clinical and radiological abnormalities of the cerebellum in patients with dystonia.
Methods: We retrospectively reviewed patients from our movement disorders research database, with predominant cervical dystonia who have been seen within last 6 months and had available routine magnetic resonance imaging (MRI). The clinical details including presence of cerebellar signs, imaging findings and results of investigations were recorded on a proforma. The results were analysed using percentages and means with standard deviation.
Results: Out of 188 patients included 26 had evidence of cerebellar abnormality on neuroimaging. 17 patients showed cerebellar atrophy and 10 of these had cerebellar signs on examination. These patients were tested negative for common inherited ataxias. 9 patients had cerebellar lesions on MRI, reported as low grade tumour (n = 2), cerebellar infarct (n = 3), cyst (n = 2), white matter hyperintensity (n = 1) and ectopia (n = 1) out of these 4 had cerebellar signs.
Conclusion: The findings from our study suggest that there may be overt clinical or radiological cerebellar involvement in 14% of cases with cervical/segmental dystonia. However, larger prospective studies are needed in this context.

1. Background

Advances in the understanding of the pathophysiology of dystonia point out to a disorder beyond basal ganglia dysfunction, and most intriguing in this regard is the emerging role of the cerebellum. Indeed, animal studies [1,2], post-mortem studies [3,4], functional imaging [5] and neurophysiological studies [6] indicate that the cerebellum might be implicated in the pathophysiology of dystonia, even though its role is still debated.

We have come across patients with predominant dystonia and neuro-radiological signs of cerebellar pathology. Based on this observation and aforementioned evidence, we sought to explore further the association of clinical and radiological cerebellar abnormalities in patients with dystonia. To this aim, we surveyed patients with predominant cervical dystonia attending our botulinum toxin clinics looking for documented evidence of cerebellar abnormalities on neuroimaging.

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2. Methods

We reviewed records from our movement disorders research database, and included patients with predominant cervical dystonia who have been seen within last 6 months and had available magnetic resonance imaging (MRI), T1, T2, FLAIR done routinely as clinically indicated as a part of the work up for dystonia and reported by a radiologist. A written informed consent was obtained by these patients on a research ethics committee approved movement disorders research database and video recording form. According to the neuroimaging results as reported by a neuroradiologist, patients were classified as having or not having, evidence of cerebellar abnormality. We retrospectively studied their medical records for the presence of cerebellar signs on examination such as finger nose testing for limb ataxia, tandem walking, ocular abnormalities, intention tremor, and if available, we also looked at the video recordings of the patients. Further documented genetic tests, additional investigations, were recorded where available.

3. Results

188 patients with dystonia cervical or segmental dystonia (with a predominant cervical involvement) attending our botulinum toxin clinics were included in this study. The clinical profile of the cervical dystonia patients was that of late-onset isolated dystonia with torticollis with or without-laterocollis, anterocollis–retrocollis, and/or shoulder elevation. The patients with segmental dystonia (n = 29, 15% of the whole cohort) had, beyond the cervical involvement, laryngeal (n = 10), oromandibular (n = 3), blepharospasm (n = 6), and upper limb dystonia (n = 10). 56 patients of the whole cohort (30%) had a tremulous cervical dystonia.

Twenty six (14% of the total) had evidence of cerebellar abnormality on neuroimaging. Seventeen patients showed cerebellar atrophy (classified as Group 1), whereas nine patients had cerebellar lesions (classified as Group 2). Table 1 details demographic and clinical features of these patients. Incidentally, we also found two patients with cervical dystonia had syringomyelia and one had incidental meningioma of sphenoid ridge.

3.1. Group 1 dystonia with cerebellar atrophy (n = 17)

Out of these patients, seven had no cerebellar signs on several examinations by a movement disorders neurologist (group 1a), while ten patients had documented upper limb ataxia on finger nose test (group 1b) (Table 2). Tests for spinocerebellar ataxias (SCAs 1, 2, 3, 6, 7, and 12) were negative for all of these patients. All the patients were also tested negative for Wilson disease and other common metabolic and inherited causes of secondary heredodegenerative dystonias.

3.1.1. Group 1a

Cervical dystonia with cerebellar atrophy, *without* cerebellar signs (n = 7). These seven patients (Table 1) had a typical adult-onset craniocervical dystonia phenotype. Five had tremulous cervical dystonia and two had craniocervical dystonia with laryngeal involvement. Both of these also had tests for DYT-6 which was negative. None of them had a family history of ataxia, dystonia or other neurological disorders. One of the patients in this group was recorded as having normal examination in the notes but a video showed very subtle cerebellar signs (video 1).

Supplementary video related to this article can be found at http://dx.doi.org/10.1016/j.parkreldis.2015.09.013.

3.1.2. Group 1b

Cervical dystonia with cerebellar atrophy and *with* cerebellar signs (n = 10). These ten patients were similar to group 1a patients but had additional documented cerebellar signs (Table 2). They did not have any other clinical features or family history. A representative case (video 2) had segmental dystonia and was tested negative for SCAs and secondary causes of dystonia with ataxia.

3.2. Group 2 cervical dystonia with cerebellar lesions (n = 9)

These nine patients had adult-onset craniocervical dystonia phenotype (Table 2) with cerebellar lesions on routine MRI reported as low grade tumour (n = 2), cerebellar infarct (n = 3), cyst (n = 2), white matter hyperintensity (n = 1) and ectopia (n = 1) (Table 2) (Fig. 1). None of the patients were aware of any clear preceding event related to the infarct and other cerebellar abnormality. There was no family history of ataxia, dystonia or other neurological disorders in any of these patients. Two of these (Table 2) were tested for SCAs (SCA 1, 2, 3, 6, 7, 12) but were negative. On examination, four had mild dysmetria on finger nose test but no gait ataxia and five did not have any cerebellar signs.

4. Discussion

We found that cerebellar abnormalities on imaging were detected in patients with late-onset cervical/segmental dystonia in 26 out of 188 patients (14%). The numbers in the study were small and it is not possible to do the sub-analysis of whether these signs were present early or later to the development of dystonia. However, this clinical observation further supports the putative involvement of the cerebellum in dystonia corroborated by electrophysiological studies [6,7] pathological studies [4,8] and advanced neuroimaging studies [9].

Abnormalities of cerebellum (mainly atrophy) have been reported as incidental findings in 4% of 644 scans in a study screening for cerebellopontine angle tumours [10]. It appears compared to the previous report [10] that cerebellar abnormalities were commoner (14%) in our patients. However, it should be acknowledged

Table 1
The two clinical groups of cerebellar involvement with dystonia. The table mentions numbers in each group for the present study with summary of demographics. (Abbreviations *SD = standard deviation*).

Group	Characteristics	Number of patients in the group	Number of patients with abnormal imaging of cerebellum	Number of patients with cerebellar signs on examination	Mean age in years (SD)	Mean disease duration in years (SD)	Male:female
Group 1a	Cervical dystonia with cerebellar atrophy, *without* cerebellar signs	7	7	0	50.4 (11.8)	10.0 (6.7)	3:4
1b	Cervical dystonia with cerebellar atrophy and cerebellar signs	10	10	10	35.8 (12.3)	15.3 (11.3)	1:9
Group 2	Cervical dystonia with cerebellar lesions	9	9	4	39.8 (12.3)	12.2 (8.5)	4:5
Total		26	26	14	41	14	8:18