

The Rett Condition - Broad Clinical Variability - A Case Report Over Three Decades

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Abstract

A forme fruste *Rett* variant female with partially preserved speech remnants is described. She was first seen by the author at an age of 4 year. She then presented with an unspecific syndrome of moderate mental retardation. At follow-up when aged 32 she had successively through the years developed a number of *Rett* characteristic abnormal behavioural patterns and neurologic deviations, together convincingly indicating a *Rett* syndrome. However, this has been discrete and atypical in original presentation and first apparent in the long term clinical profile.

It is underlined that a whole battery of *Rett* peculiarities appearing with age should be present to allow diagnostic accuracy.

Keywords

Rett syndrome - Behavioural deviation battery - Mental deficiency

Introduction

Females with *Rett* syndrome (RS) are today known to present with a much more heterogeneous pattern of phenotypes than originally realized (2). Experiences through the last ten years indicate that a number of clinical variants exist. Transitions in clinical presentation between subtypes are numerous but some main forms emerge (Table 1). The etiology of RS is still unknown. Biological markers for diagnosis are lacking. Therefore, we still have to stick to combinations of characteristic clinical criteria and profiles to distinguish the important key group of classical RS (1). For identifying atypical variants within the biological RS entity guiding diagnostic support can be obtained from the presence of clusters of particular characteristic RS manifestations.

Table 1 *Rett* syndrome (RS) phenotype expressions.

I	Classical female RS /CR/	} Subtype: Early seizure onset
II	Atypical female RS	
1. Formes frustes (FF)		
a) Original (≥ 13 years old)		
b) Tentative (10-13 years old)		
2. Late childhood regression		
3. Preserved speech		
4. Congenital		
5. Other		
III. Male RS		

Diagnostic model

We have suggested a model for elucidating RS variants (3, 4). It is based on a combined pattern of main criteria and supportive clusters of peculiar symptomatology as presented in this issue of *Neuropediatrics* page 62. The supportive manifestations comprise odd clinical symptoms and signs which are known to appear with increasing age in the majority of classical RS school girls and adolescents, also in variants according to our experiences through the years (2, 3, 4).

The following case is an example of a late recognized variant of RS. It refers to a girl with unexplained moderate mental retardation, first seen by me in 1966 at four years of age and without any suspicion of RS. At age 32, 28 years later, she had successively developed a convincing cluster of RS symptoms and signs and a long-term clinical profile compatible with an atypical RS of forme fruste type.

Case report

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This now 32-year-old woman is the first and only child to non-consanguineous parents. She was born at term, the pre- and perinatal history was normal. She was considered completely normal through her first year of life with early eye contact, head balance and turning over. After that she slowly stagnated. When aged 8-9 months she insidiously lost some already acquired hand skills and interest in manipulation. She also lost acquired nuanced double-babble and became somewhat less communicative. She did not learn to creep but bottom-shuffled for the next year. She was unable to walk unsupported before age 2 1/2 - 2 3/4 years. When seen by a pediatrician at age 2 1/2 she was noted as generally developmentally delayed with floppy lower limbs. She was able to grasp but not to use her hands in a constructive way.

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4 years of age

Seen by the author in April 1966 she was considered moderately mentally deficient (\approx IQ 50). She did not speak, was floppy, had a proprioceptive dysfunction and was noted to be "pseudoataxic". She was not considered autistic and did not show hand stereotypies.

5 years of age

She slowly had learned to handle a glass for drinking and to put a spoon to her mouth. However, her mother first had to place the food in the spoon.

8 years of age

Severe "night screaming spells" lasting for many hours were the dominating problems. The walking pattern, as described by her mother, was interpreted to be of dyspraxic type. Hand stereotypies were noted, however, not of the characteristic RS hand-wringing type.

10 years of age

Episodic hyperventilation was repeatedly re-corded, also an increasing and problematic obstipation.

18 years of age

Atypical fits occurred and could be controlled with carbamazepine.

32 years of age

Seen by the author again, she was a small (157 cm), very special woman, selectively preserved as to intellectual capacity, yet largely functioning on a moderate mental retardation level. She presented herself with a cascade of partly incomplete words thrown out explosively. The staff of the group home where she lived told that she had at best around ten understandable words. She, no doubt, understood a lot of spoken information and could clearly point out what she liked and disliked. She communicated by means of a very intense eye pointing and staring, in addition finger pointing and arm gestures. Intermittently she demonstrated the characteristic wringing RS stereotypies. She showed the RS characteristic breathing irregularities, some hyperventilation, but more of apnoeic episodes. Her bruxism of creaking type was intense, like "my knee creaking" as her mother remarked. She had from history the peculiar RS "bloating" habit, and had at examination a tympanic belly. Her fine motor performance had again deteriorated. She did no longer feed herself with a spoon. She mainly used her hands for throwing and destroying, although she had learned to "greet with her hand". The staff spontaneously remarked that she

used to have inadequate and unexpected laughing spells. They also told that she was remarkably insensitive to pain, sometimes banging her head violently on the wall laughing stereotypically.

Her gross motor function was largely good. She moved with slight asymmetry indoors. Outdoors, however, she had more difficulties and only managed a smooth surface. At neurological examination dyspraxia dominated, more pronounced in the upper than the lower limbs. There was no spasticity, dyskinesia or tremor. She had an atrophy in her right calf, considered as neurogenic in type. She had a neurogenic type of scoliosis with a double curve and, in addition, a kyphotic neck position. Her feet were of ordinary size and without trophic disturbances. Head circumference was 54 cm.

Discussion

To summarize, this 32-year-old woman was considered to represent a case of forme fruste *Rett* variant with partially preserved speech remnants. In the RS variant diagnostic model (4) she fulfills 5 of the 6 A criteria and at least 8 of the 11 supportive B manifestations. Among the latter, particular importance should be given to the successive appearance of: additional unexplained neurology (neurogenic type of scoliosis and lower limb atrophy), a characteristic RS breathing pattern and, not at least, an intense type of RS eye pointing communication

When applying the model, it is important to emphasize the necessity of a *cluster* of supporting RS manifestations (group B), particularly so when the information on main criteria (group A) is fragmentary. The presence of single manifestations, e.g. isolated handwringing in a mentally retarded girl, should always be regarded with great caution. Such signs do exist also outside the RS area! Loss of acquired skills in the critical period of late infantile development, followed by some "catch-up" is much more in support of a potential RS. Again, a whole battery of peculiarities appearing with age should be present to get convincing diagnostic accuracy.

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