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Research Paper

Rett syndrome in a set of Nigerian monozygotic twins: a case report

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ABSTRACT
Rett syndrome is an X – linked dominant severe neurodevelopmental disorder of uncertain aetiology predominantly affecting girls. It is characterised by progressive loss of acquired fine motor skills, poor social skills, intellectual impairment and seizures.
In this report, we describe the presentation of a set of monozygotic twins who presented with inability to speak, poor communication, hand stereotype and bruxism.They were delivered at 33 weeks via emergency caesarean section on account of maternal severe pregnancy induced hypertension. They were managed with sodium valproate and risperidone and have shown good seizure control and apparent improvement in language skills.

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I. INTRODUCTION

Rett syndrome is an X – linked dominant severe neurodevelopmental disorder of uncertain aetiology predominantly affecting girls.[1] It is one of the genetic causes of severe mental retardation in females.[2] The most common mutation occurs in the MECP2 gene. Most cases are sporadic and of paternal origin but some familial cases have been reported.[3,4]

Rett syndrome is characterised by an apparently normal early development followed by loss of acquired fine and gross motor skills, poor social abilities and development of stereotype hand movement. Other features include abnormal behaviour, dementia, apraxia of gait, seizures (usually generalised tonic-clonic seizures), decelerating head growth, bruxism, intellectual disability and electroencephalographic (EEG) changes.[5,6]

One essential criterion for classical Rett syndrome includes loss of previously acquired early developmental skills, usually at the age of 1–2 years. This period of regression may last for a few months to years. It is then followed by a "wake up" period with some communicative restitution and apparent preservation of ambulant ability. The last stage of late motor deterioration is characterised by severe muscle wasting, non-ambulatory state and ultimately wheelchair bound.[6]

The condition is considered to be rare in developing world, Nigeria inclusive. Most studies on this condition have been from Caucasian girls and only pockets of case reports from South Africa,[5,7] and Ghana[8]. We describe a set of monozygotic twins with Rett syndrome and hope to add to the literature on this rare condition.

CASE REPORT

A set of monozygotic twin girls presented at the child neurology clinic of the university of Benin teaching hospital fifteen months apart with similar complaints.

Twin 1

F.O the 1st of the set of twins presented at 3 years of age with complaints of abnormal behaviour of two years duration. Abnormal behaviour started suddenly and consisted of intermittent screaming and shouting in sleep which last about one hour and abnormal continuous hand wriggling, intermittent hand and nail biting, bruxism and inability to speak of two years duration. There was no prior febrile illness, loss of consciousness or trauma. She later became aggressive with frequent crying spells and withdrawal from her peers.

She is the first of a set of twins delivered at 33 weeks gestation to 37 year old lady via emergency caesarean section on account of severe pregnancy induced hypertension.The antenatal period was not adversely eventful and she cried well following delivery. She weighed 2.0kg at birth and had no adverse event during the neonatal period.Prior to onset of symptoms, motor development was normal; she could walk unsupported and could babble.

At presentation, her gait was normal, she had wriggling hand movement with scars on the dorsum of both hands from hand bitting, tones and deep tendon reflexes were normal and she had a small head (occipitofrontal circumference –50cm).Her EEG was abnormal in keeping with complex partial seizures and cranial CT scan was normal. Serum calcium and phosphate results were normal (ca^{2+} - 9.9mg/dl, PO_4^- - 5.2mg/dl). She was commenced on sodium valproate, nitrazepam and risperidone. Her seizures were controlled and the sleep problems resolved within the first month of therapy and currently she is able to say few words, less aggressive and calmer but is yet to achieve toilet training.

Twin 2

H.O. the second of the twin presented at 4 years with complaint of inability to speak, abnormal behaviour, learning difficulty, frequent incongruous laughters and bruxism of 18 months duration. Other complaints were wriggling hand movement, intermittent handbitting (and frequently hands in panties), and she was yet to achieve toilet training. She was withdrawn from school due to poor performance. She later developed sleep problems (difficulty falling asleep), became restless and preferred to be alone avoiding peer play or interaction.She cried well following delivery and weighed 1.75kg at birth. She had no problems during the neonatal period. Prior to onset of symptoms she achieved normal motor development and could say a few words.

At presentation, gait was normal, she had frequent intermittent handbiting,short attention span, had expressive aphasia, cranial nerve examination was normal, normal tones and deep tendon reflexes and her head was small (occipito-frontal circumference was 48.5cm).Electroencephalogram done was abnormal with rhythmic slow (theta) activity predominantly in the frontal area and frequent brief burst of high amplitude waves that were generalised but with right sided dominance.She was placed on sodium valproate and risperidone. Currently, violent and aggressive behaviour has significantly reduced. Speech also has improved as she is able to communicate in short phrases and sings some rhymes and achieved urine and stool continence.

II. DISCUSSION

Rett syndrome is an x-linked dominant neurodegenerative disorder predominantly affecting girls.[4,9] It is characterised by apparently normal early development followed by loss of acquired motor skills, impaired social abilities, development of stereotype hand movement, intellectual disability and EEG Abnormalities.[5,6]

The syndrome has an estimated worldwide incidence of 1:10,000 – 15,000 females below 18 years.[10] The prevalence varies from region to region. Most reported prevalence have been in Caucasians ranging from 0.44/10,000 in texas,[11] 0.586/10,000 in Serbia[2] to 0.72/10,000[12] girls below 18 years in Australia. A few cases have been reported in South Africa and one case report in Ghana.[5,8]

The cause remain unknown and the most accepted explanation is that sporadic mutation occurs in the paternal x – chromosome and thus the transfer to females.[4,5,10] TheMethyl-CpG-binding protein 2 (MECP2) mutation occurs in majority of cases.[1,9,13] Factors like maternal age, maternal diabetes mellitus, pre-eclampsia and prematurity as was present in our patients have shown no significant association with the disorder.[14] The index set of twins were delivered at late preterm following maternal pregnancy induced hypertension.

The typical presentation include apparently normal early development with subsequent unexplained intellectual disability, loss of acquired finger skills, loss of acquired words, phrases or babble, hand stereotypies, early deviant communication abilities and deceleration of head growth, bruxism, abnormal EEG, unprompted sudden laughter, sleep problems which were reported in our patients . Other features include breathing abnormalities, gait apraxia, neurogenic scoliosis, small blue/cold feet, impaired norciception and intense eye communication – "eye pointing".[6,15]

The diagnosis of Rett syndrome is a clinical one using international diagnostic criteria (eg the Trevathan diagnostic criteria).[16] Identification of MECP2 gene mutation can only support clinical diagnosis but is not used as basis for diagnosis.[9,12]There is no specific treatment for Rett syndrome. Management is only supportive and individualised. The focus of care is to manage seizures, stereotypies, risk of arrhythmias from prolonged QT syndrome,sleep disturbance, breathing problems and skeletal problems – scoliosis.[6,15]Carbamazepine and sodium valproate have shown effectiveness in controlling seizures and improvement of speech and language have been noted in many reports.[15,17,18]Our patients were on valproate which controlled the seizures.

It would have been helpful to have extensive genetic analysis of the index cases in an attempt to establish the exact gene mutation. In spite of this short coming this report shows that the condition may not be as rare in our population.

III. CONCLUSION

This report of a case of stage three Rettsyndrome in a set of twins is probably the first in a set of twins from Nigeria. It highlights also the challenges with doing genetic studies and making definitive diagnosis in resource limited societies.

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