

# AUTISM AND RING CHROMOSOME 13

**FB Assumpção Jr, E Kuczynski, C de Almeida Rocca Castanho**

## ABSTRACT

The authors describe a female carrier of ring chromosome 13 with profound mental retardation and autistic symptoms, including a brief revision of the pertinent literature.

**Key words:** *Autism; Chromosome Aberrations; Ring Chromosome 13*

## INTRODUCTION

Nowadays, autism is considered to be a developmental behavioural syndrome with multiple aetiologies, and is characterised by a deficit in social interaction and interpersonal relationships, with language and behaviour disturbances.<sup>1</sup> Sometimes, it is difficult to differentiate autism from mental retardation, in view of the fact that the qualitative handicap in social interactions and communication abilities development characteristics of autism can also be present in mental retardation.<sup>2</sup> Autism is diagnosed by signs and symptoms present until the third year of life and is related to pre-, peri-, and post-natal factors. There is an estimated prevalence of 4 to 5 cases per 10,000 population, predominating in males (male:female ratio, 3:1 to 4:1). Different genetic and neurological syndromes are described to be related to autism.<sup>3-13</sup> High rates of chromosome aberrations are described by Steffenberg,<sup>14</sup> although they have non-specific and variable presentations.<sup>15-17</sup>

The ring chromosome 13 - r(13) described in 1968 by Lejeune *et al*,<sup>18</sup> is associated with microcephaly or anencephaly, profound mental retardation, and multiple malformations such as growth retardation, facial dimorphisms, and finger anomalies.<sup>19</sup> More than 100 cases have been documented throughout the world,<sup>20</sup> and the birth prevalence for live newborns is estimated to be about 1 in 58,000.<sup>21</sup> This report is of a 10-year-old autistic girl whose genetic investigation revealed a ring chromosome 13. We believe that such a case description is fundamental to research into the aetiology of autism.

## CASE REPORT

KC is a white female aged 10 years and 6 months, from São Paulo, Brazil. She was first investigated at the age of 6 months due to hypotonia and a vague, still glance. She attended school from the age of 30 months, but did not engage in relationships with other children. KC was irritable and bit herself when she was contradicted or annoyed. She also presented with an indiscriminate affective expression. She had been prescribed different neuroleptics, but with no substantial improvement in hyperactivity or aggressiveness. KC has been losing acquired capacities since she was 4 years old. With the appearance of progressively worsening stereotypies, she was brought to the Hospital das Clínicas Child and Adolescent Psychiatry Division at São Paulo University Medical School in Brazil. KC was an

only child with no blood-related healthy siblings. Her mother had had a previous spontaneous miscarriage early in pregnancy. Two female maternal cousins died of unknown aetiology at the age of 9 after regression of development from the age of 6 years.

## PERINATAL AND MEDICAL HISTORY

KC was born with a marginal placenta via caesarean section. She had a low-birth weight, and remained in hospital for 40 days after birth. A semi-perforated anus was surgically corrected at the age of 5 months. There was also a history of cow's milk intolerance, which improved with dietary restriction. She presented with two generalised idiopathic tonic-clonic seizures and was given barbaxalone.

## NEURO-PSYCHO-MOTOR DEVELOPMENT

KC walked at the age of 18 months but did not speak or answer verbal commands, and never achieved anal or vesical control. She was totally dependent in activities of daily living.

## PHYSICAL EXAMINATION

KC had low weight and stature for her age (below the National Center Health Statistics [NCHS] 3rd percentile), her cephalic circumference was 46 cm (below the NCHS 3rd percentile). She was found to have micrognathia and mild hypotonia, no other significant neurological findings were present.

## PSYCHIATRIC EXAMINATION

KC was indifferent to the examiner's presence or her mother leaving the room. She was passive, allowing hugs with no resistance, but with no sign of anticipatory movement, although she did show affection to her mother. She did not attend to simple commands nor present deliberate gestures or attempt to get help. KC experienced laughter crises for no reason, which lasted for 2 to 3 minutes and was associated with trunk rocking. She also had glance contact but an apathetic attitude. She did not have either indicative gestures or notion of instrument use. She scored 13 on the Vineland Adaptive Behavior Scale, corresponding with profound mental retardation.

## LABORATORY STUDY

Chromosomal analysis showed ring chromosome 13. Magnetic resonance scan of the brain showed periventricular white matter and left cortical-subcortical regional alterations,

suggesting degenerative changes such as gliosis, leucoencephalopathy, or myelinisation delay, as well as lateral ventricular enlargement. She fulfilled the Diagnostic and Statistical Manual of Diseases (DSM)-IV criteria for autism,<sup>2</sup> presenting with qualitative inability in reciprocal social integration (indifference about other's existence and feelings, absent imitation, absent social games, and inability to engage with peers), qualitative inability in verbal and non-verbal communication (mutism), and restricted interests and activities repertoire (stereotypies), beginning in early childhood (usually detected by the age of 2 years).

## DISCUSSION

This patient presented with several phenotypic characteristics found in the ring chromosome 13 such as microcephaly, profound mental retardation, growth delay, micrognathia, and anorectal anomaly.<sup>19</sup> These structural chromosome aberrations originate from terminal deficiencies in both chromosomal arms, originating from the ring structure. These chromosomes can frequently divide during mitosis or meiosis, although they usually degenerate.<sup>22</sup> Despite the clear characterisation of the molecular alteration and clinical presentations, we have not found any other described patient presenting with symptoms that fulfil the diagnostic criteria for autism.<sup>2</sup> Social and affective disturbances are important characteristics of KC's behaviour and cannot be solely explained by the simple reflex of mental retardation, since patients with profound mental retardation (without autism) habitually present with affective contacts at rudimentary levels. They are also dependent of the presence of others to feel safe. In the same way, the qualitative language disorder and observed ritualistic activities cannot be characterised as typical of mental retardation.

Finally, we believe our patient is the first to be described to have autism and profound mental retardation associated with this particular chromosome aberration. We call attention to the fundamental importance of better characterisation of autistic patients carrying chromosome abnormalities with a view to clarifying the aetiology of the autistic syndrome.<sup>16</sup>

## REFERENCES

1. Gillberg C. Infantile autism: diagnosis and treatment. *Acta Psychiatr Scand* 1990;81:209-215.

2. American Psychiatric Association. Manual de diagnóstico e estatística do DSM IV. São Paulo: Artes Médicas; 1995.

3. Coleman M. The autistic syndromes. Amsterdam: North Holland Publishing Company; 1976.

4. Ritvo, ER. The UCLA-University of Utah Epidemiological Survey of Autism. The etiologic roles of rare disorders. *Am J Psychiatry* 1990;147:1614-1621.

5. Bolton P, Rutter M. Genetic influences in autism. *Int Rev Psychiatr* 1990;2:67-80.

6. Kerbeshian J, Burd L, Randall T, et al. Autism: profound mental retardation and atypical bipolar disorder in a 33-year-old female with deletion of 15q12. *J Ment Def Res* 1990;34:205-210.

7. Deikin EY, Macmahon B. Pregnancy delivery and neonatal complications among autistic children. *Am J Dis Child* 1980;134:860-864.

8. Finegan J, Quarrington B. Pre-, peri- and neonatal factors and infantile autism. *J Child Psychol Psychiatry* 1979;20:119-128.

9. Riikonen R, Amnell G. Psychiatric disorders in children with early infantile spasms. *Dev Med Child Neurol* 1981;23:747-760.

10. Gillberg C, Wahlstrom J. Chromosome abnormalities in infantile autism and other childhood psychoses: the population study of 66 carriers. *Dev Med Child Neurol* 1975;27:293-304.

11. Rutter M. Psychological sequelae of brain damage in children. *Am J Psychiatry* 1981;138:1533-1544.

12. Gillberg C, Steffenberg S. Autistic behaviour in Moebius Syndrome. *Acta Paediatr Scand* 1989;78:314-316.

13. Bloomquist HK. Frequency of the fragile X syndrome in infantile autism. *Clin Genet* 1985; 27:113-117.

14. Steffenberg S. Neuropsychiatric assessment of children with autism: the population-based study. *Dev Med Child Neurol* 1991;33:4495-4511.

15. Rasmussem K, Nielsen J, Brask BH, Saldana-Garcia P. The bisatellited marker chromosome in a mentally retarded girl with infantile autism. *Hereditas* 1976;82:37-42.

16. Kuczynski E. Anormalidades cromossômicas esporádicas associadas a síndrome autística. *Infanto Rev Neuropsiq Inf Adol* 1996;4:26-36.

17. Assumpção Jr FB. Brief report: chromosome 22 alteration associated with autistic syndrome. *J Autism Dev Disorders* 1998;28:253-256.

18. Lejeune J, Lafoucade J, Berger R. Le phenotype D (r). Étude du trois cas des chromosome D en anneau. *Ann Genet (Paris)* 1968;11:79-87.

19. Brandt CA, Hertz JM, Petersen MB, et al. Ring chromosome 13: lack of distinct syndromes based on different breakpoints on 13q. *J Med Genet* 1992;29:704-708.

20. Sousa ID, Gandarillas IM, Rodriguez MV, et al. Cromosoma 13 em anillo (tipo I) 45, XY, -13/46, XY, r (13) (p11;q34). *An Esp Pediatr* 1990;32:556-558.

21. Parcheta B, Wisniewski L, Piontek E. Clinical features in carriers with ring chromosome 13. *Eur J Pediatr* 1985;144:409-412.

22. Beiguelman B. Citogenética humana. São Paulo: Guanabara Kogan, 1982.

Dr FB Assumpção Jr, Professor of Psychiatry and Technical Director of the Hospital das Clínicas Child and Adolescent Psychiatry Division, São Paulo University Medical School, Brazil

Dr E Kuczynski, Pediatrician, Psychiatrist of Infancy and Adolescence, Mestranda in Psychiatry, College of Medicine, University of São Paulo, Brazil.

Dr C de Almeida Rocca Castanho, Psychologist, Graduanda of the Program of Functional Physiology, College of Medicine, University of São Paul, Brazil.

Address for correspondence: Dr FB Assumpção Jr

Professor of Psychiatry and Technical Director  
Hospital das Clínicas Child and Adolescent Psychiatry Division  
São Paulo University Medical School  
Brazil