Movement Disorders
CLINICAL PRACTICE

The Spectrum of Movement Disorders in Neuroacanthocytosis Syndromes: A Video Series

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The term neuroacanthocytosis (NAC) was introduced in 1982 by Yamamoto et al.[1] to describe a combination of neurologic disorders and acanthocytes occurring together. Over time, this concept has evolved and the core NAC syndromes currently comprise of Chorea-acanthocytosis (ChAc), McLeod syndrome, Huntington's disease (HD)-like 2 and Pantothenate kinase-associated neurodegeneration.[2] The largest series of NAC syndrome reported three decades ago by Hardie et al.[3] consisted of 19 cases. Following this, there has been no single centre case series, and the present study reports 24 cases of NAC syndrome recruited retrospectively via a chart review of cases diagnosed with NAC syndrome by the Parkinson's Disease and Movement Disorder Subspeciality at the department of Neurology, National Institute of Mental Health and Neurosciences, India from 2012 to 2019. Diagnosis of a NAC syndrome was based on the presence of adult-onset chorea and acanthocytosis along with supportive blood investigations and radiological findings. Four of the 24 cases underwent genetic testing and were found to have a VPS13A mutation suggestive of ChAc. This study aims to provide a video description of the spectrum of movement disorders observed in the NAC syndrome (Table 1).

Demographic and clinical details of this cohort are provided in Table 1, and Appendix S1. The male predominance observed in this cohort could be attributable to the referral system in India rather than a true skew in gender distribution. Chorea was observed in all cases. Oromandibular dystonia (OMD) was also observed in all cases, of which a majority had feeding dystonia with tongue protrusion and head extension as a compensatory mechanism (Video 1). Nine had injuries to the lip, cheek and tongue which could have occurred secondary to the OMD. Additionally, injuries to fingers were observed in two cases who had feeding dystonia, and could have occurred in an attempt to prevent tongue protrusion and subsequent expulsion of food from the mouth. OMD was also found to be partially suppressible by sensory tricks and self-concocted maneuvers in four cases (Video 2). Vocal tics, characterized by grunting, frequent loud throat clearing, production of click consonants, sniffing, and forceful exhalation were observed in most cases (Video 3). In eight cases, facial grimacing was observed in addition to the vocal tics. Head drops with axial extensions were present in three cases, and could have attributed to the head injury observed in one case. Choreiform gait was observed in 18 patients, with a rubber man gait in six (Video 4). Tremor, parkinsonism and myoclonic jerks were also observed in a few cases (Table 1, Video 5).

Other neurological symptoms included dysphagia in all cases, with choking reported by one patient. Patients had speech disturbances primarily in the form of hyperkinetic dysarthria. Generalized tonic–clonic seizures in six patients, and focal seizures in two were also observed. Patients had cognitive impairment involving the domains of working memory, executive functions, learning, verbal and categorical fluency. Finally, a host of psychiatric manifestations were observed which included depression, obsessive compulsive disorder, anxiety, hyperactivity, anger outbursts, and violent behavior (Video 6).

Neuroimaging revealed isolated caudate atrophy in 12 cases, whereas the rest had additional features in the form of striatal atrophy, T2 striatal hyperintensity, cerebellar atrophy, and diffuse cerebral atrophy (Appendix S1). Motor symptoms were managed with tetrabenazine, carbamazepine, and clonazepam which provided transient, mild to moderate benefit. Four cases received botulinum toxin for OMD with good improvement. One case with severe chorea gave consent to undergo a therapeutic trial of pallidal stimulation, i.e., bilateral globus pallidus interna (GPi)

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TABLE 1 Demographic and clinical history of patients with neuroacanthocytosis syndrome

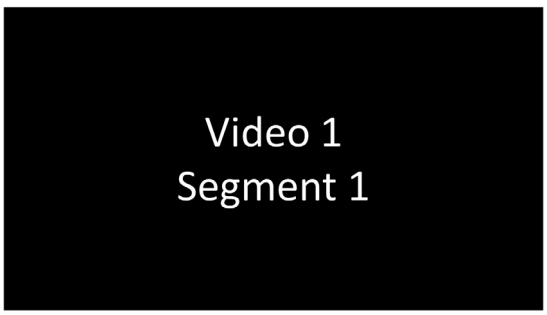
	Patients with neuroacanthocytosis (n = 24)
Gender (Female: Male)	6:18
Age at presentation (yrs)	35.45 ± 7.60
Age at onset (yrs)	29.60 ± 7.60
Symptom at onset	
Movement disorder	54.1% (13, AAO: 32.07 ± 8.28)
Non-movement disorder	45.8% (11, AAO: 26.63 ± 6.37)
Seizures	25% (6, AAO: 27.50 ± 3.25)
Behavioral disturbances	20.8% (5, AAO: 25.60 ± 8.16)
Duration of illness (years)	4.19 ± 2.90
Consanguineous parentage	50% (12)
Family history	12.5% (3)
Referral diagnosis	
Neuroacanthocytosis	41.6% (10)
Other diagnosis	58.3% (14)
Huntington's disease	50% (7)
Functional movement disorders	14.2% (2)
Meige syndrome	7.1% (1)
Structural lesion	7.1% (1)
Wilson's disease	7.1% (1)
Sydenham chorea	7.1% (1)
Progressive myoclonic epilepsy	7.1% (1)
Distribution of chorea	100 (24)
Generalized	75 (18)
Focal upper limb	16.6 (4)
Hemichorea	8.3 (2)
Truncal chorea	75 (18)
Lingual chorea	66.7 (16)
Facial grimacing	33.3 (8)
Vocal tics	75 (18)
Oromandibular dystonia	100 (24)
Feeding dystonia	62.5 (15)
Bruxism	25 (6)
Dysarthria	75 (18)
Drooling	8.3 (2)
Spitting	4.1 (1)
Parkinsonism	4.1 (1)
Tremors	16.6 (4)
Upper limb action tremor	75 (3)
Upper limb action and rest tremor	25 (1)
Myoclonic jerks	8.3 (2)
Hyporeflexia	91.6 (22)
Upper and lower limbs	36.3 (8)
Lower limb alone	63.6 (14)
Injuries	37.5 (9)
Site of injury	
Tongue, lip, cheek	100 (9)
Fingers	22.2 (2)
Head injury	11.1 (1)

(Continues)

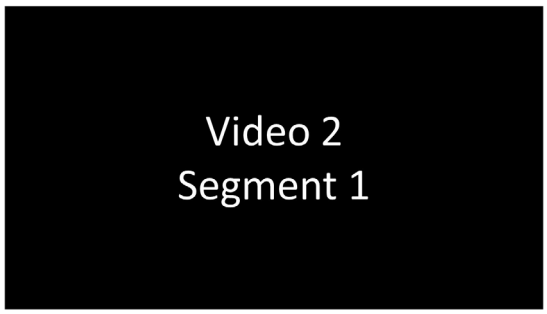
TABLE 1 *Continued*

Only four patients underwent genetic testing, and all four were found to have pathogenic VPS13A mutations.
Abbreviation: AAO, Age at onset.

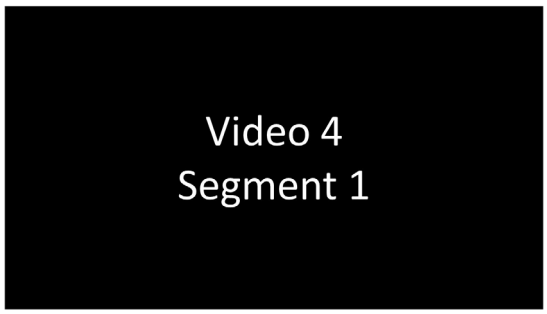
deep brain stimulation (DBS). Although he had mild improvement of chorea and gait in the first-year post-surgery, he progressively worsened thereafter.



Video 1. Feeding dystonia. Segment 1: Patient extends head backward in an attempt to swallow food which is being expelled out due to tongue protrusion. A head drop is also observed. Segment 2: There is recurrent tongue protrusion which eventually leads to complete expulsion of food from the mouth. Segment 3: The patient resorts to using her finger to retain food in the mouth, and has occasional neck extension and head drops. Segment 4: Occasional tongue protrusions are observed, and the patient attempt to hold the jaw shut by placing his hand under his jaw. Segment 5: Tongue protrusions with recurrent expulsion of food is observed, and the patient uses his finger to retain food within his mouth. Note: Injuries to the lip are also observed.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13269



Video 2. Maneuvers performed by patients to reduce injury due to oromandibular dystonia. Segment 1: Recurrent biting of lower lip is observed. The patient, places a towel in the mouth to reduce the bites. Segment 2: This patient places a coin between the upper and lower jaw in an attempt to reduce lip injuries. Segment 3: Repetitive touching of perioral region. Occasional head drops, neck extensions and vocalizations are also observed. Segment 4: Dental guard is used to reduce the lip injuries due to the OMD which can be observed when the patient stands up and walks.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13269



Video 4. Gait. Segment 1: Classical rubberman type of a gait which is characterized by intermittent truncal flexion, extension spasms and occasional knee flexion. Segment 2: Patient tends to fling limbs while walking, and has occasional head drops. Segment 3: Significant chorea of limbs present while walking. Segment 4: Occasional buckling of right leg, with truncal flexion and extension while walking which gives the appearance of a bouncing gait.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13269

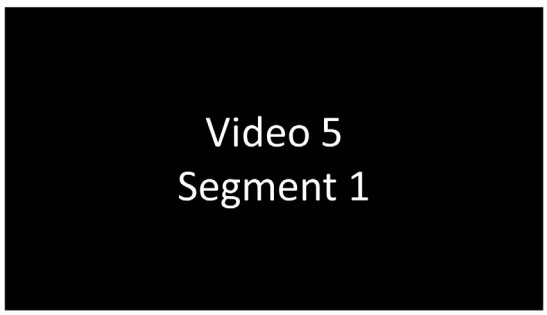
NAC syndrome may be often misdiagnosed as HD in a patient with adult-onset chorea with neuropsychiatric manifestations and cognitive impairment. However, features such as prominent oromandibular dystonia, self-mutilation, seizures, myopathy, and neuropathy, in a case of sporadic or autosomal recessive adult-onset chorea, should suggest the possibility of NAC specifically ChAc, rather than HD.[4]

The NAC syndrome has a wide spectrum of clinical features. Chorea may not necessarily be the symptom at onset and a strong index of suspicion should exist when cases present with seizures or behavioral disturbances, and a family history suggestive of neuroacanthocytosis or consanguineous parentage. Cases of ChAc have a propensity for characteristic head drops, axial extension,[5] and feeding dystonia,[6,7] which may prove to be crucial signs in differentiating it from other NAC syndrome disorders.

Author Roles

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

Video 3. Vocalizations Segment 1: Labial, and lingual click consonants, inspiratory sighs. Segment 2: Labial click consonants, bruxism. Segment 3: Lingual and labial click consonants, and grunts. Segment 4: Loud vocalizations in a patient with predominant psychiatric symptoms.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13269



Video 5. Tremor and myoclonus. Segment 1: Bilateral upper limb action tremor with intermittent myoclonic jerks. Segment 2: Bilateral upper limb jerky action tremor predominantly involving fingers.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13269

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Video 6. Behavioral disturbances, head drops with axial extension, and stereotypies.
Video content can be viewed at https://onlinelibrary.wiley.com/doi/10.1002/mdc3.13269

K.N.: 1A, 1B, 1C, 2A, 2B, 3A
S.P.: 1A, 1B, 1C, 2A, 2B, 3A
V.V.H.: 1B, 1C, 2A, 2B, 3B
N.K.: 1A, 1B, 2C, 3B
R.Y.: 1A, 1B, 2C, 3B
P.K.P.: 1A, 1B, 2A, 2C, 3B

Disclosures

Ethical Compliance Statement: The authors confirm that approval was obtained from the Institutional Review Board for this work. Informed written consent was obtained from the patient. 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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Supporting Information

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

Appendix S1. Supporting information.