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References


Atypical Stereotypies and Vocal Tics in Rett Syndrome: An Illustrative Case

Hand stereotypies are the signature sign of Rett syndrome (RTT) and their presence plays a key role in diagnosis. We have found that hand movements, which may involve the hands together or apart, are very standardized in individual girls. We also found additional stereotypies (including vocal ones) that changed over time, not previously reported in RTT and we hypothesized the existence of tics in this disorder.

Most studies stress that stereotyped hand movements coincide with or follow the disappearance of purposeful prehension in RTT; however, more recently, different studies reported stereotypies as coinciding with or preceding the loss of purposeful hand movements in this disorder. Thus we believe that the particularly compulsive stereotypies in patients with RTT are likely to contribute to loss or reduction of hand use.

We present the case of a girl with RTT with a very atypical presentation that illustrates the complexity of movement disorders and psychiatric symptoms that can be present in RTT and their probable interference in function.

In a center for autistic children a child psychiatrist noticed that one 6-year-old girl stood out from the majority of the other children in that she had intense eye contact.

This girl was the second child of an unrelated and healthy couple and her perinatal history was normal. Family history was unremarkable for tics, obsessive-compulsive symptoms, and neurologic or psychiatric problems. When she was born her occipital frontal circumference (OFC) was below the 5th percentile but increased progressively to 50 percentile by 6 months of age. She achieved head control at 3 months, grasped an object at 4 months, and had intentional prehension at 5 months. She walked unsupported and uttered her first words at 13 months. She never crawled.

She had a high pitched voice and echolalia. She spoke complex frequently coprolalic phrases and her vocabulary was notable for unusual words. She had some phobias and repetitive compulsive behaviors such as switching lights on and off and opening and closing drawers. She never acquired sphincter control.

At 4 years old she met DSM-IV diagnostic criteria for autistic disorder and developmental quotient (QD) evaluation...
with Griffiths Scale revealed mild mental retardation (global QD of 55%). Her clinical report indicates that by that time she already had hand stereotypies.

We evaluated her for the first time when she was 6 years and 9 months because of an increase in hand stereotypies accompanied by deterioration in manual abilities. She was a thin girl with bizarre face expression, intense eye contact and complex rhythmical movements with separate hands (Fig. 1 and video 1), and even more complex hand stereotypies with only one hand against her mouth or other people or dolls mouths (Fig. 1 and videos 1 and 2). She was able to manipulate objects but this was constantly interrupted by compulsive hand stereotypies (video 2).

She also closed her eyes repetitively, protruded her lips or grimaced (Fig. 1).

She answered simple questions in a high pitched voice and had echolalia only for unusual words.

Neurological examination, except for the mental retardation, autistic traits, and stereotypies, showed no abnormalities. OFC was in the 75th centile, height at the 50th, and weight below the 5th centile.

Cerebral MRI and EEG were normal. Genetic test confirmed the diagnosis of Rett syndrome with a missense mutation in the MECP2 gene (R133C). X-chromosome inactivation pattern (XCI) did not show a skewed XCI pattern.

At the age of 8 she presented frequent episodes of hypopnea and apnea which started 1 year earlier. She maintained the ability of speak, although spontaneous language has decreased. She also continued to have echolalia and coprolalia. She maintained the same manual stereotypies and showed new stereotypies with other topographies as mouth opening and rolling of the tongue (Fig. 1). She had no epilepsy but had occasional screaming or laughing spells. A resting and postural tremor of the upper limbs was now evident.

We think that the more mildly affected girl described here highlights the phenotypic variability of RTT. She was diagnosed as having classic autism and it was only after the age of 5, following a progressive increase in manual stereotypies, that she partially lost prehension. Some studies of autism report that stereotypies are correlated with its severity and with cognitive deficiency. In our patient, stereotypies also increased with the cognitive regression she experienced at 5 years.

Obsessions for repetition and sameness have not been described in RTT, perhaps because these girls are so profoundly retarded. One of her hand stereotypies is obsessively self-directed at her mouth or directed to the mouths of people or her dolls, which may be analogous to autistic interest in parts of objects.

Her hand stereotypies are very complex and the movements, albeit in the midline, are quite different from those we described in a series of RTT patients. Additionally, she has echolalia and coprolalia, vocal tics that have previously been reported in autism but never in RTT.

We conclude that in RTT, like in other disorders, stereotypies can be accompanied by tics and behavioral disturbances such as obsession and compulsion. However, its pathophysiology remains to be explained as well as the relation between these motor-behavioral disorders.

LEGENDS TO THE VIDEO

Segment 1. Complex self-directed hand stereotypes and complex hand stereotypes with separated hands.

Segment 2. This video illustrates the manual abilities of the patient. We also can observe complex hand stereotypes with only one hand against her mouth or dolls mouths. She was able to manipulate objects but this was constantly interrupted by compulsive hand stereotypes.

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Marked Diurnal Fluctuation and Rest Benefit in a Patient with Parkin Mutation

Video

Mutations in the gene encoding parkin cause autosomal recessive juvenile Parkinsonism (ARJP), a disease characterized by a highly beneficial response to levodopa (L-dopa), prominent dystonia, hyperreflexia, severe motor fluctuation, and more symmetric symptom onset. Although patients with parkin-associated ARJP may benefit from sleep, the detailed clinical characteristics of diurnal fluctuation and rest benefit have not been clearly demonstrated. We describe a juvenile Parkinson patient with parkin mutation who showed marked diurnal fluctuation and rest benefit together with excellent L-dopa response.

A 22-year-old man was admitted because of progressive gait disturbance, tremor, and bradykinesia for 6 years. At age 16, he began to experience abnormal forceful flexion of the left toes when playing basketball, but this abnormal posturing disappeared after he rested for about 10 minutes. Over time, these action-induced involuntary movements became worse, involving all four limbs and disturbing his daily activities. Four years later, he developed tremulousness of the arms and slowness of body movements. At that time, he was diagnosed at another hospital with “conversion disorder” because of the dramatic fluctuation of his symptoms. One year before admission, he experienced severe heaviness and slowness of his entire body, and he could no longer participate in any sports activities. There was no significant past medical history or neuroleptic exposure and no family history of neurological disorders.

On admission, he showed severe bradykinesia and rigidity of both arms and legs, along with postural tremor of both hands and dystonic posturing of both feet (see Video, Segment 1). He had severe postural instability, and his gait was very unstable without arm swings. His parkinsonian features showed marked diurnal fluctuation. On awakening in the morning, he had mild bradykinesia without rigidity or tremor, and his gait was normal (see Video, Segment 2). In the afternoon, his parkinsonian features recurred and became much worse in the evening, with severe micrographia, but dramatically improved after 10 minutes of rest (see Video, Segment 3). His UPDRS III subscore was 3 on awakening, increasing to 71 in the evening, but decreasing to 31 after lying in bed for 10 minutes. He was prone to mild irritability after disease onset. There was no cognitive impairment. Motor power and sensation were normal, deep tendon reflexes were normoactive and symmetric, and plantar responses were flexor bilaterally.

Complete blood count, biochemical screen, erythrocyte sedimentation rate, C-reactive protein, serum ceruloplasmin and

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FIG. 1. Multiplex ligation-mediated probe amplification (MLPA) results of the patient and his parents. In the parkin (PARK2) gene, patient’s father has a heterozygous deletion of exon 3 and his mother carries a heterozygous deletion from exon 1 to 4. The patient is compound heterozygous for these two deletions. The height of each peak reflects the gene dosage of the target region detected by each probe in this family (blue) or simultaneously tested controls (red). Open arrows show reduced peak height of target exons in the PARK2 gene. Filled arrow shows no peak representing homozygous deletion.