Variable expression of Rett syndrome in two cases

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Abstract

Rett syndrome is pervasive neurodevelopmental disorder presented as a regression in motor development, mental deterioration with speech disabilities .

The disorder is characterized by normal early development followed by loss of purposeful use of the hands, distinctive hand movements, slowed brain and head growth, gait abnormalities, seizures, and mental retardation.

It is X linked disorder, due to MECP2 gene mutation and affects females

Incidence rates are 1:20000 to 1:40000 life female births

Several stages of the diseases are described – early normal development followed by rapid deteriorisation of motor and mental functions.

Early in childhood, affected girls lose purposeful use of their hands and begin making repeated hand wringing, washing, or clapping motions. They tend to grow more slowly than other children and have a small head size (microcephaly). Other signs and symptoms can include breathing abnormalities, seizures, an abnormal curvature of the spine (scoliosis), and sleep disturbances.

A case report

Two girls were born:

one with prolonged delivery, one with severe prematurity of 28 GW. Motor development was satisfactory within first year of life in both cases, gross motor and fine motor skills were satisfactory as well as communication abilities .

The deterioration became with ataxia, gait apraxia, imparement of receptive and expressive language, drooling, stereotipic hand movements at same age- 21 months. There were breathing disorders during sleep , repetitive vomiting.

neurological examination showed head and body growth retardation, lost eye contact, spasticity on distal extremities, inability to walk , initial thoracic scoliosis. Seizures started during sleep in both cases

The work up – EEG was with mostly focal spike and wave changes, MRI PVL in one case at the other cortical atrophy.

. We excluded metabolic disorders amino and organic acidurias, peroxisomal and lisosomal enzyme disorders, acylcarnitine and creatine deficiency disorders.

mutational analysis confirmed the MECP2 mutation. (Beograd and Vienna)

Perinatal history, initial work up
stage 1

Case 1	Case 2
• large baby • BW4600g, HC 36cm,l 52cm • A/S 7/8 • prolonged delivery, • normal development 1st year, speeks few words • Started to walk at 15 months • interested in games and other children	• premature baby • Bw 1220gr Hc 27sm l 47cm • A/S 4/5/5 • Wentilation artefitial • Seets at 10 months, plays with toys at 12, • Speeks few words 1st year • Starts to walk at 18 months poorly

Destructive stage 2

• 21months age • muscle cramps • motor ability started to deteriorate • speech completely stopped. • tics provoked with crying	• 21 months age • stoped walking • lost interest in toys • speech stopped • poor sleep with episodes of nightmares • Seizures and vomiting during the night

Work up at 4 years of age
stage 2- 3

• Small head circumpherece • Not able to seat and stand , walks with difficulties – ataxia, gait apraxia • Not interested in toys and other person • Sleep disturbancies • Frequent breathing difficulties • Spasticity in lower extremities with preserved tendon reflekses • Thoracic Scoliosis • Restricted purposefull hand movements	• Small head circumpherence • Seets and walks only with help, • Walks on toes • Fear of other person • Eye contact lost • Hand clapping • Motor tonic seizures during sleep • Difficulties of swollowing, drooling • Regular vomiting • fine intention tremor

Investigations:

• EEG: unstable basic alfa activity with not specific changes • MRI mild frontal cortical atrophy • Metabolic aminoacid and organic acid screening normal • Kariotype 46xy	• EEG high amplitude spike wave complexes at both but dominantly right temporal zones • MRI periventricular leucomatatia • Metabolic aminoacid and organic acid screening normal • Kariotype 46xy • Creatine and carnitine deficiency excluded • Screening for peroxisomal and lisosmal enzyme disorders normal

DNA analysis

• Deletion in the third portion of the third exon of MECP2 gene. • The deletion of 41 nucleotide was a fremeshift mutation i the rest of a gene. The consequence was apsence of 13 normal aminoacids and existance of different ones. • There is no evidence of this mutation at the DNA analysis of the mother • (Institute of mother and child Beograd, Srbia)	• Heterozigous sequence variant pR168X(GGA>TGA, Arg>stop) in exon 4 of MeCP2 gene • There is no evidence of this mutation at the DNA analysis of the mother • (Genetic laboratories Medgen.at Vienna, Austria)

Discussion

We report on two cases of girls with Rett syndrome, with variable presentation

One of the girls was born with severe prematurity, low birth weight and supported with artificial ventilation, but development was not suggestive for cerebral palsy

The difficulties of recognition are due to nearly normal development at the first year

Genetic analyses of MeCP 2 gene is not available in Macedonia so far.

Multidisciplinary approach for treatment needed but always available