Tzu Chi Medical Journal 24 (2012) 90–91

Contents lists available at SciVerse ScienceDirect

Tzu Chi Medical Journal

journal homepage: www.tzuchimedjnl.com

Clinical Practice and Therapeutics

Dup(3) (p23p25) syndrome and array-based comparative genomic hybridization

Chun-Ying Weng [a], Peng-Yeong Woon [b], Pei-Chun Lai [a], Yu-Hsun Chang [a], Tzu-Ying Li [a], Yi-Ning Su [c], Jye-Siung Fang [b], Shao-Yin Chu [a,d,*]

[a] Department of Pediatrics, Buddhist Tzu Chi General Hospital, Hualien, Taiwan
[b] Department of Molecular Biology and Human Genetics, Tzu Chi University, Hualien, Taiwan
[c] Department of Medical Genetics, National Taiwan University Hospital, Taipei, Taiwan
[d] Department of Medical Education, Buddhist Tzu Chi General Hospital, Hualien, Taiwan

ARTICLE INFO

Article history:
Received 1 August 2011
Received in revised form
20 September 2011
Accepted 3 October 2011

A high resolution peripheral blood G-banded chromosome study was arranged for a 3-month-old female infant due to the presence of multiple congenital anomalies (MCA), including: flat face, flat occiput, flat nasal bridge, retrognathia, fish mouth, low set and dysplastic ears, temporal narrowing, short neck and prominent nuchal fold, and clinodactyly and hypoplastic toe nails (Fig. 1). Soon after birth, the infant was found to have mild whole body edema with hypoalbuminemia of an unknown cause and congenital heart disease, which included patent ductus arteriosus (PDA) and tricuspid regurgitation. No evidence of congestive heart failure or PDA persisted after two doses of oral indomethacin. Preterm labor had not occurred and the infant's birth weight was 3.2 kg. During follow-up at an outpatient clinic, weak crying, extended daytime sleeping, and delayed developmental milestones were noted by the early infant developmental screening program.

Karyotyping revealed 46,XX, dup(3) (p23p25) (20 cells); a surprising *de novo* chromosomal aberration due to the fact that parental peripheral blood chromosome studies were normal. No similar chromosomal anomaly has been identified in Taiwan or in the scientific literature. Chromosomal microarray (CMA) by array-based comparative genomic hybridization (aCGH) was carried out in order to determine copy number of the chromosomal aberration and revealed: arr 3p26.3p24.2 (RP11-63O1→RP11-1149N13) ×3 (Fig. 2).

In 2010, consensus was that CMA is a first-tier clinical diagnosis method for patients affected by multiple congenital anomalies, autism spectrum disorder, unexplained developmental delay, or intellectual disability because CMA has greater sensitivity when detecting submicroscopic deletions or duplications. The density of aCGH is sufficient to allow detection of copy number changes around 1 Mega base-pair (Mbp). This should be compared to G-banded karyotyping which detects genomic imbalances in the range of 5–10 Mbp on occasion. CMA represents a greater than 10-fold improvement in resolution and narrows down potential indications from G-banded karyotyping to obvious chromosomal diseases, e.g. Down syndrome, especially when there is a family history of chromosomal rearrangement or a history of multiple miscarriages.

As part of the patient's clinical care and with the parents' informed consent, there were clear indications that supported carrying out aCGH, making it possible to pinpoint the more precise genomic variations. Nonetheless, issues associated with chromosomal variations of uncertain clinical significance are still present. The fact that there are no uniform guidelines for determining the clinical significance of genetic variation identified by aCGH poses a challenge. In this context, poor correlation between phenotype and genotype remains a major issue that needs to be explored. In many cases, the benefits of CMA do not yet directly affect the patient.

Further reading

[1] Shinawi M, Cheung SW. The array CGH and its clinical applications. Drug Discov Today 2008;13:760–70.
[2] Miller DT, Adam MP, Aradhya S, Biesecker LG, Brothman AR, Carter NP, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. Am J Hum Genet 2010;86:749–64.
[3] Shaffer LG, Slovak ML, Campbell LC. International Standing Committee on Human Cytogenetic Nomenclature (ISCN): an international system for human cytogenetic nomenclature. KARGER; 2009:122–3.

* Corresponding author. Department of Pediatrics, Buddhist Tzu Chi General Hospital, 707, Section 3, Chung-Yang Road, Hualien, Taiwan. Tel.: +886 38561825x3649; fax: +886 38563532.
E-mail address: chu_chu@tzuchi.com.tw (S.-Y. Chu).

doi:10.1016/j.tcmj.2011.12.001

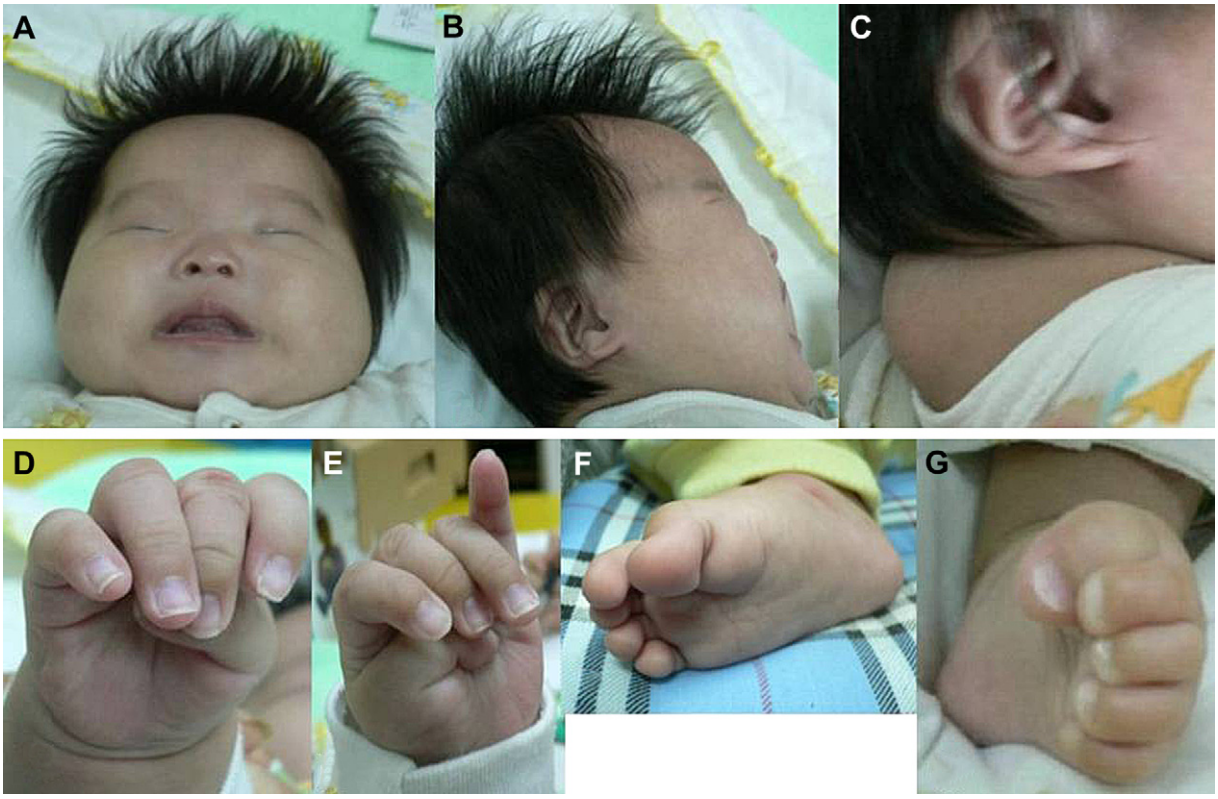

Fig. 1. Dup(3) (p23p25) syndrome. (A) Flat face, full cheeks, fish mouth, flat nasal bridge, hypertelorism, temporal narrowing. (B) Flat occiput, retrognathia, low set dysplastic ears. (C) Prominent nuchal fold, short neck. (D, E) Overlapping fingers. (F) Prominent toetip pads. (G) Hypoplastic toenail (published with the parents' consent).

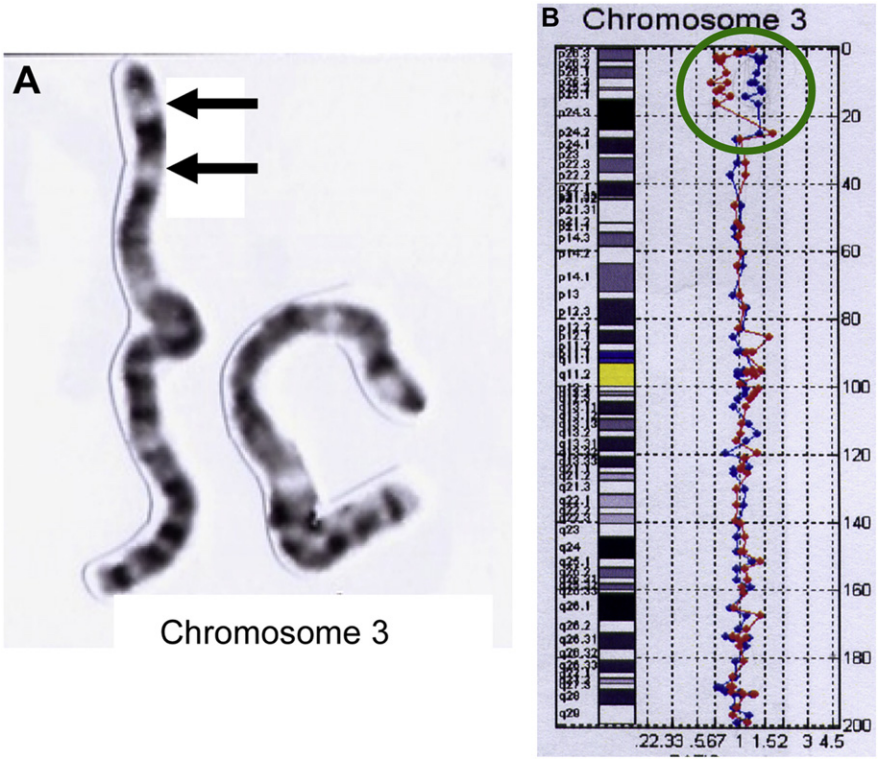

Fig. 2. (A) Karyotype result: 46,XX, dup(3) (p23p25). Double arrow indicates the duplication area. (B) Array-based comparative genomic hybridization result (circled) from 3p26 to 3p24.2 (2495414→16469054), which shows the presence of a 14 MB gene duplication.