Movement Disorders
CLINICAL PRACTICE

CASE SERIES

Dystonia in Patients With Spinocerebellar Ataxia Type 2

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Abstract: Dystonia has been described in various genetically proven spinocerebellar ataxias (SCAs), most often in SCA3, SCA17, and SCA2 patients. In this report, we describe different types of dystonia observed in 5 of our 11 SCA2 patients. All our patients had cranial and/or cervical dystonia with focal or segmental distribution. Except for 1 case with isolated cervical dystonia, all other patients had lower cranial affection of variable severity. Although it is difficult to describe ataxia-dystonia syndrome that would be highly characteristic for SCA2, we suggest that occurrence of dystonia in a patient with slowly evolving cerebellar disease should, besides SCA3 and SCA17, also suggest SCA2 testing. In patients with lower cranial dystonia, especially jaw and tongue dystonia, SCA2 should be considered during the diagnostic workup.

Dystonia has been described in various genetically proven spinocerebellar ataxias (SCAs), most often in SCA3, SCA17, and SCA2 patients, but also, less commonly, in SCA1, SCA14, and SCA6.[1] Dystonic features in SCA often emerge in the context of already developed cerebellar ataxia, when they do not pose a significant diagnostic problem. However, SCA patients with prominent focal dystonia and only mild cerebellar disease, as well as those with dystonia appearance preceding cerebellar symptoms, have been also described.[2]

The prevalence of dystonia in SCA2, an autosomal-dominant cerebellar ataxia caused by the trinucleotide cytosine-adenine-guanine (CAG) repeat expansion in the ataxine-2 gene, varied from 14% to 17%,[1,2] although Boesch et al.[3] reported an estimate of up to 61%. Cervical dystonia, in particular, may be an initial symptom in SCA2 patients, preceding cerebellar symptoms for many years.[3]

In this report, we describe different types of dystonia observed in 5 of our SCA2 patients with long-term follow-up data.

Case Reports

The study comprised 11 consecutive patients with SCA2 (9 have been previously reported on),[4] who were regularly followed (N.T.D.-M., V.S.K.) in 4- to 6-month intervals for an average of 12.6 years (range, 9–17). The patients' histories were thoroughly reviewed, as well as archived video clips, when available. At study entry, clinical examination of all patients was performed and new video material was recorded. The Scale for the Assessment and Rating of Ataxia (SARA) was used to assess disease severity.[5] Dystonia was identified in 5 patients (45%) whose demographic, clinical, and genetic data are presented in Table 1. None of them were exposed to antipsychotic medications or any other dopamine antagonists. Brain MRI scans were performed to exclude other possible causes of dystonia. Before inclusion in the study, written informed consent that included video recording and publishing consent was obtained from 10 patients, whereas for a patient who passed away (case 5), written informed consent was obtained from her legal representative (daughter). The ethical committee of the School of Medicine University of Belgrade approved the study.

Case 1

A female patient, with an onset of cerebellar symptoms at the age of 18, developed oromandibular dystonia 7 years later (see Video 1, part Ia). Dystonia worsened over years and resulted in

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TABLE 1 Demographic and clinical features of patients with SCA2 associated with dystonia

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	36	60	50	37	61
Sex	Female	Female	Female	Female	Female
Disease duration (years)	18	17	27	19	9
Follow-up (years)	12	17	10	15	9
CAG^n	23/35	22/27	23/40	23/42	22/38
Family history	Positive	Negative	Positive	Positive	Positive
Initial symptom	Gait instability	Cervical dystonia	Gait instability, dysarthria	Gait instability	Gait instability
Age at onset of cerebellar signs (years)	18	55	23	18	52
Age at onset of dystonia (years)	25	43	49	26	58
Course of dystonia	Slow progression	Slow progression	Rapid progression	Slow progression	Steady
Current clinical features					
Cerebellar features	Cerebellar dysarthria, limb and truncal ataxia, slow saccades, wheelchair bound	Cerebellar dysarthria, limb and truncal ataxia	Saccadic speech, dysphagia, slow saccades, limb and truncal ataxia, titubation, hyporeflexia, wheelchair bound	Cerebellar dysarthria, limb and truncal ataxia, slow saccades, titubation	Cerebellar dysarthria, slow saccades, limb and truncal ataxia, titubation, hyper-reflexia
SARA score	33	9.5	35	18	16
Dystonia	Jaw-opening dystonia	Blepharospasm, orobuccal dystonia, antecollis	Dystonic lingual tremor, jaw-opening dystonia	Facial dystonia, oromandibular dystonia, dystonic posture of hands	Right laterocollis
Sensory trick	No	Yes	No	No	No
Response to botulinum toxin injections	na	Excellent	na	na	Excellent

na, not applicable.

disabling jaw-opening dystonia (see Video 1, part Ib). This patient also developed severe rest and postural tremor of the limbs, which was treated with levodopa without success.

Case 2

A female patient initially presented with cervical dystonia at the age of 43 years. Within the subsequent 5 years, she developed segmental dystonia that included blepharospasm, orobuccal dystonia, and cervical dystonia (predominant ante- and mild laterocollis; see Video 1, part IIa). She had an excellent response to botulinum toxin injections. Cerebellar dysarthria and mildly ataxic gait occurred several years after dystonia manifested. The precise time latency from dystonia to ataxia development could not be precisely determined, because both the patient and physicians paid little attention to ataxic features until the age of 55, when she complained of unsteady, ataxic gait as her leading symptom (see Video 1, part IIb).

Case 3

A female patient presented to us at the age of 40 with a long history of gait instability and speech problems. Examination revealed slow saccades, cerebellar dysarthria, titubation, and ataxia (see Video 2, part IIIa). After 27 years of progression of cerebellar symptoms, when she was wheelchair bound, intense and disabling jaw and tongue involuntary movements developed, which interfered with speech and feeding. They consisted of jaw-opening dystonia with almost rhythmic tongue protrusion, consistent with the dystonic tremor of the tongue (see Video 2, part IIIb). When these movements developed, the patient was already edentulous for many years.

Case 4

A 26-year-old female patient developed asymmetrical facial dystonia with oromandibular dystonia 8 years after the onset of cerebellar symptoms (see Video 2, part IVa). Facial dystonia was most prominent at rest, whereas oromandibular dystonia became apparent with activation, especially speech. At the latest neurological examination, in addition to progression of ataxia, dystonic posture of her hands was observed (see Video 2, part IVb).

Case 5

A female patient, suffering from slowly progressive ataxia for 6 years, developed mild cervical dystonia (right laterocollis) at

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the age of 58. She was successfully treated with botulinum toxin injections, and during the 3-year follow-up, dystonic features had a steady course (see Video 2, Part V).

Discussion

Because 45% of our patients with SCA2 had dystonia, our experience was in line with those that reported high prevalence of dystonia in patients with SCA2.[3] Notably, all of our patients were women. Also, all of them had cranial and/or cervical dystonia with focal (cases 1, 3, 4, and 5) or segmental distribution (case 2). Only one of them (case 2) had a sensory trick. It is clinically important to differentiate cervical dystonia from head tilt, which has been described in cerebellar lesions of different origin. Except for case 5 with isolated cervical dystonia, all other patients had lower cranial affection of variable severity (Table 1). This finding contradicted the data of Boesch et al.,[3] who observed cervical dystonia as the only dystonic feature in 11 of 18 patients with SCA2 accompanied with dystonia. Oromandibular dystonia has already been described in SCA2,[6] as well as in SCA8 patients,[7] but also in cases of cerebellar infarction.[8] Striking presentation of jaw-opening dystonia observed in case 4 closely resembled those observed in patients with the iron accumulation disorders. The unusual presentation of lingual protrusion dystonia with dystonic tremor of the tongue (case 5), to our knowledge, has not been described in association with SCAs. Lingual protrusion dystonia is a rare type of dystonia observed in approximately 4% of patients with dystonia in specialized clinics, with almost half being tardive phenomenon.[9]

In only 1 patient (case 2), dystonia preceded cerebellar signs, whereas in the remaining 4 it developed after 6, 7, 8, and even 27 years of cerebellar ataxia progression. Treatment with botulinum toxin was very successful in 2 of the treated patients. Interestingly enough, dystonia in SCA2 may, at least transiently, respond to L-dopa.[10] Although 1 of our patients developed rest tremor (case 1) and parkinsonism was described in SCA 2 patients,[1] we believe that this tremor was probably the result of damage to cerebellar outflow pathways.

According to recently proposed classification of dystonia, clinical recognition of dystonia syndromes is strongly recommended, given that this can provide valuable diagnostic clues.[11] Syndrome of adult-onset cerebellar ataxia accompanied with dystonia is probably rare and in its differential diagnosis includes screening for metabolic diseases, such as Wilson's disease, Nieman-Pick type C,[12] cerebrotendinous xanthomatosis,[13] and so on, although in these cases dystonia and cerebellar signs develop in the context of broader clinical picture. Dystonia has also been described in recessive ataxias, such as ataxia-telangiectasia. In particular, high prevalence of lower cranial dystonia in our patients suggests that SCA2 might be added to the list of diseases with prominent oromandibular dystonia, such as iron accumulation disorders, Wilson's disease, GM1 gansliosidosis, tardive dystonia,[12] and so on.

It is unknown whether the underlying mechanism(s) of dystonia associated with cerebellar damage are related to cerebellar or extracerebellar alterations.[14] It has been suggested that cerebellar degeneration leads to decreased inhibition of motor cortex.[15] Postmortem studies reported alterations in the basal ganglia of patients with SCA2 (pallidum, STN, and ventral thalamic nuclei).[16] Prudente et al.[14] proposed concept of dystonia as a disorder of network comprising both basal ganglia and cerebellum.

Although it is not possible to describe ataxia-dystonia syndrome that would be highly characteristic for SCA2 based on this small case series, we suggest several points that might be of interest in clinical work. Occurrence of dystonia in a patient with slowly evolving cerebellar disease should, besides SCA3 and SCA17, also suggest SCA2 testing. In particular, presence of lower cranial dystonia in patients with ataxia may be a red flag for SCA2 testing. In selected patients with lower cranial dystonia, especially jaw and tongue dystonia, SCA2 might be considered during the diagnostic workup.

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

V.M.: 1B, 1C, 2B, 2C, 3A
N.T.D.-M.: 1A, 1B, 1C, 2A, 3B
I.S.: 1B, 1C, 2B, 2C, 3A
I.P.: 1A, 1B, 1C, 2A, 3B
M.S.: 1B, 1C, 2A, 3B
V.S.K.: 1A, 1B, 1C, 2A, 3B

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Supporting Information

Videos accompanying this article are available in the supporting information here.

Video 1. Case 1, Part Ia: Examination at age 28: mild jaw-opening dystonia, limb ataxia, dysarthria, and gait ataxia are shown. Case 1, Part Ib: Examination at age 34: severe jaw-opening dystonia. Case 2, Part IIa: Examination at age 48: blepharospasm, orobuccal dystonia, and cervical dystonia. Case 2, Part IIb: Examination at age 60: blepharospasm, orobuccal dystonia, sensory trick, antecollis, limb ataxia, and gait ataxia.

Video 2. Case 3, Part IIIa: Examination at age 40: slow pursuit, ataxia, and titubation and no dyastonia. Case 3, Part IIIb: Examination at age 50: jaw-opening dystonia, tongue protrusion, limb ataxia, and titubation. Case 4, Part IVa: Examination at age 26: gait ataxia, facial myokimia, and limb ataxia. Case 4, Part IVb: Examination at age 37: facial myokimia, oromandibular dystonia, dysarthria, and dystonic posturing of the hands. Case 5, Part V: Examination at age 61: saccadic speech, slow pursuit, limb ataxia, and right laterocollis.

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