

RETT Syndrome: A Tryst with Development and Dilemma

Subham Basu¹, Subhajit Saha²

¹MBBS Internees, Department of Pediatrics , IQ City Medical College & Hospital , Durgapur, West Bengal, India
¹sbhmbasu[at]gmail.com

²MBBS Internees, Department of Pediatrics , IQ City Medical College & Hospital , Durgapur, West Bengal, India
²zeviar0[at]gmail.com

Abstract: *“What the eye doesn’t see and the mind doesn’t know doesn’t exist even if it does”- quoted by English writer D H Lawrence is most commonly used in the medical field and to cite a perfect example of it we present a rare disease, Rett Syndrome which we although know , doesn’t strike in our mind. It is a rare X-linked dominant and severe neurodevelopmental disorder found only in females falling under Autism Spectrum Disorder(ASD) causing severe intellectual disability. We report one such case of a 16 year old girl who remained misdiagnosed as cerebral palsy for a long period of time , presented to the Accident and Emergency of IQ City Medical College & Hospital with history of fever, multiple episodes of generalised tonic clonic convulsions , stereotypical hand movements and history of neuro-developmental regression.*

Keywords: Rett syndrome, ASD, Cerebral Palsy, Neurodevelopmental Regression

1. Introduction

Rett syndrome (RS) was first described by an Austrian physician, Andreas Rett hence the name. Initially believed as a neurodegenerative disorder was later proved to be of genetic origin, caused due to mutation in the Methyl CpG binding protein 2 (MECP2) gene. It is characterized by developmental arrest noted as per delayed developmental milestones, loss of communication, deceleration of head growth from 6 to 18 months of age, stereotypical hand movements, severe dementia with autistic features, ataxic gait, seizures. Diagnosis is mainly clinical after excluding the neurodegenerative and other causes of delayed milestones. There is a large variability in motor disability patterns with age even within the nucleus group of "Classical RS".

In Indian scenario the incidence is about 1 in 10,000 to 15,000 live births although information is very limited due to underdiagnosis. 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.

2. Case Report

A 16 year old girl presented to our Accident & Emergency Department in a drowsy condition with chief complaints of fever, occasional episodes of seizure with stereotypical hand movements for last 3 days which got aggravated since morning with no history of diarrhoea and cough. On detailed enquiry it was learnt that a private setup previously diagnosed it as a case of cerebral palsy with uncontrolled seizure at her age of 2 years. On taking further history we got to know the seizure episodes started 10 years ago and were occasional with ictal cries for which she was on anti-epileptic medication. On initial examination at the emergency room , the girl was drowsy with GCS-E₄ V₄ M₄ and hemodynamically stable with oxygen saturation at 97%

with 2L/min O₂ via simple face mask and a CBG of 113mg/dl. The patient was managed with Inj. Levera , Inj. Lopez and Inj. Eptoin in the emergency room and was admitted in Pediatrics Intensive Care Unit for further observation and care.

After admission her anthropometric measurements were assessed as weight being 21.4 kg with a percentile of 0.1% and a Z-score of -12.98 and head circumference of 47.5cm which was <1% percentile (-6.4 SD).

Relevant basic blood investigations were sent to rule out other causes such as infections, electrolyte imbalance etc. The treatment commenced with i.v. fluids, broad spectrum antibiotics and convulsions were managed and prevented by Inj. Levetiracetam. Now for finding the underlying cause her detailed developmental history was taken which revealed that she started speaking in monosyllables from 1.5 years of age, after which around 3.5-4 years she stopped speaking and is currently unable to speak . At around 6 months of age she was able to sit with support, which regressed completely at around 1.5 years. The girl hasn't attained her menarche and is unable to receive basic education. A pattern was observed in the mother's obstetric history with score P₃ L₁ of which two boy babies died few weeks after birth and the girl baby being our patient. The history came out to be inconsistent with the findings of cerebral palsy therefore the previous diagnosis was ruled out. Thus, further investigations were ordered. The basic blood investigations were all within normal limits. MRI Brain gave an impression of diffuse volume loss in pons and both cerebelli with widened folia and subarachnoid spaces and that of appropriate myelination for age. After the reports Autoimmune Encephalitis was initially suspected for which blood for antibody profile (LGI 1) was ordered and Inj. Methyl Prednisolone was prescribed but no improvement was noted with the report ruling out Autoimmune Encephalitis. Now on retracing our steps it was observed that the history pointed towards a rare disorder, Rett Syndrome. To confirm the diagnosis, MECP-2 gene

testing was performed, the report of which proved she was suffering from Rett Syndrome.

The management focussed on anti-epileptics for prevention of seizures with high protein diet for growth retardation, parent counselling about the condition and regular follow-up with physio and speech therapy.

3. Discussion

Initially thought to be strictly affecting females, the disease has also been identified in males. The incidence in males is unknown, partly owing to the low survival of male fetuses with the RS-associated MECP2 mutations. The MECP2 gene contains instructions for the synthesis of methyl cytosine binding protein 2, which is needed for neural development. In less than 10% of cases of RS, mutations in the gene cyclin-dependent kinase, like 5 (CDKL5) or FOXP1, have been found. Sporadic mutation is seen in at least 95% of RS cases and the cause is a de novo mutation that is not inherited from either parent.

The parents report normal physical and mental development for the first 6-8 months of life, as evidenced by physical growth and psychomotor and verbal behaviour. A pattern of deceleration across all growth measurements, especially microcephaly, following the first 6 months of life is witnessed in most persons with RS. Growth retardation may be suggestive of nutritional factors. Stereotyped hand movements represent one of the most distinguishing characteristics of the RS. A loss of social interaction skills is frequently observed during the pre-school years, but social interest often increases later. Although most girls with RS demonstrate abnormal EEG tracings, seizure activity is not universal. By adolescence, approximately 75% of patients are in wheelchairs or bedridden. Other common concomitant features are breathing problems (hyperventilation, breath holding and air or saliva expulsion), bruxism and scoliosis.

An integrated, multidisciplinary approach comprising of symptomatic, supportive medical management, therapy and supportive services is needed. Pharmacotherapy, in the form of bromocriptine, magnesium citrate, L-carnitine, naltrexone and levodopa have been tried for symptom control without reasonable success.

4. Conclusion

Though the discovery of the disorder dates long back, still much is unknown to us, the reason being under diagnosing or misdiagnosing the condition commonly as cerebral palsy. It is necessary to spread awareness of this disorder as it may help early detection and timely intervention to help both the patient and their family. Cytogenetic analysis should be done for epileptic patients with mental retardation. As ours is a developing nation with limited resources it is advisable that all female children with low intelligence, autistic character, developmental regression following an initial normal period of development to be suspected of having Rett Syndrome unless contradictory evidence is found.

5. Future Scope

More literature is required for better understanding and early detection of this disease which will help us to provide the patients and their family members a proper explanation and for the medical community, to formulate a better treatment protocol in managing the condition.

References

- [1] Arora, S. C. (n.d.). *The Ironies of Human Mind: A Case of Rett Syndrome*. Retrieved February 2022, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4006212/>
- [2] Era R Sharma, A. V. (n.d.). *Silent angel: A case report on Rett syndrome*. Retrieved January 2021, from <https://www.mjdrdypu.org/article.asp?issn=0975-2870;year=2015;volume=8;issue=2;spage=247;epage=249;aulast=Sharma>
- [3] GUPTA, V. (n.d.). *RETT'S SYNDROME : A CASE REPORT*. Retrieved January 2021, from Indian Journal of Psychiatry, 2001, 43 (1), 81 - 84 : <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2955941/pdf/IJPsy-43-81.pdf>
- [4] Michael A. Buccino, J. A. (n.d.). *Rett syndromema: rare and often misdiagnosed*. Retrieved February 2022, from <https://www.aapd.org/globalassets/media/publications/archives/buccino-11-02.pdf>
- [5] Pathak, M. (n.d.). *Rett Syndrome: A Case Report*. Retrieved February 2022, from Journal of Nepal Paediatric Society: <https://www.nepjol.info/index.php/JNPS/article/view/1402>
- [6] Pathak, M. (n.d.). *Rett Syndrome: A Case Report*. Retrieved January 2022, from Journal of Nepal Paediatric Society: <https://www.nepjol.info/index.php/JNPS/article/view/1402>

Author Profile



Dr. Subhajit Saha is an MBBS intern currently under Department of Pediatrics at IQ City Medical College and Hospital, Durgapur, West Bengal, India.



Dr. Subham Basu is an MBBS intern currently under Department of Pediatrics at IQ City Medical College and Hospital, Durgapur, West Bengal, India.