www.jcimcr.org

JCIMCR OPEN ACCESS Journal of Clinical Images and Medical Case Reports

ISSN 2766-7820

Case Report

Open Access, Volume 3

Monosomy 18p and trisomy 17q in a boy with unilateral absence of the right pulmonary artery

Melissa Calzada-Dávila[1]*; Geovana Calvo Anguiano[1]; Silvia Cecilia Britton Robles[2]; Gabriel Rodríguez Camelo[3]; Gloria Cristina Aguilar Arredondo[2]; Olga Judith Santín Saeb[2]; Gloria García Castañeda[1]; Laura E Martínez de Villarreal[1]; Graciela Arelí López-Uriarte[1]

[1]Genetics Department, Hospital Universitario "Dr. José Eleuterio González" and Medicine Faculty, Autonomous University of Nuevo León, Monterrey, Mexico.

[2]Pediatric Cardiology and Hemodynamics, Hospital Zambrano Hellion-TecSalud, Monterrey, Mexico.

[3]Neonatology Service, Hospital Zambrano Hellion-TecSalud, Monterrey, Mexico.

***Corresponding Author: Melissa Calzada-Dávila**
Genetics Department, Hospital Universitario "Dr. José Eleuterio González" and Medicine Faculty, Autonomous University of Nuevo León, Monterrey, Mexico.
Email: calzada_mel@hotmail.com

Received: Apr 29, 2022
Accepted: May 30, 2022
Published: Jun 06, 2022
Archived: www.jcimcr.org

DOI: www.doi.org/10.52768/2766-7820/1871

Abstract

Unilateral absence of the pulmonary artery (UAPA) is an infrequent finding, with an estimated prevalence of 1 in 200,000 young adults. The percentage of syndromic UAPA is not known but mostly does not have a syndromic association, only being reported with the 22q11 deletion syndrome. We present the case of a baby boy with peculiar facies and UAPA, who developed severe bilateral pulmonary fibrosis, his molecular cytogenetics identify an unbalanced structural rearrangement leading to trisomy 17q25.1-qter and monosomy of 18p11.21-pter. There are no reported cases of severe bilateral pulmonary fibrosis associated with UAPA in early infancy and we speculate the genetic mechanism that could explain this phenomenon. Besides, this is the second report in the literature of partial trisomy 17q and partial monosomy 18p, with an inherited maternal origin.

Keywords: Inherited unbalanced translocation; Monosomy 18p; Trisomy 17q; Unilateral absence of the right pulmonary artery; UAPA.

Abbreviations: UAPA: Unilateral absence of the pulmonary artery; CMA: Chromosomal microarray; CNV: Copy number variants; WoG: Weeks of gestation; aCGH: array-based comparative genomic hybridization.

Introduction

Unilateral absence of the pulmonary artery (UAPA) is an infrequent finding, with an estimated prevalence of 1 in 200,000 young adults [1]. It may be isolated, but it is more often associated with other congenital cardiac defects [2]. Two types of clinical presentations have been reported: it can be either a random finding during imaging or it can present with hemoptysis or progressive dyspnea on exertion [3]. The embryologic cause of UAPA is still a matter of debate [4] and mostly does not have a syndromic association, only being related to the 22q11 chromosome deletion syndrome [3,5].

Chromosomal microarray (CMA) detects losses and gains of DNA material that is smaller than 1Mb, or less, also called copy number variants (CNV) [6]. The CMA provides a molecular diagnosis in 15 to 20% of cases of intellectual disability, developmental delays, autism, or congenital anomalies [7]. The CNV can occur either de novo or through parental transmission [8].

We present the case of a male baby with UAPA and peculiar facies, in whom it was possible to characterize an unbalanced structural rearrangement leading to trisomy 17q25.1-qter and monosomy of 18p11.21-pter. This is the second report in the literature with these two rearrangements together, instead our case has a congenital heart disease, and it was originated by an inherited rearrangement.

Case presentation

The proband was 1-month-old Mexican boy who was diagnosed prenatally with increased nuchal translucency (7 mm) at 11th weeks of gestation (WoG). Non-invasive prenatal test was performed with a normal result at 14.1 WoG (screening for trisomy 21, 13, 18, sexual aneuploidies and five microdeletion syndromes). The boy was born to 33y.o. healthy mother and 36 y.o. father, non-consanguineous, who already had a previous spontaneous miscarriage at 8 WoG.

Upon delivery at 36 WoG, measurements at birth were normal. Clinical examination revealed respiratory distress, so he was admitted to the neonatal intensive care unit. He had dysmorphic features, widely spaced nipples, right cryptorchidism, sacral dimple, aberrant plantar creases, and 3rd left toe was hypoplastic (Figure 1).

The echocardiogram was suspicious of absence of the right pulmonary artery and aortic coarctation which were later confirmed with a cardiac CT-scan and lung ventilation/ perfusion scan. Patent ductus arteriosus, atrial septal defect and severe pulmonary hypertension were also identified. He underwent cardiac catherization aiming pulmonary artery revascularization. However, revascularization wasn't successful and balloon aortoplasty was performed with a residual gradient of 10mmHg. His evolution during hospitalization was torpid, requiring aggressive management of pulmonary hypertension. He was discharged 2 months later, with ambulatory pharmacological treatment and supplemental oxygen support at home.

Genomic DNA from peripheral blood was analyzed by array-based comparative genomic hybridization (aCGH). The chromosomal microarray showed a terminal gain on 17q (17q25.1 to 17q25.3) with a size of 7783 Kb and 280 genes involved; in addition to a terminal deletion on 18p (18p11.21 to 18p11.32) with a size of 13135 Kb and 94 genes involved.

To determine the origin of the unbalanced rearrangement, analysis of parental chromosomes was solicited. The conventional chromosomal analysis revealed a balanced translocation between 18p and 17q in the mother, and a normal karyotype in the father. Thus, the proband was found to have a maternally derived unbalanced translocation. A segregation analysis was performed to complete the genetic counseling. Finding that the theoretical chance for them to have a normal chromosomally balanced embryo is 12.5%.

The patient was readmitted 2 months later due to a pulmonary hypertension crisis which led to cardiac arrest. After successful reanimation, he required intubation and mechanical ventilation. Cardiac catheterization was performed for stent angioplasty of the right pulmonary artery which originated from the common brachiocephalic trunk (Figure 2A). Once stabilized, an extended resection and end-to-end anastomosis for aortic coarctation was performed. He had a poor clinical evolution during hospitalization, presenting severe left pulmonary fibrosis (Figure 2B) and bilateral pneumothorax, which led to acute respiratory failure and death one month later.

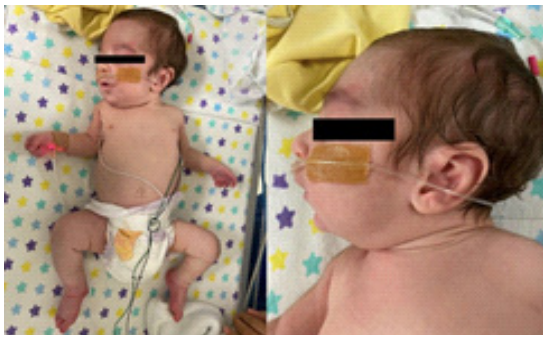

Figure 1: Dysmorphic features including telecanthus, wide nasal bridge, bulbous nasal tip, down-turned mouth, thin upper lip, low-set and posteriorly rotated ears, micro-retrognathia, short and webbed neck and redundant nuchal fold.

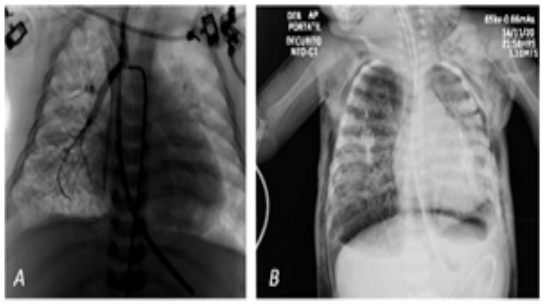

Figure 2: A. Cardiac catherization showing stenting of the right pulmonary artery. B. Chest X-ray showing extensive bilateral infiltrates corresponding to severe pulmonary fibrosis.

Discussion

Trisomy of the distal portion of long (q) arm of chromosome 17 is a rare, but recognized, syndrome, with ~20 cases reported till 2018 [9]. Instead, the partial monosomy 18p is a well-recognized syndrome, with around 150 reported cases [10]. The first report of partial trisomy 17q and partial monosomy 18p was made in 2003, they reported a girl with de novo unbalanced translocation [11]. Her facial appearance was quite similar to our case. At 11 months of age, she was reassessed and presented profound psychomotor retardation, failure to thrive, microcephaly, and splenomegaly. Subsequently, the follow-up of the patient was lost (personal communication with Dr. Velagaleti). There is very little information about UAPA in infancy [3] and, as far as we know, had only previously been associated with the 22q11 deletion syndrome [3,5].

We hypothesize that deletion of 94 genes on 18p11.32 could be the cause of the clinical features [12]. Of these deleted genes, *LAMA1, NDUFV2, PTPRM, MYL12A*, and *MYL12B*, may be genes of interest for their possible involvement in the congenital defects of the patient since they fulfill functions of regulation of cell processes including proliferation, cell growth, regulation in the development of cardiac muscle, blood vessel and morphogenesis. Mainly *LAMA1* that was found by Lee et al. (2018) in a murine model identified as a genetic modifier of TGF-β1 effector responses that significantly affects the development of

pulmonary fibrosis [13]. Another interesting gene with possible association to clinics is *NDUFV2*, reported before in early onset hypertrophic cardiomyopathy and encephalopathy [14].

Regarding the duplication in 17q25.1, no reports were found in the literature that links any candidate gene or gene with significance in congenital heart disease and the clinical characteristics of the patient. Although we cannot completely rule out a synergistic effect in the determination of the phenotype.

Conclusion

In summary, we present the first case of an inherited translocation resulting in trisomy for the 17q region and monosomy for the 18p. This is, to the best of our knowledge, the second infant with this unbalanced rearrangement, and the first associated with unilateral absence of the right pulmonary artery.

Declarations

Acknowledgements: The authors would like to thank the patient's parents for their support and consent.

Conflict of interest: There are no conflicts of interest.

References

1. Bouros D, Pare P, Panagou P, Tsintiris K, Siafakas N. The varied manifestation of pulmonary artery agenesis in adulthood. Chest. 1995; 108(3): 670-6. doi: 10.1378/chest.108.3.670. PMID: 7656614.

2. Kruzliak P, Syamasundar RP, Novak M, Pechanova O, Kovacova G. Unilateral absence of pulmonary artery: pathophysiology, symptoms, diagnosis and current treatment. Arch Cardiovasc Dis. 2013; 106(8-9): 448-54. doi: 10.1016/j.acvd.2013.05.004. Epub 2013 Aug 9. PMID: 23938302.

3. Christou E, Bourousis E, Servos G, Xatzipsalti M, Kaditis AG, Delis D, Vazeou A. Unilateral pulmonary artery agenesis in an infant with 22q11.2 deletion syndrome. Pediatr Pulmonol. 2020; 55(9): 2184-2186. doi: 10.1002/ppul.24867. Epub 2020 Jun 12. PMID: 32531097.

4. Raymond A, Pedretti E, Privitera G, Cicero C, Biasucci G. Neonatal diagnosis of isolated absence of the right pulmonary artery: a case report and review of the literature. Ital J Pediatr. 2018; 44(1): 27. doi: 10.1186/s13052-018-0465-1. PMID: 29463283; PMCID: PMC5819273.

5. McElhinney DB, Clark BJ 3rd, Weinberg PM, Kenton ML, McDonald-McGinn D, Driscoll DA, et al. J Am Coll Cardiol. 2001; 37(8): 2114-9. doi: 10.1016/s0735-1097(01)01286-4. PMID: 11419896.

6. Bi W, Borgan C, Pursley AN, Hixson P, Shaw CA, Bacino CA, et al. Comparison of chromosome analysis and chromosomal microarray analysis: what is the value of chromosome analysis in today's genomic array era? Genet Med. 2013; 15(6): 450-7. doi: 10.1038/gim.2012.152. Epub 2012 Dec 13. PMID: 23238528.

7. Mefford HC, Batshaw ML, Hoffman EP. Genomics, intellectual disability, and autism. N Engl J Med. 2012; 366(8): 733-43. doi: 10.1056/NEJMra1114194. PMID: 22356326; PMCID: PMC4107681.

8. Ganguly BB, Kadam V, Kadam NN. Clinical expression of an inherited unbalanced translocation in chromosome 6. Case Rep Genet. 2011; 2011: 396450. doi: 10.1155/2011/396450. Epub 2011 Sep 25. PMID: 23074675; PMCID: PMC3447228.

9. Upadia J, Philips JB 3rd, Robin NH, Lose EJ, Mikhail FM. A case report of chromosome 17q22-qter trisomy with distinct clinical presentation and review of the literature. Clin Case Rep. 2018; 6(4): 612-616. doi: 10.1002/ccr3.1298. PMID: 29636925; PMCID: PMC5889218.

10. Brenk CH, Prott EC, Trost D, Hoischen A, Walldorf C, Radlwimmer B, et al. Towards mapping phenotypical traits in 18p- syndrome by array-based comparative genomic hybridisation and fluorescent in situ hybridisation. Eur J Hum Genet. 2007; 15(1): 35-44. doi: 10.1038/sj.ejhg.5201718. Epub 2006 Oct 4. PMID: 17024214.

11. Velagaleti GV, Jalal SM, Michaelis RC, Rowe TF, Nichols JR, Lockhart LH. Molecular cytogenetic characterization of a de novo unbalanced translocation leading to trisomy 17q25-->qter and monosomy 18p11.3-->pter in a girl with dysmorphic features. Clin Dysmorphol. 2003; 12(1): 29-33. doi: 10.1097/00019605-200301000-00005. PMID: 12514362.

12. Brenk CH, Prott EC, Trost D, Hoischen A, Walldorf C, Radlwimmer B, et al. Towards mapping phenotypical traits in 18p- syndrome by array-based comparative genomic hybridisation and fluorescent in situ hybridisation. Eur J Hum Genet. 2007; 15(1): 35-44. doi: 10.1038/sj.ejhg.5201718. Epub 2006 Oct 4. PMID: 17024214.

13. Lee CM, Cho SJ, Cho WK, Park JW, Lee JH, Choi AM, et al. Laminin α1 is a genetic modifier of TGF-β1-stimulated pulmonary fibrosis. JCI Insight. 2018; 3(18): e99574. doi: 10.1172/jci.insight.99574. PMID: 30232270; PMCID: PMC6237225.

14. Bénit P, Beugnot R, Chretien D, Giurgea I, De Lonlay-Debeney P, Issartel JP, Corral-Debrinski M, Kerscher S, Rustin P, Rötig A, Munnich A. Mutant NDUFV2 subunit of mitochondrial complex I causes early onset hypertrophic cardiomyopathy and encephalopathy. Hum Mutat. 2003; 21(6): 582-6. doi: 10.1002/humu.10225. PMID: 12754703.