

Asymmetry of Tremor in Spinocerebellar Ataxia 12- Exception or Rule?

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Spinocerebellar Ataxia 12(SCA12) is a rare form of SCA, predominantly reported in the ethnic Agarwal population originating from North India. It generally presents with late onset upper limb tremor followed by ataxia.¹ Tremor in SCA12 remains poorly studied to date. Since action tremor is the most common and earliest sign in SCA12, it is often mis-diagnosed as Essential tremor.²

In SCA12, CAG repeat associated neuro-toxic protein accumulation accelerates degeneration in the cerebello-cortical region.³ Since toxic protein associated neuro-degeneration is a diffuse process, one may expect appendicular features of SCA12 to reflect symmetry. But asymmetrical hand tremor was documented in one patient of Indian origin by Kalia et al.⁴ They stated that previous reports did not comment about tremor symmetry, this remains largely true to date. In this paper we have

tried to explore if asymmetry of symptoms in SCA12 is an exception or a common finding.

We studied 22 cases of SCA12 with a focus on laterality and associated phenomenology of symptoms. Mean disease duration in our study population was 8.2 (±4.7) years. Tremor was clinically analyzed by a movement disorders neurologist. The findings have been summarized in Table 1. When we look into upper limb findings, all 22 (100%) patients had intention tremor, 21 (95%) had dysmetria, 21 (95%) patients had postural tremor and 12 had rest tremor. Interestingly, postural tremor did not depict re-emergence, which is commonly seen in Parkinson's disease.

Twenty (91%) patients had asymmetrical upper limb tremor and 10 (45%) had asymmetrical dysmetria. Out of these 20 patients, 19(90%), 10 (83%) and 5 (29%) had asymmetry in

TABLE 1 Appendicular features of SCA 12 – We focused on tremor and dysmetria in upper and lower limb. Majority of upper limb shows asymmetry, in postural>rest>action tremor. In lower limb, dysmetria although common is symmetrical and action tremor is rare. Holmes' tremor was seen in several patients and Parkinsonism was rare

S No.	UL					Holmes' Tremor	DD	LL Action Tremor	LL Dysmetria	
	*Asymmetry in UL tremor	Postural tremor	UL Action tremor	UL Rest tremor	UL Dysmetria					
1	Present	R > L	Symmetry	Absent	Symmetry	—	7 yr	Absent	Symmetry	
2	Present	Absent	Symmetry	L > R	L > R	—	6 yr	Absent	Symmetry	
3	Absent	Symmetry	Symmetry	Symmetry	R > L	—	Present	16 yr	Absent	Symmetry
4	Present	R > L	Symmetry	R > L	Symmetry	—	Present	10 yr	Absent	Symmetry
5	Present	Symmetry	Symmetry	L > R	Absent	—	Present	9 yr	Absent	Symmetry
6	Present	R > L	Symmetry	R > L	R > L	Parkinsonism+	Present	5 yr	Absent	Symmetry
7	Present	L > R	Symmetry	L > R	Symmetry	—	Present	7 yr	Absent	Symmetry
8	Present	R > L	Symmetry	L > R	Symmetry	—	Present	4 yr	Absent	Absent
9	Present	R > L	Symmetry	Absent	R > L	—	Present	20 yr	Absent	Symmetry

(Continues)

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TABLE 1 Continued

S No.	*Asymmetry in UL tremor	UL Postural tremor	UL Action tremor	UL Rest tremor	UL Dysmetria	Parkinsonism	Holmes' Tremor	DD	LL Action Tremor	LL Dysmetria
10	Present	R > L	Symmetry	Absent	Symmetry	—	—	7 yr	Absent	Absent
11	Present	R > L	Symmetry	Absent	Symmetry	—	—	14 yr	Symmetry	Absent
12	Present	R > L	R > L	Absent	R > L	—	—	5 yr	Absent	Symmetry
13	Present	L > R	Symmetry	L > R	R > L	—	Present	3 yr	Absent	Symmetry
14	Present	L > R	Symmetry	Absent	Symmetry	Parkinsonism+	—	6 yr	Absent	Symmetry
15	Present	R > L	R > L	Absent	R > L	—	—	14 yr	Absent	Symmetry
16	Present	L > R	Symmetry	Absent	Symmetry	—	—	5 yr	Absent	Symmetry
17	Present	R > L	Symmetry	R > L	Symmetry	—	Present	5 yr	Absent	Absent
18	Absent	Symmetry	Symmetry	Symmetry	L > R	—	Present	14 yr	Absent	Symmetry
19	Present	R > L	R > L	R > L	R > L	—	Present	10 yr	Absent	Absent
20	Present	L > R	R > L	L > R	R > L	—	Present	1 yr	Absent	Symmetry
21	Present	R > L	Symmetry	Absent	Symmetry	—	—	3 yr	Absent	Symmetry
22	Present	L > R	Symmetry	Absent	Symmetry	—	—	10 yr	Absent	Absent

Asymmetry*: The patient was said to have asymmetrical tremor, if any/all of rest, action or postural tremor were asymmetrical. Parkinsonism: If any patient had bradykinesia or/and rigidity they were said to have Parkinsonism.

Abbreviations: UL, Upper limb; LL, Lower Limb; DD, Disease duration: time since onset of first symptom.



Video 1. In the upper limb – Patient 1, has asymmetrical rest and postural tremor with symmetrical dysmetria and intention tremor, Holmes' tremor is present. Patient 2 has asymmetrical postural tremor, intention tremor and dysmetria. Patient 3 has asymmetrical postural tremor but symmetrical dysmetria, rest and intention tremor, Holmes' tremor and head tremor were present. Patient 4 has asymmetrical dystonic posturing and postural tremor (Right>Left) but symmetrical intention tremor. In the lower limbs – Patient 3 had symmetrical dysmetria but no intention tremor. Asymmetrical upper limb tremor and dysmetria along with symmetrical lower limb dysmetria was commonly seen in our cohort of patients with SCA12. Video content can be viewed at <https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13237>

postural, rest and intention tremor respectively. Notably, postural tremor showed the highest rate of asymmetry. Only two patients had symmetry in upper limb tremor at presentation but their symptoms started 14 and 16 years ago respectively. Even in these

two patients, tremor began on one side and took 5–7 years to equally involve the upper limbs. Twelve patients had simultaneous rest, postural and action tremor, which is defined as Holmes' tremor (HT).⁵ When analyzing lower limb data, only one patient had action tremor and it was symmetrical. Sixteen patients had dysmetria, all of which was symmetrical.

Our findings suggest that asymmetry is a commonly found character of upper limb tremor in SCA12, which can be seen in the representative video segments (Video 1), provided as a supplement to this manuscript. Written informed consent was obtained and ethical approval was taken. Theoretically, HT can be found in any cerebellar outflow tract disorder, but we duly document it in SCA12 for the first time.⁵

Lower limb tremor was found in only one patient, and it was symmetrical. Dysmetria was more common in lower limbs as compared to tremor, and that too was symmetrical. The clear incongruence in upper and lower limb symptoms in tremor disorders is well reported but unexplained. Well-developed laterality in the upper limbs might make central oscillations manifest better on one side. These oscillations may be dampened in the lower limb due to more crosstalk between bilateral neural tracts.

Through our preliminary observation, we conclude that asymmetrical upper limb tremor is a hallmark of SCA12.

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; (4) Supervision.

S.B.: 1A, 1B, 1C, 2C, 3A, 3B

S.C.: 2A, 2C, 3B

U.S.: 1C, 2C, 3C

P.B.: 1C, 2C, 3C

H.K.: 1A, 1B, 1C, 2A, 3B, 4

Disclosures

Ethical Compliance Statement: This study was approved by the Institute of Neurosciences Kolkata, Institutional Ethics Committee. Written informed consent to publish case reports and videos was obtained from all participants. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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