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RETT SYNDROME: A CASE REPORT

Paediatrics

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ABSTRACT

Background-Rett syndrome is a very rare disorder characterised by severe neurodevelopmental delay affecting mostly girl child due to mutation of MECP-2 gene. The cause of this remains unknown but brain dysfunction and genetic factors have been implicated. **Clinical features-** We present one such case of 3 year 8-month-old female with no prior diagnostic intervention who presented with multiple episodes of convulsion (GTCS). History revealed normal physical development and normal achievement of developmental milestone for the first 1yr of life, followed by regression of acquired hand skills and speech, and appearance of midline stereotypical hand movement after 1.5 years of age. **Treatment-** Mainstay of treatment focussed on counselling of parents about the illness and taking multidisciplinary approach. Patient was discharged in a stable condition with antiepileptic drugs for controlling seizures, given high calorie diet for proper growth and referred to DEIC Unit of our Department for physiotherapy and speech therapy which will eventually help to increase the quality of life. **Conclusion-** This case report emphasises the importance of being aware of rare yet significant disorder of interest because early identification and timely intervention can help both the patient and their families in improving quality of life.

KEYWORDS

MECP-2, Regression, Rett syndrome, Stereotypical midline hand movement.

INTRODUCTION:

Andreas Rett, an Australian physician, first described Rett syndrome after seeing two girls seated in his waiting room displaying strikingly similar handwringing mannerism. Unable to find a known classification of this disorder, Rett published a report in German in 1966 describing a syndrome consisting of stereotypic hand movements, ataxia, dementia, autistic behaviour, cortical atrophy and hyperammonaemia – it was termed cerebroatrophic hyperammonaemia, a term that was later discarded [1].

Meanwhile, unaware of Rett's work, Bengt Hagberg in Sweden reported patient's displaying similar symptoms. In 1980 he presented a paper at European Federation of Child Neurology Societies describing 16 girls[2]. After that Rett Syndrome was recognized, characterized by neurodevelopmental arrest, loss of communication skills, diminished interest in surroundings, deceleration of head growth from 6-18 months of age, stereotypical hand movements, severe dementia with autistic features, ataxic gait, hyperventilation and seizures [3]. This syndrome is independently recognised throughout the world and is a rare condition with a prevalence estimated 1 in 15000 female births[2].
INDIAN SCENARIO – The first Indian case of Rett Syndrome was reported in 1944[4]. The incidence in India is about 1/10,000-22,000 live births [5]. Paucity of knowledge in Indian Literature misdiagnosed Rett syndrome as a case of Cerebral palsy.

CASE REPORT

A 3year 8 months old, female child born out of non-consanguineous marriage, 1st order by birth, presented to our hospital with complaints of multiple episodes of Generalised Tonic Clonic type of convulsion (GTCS), each episode lasting for 2-3 mins. On the next day of admission intermittent clonic movement of left upper limb was seen. There was no associated history of fever, vomiting, loose stool, cough and cold or feeding difficulty.

On general examination there was no pallor, icterus, cyanosis, clubbing and edema. Vitals were stable. There was no facial dysmorphism, skin pigmentation, bulging over the spine, dimpling or tuft of hair over sacral region or skeletal deformity noted. Anthropometry revealed a length of 93cm; weight- 8 kg; Mid upper arm circumference (MUAC)- 13 cm and a head circumference of 43cm. On plotting on WHO Growth Chart for girls, weight for length was < 3rd percentile, weight for age was < 3rd percentile, length for age was between 3rd and 15th percentile and head circumference was < 3rd percentile. On neurological examination, the patient was conscious and alert. Hypotonia was noted in all four limbs. Superficial and deep reflexes were normal. Bladder bowel control is achieved. There were no signs of meningeal irritation.

As per mother, the pregnancy was uncomplicated and delivered by LUCS at 42 weeks gestational age, singleton pregnancy. The baby cried immediately after birth, birth weight was 2.25kg and was admitted at SNCU as a case of low birth weight with feeding difficulty for 7 days. Immunisation is up to date.

Developmental history revealed that all milestones were achieved as per age till 1.5 years of age- social smile at 2 months, head holding at 3 months, could speak bisyllables by 7months, sit with support at 6 months, stand with support at 1 year , walk with support at 1.5 years, bidextrous grasp at 8 month and monodextrous grasp at 1 year of age and could follow mother's command for feeding and playing. There were no significant developmental problems but could be considered as late normal.

After the age of 1.5 years, mother noticed that the child was not gaining milestones as per her peers of same age group, the child gradually lost interest in surrounding, made no eye contact with mother or any other people, did not respond to mother's voice command for feeding, playing and did not follow any illuminating object. The child did not achieve any further milestone but rather began to lose already acquired hand skills of bidextrous and monodextrous grasp, at 2 yrs of age she could not sit with support and at 2.5 years of age she could not stand and walk with support. Speech had regressed to mere babbling. On observation we found that the patient had a characteristic midline stereotypical hand movement, repeatedly made a fist with both her hands and touched them to her face with thumb sucking behaviour. She also shows characteristic rocking movement and had truncal ataxia. There is no history of seizure disorder or intellectual disability in any first- or second-degree relative.

Routine laboratory investigations and thyroid profile were normal. There was no abnormality found in MRI of Brain but EEG was abnormal suggestive of seizure disorder.

Mutation analysis study could not be done due to unavailability of

resource in our hospital. Party could not afford for the same to be tested at higher centre but the clinical profile was so characteristics that we could make a diagnosis of Rett syndrome with sufficient confidence.

Fig: Showing midline stereotypical hand movement

MANAGEMENT-

1. Mainstay of treatment was counselling of parents about the illness and prognosis of the illness and taking multidisciplinary approach.
2. Growth retardation was handled by advising high calorie well balanced diet with locally and easily available foods.
3. Regular follow-up with physiotherapy at DEIC was advised.
4. Syrup levetiracetam and Syrup Valproate was used for controlling convulsion.
5. Regular follow up for monitoring of physical changes such as scoliosis, gastrointestinal issues was advised.
6. Occupational therapy was started to improve purposeful use of the hands for activities such as dressing and feeding.
7. Speech therapy was introduced to improve child's language milestone by teaching nonverbal ways of communicating and for social interaction.
8. Early intervention programs, school and social services may help with integration of various programmes in school, work and social activities.

CASE DISCUSSION

Rett syndrome occurs due to mutation in MECP-2 gene. Initially it was thought to be strictly affecting females, the disease has also been identified in males. Male foetuses with Rett syndrome, associated with MECP-2 mutation has low survival rate. There have been several cases of 46XY karyotype males with a MECP-2 mutation carried to term were affected and died before the age 2 years[6].

Clinical features of Rett syndrome including the age of onset and severity of symptoms, varies from child to child. As there is no known biochemical, genetic, or morphological markers, diagnosis is based on clinical phenotype dependent upon the coexistence of three groups of features[7]-

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

So, we can say she definitely had Rett syndrome as there was regression of milestones, a pattern of deceleration across all growth measurement including head size and appearance of stereotypical abnormal hand movements.

Abnormal hand movements become gradually more stereotyped, less purposeful and occurs always in midline. By 5 years characteristics hand wringing, licking, sucking and biting occurs in virtually all children[7].

Language never progresses beyond 2 or 3 phrases or words. Gait apraxia and, truncal ataxia may develop. Hyperreflexia with sustained clonus can be found. Hyperventilation, breath holding, bruxism and tremulousness are all common but not specific to Rett syndrome[8].

Although most girls with Rett Syndrome demonstrate abnormal EEG tracing, seizure activity is not universal. By adolescence, approximately 75% patients are in wheelchair bound or bedridden[2].

Genetics- The MECP-2 gene contains instructions for the synthesis of methyl cytosine binding protein 2(MECP-2 protein), which is needed for neural development especially synaptic functions. Mutations in gene cyclin dependent protein kinase 5(CDK5) OR FOXG1 have been found in less than 10%cases. Sporadic mutation is seen in at least 95% of Rett syndrome cases. There mutation is de novo and not inherited from either parent[9].

Management-An integrated multidisciplinary approach is needed consisting of counselling of patient, symptomatic treatment, supportive medical management, speech and physiotherapy and social support services. Pharmacotherapy in the form of bromocriptine, magnesium citrate, L-carnitine (may help improve language skills, muscle mass, alertness, energy, and quality of life), naltrexone (to stabilize breathing irregularities) and levodopa (to alleviate muscle stiffness) have been tried for symptoms control without reasonable success[10]. Seizures are tried to control with the help of Antiepileptic drugs like levetiracetam, valproate, lamotrigine, etc. High calorie and high fat ketogenic diet have reported weight gain along with diminished stereotype behaviour and better seizure control. Early intervention programs and school and social services may help with integration into school, work and social activities. Currently there is no curative treatment available, but trials with IGF (insulin like growth factor 1) has been shown to partially reverse signs in MECP-2 mutant mice[11].

CONCLUSION

There are many areas of Rett syndrome which are yet to be discovered. All female children with regression of acquired milestones, low intelligence and autistic symptoms following a normal period of development should be suspected of having RS until proven otherwise.

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Declaration Of Consent:
Proper informed consent has been taken from the legal guardian of the patient regarding the publication of the information.

CONFLICT OF INTEREST- None.

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