RETT'S SYNDROME : A CASE REPORT

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ABSTRACT

Rett's syndrome is a rare condition affecting only the girl child. It presents as a pervasive developmental disorder with a remarkable behavioural phenotype. The cause for this remains unknown but genetic factors and brain dysfunction have been implicated. This case report emphasises the importance of being aware of rare yet significant disorders of interest to neuro-developmental psychiatrists.

Key words: Rett's syndrome, pervasive developmental disorder, developmental disability, learning disability, speech regression, growth retardation

Rett's Syndrome (RS) was first described in 1966 by Andreas Rett in Vienna (Rett, 1966). During the 17 years period (1966-83), only 3 original medical reports were presented. In the period 1984-90, more than 200 research studies appeared. Since this time a great deal of new biochemical, physiological and genetic data has been collected. Rett's syndrome, is a profoundly handicapping and a progressive neurological disorder. It is one of the most frequent causes of mental retardation which only affects girls. This syndrome has been independently recognised throughout the world and is a rare condition with a prevalence estimated at 1 in 15,000 female births (Hagberg, 1985).

Clinical Picture

After 6-12 months of nearly normal development there is a period of developmental stagnation, followed by, from 12 to 18 months by a regression in language skill, deceleration of head circumference, the appearance of seizures (in 80% of cases) and the emergence of the remarkable behavioural profile. Typically there is an autistic withdrawal accompanied by seizures, stereotypic midline hand movements - notably hand wringing, agitation, hyperventilation and breath holding accompanied by screaming attacks. Then follows a truncal ataxia, hyperreflexia, spasticity and dystonia to leave an adult who is severely mentally and physically handicapped (Naidu et al., 1986). Depression and anxiety are frequent, with self-injury and panic when threatened. Myoclonus, although reported in some series has never been characterised. Growth failure is a major aspect of the development arrest in RS. Small hands and feet have been reported anecdotally. There is a large variability in motor disability patterns with age even within the nucleus group of "Classical RS". About 80% become severely invalidated, more or less completely immobilised. In contrast, 15-20% seem to remain relatively spared through the years and with possibilities to walk and struggle around. Also the amount of preserved intellectual capacity varies considerably between RS females, independent of ageing and profile of motor incapacity. Memorizing and recognising are the abilities which seem to be spared in many elderly RS women. They seem to recognise and know more than we realise but experience extensive difficulties to sort out, integrate, process and express their "thinking" for communication. Vision, hearing and smelling are mainly intact. Involvement of the autonomic nervous system in RS is suggested by neonatal
level of cardiac vagal tone, poor autonomic integration and multiple breathing dysrythmias showing medullary immaturity in RS.

The mortality rate in RS is 1.2% per annum, 48% of deaths occurring in debilitated people, 13% from natural causes, 13% with prior seizures and 26% sudden and unexpected (Kerr et al., 1997).

CASE REPORT

A four and half year old female child was seen with the concern of absence of speech and failure to learn. Elder of the two siblings in a healthy family of a young Sikh couple, she was born to a non-consanguinous marriage, and had a younger brother about 30 months old at the time of initial assessment. Born in a normal delivery at full term, she weighed 3100 gm at birth, with a head circumference of 33 cm. There were no significant developmental problems but could be considered as late normal. She sat at 8 and walked at 14 months. She learned some single words by age 20 to 22 months. Later by about 28 months she is reported to have acquired a vocabulary of some 20 words, and by 30 months learned to communicate by joining 3 to 4 words. This point was emphasised by her mother, who saw a relation (actually a temporal coincidence) of her deterioration with the coming of the second child. It is from around that time i.e. around 30 months, that she is said to have lost her speech and deteriorated. Fine motor abilities were also almost normal until the same period after which hand skill deterioration was observed. However, she still managed to eat with a spoon and retained even some sort of pincer grasp, but she no more played constructively with use of her hands. The girl was pleasing in appearance, but was short and overweight, with no dysmorphic features. She could sit comfortably and independently, walked and ran with a wide based gait and without failure.

The child's expressive speech included unintelligible sounds and screams, and her ability to comprehend speech was impaired but not totally lacking. It was possible to make eye contact with her and she did not show aversion to physical contact. There was a delay in achieving sphincteric control (but not regression as she had not achieved continence when regression started) and indicated her need to void through vocalisation or showing uneasiness of being incontinent. Her head circumference measured 46.5 cm, but had no physical deformity such as scoliosis, kyphosis or a systemic defect. She had typical midline purposeless hand movements - wringing, clapping and mouthing. She also had episodic hyperventilation, grinding of teeth, and grimacing of the face. There was no history of having had a seizure so far, and EEG's were almost normal. MRI scan done did not reveal any structural brain lesion that would explain the regression and arrest of her development. There was no history of mental retardation in any first or second degree relatives and no suggestion of similar or other type of pervasive developmental disorder was present. She screamed intermittently without any obvious reason.

DISCUSSION

The spectrum of pervasive developmental disorders and conditions associated with learning disability is wide. This child meets the diagnostic criteria of Rett's syndrome. She definitely had regression of language and small head size with developmental delay especially of intellectual abilities with severe learning disability in addition to the typical motor features as described for the Rett's syndrome. Rett's syndrome is classified separately (F 84.2) under the category of pervasive developmental disorders (F 84) in the ICD-10. As there are no known biochemical, genetic, or morphological markers, diagnosis is based on clinical phenotype dependent upon the co-existence of three groups of features (Trevathan and Moser, 1988).

1. A history of slowing of development always followed by loss of previously acquired skills.
2. Marked changes in emotional development and behaviour especially withdrawal and anxiety.
3. Emergence of a variety of stereotyped behaviours, most commonly involving the hands.
RETT'S SYNDROME

The differential diagnosis is not usually difficult after the age of 4 or 5 years. Olsson and Rett (1987) suggest that the similarity with autism is more apparent than real, with most affected girls showing a level of social interest, communication and play that is appropriate to their very low mental age. Other conditions that may need to be considered in differential diagnosis are the disintegrative disorder, mesial encephalitis, cerebral lipoidoses and leukodystrophies. Despite the commonly held opinion that there is regression after a period of normal development, it has been reported that the girl with RS may not be normal at birth. They tend to have lower birth weights, lower head circumference at birth after corrections, some perinatal difficulty and development of behaviour may have been unusual in the first 6 months (Leonard and Bower, 1998). From as early as 12 months, abnormal hand movements appear, such as twirling of the hands at the sides, tapping the chest, pulling hair or ears. Gradually the movements become more stereotyped, less purposeful and occur increasingly in the midline, sometimes being performed behind the child's back, but always in the midline (Naidu et al., 1986). By 5 years characteristic hand-wringing, licking, sucking and biting occur in virtually all children. There is little doubt that these movements are a direct outcome of the biological basis of Rett's syndrome (Iwata et al., 1986).

Furthermore the hand stereotypies are part of a more general neurodevelopmental abnormality; language never progresses beyond the possession of 2 or 3 phrases or words and there are signs of poor motor development; gait apraxia may develop, some children being unwilling to walk at all, and hyperreflexia with sustained ankle clonus can be found. Hyperventilation, breath-holding, bruxism and tremulousness are all common, but not specific to Rett's syndrome (Naidu et al., 1986). With increasing awareness of RS, referrals for conditions appearing with striking 'Rettoid' clinical manifestations, but not fulfilling the RS criteria are seen.

Thus Rett's syndrome represent a neurodevelopmental disorder of uncertain pathogenesis, featuring an apparent arrest in normal maturation during the perinatal period. RS is commonly thought of as an X-linked dominant disorder lethal to hemizygous males. Familial cases of RS are rare. The few familial cases would arise through mosaicism or because of occasional females failing to manifest the disorder through skewed X inactivation in relevant cell types. Studies using multiple informative markers indicate that the RS locus is likely to be located close to one of the X-chromosome telomeres, most likely region for the RS gene is the distal part of Xq (Xq28) (Xiang et al., 1998).

In trying to explain origin of RS, a two-step process could be reasonable to suspect. A genetic age-dependent deficiency as a basic predisposing factor (with a complex type of recessive transmission?) with superimposed trigger factors which could be of alternative types, specifically acting on the developing brain cell program. Abnormalities in multiple neurotransmitter/receptor systems (dopaminergic, glutamatergic, and cholinergic), whether primary or secondary, underscore the pervasive effects of this maturation arrest.

There is no specific treatment for the symptoms of Rett's syndrome. Many of the drugs used in other handicapping conditions have a place in the management of RS. Physiotherapy and hydrotherapy can greatly help the girls, not only by preventing stiffness and deformities in the joints, but also by encouraging movement, walking and toning of the muscles. Lamotrigine has been reported useful in controlling seizures in RS, and even bad tantrums may improve, making the girl happier, more alert, more able to concentrate and improved in contacting (Stenbom et al., 1998).

This case is reported, firstly for the rarity of RS and secondly for its clinical interest to neurodevelopmental psychiatrists. Assessing children with learning and developmental disabilities poses interesting challenges in diagnosis and management. Familiarity with significant even if
uncommon conditions should be aimed at during the specialist training. Difficulties dealing with developmentally disabled children includes bringing acceptance in the affected child's family. Therefore a correct diagnosis helps to address many issues related to working with the affected family.

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