

Novel chromosomal translocation t(7;14)(q36.3;q11.2)dn in a female child with dysmorphic features

Jean-Pierre Antunes Gonçalves^{1,2}, Liliana Pinheiro³, Maria João Magalhães¹, Arnaldo Cerqueira¹, Eduarda Abreu³, Albina Silva³, Carla Sá³, Almerinda Pereira³

¹Pediatric Department, Braga Hospital, Braga, Portugal

²Community Health, School of Health Sciences, University of Minho, Portugal

³Neonatology, Braga Hospital, Braga, Portugal

Abstract

When evaluating a newborn with peculiar phenotype it is mandatory to perform chromosomal studies. In this case report, the genetic study revealed a novel *de novo* translocation involving chromosome 7 and 14, thus establishing the following karyotype: as 45,XX,der (7)t(7;14)(q36.3;q11.2),-14dn.ish 7q36.3(VIJyRM2185 enh).mpla 7qsubtel(P036-E1,P070-B2)x3,14q11.2(P036-E1,P070-B2)x1.

Keywords

Phenotype, translocation, karyotype.

Corresponding author

Jean-Pierre Antunes Gonçalves; Hospital, Sete Fontes – S.Victor, 4710-243 Braga, Portugal; tel. +351253027000; fax +351253027999 (Hospital); email: pierre_3.14r@hotmail.com.

How to cite

Gonçalves J-P, Pinheiro L, Magalhães M, Cerqueira A, Abreu E, Silva A, Sá C, Pereira A. Novel chromosomal translocation t(7;14)(q36.3;q11.2)dn in a female child with dysmorphic features. J Pediatr Neonat Individual Med. 2014;3(1):e030101. doi: 10.7363/030101.

Introduction

There are almost 1.550 genes on chromosome 7 [1] and 1.200 genes on chromosome 14 [2] that code for hundreds of different proteins with different functions. In most unbalanced translocation it is not possible to predict what phenotypes or abnormalities to expect and how severe the last may be.

Besides the scarce information about translocation involving chromosomes 7 and 14, it has been described that deletions on chromosome 7 are associated with a range of phenotypes including craniofacial malformations

(frontal prominent, craniosynostosis, microcephaly, malformed ears, changes in the eyes and eyelids), congenital heart problems, distal limbs and genitalia malformations and moderate to severe retardation of psychomotor development [3-5].

In this report the authors present a child with a *de novo* translocation involving chromosome 7 and 14:45,XX,der(7)t(7;14)(q36.3;q11.2),-14dn.

Clinical report

The patient is a female newborn referred for evaluation of dysmorphic features and little spontaneous movement in the neonatal period.

Prenatal ultrasound studies revealed a single umbilical artery. She was born at 38 weeks by caesarean delivery to a 35-year-old healthy gravida 2 para 2 mother. The family history is negative for birth defects, mental retardation, infant deaths or metabolic disorders.

Pregnancy, labour and delivery were uncomplicated. Her weight, height and head circumference were adequate for gestational age. Apgar scores were 8 at 1 and 5 minutes and 10 at 10 minutes after birth. Shortly after birth she presented with transient tachypnea of the newborn and was admitted in neonatal intensive care unit.

Physical examination showed low implantation of ears, hypertelorism (**Fig. 1**), short neck, mild axial hypotonia and little spontaneous movement.

Blood and cerebrospinal fluid cultures, thyroid function, metabolic studies and transfontanelar and abdominal ultrasounds were normal. Echocardiography showed patent foramen ovale and a small apical muscular interventricular communication with left-to-right shunting (**Fig. 2**).

Classical karyotyping using conventional high resolution GTG banding (where GTG is G-banding with trypsin-Giemsa) [6] was performed on metaphases obtained from PHA-stimulated lymphocytes from the patient and her parents, according to standard procedures.

CTG-banded chromosomes (where CTG is C-banding with trypsin-Giemsa) obtained from the lymphocytes of the proband revealed 45,XX chromosomes with a translocation involving the long arms of chromosomes 7 and 14. There is only one normal chromosome 14. This chromosome analysis revealed the breakpoint at 7q36.3 and 14q11.2. The proband's karyotype was designated 45,XX,der(7)t(7;14)(q36.3;q11.2),-14.

To detect duplications and deletions a multiplex-ligation probe amplification (MLPA) analysis [7]

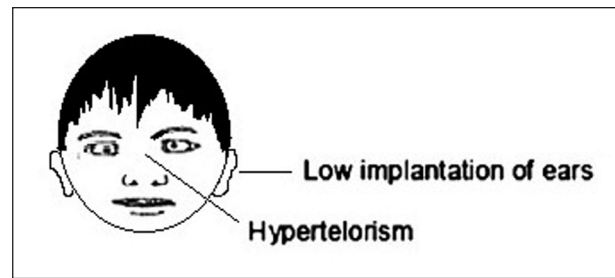


Figure 1. Patient phenotype diagram showing a low implantation of ears, and hypertelorism.

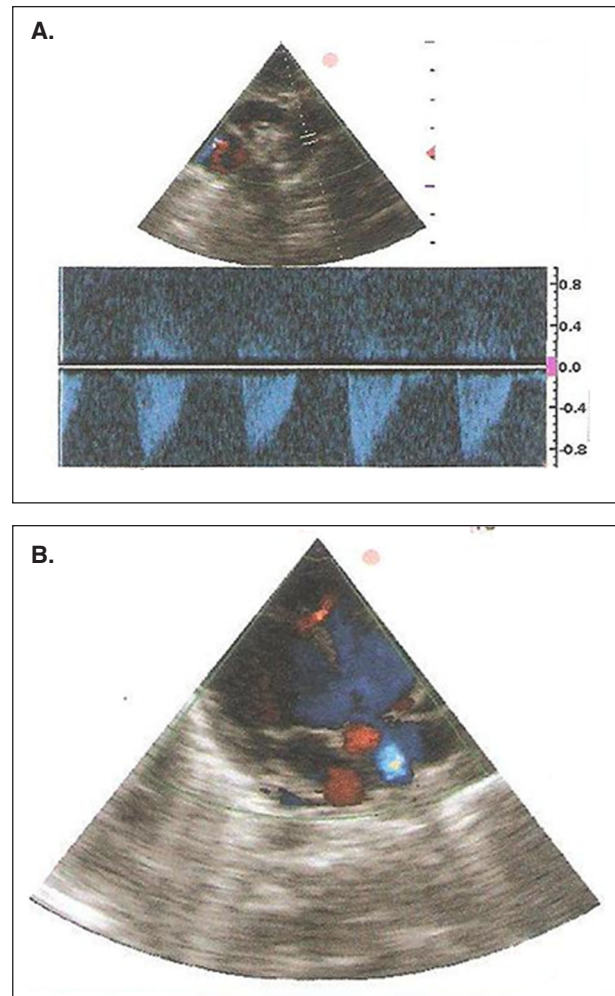


Figure 2. Echocardiography showed patent foramen ovale (A) and interventricular communication (B).

was performed using a human subtelomeric probe-set for all chromosomes. The SALSA – multiplex ligation-dependent probe amplification kits (P036 and P070) were developed and manufactured by MRC-Holland. The preparation and sequences of the probes have been described elsewhere [8].

Fluorescence in situ hybridisation (FISH) was performed to assist in identifying a possible subtelomeric duplication of chromosome 7 long

arm. A subtelomeric probe of chromosome 7 was used (VIJyRM2185).

A microdeletion in the long arm of chromosome 14 (band 14q11.2) and a subtelomeric tandem duplication of chromosome 7 (band 7q36.3) were detected in MLPA and FISH analyses, respectively.

Therefore, the genetic studies revealed a *de novo* translocation involving chromosome 7 and 14: 45,XX,der (7)t(7;14)(q36.3;q11.2),-14dn.ish 7q36.3(VIJyRM2185 enh).mpla 7qsubtel(P036-E1,P070-B2)x3,14q11.2(P036-E1,P070-B2)x1 (Fig. 3 and Fig. 4).

Since the phenotypically normal parents showed normal karyotype, this abnormality was considered *de novo*.

She was discharged for outpatient consultation at age of 13 days.

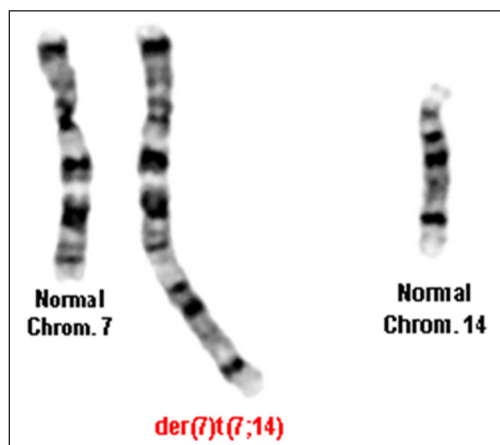


Figure 3. Partial karyotype of the proband, showing normal chromosomes 7 and 14 and der(7)t(7;14) after GTG banding (where GTG is G-banding with trypsin-Giemsa).

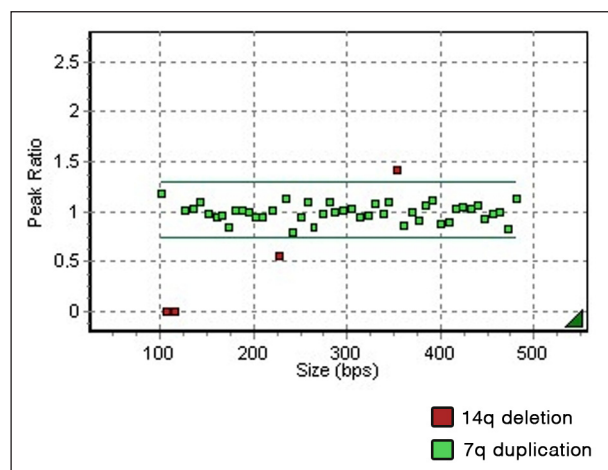


Figure 4. Multiplex-ligation probe amplification (MLPA) results showing a 14q deletion and a 7q duplication.

Currently (4-month-old), she is feeding normally. Her weight is 5.830 g (25th centile), length is 64.5 cm (75th to 90th centiles) and head circumference is 43 cm (75th to 90th centiles). She is alert, visually tracks and has a social smile. She has normal head and trunk control and the neurologic examination is normal.

Discussion

As far as we have investigated, this is the first report of a new cytogenetics imbalance: a tandem dup7q36.8 and a 14q11.2 microdeletion. Since the phenotypically normal parents showed normal karyotype, this abnormality is considered *de novo*.

Here, we used multiplex ligation-dependant probe amplification combined with FISH and cytogenetic studies, which allows us to find this translocation. MLPA facilitates the amplification and detection of multiple targets with a single primer pair. In a standard multiplex PCR reaction, each fragment needs a unique amplifying primer pair. These primers being present in a large quantity result in various problems such as dimerization and false priming. With MLPA, amplification of probes can be achieved. Thus, many sequences (up to 40) can be amplified and quantified using just a single primer pair. MLPA reaction is fast, inexpensive and very simple to perform.

Various techniques including DGGE (denaturing gradient gel electrophoresis), DHPLC (denaturing high performance liquid chromatography), and SSCA (single strand conformation analysis) effectively identify SNPs (single nucleotide polymorphisms) and small insertions and deletions. MLPA, however, is one of the accurate, time-efficient techniques to detect genomic deletions and insertions. MLPA can successfully and easily determine the relative copy number of all exons within a gene simultaneously with high sensitivity.

Alternatively, array comparative genomic hybridization (aCGH) can be used in order to complement the cytogenetic findings, and define accurately the deletion breakpoints and the extent of the deletion. For technical and financial limitations we are not able to provide these analyses. Consequently, it is not possible to establish a precise genotype-phenotype correlation.

This case report suggests that molecular cytogenetic techniques should be used to investigate unpublished translocations, especially when they seems to be associated with dysmorphic features, mild hypotonia in neonatal period and cardiac abnormalities.

Genetic analysis in this case was of significant benefit to the patient's family because it provided a possible explanation for the child's problems.

Knowledge about clinical anomalies associated with translocation involving chromosomes 7 and 14 are still scarce and so we hope this case report could represent an improvement to better characterize this genetic disorder.

Acknowledgements

We would like to thank N. Oliva-Teles, M.C. Ribeiro, M. Mota-Freitas for their assistance with the cytogenetics analyses.

Declaration of interest

The Authors declare that they don't have any financial interests or affiliations with institutions, organizations, or companies that are mentioned in the manuscript or whose products or services are discussed.

References

- Hillier LW, Fulton RS, Fulton LA, Graves TA, Pepin KH, Wagner-McPherson C, Layman D, Maas J, Jaeger S, Walker R, Wylie K, Sekhon M, Becker MC, O'Laughlin MD, Schaller ME, Fewell GA, Delehaunty KD, Miner TL, Nash WE, Cordes M, Du H, Sun H, Edwards J, Bradshaw-Cordum H, Ali J, Andrews S, Isak A, Vanbrunt A, Nguyen C, Du F, Lamar B, Courtney L, Kalicki J, Ozersky P, Bielicki L, Scott K, Holmes A, Harkins R, Harris A, Strong CM, Hou S, Tomlinson C, Dauphin-Kohlberg S, Kozlowicz-Reilly A, Leonard S, Rohlfing T, Rock SM, Tin-Wollam AM, Abbott A, Minx P, Maupin R, Strowmatt C, Latreille P, Miller N, Johnson D, Murray J, Woessner JP, Wendl MC, Yang SP, Schultz BR, Wallis JW, Spieth J, Bieri TA, Nelson JO, Berkowicz N, Wohldmann PE, Cook LL, Hickenbotham MT, Eldred J, Williams D, Bedell JA, Mardis ER, Clifton SW, Chissoe SL, Marra MA, Raymond C, Haugen E, Gillett W, Zhou Y, James R, Phelps K, Iadamoto S, Bubb K, Simms E, Levy R, Clendenning J, Kaul R, Kent WJ, Furey TS, Baertsch RA, Brent MR, Keibler E, Flicek P, Bork P, Suyama M, Bailey JA, Portnoy ME, Torrents D, Chinwalla AT, Gish WR, Eddy SR, McPherson JD, Olson MV, Eichler EE, Green ED, Waterston RH, Wilson RK. The DNA sequence of human chromosome 7. *Nature*. 2003;424(6945):157-64.
- Heilig R, Eckenberg R, Petit JL, Fonknechten N, Da Silva C, Cattolico L, Levy M, Barbe V, de Berardinis V, Ureta-Vidal A, Pelletier E, Vico V, Anthonard V, Rowen L, Madan A, Qin S, Sun H, Du H, Pepin K, Artiguenave F, Robert C, Cruaud C, Brûls T, Jaillon O, Friedlander L, Samson G, Brottier P, Cure S, Ségurens B, Anière F, Samain S, Crespeau H, Abbasi N, Aiach N, Boscus D, Dickhoff R, Dors M, Dubois I, Friedman C, Gouyvenoux M, James R, Madan A, Mairey-Estrada B, Mangenot S, Martins N, Ménard M, Oztas S, Ratcliffe A, Shaffer T, Trask B, Vacherie B, Bellemere C, Belser C, Besnard-Gonnet M, Bartol-Mavel D, Boutard M, Briez-Silla S, Combette S, Dufossé-Laurent V, Ferron C, Lechaplais C, Louesse C, Muselet D, Magdelenat G, Pateau E, Petit E, Sirvain-Trukniewicz P, Trybou A, Vega-Czarny N, Bataille E, Bluet E, Bordelais I, Dubois M, Dumont C, Guérin T, Haffray S, Hammadi R, Muanga J, Pellouin V, Robert D, Wunderle E, Gauguet G, Roy A, Sainte-Marthe L, Verdier J, Verdier-Discala C, Hillier L, Fulton L, McPherson J, Matsuda F, Wilson R, Scarpelli C, Gyapay G, Wincker P, Saurin W, Quétier F, Waterston R, Hood L, Weissenbach J. The DNA sequence and analysis of human chromosome 14. *Nature*. 2003;421(6923):601-7.
- Chotai KA, Brueton LA, van Herwerden L, Garrett C, Hinkel GK, Schinzel A, Mueller RF, Speleman F, Winter RM. Six cases of 7p deletion: clinical, cytogenetic, and molecular studies. *Am J Med Genet*. 1994;51(3):270-6.
- Schwarzbraun T, Windpassinger C, Ofner L, Vincent JB, Cheung J, Scherer SW, Wagner K, Kroisel PM, Petek E. Genomic analysis of five chromosome 7p deletion patients with Greig cephalopolysyndactyly syndrome (GCPS). *Eur J Med Genet*. 2006;49(4):338-45.
- Hinkel GK, Tolkendorf E, Bergan J. [7p-deletion syndrome]. [Article in German]. *Monatsschr Kinderheilkd*. 1988;136(12):824-7.
- Hou JW, Wang TR. Chromosomal rearrangements detected by FISH and G-banding. *J Formos Med Assoc*. 1996;95(9):686-91.
- Kozlowski P, Jasinska AJ, Kwiatkowski DJ. New applications and developments in the use of multiplex ligation-dependent probe amplification. *Electrophoresis*. 2008;29(23):4627-36.
- Schouten JP, McElgunn CJ, Waaijer R, Zwijnenburg D, Diepvens F, Pals G. Relative quantification of 40 nucleic acid sequences by multiplex ligation-dependent probe amplification. *Nucleic Acids Res*. 2002;30(12):e57.