Letter to the Editor
Diagnostic Genetics

Ann Lab Med 2018;38:77-79
https://doi.org/10.3343/alm.2018.38.1.77
ISSN 2234-3806 • eISSN 2234-3814

ANNALS OF LABORATORY MEDICINE

Deletion of 20p13 and Duplication of 20p13p12.3 in a Patient with Delayed Speech and Development

Soon Sung Kwon, M.D.[1], Jieun Kim, M.D.[2], Saeam Shin, M.D.[3], Seung-Tae Lee, M.D.[1], Kyung-A Lee, M.D.[1], and Jong Rak Choi, M.D.[1]

Department of Laboratory Medicine[1], Yonsei University College of Medicine, Seoul; Department of Laboratory Medicine[2], Soon Chun Hyang University College of Medicine, Seoul; Department of Laboratory Medicine[3], Hallym University College of Medicine, Seoul, Korea

Dear Editor,

Few cases involving deletions and duplications of the short arm of chromosome 20 have been reported; these patients present various phenotypes, including developmental delays and dysmorphic features [1-10]. In the majority of cases, 20p deletions and duplications are accompanied by defects in other chromosomes [1-3]. Here, we report a patient with a complex partial deletion and duplication involving 20p only, identified by chromosomal microarray (CMA).

A 3-year-old girl visited Severance hospital located in Shinchon, Seoul, in 2015 for evaluation of delayed speech and development. The patient had been managed for speech and developmental delays in our center for a year. There was no family history of delayed development, and her older sister and brother showed normal development. The patient was born at 34 weeks of gestation by cesarean section, and her birth weight was 3,840 g. Her growth parameters, weight, height, and head circumference were within normal ranges. Physical examination indicated mild craniofacial dysmorphisms, including a bulging head, prominent forehead, widely spaced eyes, wide nasal bridge, and a prominent lower jaw. She also exhibited pes plano valgus. Psychological assessment revealed psychomotor retardation with delayed social development. Direct sequencing of *MECP2* revealed no pathogenic variant. Conventional G-banding chromosome analysis showed a duplication in 20p; however, the affected regions could not be designated accurately. Further CMA testing revealed a 928-kb deletion in 20p13 and a 6.6-Mb duplication of 20p13p12.3; the final karyotype was designated as arr 20p13 (61,661-1,043,325)×1, 20p13p12.3(1,045,639-7,604,026)×3. The patient's speech development improved and normalized following two years of speech training. The genetic analysis in this study was conducted with the written informed consents from the parents of the patient. This study was exempted from approval by the institutional review board of the hospital (Fig. 1).

Although various clinical features such as dysmorphic face, and language and developmental delay have been associated with partial 20p deletion and duplication, correlations between deletions, duplications, and phenotype are complicated by accompanying defects in other chromosomes. Deletions involving the short arm of chromosome 20 are rare. Most of these include the deletion of *JAG1* located in 20p12.2, known to be related to Alagille syndrome, which affects the liver, heart, and other organs and manifests distinctive facial features [9]. Deletions of 20p13 excluding *JAG1* are rarer and have been reported to be related to motor and speech development delays, varying degrees of mental retardation, various forms of epilepsy, and mild

Received: February 1, 2017
Revision received: May 10, 2017
Accepted: September 19, 2017

Corresponding author: Jieun Kim
Department of Laboratory Medicine, Soon Chun Hyang University College of Medicine, 59 Daesagwan-ro, Yongsan-gu, Seoul 04401, Korea
Tel: +82-2-2228-1745, Fax: +82-2-2228-6113
E-mail: jkim1220@schmc.ac.kr

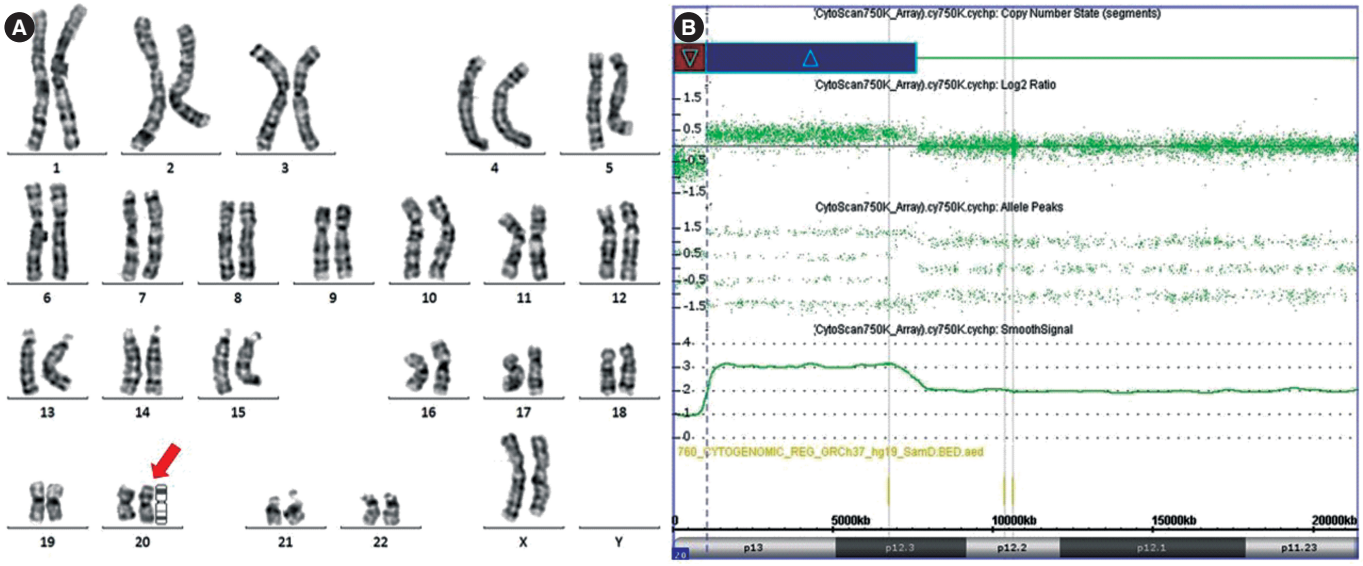

Fig. 1. Karyotype and microarray results of the present case. (A) A duplication in 20p was revealed by conventional G-banding chromosome analysis. (B) Chromosomal microarray revealed a subtelomeric deletion of 20p accompanied by a duplication of 20p13p12.3.

facial dysmorphisms [8]. The clinical features of patients with 20p duplications overlap with those with 20p deletions. The characteristic features of 20p duplications include dysmorphic facial features, developmental delay, poor coordination, mental retardation, speech delay, and dental anomalies [1-3].

To date, only two case studies have reported duplications in the short arm of chromosome 20 accompanied by a subtelomeric deletion of 20p [4, 5]. In these two cases, the common features of the affected patients included facial dysmorphisms, psychomotor retardation, delayed development, and speech difficulties. Our patient presented with similar phenotypic traits; however, the degree of the abnormalities was milder than those in the previously reported patients (Table 1).

Differences in the sizes of the deletions and duplications may account for the variance in clinical feature severity. In the previously reported cases, the subtelomeric deletions of 20p13 were 1.64 Mb and 2.02 Mb in size, and the duplications were 18.9 Mb and 18.2 Mb in size, whose affected sizes were larger than that in our patient. Moreover, the 20p genetic aberrations in those two cases consisted of inverted duplications associated with a terminal deletion, which were confirmed by FISH analysis. However, in our case, the presence or absence of an inverted duplication and deletion could not be confirmed because FISH analysis was not performed.

Of the genes located in the subtelomeric region of 20p, *SOX12* and *NRSN2* have been associated with developmental delay, especially language development [10]. Indeed, a few previous cases of 20p13 deletion accompanied by language developmental delay [4, 5, 7, 8, 10], as well as our patient, harbored a deletion of the chromosomal region, in which *SOX12* and *NRSN2* are located. Although partial deletion and duplication of 20p were identified in our patient, her dysmorphic findings, except for speech development delay, were not consistent with the clinical features in previous reports. This case enhances our understanding of this genomic region and also underlines the importance of genomic studies using CMA in diagnosing patients with unexplained developmental delays and confirming genomic rearrangements that are difficult to identify by conventional karyotyping.

Table 1. Phenotypic traits of the cases with 20p duplications and deletions

Phenotypic traits	Leclercq et al. (2009) [4]	Trachoo et al. (2013) [5]	Present case
Psychomotor retardation	+	+	+
Mental retardation	+	+	-
Poor motor coordination	+	+	+
Poor speech	+	+/-	+
Round face with prominent cheeks	+	+	-
Wide nasal bridge	+	+	+
Prominent forehead	+	+	+
Short nose with large nostrils	+	+	-

https://doi.org/10.3343/alm.2018.38.1.77

Authors' Disclosures of Potential Conflicts of Interest

The authors have declared no conflict of interest.

REFERENCES

1. Freitas EL, Gribble SM, Simioni M, Vieira TP, Silva-Grecco RL, Balarin MA, et al. Maternally inherited partial monosomy 9p (pter --> p24.1) and partial trisomy 20p (pter --> p12.1) characterized by microarray comparative genomic hybridization. Am J Med Genet Part A 2011;155A:2754-61.
2. Meloni Vde F, Piazzon FB, Soares Mde F, Takeno SS, Christofolini DM, Kulikowski LD, et al. Cytogenomic characterization of an unexpected 17.6 Mb 9p deletion associated to a 14.8 Mb 20p duplication in a dysmorphic patient with multiple congenital anomalies presenting a normal G-banding karyotype. Gene 2012;496:59-62.
3. Oegema R, van Zutven LJ, van Hassel DA, Huijbregts GC, Hoogeboom AJ. Unbalanced three-way chromosomal translocation leading to deletion 18q and duplication 20p. Eur J Med Genet 2012;55:265-8.
4. Leclercq S, Maincent K, Baverel F, Tessier DL, Letourneur F, Lebbar A, et al. Molecular cytogenetic characterization of the first reported case of inv dup del 20p compatible with a U-type exchange model. Am J Med Genet Part A 2009;149A:437-45.
5. Trachoo O, Assanatham M, Jinawath N, Nongnuch A. Chromosome 20p inverted duplication deletion identified in a Thai female adult with mental retardation, obesity, chronic kidney disease and characteristic facial features. Eur Med Genet 2013;56:319-24.
6. Kang JE, Park MY, Cheon CK, Lee HD, Hwang SH, Yi J. A case of partial trisomy 20p resulting from meiotic recombination of a maternal pericentric inversion. Ann Lab Med 2012;32:91-4.
7. Martin MM, Vanzo RJ, Sdano MR, Baxter AL, and South ST. Mosaic deletion of 20pter due to rescue by somatic recombination. Am J Med Genet Part A 2016;170A:243-8.
8. Moutton S, Rooryck C, Toutain J, Cailley D, Bouron J, Villega F, et al. Dysmorphic features in subtelomeric 20p13 deletion excluding JAG1: a recognizable microdeletion phenotype? Eur J Med Genet 2012;55:151-5.
9. Zhang F, Deleuze JF, Aurias A, Dutrillaux AM, Hugon RN, Alagille D, et al. Interstitial deletion of the short arm of chromosome 20 in arteriohepatic dysplasia (Alagille syndrome). J Pediatr 1990;116:73-7.
10. An Y, Amr SS, Torres A, Weissman L, Raffalli P, Cox G, et al. SOX12 and NRSN2 are candidate genes for 20p13 subtelomeric deletions associated with developmental delay. Am J Med Genet Part B Neuropsychiatr Genet 2013;162B:832-40.