Myoclonus-Dystonia Syndrome Associated with Russell Silver Syndrome

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Keywords
myoclonus-dystonia; uniparental disomy; SGCE; Russell-Silver; genomic imprinting

Myoclonus-Dystonia Syndrome (MDS, DYT11) is a movement disorder characterized by myoclonus predominant in upper body regions and focal or segmental dystonia. MDS typically results from autosomal dominant loss-of-function mutations in the epsilon-sarcoglycan gene (SGCE) on chromosome 7q21. We describe MDS due to maternal uniparental disomy of chromosome 7 (mUPD7) associated with Russell Silver Syndrome (RSS), rather than SGCE gene mutation.

A 7-year-old girl with RSS presented for evaluation of involuntary movements of two years’ duration. Parents described generalized and multi-focal jerks of the head, limbs, and trunk, worsened by intercurrent illness and fatigue. The jerks sometimes resulted in accidental dropping or throwing of items. The involuntary movements were neither suppressible nor associated with premonitory sensation. Cognition, behavior, and mood were normal. Development was notable for mild gross and fine motor delays. The diagnosis of RSS was made at age 1 year based on intrauterine growth restriction, post-natal failure to thrive, and characteristic facial features. Microsatellite marker testing on the patient and her parents was indicative of maternal uniparental disomy for the entirety of chromosome 7. There was no known family history of similar symptoms.
On examination, the patient was small for age with preserved head size (head circumference 50\textsuperscript{th} %ile, length and weight <5\textsuperscript{th} %ile). She had a triangular-shaped face, mild frontal bossing, scooped nasal bridge, small mouth, flat philtrum, and mild lower limb size asymmetry, all consistent with RSS. There was diffuse hypotonia with diminished muscle bulk, but full strength. Multifocal myoclonus was present at rest and worsened with action without stimulus sensitivity. The myoclonus was most prominent in the head, shoulders, torso, and upper extremities. Focal dystonia of the right upper extremity was elicited with prolonged writing. Dystonia was not evident in other body regions.

Clinical evaluation included electroencephalogram, which showed generalized spike-wave discharges but no electrographic change during the periods of myoclonus. SGCE analysis did not identify any deletions. Treatment of the involuntary movements with medication was not pursued.

Discussion

The combination of multi-focal myoclonus and focal dystonia are consistent with MDS. The SGCE gene on chromosome 7 associated with MDS is maternally imprinted\textsuperscript{2}. In this case, RSS is due to mUPD7, which occurs in approximately 10% of cases\textsuperscript{3}. mUPD7 is also the likely cause of the patient’s MDS. There are two prior reports of MDS in patients with RSS caused by mUPD7 – one 36-year-old male who presented to a movement disorders clinic for evaluation of myoclonus, and one 6-year-old female with atypical RSS features\textsuperscript{4,5}. In the adult, the RSS diagnosis was made during the movement disorder evaluation. Our patient was previously erroneously diagnosed with essential tremor and then epilepsy.

We suspect that MDS, in those with RSS due to mUPD7, will be an increasingly recognized aspect of the clinical phenotype. Recognition of RSS features will be important for clinicians evaluating children with movement disorders, and recognition of MDS will be important for pediatric geneticists caring for children with RSS so that medications for involuntary movements and additional subspecialty referrals related to RSS complications are appropriately targeted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Financial Disclosures

Dr. Augustine is funded by NIH grant K12NS066098, and receives research support from the Food and Drug Administration, Tourette Syndrome Association and Batten Disease Support and Research Association. She received an honorarium for speaking at the 2012 AAN annual meeting.

Dr. Blackburn has no financial disclosures.

Dr. Pellegrino receives funding from Genzyme Therapeutics for work as a principal investigator in clinical trials.

Mr. Miller has no financial disclosures.

\textit{Mov Disord.} Author manuscript; available in PMC 2015 November 13.
Dr. Mink is funded by NIH grants R01NS060022, R01NS039821, CDC grant U01DD000510. He serves on the Tourette Syndrome Association Scientific Advisory Board, on the Dystonia Medical Research Foundation Medical and Scientific Advisory Committee, and on the Batten Disease Support and Research Association Medical Advisory Board. He receives honoraria from the American Academy of Neurology for work as Associate Editor of Neurology and from Edison Pharmaceuticals for serving on a Data and Safety Monitoring Board.

Funding source: Not applicable

References


