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Myoclonus-Dystonia Syndrome Associated with Russell Silver Syndrome

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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[12]. 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.

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On examination, the patient was small for age with preserved head size (head circumference 50th%ile, length and weight <5th%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[2]. In this case, RSS is due to mUPD7, which occurs in approximately 10% of cases[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[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.

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References

1. Zimprich A, Grabowski M, Asmus F, Naumann M, Berg D, Bertram M, et al. Mutations in the gene encoding [epsiv]-sarcoglycan cause myoclonus-dystonia syndrome. Nat Genet. 2001; 29(1):66–69. [PubMed: 11528394]
2. Grabowski M, Zimprich A, Lorenz-Depiereux B, Kalscheuer V, Asmus F, Gasser T, et al. The epsilon-sarcoglycan gene (SGCE), mutated in myoclonus-dystonia syndrome, is maternally imprinted. Eur J Hum Genet. 2003; 11(2):138–44. [PubMed: 12634861]
3. Abu-Amero S, Monk D, Frost J, Preece M, Stanier P, Moore GE. The genetic aetiology of Silver–Russell syndrome. Journal of Medical Genetics. 2008; 45(4):193–99. [PubMed: 18156438]
4. Guettard É PML-HK, et al. MYoclonus-dystonia due to maternal uniparental disomy. Archives of Neurology. 2008; 65(10):1380–85. [PubMed: 18852357]
5. Stark Z, Ryan MM, Bruno DL, Burgess T, Savarirayan R. Atypical Silver–Russell phenotype resulting from maternal uniparental disomy of chromosome 7. American Journal of Medical Genetics Part A. 2010; 152A(9):2342–45. [PubMed: 20684011]