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Short communication

Dystonia with aphonia, slow horizontal saccades, epilepsy and photic myoclonus: A novel syndrome?

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ABSTRACT

Background: Dystonia with anarthria and/or aphonia is a rare syndromic association. Here we present two cases with slowly progressive, severe generalized dystonia and aphonia, slow horizontal saccades, epilepsy and photic myoclonus.
Methods: Detailed clinical data were collected over two decades in the female (index) patient and for nine years in her similarly affected son. Sanger sequencing followed by exome sequencing was performed.
Results: Both patients had leg onset generalized dystonia with gradual rostral spread including prominent facial and oro-mandibular involvement. The index patient was anarthric, her son aphonic. Both had saccadic slowing, more marked for the horizontal plane, and subclinical epileptic activity. The index patient also had photic myoclonus and a combined axonal and demyelinating neuropathy. Known genetic causes of similar syndromes were not identified.
Conclusion: These cases with caudo-rostrally spreading generalized dystonia with prominent facial and oro-mandibular involvement, severe speech impairment, marked slowing of horizontal saccades, and photic myoclonus likely represent a novel entity.

1. Main text

Prominent oro-laryngo-mandibular involvement in combined generalized dystonia [1] usually signifies a progressive neurodegenerative disease. In some of these syndromes prominent tongue protrusion has been noted and can guide diagnostic considerations [2]. However, reports on cases with generalized dystonia and anarthria (i.e. the inability to articulate) and/or aphonia (i.e. the inability to vocalize) without prominent tongue protrusion are scarce [3–10]. Here, we present a unique clinical syndrome of generalized dystonia with aphonia, slow horizontal saccades, epilepsy and photic myoclonus in a German woman and her son (pedigree shown in Fig. 1A), which, to our knowledge, has not been previously described in the literature.

2. Methods

2.1. Clinical

Clinical details have been gathered over a period of 19 years for the female patient and 9 years for her son. Detailed methodologies on neuropathological and genetic investigations are provided in the Supplementary material section. Informed consent was obtained for all examinations, including video recordings for publication and was in accordance with German law, the local ethics committee and the declaration of Helsinki.

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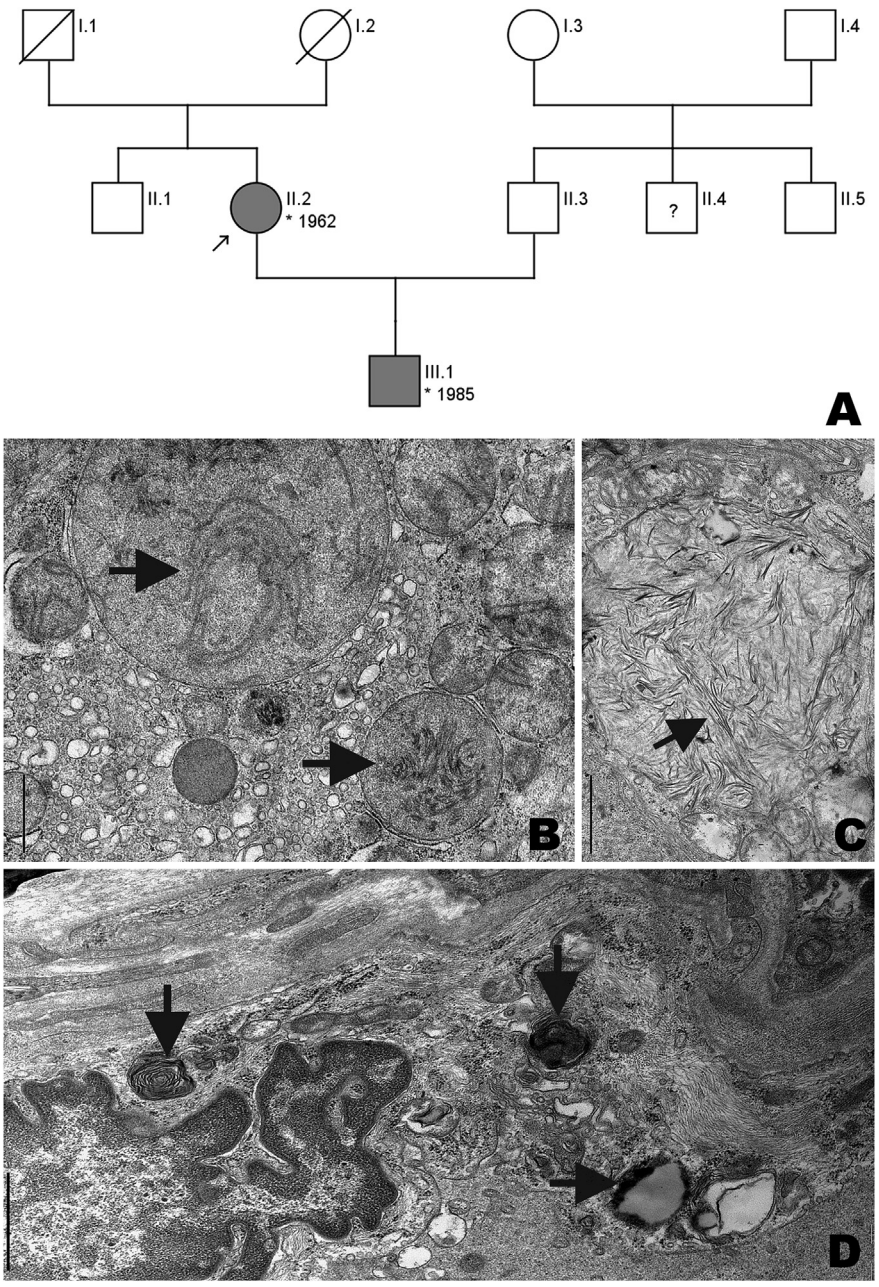

Fig. 1. A. Pedigree of the reported family. Affected members are marked with black symbols. The index patient is indicated by an arrow. Family member I1 (father of index patient) died at the age of 77 as a result of cardiac infarction and I2 (mother of index patient) at the age of 67 after suffering a stroke. Family member II4 was diagnosed with schizophrenia at late adolescence and died at his early thirties by an autoimmune disorder of unclear cause and is indicated with a question mark. B–D. Electron microscopic findings in skin biopsies of case 2. Large mitochondria with irregular cristae (B); Area with randomly scattered straight and curved filaments with a diameter of 18 nm in a cell of an eccrine gland in the axilla, same gland as in B (C); Myocyte of an arteriole with lysosomes and membrane bodies and mitochondria with irregular cristae (D); changes indicated with black arrows; scale bars = 1 μm.

3. Results

3.1. Clinical description

3.1.1. Case 1

Shortly after giving birth to her only son at the age of 23, this 51-year old woman developed gait difficulties with instability, inward feet rotation and difficulties reaching objects. She also developed pronounced problems with articulation and phonation. When suddenly exposed to light she reported to have brief generalized jerks.

On clinical examination (at the age of 51; video 1) her gingiva was hypertrophic. She had difficulties initiating saccades with compensatory eye blinking and marked slowing of saccadic velocity, more pronounced in the horizontal plane. Smooth pursuit was intact. There was no nystagmus. She had severe oromandibular dystonia with jaw opening dystonia. She was anarthric with only very limited phonation (short vocalizations). There was marked generalized