Case Report: Retracing Atypical Development: A Preserved Speech Variant of Rett Syndrome

Peter B. Marschik · Christa Einspieler · Andreas Oberle · Franco Laccone · Heinz F. R. Prechtl

Published online: 18 February 2009 © Springer Science+Business Media, LLC 2009

Abstract The subject of the present study is the development of a girl with the preserved speech variant of Rett disorder. Our data are based on detailed retrospective and prospective video analyses. Despite achieving developmental milestones, movement quality was already abnormal during the girl’s first half year of life. In addition, early hand stereotypies, idiosyncratic vocalizations, asymmetric eye opening, and abnormal facial expressions are early signs proving that this variant of the Rett complex, too, manifests itself within the first months of life.

Keywords Autism spectrum · Development · Genetic disorder · General movements · Language · MECP2 · Stereotypies

A Rett variant shares with the classical Rett syndrome the same staging and a number of symptoms including hand stereotypies. Girls with the Preserved Speech Variant (PSV) preserve or recover speech and language abilities to a certain extent and can potentially improve their purposeful hand movements (Zappella 1992; Hagberg and Skjeldal 1994; Zappella et al. 1998; Renieri et al. 2008). The majority of patients carries either missense mutations, especially the p.R133 change, late truncating mutations in the MECP2 gene but also at least in one case an early truncating mutation (Renieri et al. 2008). As the diagnosis of Rett syndrome and its variants is tentative until at least toddler age, there is little comprehensive knowledge of pre-diagnostic development. The only objective evaluation of possible behavioral abnormalities before regression consists in a close analysis of family videos from the first 2 years of life. We provide a unique case report of a girl with a PSV, having observed her neurological and socio-communicative development longitudinally over a period of 10 years.

Subject At the age of three, a girl born in Germany in 1998 was clinically diagnosed with Rett syndrome. Genetic testing at 3 years and 9 months of age revealed a large intragenic deletion (c.378-43_964delinsGA). This mutation most probably causes a complete loss of function of MeCP2. The patient meets, however, the inclusion criteria for Rett variants (Hagberg and Skjeldal 1994) and is now classified as PSV (Zappella et al. 1998). The girl was a singleton birth at 40 weeks of gestation; birth weight 2,970 g; length 53 cm; occipitofrontal circumference 34 cm; Apgar scores 9 (1 min) and 10 (5 min).

Methods The focus of this report lies on longitudinal observations of age-specific motor and postural patterns as well as the
child’s behavior, documented by videotapes. We retrospec-
tively analyzed family videos, parental diaries and the
medical history of the first years of life. Prospectively, the
following assessments were applied: the Austrian Rett sur-
vey; behavioral observations in the girl’s natural
surroundings; the Austrian Communicative Development
Inventories (Marschik et al. 2007); spontaneous speech
samples; various language development tests. Observational
data were obtained by means of the Observer program
(Noldus Information Technology, The Netherlands). Two
independent scorers (CE, PBM) achieved a high interscorer
agreement (Cohen’s Kappa = 0.91).

General Motor Performance
At 6 months of age the girl could roll from supine to prone
and back; she had a good anticipatory shift of the center of
gravity before reaching sideward or upward while sitting;
she crawled at 9 months and stood free at 11 months; she
walked independently at 14 months. At 17 months she
performed coordinated belly dancing. Despite achieving
the gross motor milestones, she showed abnormal move-
ments during her first months of life. The body movements
that are most common at this early stage are so-called
general movements with a strictly age-specific appearance
(review: Einspieler and Prechtl 2005). Our test subject
showed fidgety general movements that were abnormal and
slow in comparison with normal fidgety movements (i.e.
contiguous small movements of moderate speed with a
variable acceleration of neck, trunk and limbs in all
directions) (Prechtl et al. 1997).

Although the girl developed coordinated crawling, she
exhibited excessive rolling between 8 and 10 months of
age. At 2 years and 4 months of age her gait became
instable and the gait width was broad, invariable and
maladjusted.

Hand and Finger Movements
Aged 3 months, the girl reached for objects; at 8 months
she demonstrated good pincer grasping; at 10 months she
started using gestures to express needs, including index
finger pointing; at 14 months she could feed herself and
drink from a cup. However, when she started pincer
grasping she also touched objects with undifferentiated
movements with her fingers mainly extended. Stereotypical
hand movements for the first time occurred at the age of
6.5 months in terms of repetitive uni- or bilateral hand
pronation with simultaneous wrist dorsiflexion and finger
spreading. These stereotypical hand movements co-occurred
but were not synchronized with repetitive opening and
closing of the mouth. Aged 16 months, she occasionally
exhibited wiping hand movements; at the age of two, we
observed the first excessive hand rubbing after the girl got
frustrated.

Facial Expressions
Every now and then, blinks were rare. At 7 months of age
the girl even showed a prolonged phase of staring. In
addition, eye opening after a blink was sometimes per-
formed asymmetrically. At 2 years and 4 months of age,
the first awkward mouth movements and bizarre grimaces
were observed. At the age of 6 months, repetitive
unmodulated vocalizations were present. At the same age
the girl showed bursts of abnormal facial expressions
consisting of several repetitions of the following sequence:
head in midline with neutral facial expression (second 1);
head turned sideward with a crying expression often
combined with atypical inspiratory vocalization (second 2);
head in midline with neutral facial expression (second 3);
etc.

Early Communication
Normal babbling was interspersed with atypical episodes of
forceful and/or inspiratory vocalizations often associated
with grimaces of effort. Intentional gestures were limited
and partly used in an inappropriate manner. The girl uttered
her first words around her first birthday but was unable to
combine words before the regression period.

Apparently Reduced Nociceptive Sensitivity
It was remarkable that the girl did not complain when her
excessive rolling locomotion was stopped by bumping into
the door frame; when walking barefoot on gravel; when
falling down; and even when plunging her head under
water.

Regression Period
By the time the girl was aged two her parents were seri-
ously concerned: previously acquired language skills had
worsened or entirely disappeared; she withdrew from
normal social contact; she would run around aimlessly and
in a disquieting manner, often screaming; purposeful hand
movements had deteriorated; she gradually lost the ability
to feed herself and half a year later stopped using her right
hand. Rubbing and washing hand movements as well as
hand-to-mouth and hand-to-tongue contact and manipulations became more frequent. Our video analysis has confirmed the parents’ concerns.

At the age of three, Rett syndrome was clinically diagnosed. Her gait had remained unstable; her muscle tone was low; reduced nociceptive sensitivity was confirmed. Autistic features became more prominent and her behavior was increasingly dominated by routines, obsessions and ritual actions.

Post-regression Period

Over the next 4 years lost or fragmentarily preserved skills were slowly regained. This period was marked by a slow but steady improvement of gross and fine motor functions, a reduction of autistic behavior; and by a recovery of speech and language. Her phonological and morphosyntactic skills, the lexicon size and composition as well as the complexity of phrasal structures slowly increased, albeit frequently accompanied by idiosyncratic vocalizations, rhythmic prosodic events, and out of context speech.

Current Status

Today, at 10 years of age, the girl has a relatively complex language system with a lexicon size comparable with that of a preschooler. Nevertheless, she has a limited accuracy of articulation and a significant phonological deficiency. There are also morpho-syntactic and socio-pragmatic limitations as well as dysfluency of speech, mostly caused by immediate echolalia or repetitive questioning.

She still shows autistic behavioral characteristics such as finding it hard to recognize borders of intimacy. She needs fixed patterns and shows obsessive behavior (e.g. repetitive checking if there is enough bread). She can be described as hyperkinetic, highly distractible and unable to make decisions. She is hypersensitive to noise and, once excited, can hardly be calmed. She exhibits distinct mood disturbances, unprovoked bursts of anger and seemingly motiveless episodes of sadness or laughter.

She preferably uses her left hand although dyspraxia is noticeable. Hand stereotypies, which are more frequent in her right hand, predominantly consist of hand-to-mouth/tongue contacts. Bilateral hand stereotypies like washing, rubbing, or clapping movements are rare. She has regained the ability to feed herself and even uses forks and knives. Gait and balance are more stable now, but for long distances she uses a wheelchair.

The girl’s head circumference is still below the 3rd percentile while weight and height are within the normal range. She shows the following satellite signs typical for Rett syndrome (Kerr et al. 2001): mild scoliosis; muscle hypotonia; hypersalivation; moderate circulation problems in terms of cold extremities; sleep disturbances; crying spells; aerophagea and hyperventilation during episodes of excitement or anger.

It is worthwhile mentioning that beside her musical aptitude the girl takes riding lessons, does trampolining and likes swimming. Furthermore, she is able to handle a computer mouse when playing drag and drop games.

Discussion

The uniqueness of this case report is twofold: (1) we provide a longitudinal assessment of a girl with PSV based on comprehensive video data; and (2) we focused not only on the achievement of developmental milestones but also on the quality of the performance. Our detailed analysis has revealed that as early as during the first half a year of life the main pattern of motor activity (i.e. the general movements) was clearly impaired. Abnormal, slow fidgety movements, as observed in the reported case, have also been described in girls with classical Rett syndrome (Einspieler et al. 2005a, b). These abnormal movements, which correspond with neuropathological reports on brainstem impairments (Armstrong 2005), indicate deficiencies in the brainstem at this early age. In addition to these abnormal fidgety general movements, the early appearance of hand stereotypies, idiosyncratic vocalizations, prolonged asymmetric eye opening after a blink, and bursts of abnormal facial expression are in accordance with previous studies on girls with classical Rett syndrome (Einspieler et al. 2005a), which proves conclusively that this variant of Rett disorder, too, manifests itself within the first months of life. This contradicts other reports describing a normal development of girls with PSV during their first 6 months of life (Zappella 1992; Zappella et al. 1998). This discrepancy might be explained in terms of different methodological approaches: While the data of other PSV case reports on the pre-regression period are based on parental interviews and medical records, ours is the first study on the early development of a girl with PSV carried out by means of standardized video analysis. It may also be possible, that a subgroup of PSV Rett patients carrying an early truncating mutation (Renieri et al. 2008; this case) may have more likely subtle signs in their first 6 months of life. An investigation by standardized video analysis of a larger cohort of PSV patients carrying “mild” mutations could provide data to the issue of early developmental dysfunctions of those patients.

The comprehensive longitudinal analysis has revealed not only the early onset of conspicuous signs but also that these signs are interspersed with typical patterns of motor...
and communicative development. The conspicuity became more and more prominent as the onset of regression was approaching. These findings might potentially help to identify a possible genetic mutation in children at an early age.

Acknowledgments We would like to thank our test subject and her extended family in Germany and Austria for their participation, cooperation, effort and kindness. We would further like to thank Dr. Alison M. Kerr for her continuous support and encouragement; Professor Angus Clarke for sharing his expertise in genetics; and scriptophil.die textagentur (Miha Tavcar) for editing the article. This study was supported by the Austrian Science Fund (FWF; P19581-B02) and the Lanyar Foundation (P325).

References

Armstrong, D. D. (2005). Neuropathology of Rett syndrome. Journal of Child Neurology, 20, 747–753. doi:10.1177/0883073805020082401.

Einspieler, C., & Prechtl, H. F. R. (2005). Prechtl’s assessment of general movements: A diagnostic tool for the functional assessment of the young nervous system. Mental Retardation and Developmental Disabilities Research Reviews, 11, 61–67. doi:10.1002/mrdd.20051.

Einspieler, C., Kerr, A. M., & Prechtl, H. F. R. (2005a). Is the early development of girls with Rett disorder really normal? Pediatric Research, 57, 696–700. doi:10.1203/01.PDR.000015945.94249.0A.

Einspieler, C., Kerr, A. M., & Prechtl, H. F. R. (2005b). Abnormal general movements in girls with Rett disorder: The first months of life. Brain & Development, 27, 8–13. doi:10.1016/j.braindev.2005.03.014.

Hagberg, B., & Skjeldal, O. H. (1994). Rett variants: A suggested model for inclusion criteria. Pediatric Neurology, 11, 5–11. doi:10.1016/0887-8994(94)90082-5.

Kerr, A. M., Nomura, Y., Armstrong, D., Anvret, M., Belichenko, P. V., Budden, S., et al. (2001). Guidelines for reporting clinical features in cases with MECP2 mutations. Brain & Development, 23, 208–211. doi:10.1016/S0387-7604(01)00193-0.

Marschik, P. B., Einspieler, C., Garzarolli, B., & Prechtl, H. F. R. (2007). Events at early development: are they associated with early word production and neurodevelopmental abilities at the preschool age? Early Human Development, 83, 107–114. doi:10.1016/j.earlhumdev.2006.05.009.

Prechtl, H. F. R., Einspieler, C., Cioni, G., Bos, A. F., Ferrari, F., & Sontheimer, D. (1997). An early marker for neurological deficits after perinatal brain lesions. Lancet, 349, 1361–1363. doi:10.1016/S0140-6736(96)10182-3.

Renieri, A., Mari, F., Mencarelli, M. A., Scala, E., Ariani, F., Longo, I., et al. (2008). Diagnostic criteria for the Zappella variant of Rett syndrome (the preserved speech variant). Brain & Development, doi:10.1016/j.braindev.2008.04.007.

Zappella, M. (1992). The Rett girls with preserved speech. Brain & Development, 14, 98–101.

Zappella, M., Gillberg, C., & Ehlers, S. (1998). The preserved speech variant: A subgroup of the Rett complex: A Clinical report of 30 cases. Journal of Autism and Developmental Disorders, 28, 519–526. doi:10.1023/A:1026052128305.