

## **CLINICAL SEVERITY AND MULTIDIMENSIONAL APPROACH IN RETT SYNDROME: TWO CASE REPORTS**

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Rett Syndrome (RTT .OMIM#312750) is a rare neurologic disease, whose incidence is approximately 1: 10.000 live individuals births, primarily affecting females. It is an X-linked progressive neurodevelopmental disorder, often due to “de novo” mutations, mainly involving MECP2 gene in the classic or typical form of disease, sometimes involving CDKL5 gene in Hanefeld’s variant or early seizure variant and sometimes involving FOXP1 gene in congenital variant.

Rett Syndrome’s diagnosis is based on consensus clinical criteria, that were developed in 2001 by European Society of Pediatric Neurology in 2001 and then revised in 2010. These criteria are a useful tool both for start genetic testing and, if these testing are negative, to obtain a correct diagnosis.

In 1986 Hagberg and Witt-Engerstrom described four consecutive phases of disease for typical RTT. Over the years at least 5 different specific variant forms have been described of atypical Rett Syndrome, including the preserved speech variant, the early seizure variant and the congenital variant, characterized by psychomotor developmental delay that occurs in the first months of life and finally a late regression variant, besides mild variant forms with milder symptoms.

In typical RTT clinical picture, even though characterized by predominantly neurological symptoms, is also comprehensive of extra neurological symptoms such as scoliosis, breathing disturbances, cardiovascular and gastrointestinal problems.

We report two girls affected by Rett Syndrome with higher clinical complexity. This report shows that Rett Syndrome is characterized by a broad spectrum of severity disease, that requires a multidisciplinary approach.