Gene 498 (2012) 296–299

Contents lists available at SciVerse ScienceDirect

Gene

journal homepage: www.elsevier.com/locate/gene

Short Communication

A case of del(13)(q14.2)(q31.3) associated with hypothyroidism, hypertriglyceridemia, hypercholesterolemia and total ophthalmoplegia

Baris Malbora [a,*], Cihan Meral [a], Nihan Malbora [b], Deniz Sunnetci [c], Naci Cine [c], Hakan Savli [c]

[a] Department of Pediatrics, Gulhane Military Medical Academy, Istanbul, Turkey
[b] Department of Pediatric Surgery, Gazi University Faculty of Medicine, Ankara, Turkey
[c] Department of Medical Genetics, Kocaeli University Faculty of Medicine, Kocaeli, Turkey

ARTICLE INFO

Article history:
Accepted 2 February 2012
Available online 22 February 2012

Keywords:
Chromosome 13q deletion
Ophthalmoplegia
Hypertriglyceridemia
Hypercholesterolemia
Hypothyroidism
Array-CHG

ABSTRACT

13q deletion syndrome is caused by the absence of a portion of the long arm of chromosome 13. This syndrome is a rare condition characterized by a wide range of clinical findings. Phenotype varies with the location and size of the deletion. We report a female dizygotic twin with a proximal deletion of 13q and failure to thrive, hypotonia, and multiple anomalies included pytosis and total ophthalmology at right side, strabismus at left, bilateral iris heterochromia and telecantus. She had a broad nasal bridge with flat philtrum, micrognathia and antevert ear lobes. Her umbilicus had vanished. Her left coxa was dislocated and left toes were overlapped. She was also found to have hypertriglyceridemia, hypercholesterolemia, and hypothyroidism. Chromosome analysis showed a proximal deletion of chromosome 13 [karyotype 46,XX,del(13) (q14.2q31.3)] which was confirmed by high-resolution microarray based comparative genomic hybridization.
The described patient is unique among similar rare cases with different deletion breakpoints. It is the first case of 13q14.2q31.3 deletion where the breakpoints are clearly defined, indicating the importance of detailed clinical description and high-resolution genomic analysis for characterization of rare genetic syndromes.

1. Introduction

13q deletion syndrome is caused by the absence of a portion of the long arm of chromosome 13, as first reported by Allderdice et al. (1969). This syndrome is a rare condition characterized by a wide range of clinical findings. Phenotype varies with the location and size of the deletion. Clinical features include low birth weight, microcephaly, mental and growth retardation, brain malformations, craniofacial dismorphism, iris heterochromia, retinoblastoma, heart defects, vertebral anomalies, skeletomuscle system deformities, digestive and urogenital abnormalities (Ballarati et al., 2007; Kirchhoff et al., 2009; Mitter et al., 2011; Quélin et al., 2009).

We report a female dizygotic twin with an interstitial deletion of chromosome 13 [karyotype 46,XX,del(13) (q14.2q31.3)], who, in addition to having total ophthalmoplegia and multiple anomalies, was also found to have hypertriglyceridemia, hypercholesterolemia and hypothyroidism, features not previously reported in 13q deletion patients.

2. Clinical report

The patient is a female dizygotic twin, born at 36 week and 4 day gestation by cesarean section secondary to premature rupture of membranes to a 28-year-old Gravida 1 Para 2 woman and her 31-year-old unrelated husband. Birth weight was 1570 g (<3rd centile) and length was 45 cm (<3rd centile), and head circumference of 31.1 cm (<3rd centile) while the dizygotic twin brother's birth measurements were weight of 2950 g (10–25th centile) and length of 48.2 cm (10–25th centile), and head circumference of 33.7 cm (10–25th centile). She developed respiratory distress syndrome at 3rd day of life and treated in the neonatal intensive care unit for 1 month. Weight gain was very slow in contrast to her twin brother who had no serious perinatal complications and was thriving.

At physical examination, the patient was 23 months old and her body weight, height, and head circumference were below 3rd centile (5690 g, 67 cm, 40.5 cm, respectively). She was hypotonic and had pytosis and total ophthalmoplegy at right side, and strabismus at left. There was bilateral iris heterochromia and telecantus (Fig. 1A–C). She had a broad forehead, a broad nasal bridge with flat philtrum, micrognathia and antevert ear lobes. Her umbilicus had vanished. Her left coxa was dislocated and left toes were overlapped.

On lipid profile, hypercholesterolemia, hypertriglyceridemia and elevated liver enzymes were noted [total cholesterol: 363 mg/dL (normal range, 130–210), triglyceride: 327 mg/dL (normal range, 20–110), high density lipoprotein: 29 mg/dL (normal range, 35–75),

Abbreviations: BAC, bacterial artificial chromosome; CGH, comparative genomic hybridization; del, deletion; DNA, deoxyribo nucleic acid; EEG, electroencephalography; VLDL, very low density lioprotein.

* Corresponding author at: Department of Pediatrics, Gulhane Military Medical Academy, Selimiye Mahallesi, Tıbbiye Caddesi, 34668 Istanbul, Turkey. Tel.: +90 5336413841; fax: +90 216 3487880.
E-mail address: barismalbora@gmail.com (B. Malbora).

0378-1119/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.gene.2012.02.002

Fig. 1. She had pytosis and total ophthalmoplegy at right, strabismus at left (A), bilateral iris heterochromia and telecantus (B and C).

low density lipoprotein: 109 mg/dL (normal range, 60–130), very low density lipoprotein: 65.4 mg/dL (normal range, 6–25), aspartate aminotransferase: 181 IU/dL (normal range, 5–34), alanine aminotransferase: 156 IU/dL (normal range, 0–55), gamma glutamyl transferase: 1164 IU/dL (normal range, 5–36), alkaline phosphatase: 435 IU/dL (normal range: 5–287), lactate dehydrogenase: 349 IU/dL (normal range, 110–295)]. However, her parents and twin brother had normal lipid profiles. Endocrinologic tests revealed insulin like growth factor-1: <25 ng/mL (normal range, 51–303), marked decrease in free-T3 [0.8 pmol/L (normal range, 12.3–22.8)], free-T4 [0.1 pmol/L (normal range, 3.7–8.5)], and increased thyroid stimulating hormone [138 μIU/mL (normal range, 0.5–6.5)]. Growth hormone, insulin like growth factor binding protein-3, cortisol and prolactine levels were normal. Brain magnetic resonance imaging of the patient shows olivopentocerebellar atrophy. An EEG showed no epileptiform discharges.

3. Cytogenetic and molecular analysis

Peripheral blood of the patient was cultured and harvested according to standard procedures.

Total of 40 metaphase plaques were evaluated and 46,XX, del(13)(q14q31?) karyotype is determined (Fig. 2). Total genome scanning at 1 Mb resolution for microdeletion/duplication via BAC-based comparative genomic hybridization array (array-CGH) method is substantiated to the peripheral blood sample of the patient. Genomic DNA is isolated from the peripheral blood sample using DNeasy Blood&Tissue kit (Qiagen, Hilden, Germany). DNA quality is confirmed with gel electrophoresis, while quantity is confirmed with spectrophotomery (NanoDrop ND-1000; NanoDrop Technologies, Wilmington, DE). As array-CGH platform, CytoChip Focus Constitutional v1.1 (BlueGnome, Cambridge, U.K.) is used. Having adequate quality and quantity, the patient's DNA and the reference DNA (Human Genomic DNA: Female; Promega Corporation, Madison, USA) are labeled according to CytoChip protocol. The labeled patient's DNA and reference DNA are combined and left for hybridization with array-CGH microchips for 20 h at 47 °C as described in the protocol. At the end of the hybridization and washing process, the microchips are scanned with Agilent Microarray scanner (Agilent Microarray Scanner G2505B; Agilent Technologies, Palo Alto, CA). The scanned images

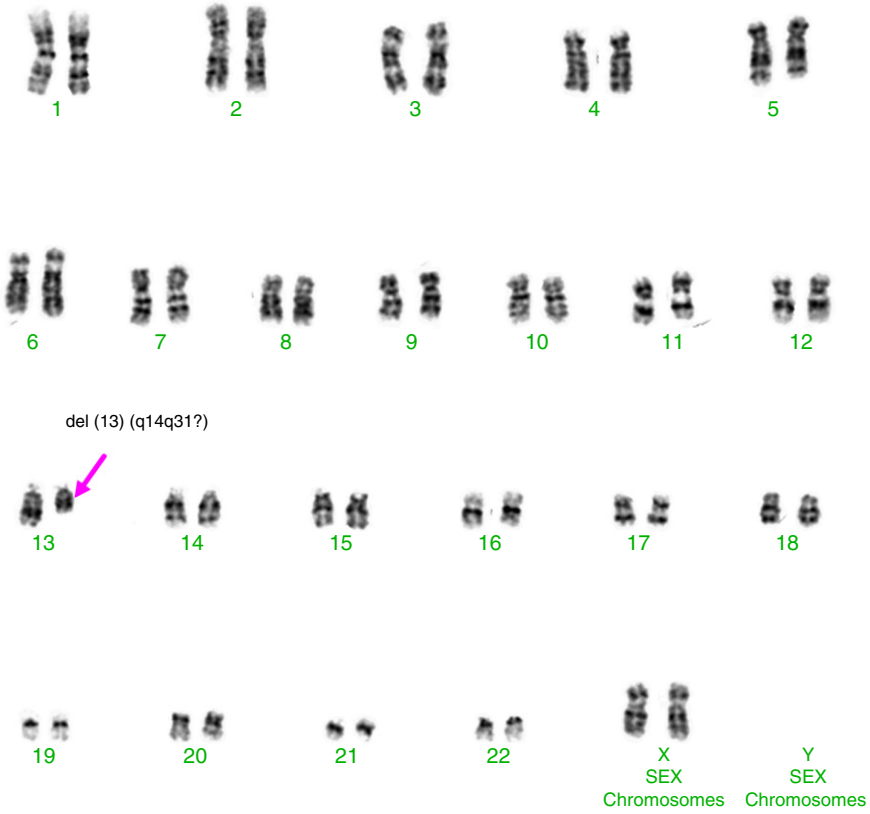

Fig. 2. Giemsa stained karyotype showing the 46,XX,del(13)(q14q31?).