European Journal of Medical Genetics 54 (2011) 329–332

Contents lists available at ScienceDirect

European Journal of Medical Genetics

journal homepage: http://www.elsevier.com/locate/ejmg

Short report

De novo mosaic ring chromosome 18 in a child with mental retardation, epilepsy and immunological problems

Adriana Lo-Castro [a,*], Nadia El-Malhany [a], Cinzia Galasso [a], Alberto Verrotti [b], Anna Maria Nardone [c], Diana Postorivo [c], Cristina Palmieri [c], Paolo Curatolo [a]

[a] Department of Neuroscience, Paediatric Neurology Unit, "Tor Vergata" University of Rome, Viale Oxford 81, 00133 Rome, Italy
[b] Department of Paediatrics, University of Chieti, Via dei Vestini 5, 66100 Chieti, Italy
[c] Department of Medical Genetics, "Tor Vergata" University of Rome, Viale Oxford 81, 00133 Rome, Italy

ARTICLE INFO

Article history:
Received 10 October 2010
Accepted 1 February 2011
Available online 17 February 2011

Keywords:
Developmental delay
Dysmorphisms
Epilepsy
Mental retardation
Immunological disorders
Ring chromosome 18 mosaicism

ABSTRACT

Ring chromosome 18 [r(18)] is a disorder in which one or both ends of chromosome 18 are lost and joined forming a ring-shaped figures. R(18) patients can therefore show features of 18q−, 18p− syndrome or a combination of both, depending on the size of the 18p and 18q deleted regions.

The phenotype of the r(18) is characterized by developmental delay/mental retardation, typical facial dysmorphisms, major abnormalities and immunological problems.

Here we report a case of *de novo* mosaic r(18) with a characterization by array-based comparative genomic hybridization analysis, and discuss the phenotypic correlation in r(18) also through a comparison with previously described cases of the literature.

1. Introduction

The severity of ring chromosome 18 syndrome's [r(18)] phenotype is variable, depending on the size of the 18p and 18q deleted regions. Frequently, r(18) patients show a clinical phenotype of 18q deletion syndrome (18qDS) (MIM # 601808), characterized by dysmorphisms, microcephaly, short stature, congenital aural atresia, foot deformities, immunological problems, mild-severe mental retardation (MR), hypotonia, and white matter abnormalities or delayed myelination [1–3]. Less frequently, r(18) patients share characteristics in common with the 18p deletion syndrome (18pDS) (MIM # 146390), which is characterized by dysmorphic features, mild microcephaly, short stature (frequently due to growth hormone deficiency), immunological problems, skeletal abnormalities, variable degrees of MR with marked speech impairment and/or behavioral disorders, brain malformations evocative of holoprosencephaly spectrum disorders and, occasionally, alopecia and dystonia [1–5].

R(18) is a relatively frequent condition among the ring chromosomes and, up to now, about 70 cases of r(18) syndrome have been reported [1,6]. However, only few cases of mosaicism r(18) associated with other chromosome 18 aberrations have been described [1,2,6–13]. We performed a Pubmed peer-review of mosaic ring chromosome 18 articles, to discuss the clinical features and the neurocognitive phenotype of previously reported cases and our patient (Table 1). Only articles published in English were reviewed.

2. Case report

The proband was a 9 years old girl referred because of dysmorphisms, short stature, mental retardation, and behavioral problems. The girl was the first child of healthy, non-consanguineous parents; the other son is healthy, and the family history was not contributory. Vaginal bleeding occurred at the third month of gestation. She was born at 41 weeks of gestation by cesarean section due to uterine inertia. At birth the weight was 3520 g, length 49,5 cm and occipital–frontal circumference 33.5 cm (50th, 75th, and 10–25th centiles, respectively). Apgar scores were 7 and 8 at 1 and 5 min. A low growth was noted in the neonatal period, associated to frequent infections. She walked without support at 30 months and starting speaking single words when she was 1 year old. During her second year of life a suspect of celiac disease was confirmed by diagnostic serologic tests (positivity to anti-transglutaminase and

* Corresponding author. Tel.: +39 06 20900249; fax: +39 06 20900018.
E-mail address: a.locastro@libero.it (A. Lo-Castro).

1769-7212/$ – see front matter © 2011 Elsevier Masson SAS. All rights reserved.
doi:10.1016/j.ejmg.2011.02.004

Table 1
Clinical comparison between previously reported ring 18 mosaicisms and our case.

Authors	Age and sex	IUGR	Dysmorphisms	Short stature	Major abnormalities	Immunological and endocrinological problems	Microcephaly	MR/DD	Seizures	Other neurologic findings	MRI findings	Other cognitive and behavioral problems
Fryns et al., 1992	Pt 1: 2 y, M	?	−	−	−	−	−	Moderate–severe DD	−	−	?	Autism
	Pt 2: 37 y, F	?	−	+	−	−	−	Severe MR	−	−	?	Autism
Maaswinkel-Mooij et al., 1993	27 y, M	−	+	−	Aplasia of the right thumb and other skeletal abnormalities, peri-papillary atrophia of fundus oculi	−	−	MR	FC	Spastic diplegia of legs	CT scan: dysgenesis of corpus callosum	Friendly disposition, language and motor delay
Nakayama et al., 1997	3 y, M	+	+	+	Cleft/lip palate, ASD, bilateral hypoplastic kidney	−	+	Severe DD	−	−	Hypointensity of GM, hyperintensities in WM with immature pattern	Severe language i mpairment
Litzman et al., 1998	14 y, F	−	+	+	Skeletal abnormalities	Decreased IgG, IgA, and IgM		Severe DD	−	Extensor hypertonus of lower extremities at birth, subsequently generalized hypotonia and L2–S2 areflexia	?	Severe language impariment
Stankiewicz et al., 2001	Case 6: 11 y, F	−	+	+	VSD, hypoplastic labia majora, vesicoureteral reflux	−	+	Mild MR	−	−	Cerebral cortex atrophy, internal hydrocephalus	Speech delay
	Case 7: 10 y, F	−	+		−	−	−	Moderate MR	−	−	?	Speech delay
Baumer et al., 2002	11 y, F	−	+	+	−	−	+	Mild MR?	−	−	Normal	Learning difficulties, expressive and receptive language delay, little friendly disposition
Souraty et al., 2007	2.5 y, F	+	+	+	Cleft/lip palate, umbilical hernia, thoracic hemi-vertebrae, short claviculae, VSD	−	+	Severe DD	−	Horizontal nystagmus	Cortical atrophy, enlarged ventricles, thin corpus callosum	Language impairment
Koç et al., 2008	6.5 y, F	−	+	+	−	−	+	Mild MR	+	−	Normal	Severe language impairment, hyperactivity
Geretzul et al., 2008	27 y, F	−	+	+	Cleft/lip palate, fusion of C2–C3 vertebrae	Hashimoto thyroiditis, primary hypogonadism, ectodermal dysplasia	+	+	−	Hypotonia	?	Language impairment
Mello et al., 2008	20 m, M	−	+	+	Aortic stenosis and tricuspid valve insufficiency, gastresofageal reflux, micropenis	−	+	Mild DD	−	Hypotonia, fine and gross motor delay	?	−
Our case	9 y, F	−	+	−	Mild mitral insufficiency with mitralic flap dysplasia, right ptotic kidney	Autoimmune hypothyroidism, celiac disease	−	Mild MR	+		Aspecific WM hyperintensities	Visuo-spatial deficits, poor attention, hyperactivity

+ = present; − = not present; ? = not reported; ASD = atrial septal defect; DD = developmental delay; F = female; FC = febrile convulsion; GM = gray matter; IUGR = intrauterine growth retardation; m = months; M = male; MR = mental retardation; Pt = patient; VSD = ventricular septal defect; W = week; WM = white matter; y = years.