



## De Novo Pure Trisomy 20p: Report of a Novel Case of a Marker Chromosome and Literature Review

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Dear Editor,

Trisomy 20p is a rare genetic disorder manifesting as intellectual disability, speech delay, specific facial features, and delayed motor milestones. Severity of the symptom depends on chromosome 20p duplication size; larger chromosomal duplications usually result in more serious symptoms [1]. Most previously reported cases involved partial trisomy 20p derived from a parental reciprocal translocation, chromosome inversion, or a small supernumerary marker chromosome (sSMC) [1-5]. However, only a few cases of pure trisomy 20p (involving whole short arm of chromosome 20) have been reported [1, 5-9].

We report a case of pure trisomy 20p arising from a *de novo* marker chromosome, 20p(47,XX,+mar), with a non-reciprocal translocation, which was characterized at the molecular level by comparative genomic hybridization (CGH). To the best of our knowledge, this is the first case of *de novo* pure trisomy 20p arising from a marker chromosome in Korea. In addition, we reviewed previously reported cases of trisomy 20p syndrome and compared them with the phenotype of our patient. We received informed consent from the patient for all the genetic testings. This study was approved by the Institution Review Board of Korea University Guro Hospital, Seoul, Korea (IRB-2019GR0429).

The patient was referred at 30 months of age, in June 2017,

to Korea University Guro Hospital, Seoul, Korea, for an evaluation of developmental and speech delay. She was the last of four children of unrelated healthy Korean parents aged 39 (mother) and 40 years (father), respectively. Physical examination showed facial asymmetry, micrognathia, strabismus, and a large ear; neither cardiac syndrome nor renal abnormalities were observed. The neurological examination revealed poor coordination in gross and fine motor skills. Brain magnetic resonance imaging did not reveal any structural abnormalities in the auditory system.

In the developmental and speech delay evaluation, the scores were <0.1% of the scales defining moderate mental retardation in the Korean Bayley Scales of Infant and Toddler Development-II and <1% of the scales indicating speech delay Sequenced Language Scale for Infants. However, the Childhood Autism Rating Scale score was 27 (cutoff: 30); thus, she was classified as a non-autistic child.

The cytogenetic examination was carried out on peripheral blood of the patient and her parents. Chromosome harvesting and karyotyping were performed following a standard protocol, phytohemagglutinin-stimulated peripheral blood culture.

The proband's karyotype was defined as 47,XX,+mar in metaphase (Fig. 1A), while the mother and father had normal karyotypes of 46,XX and 46,XY, respectively. Genomic DNA was ob-

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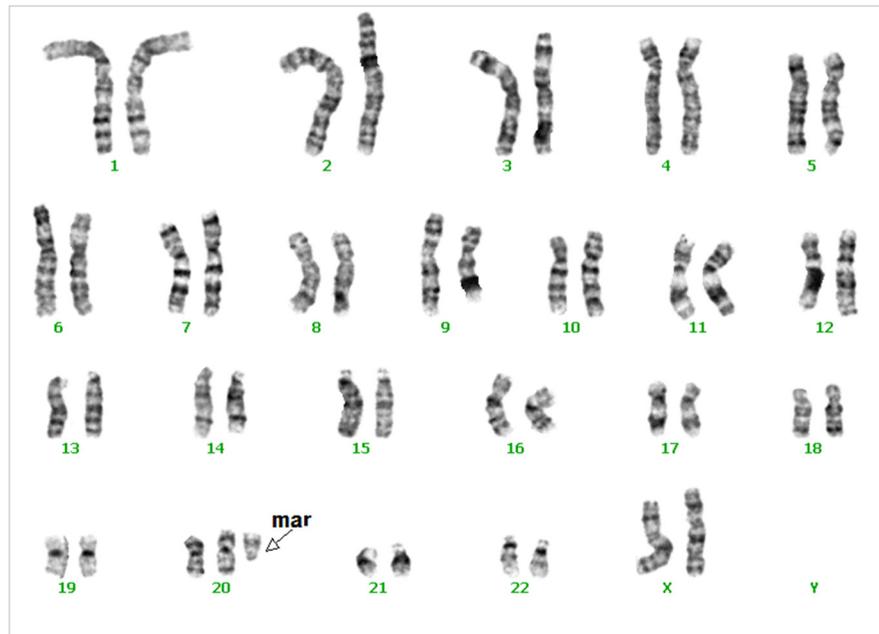


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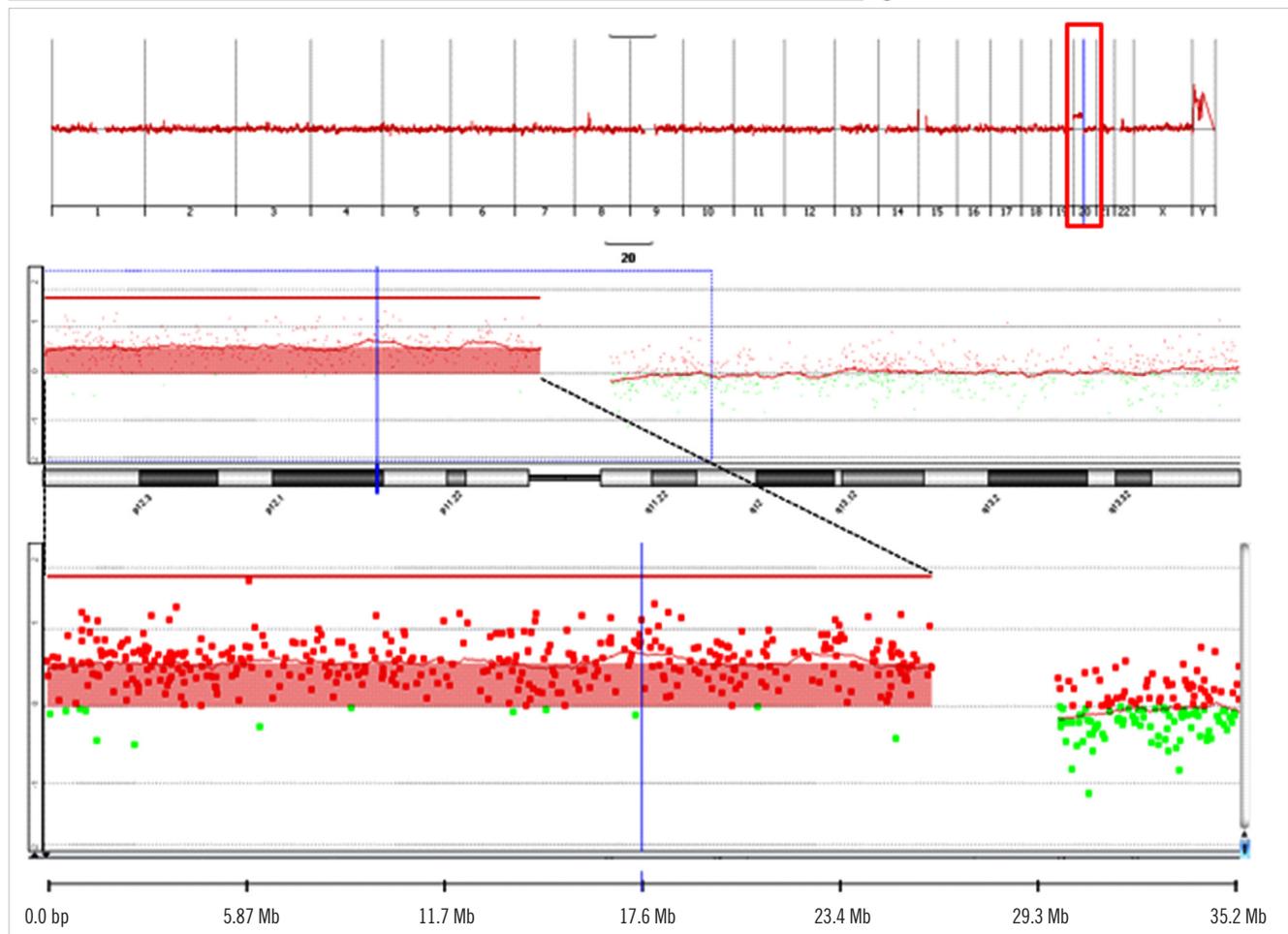
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tained from patient's peripheral blood and subjected to array-CGH analysis (Fig. 1B). Molecular characterization of the sSMC

identified it as  $\text{arr}[\text{GRCh38}] \text{20p13p11.1}(140880\_26207158) \times 3$  (Fig. 1). According to the array-CGH results, the sSMC of our



**Fig. 1.** Chromosome analysis and array CGH. (A) Karyotype of the patient showing the marker chromosome (arrow). (B) Detailed views of the microarray plots for the patient. The horizontal axis shows megabases (Mb) from the chromosome 20 (26.06 Mb duplication), and the vertical axis shows the fold-change in copy number variation (red dot: patient DNA tagged with red fluorescence, green dot: reference control DNA tagged with red fluorescence). Abbreviation: CGH, comparative genomic hybridization.



**Table 1.** Summary of the clinical features of pure trisomy 20p cases

Our patient	van Langen, et al. (1996) [6]	Oppenheimer, et al. (2000) [1]	Sidwell, et al. (2000) [7]	Chaabouni, et al. (2007) [8]	Bartolini, et al. (2013) [9]	Liehr (2018) [5]	
Karyotype	47,XX,+mar. arr[GRCh38] 20p13p11.1 (140880_26207158) x3 dn	46,XY,der(12) t(12;20) (p13.3;p11.1) pat	46,XX,der(12) t(12;20) (p13.3;p11.1) pat	46,XY,der(4) t(4;20) (pter;q11.1), i(20)(q11.1)	46,XY,der(20) (pter→q13.3:: p11.2→pter)	47,XX,+mar(20) (pter→q11.1.) [29]/46,XX[19] (20-Uu-1) 2-2)*	47,+min(20) (pter→q10.) (20-W-p13/ 3-2)*
Parents	46,XX 46,XY	46,XX 46,XY,t(12;20) (p13.3;p11.1)	46,XX 46,XY	46,XX 46,XY	46,XX 46,XY	Unknown	Unknown
Mental retardation	+	+	+	+	+	Unknown	+
Speech delay	+	+	+	+	+	Unknown	Unknown
Motor develop delay	+	+	+	+	+	Unknown	+
Strabismus	+	-	-	-	+	Unknown	Unknown
Micrognathia	+	+	+	+	+	Unknown	+
Large ears	-	Unknown	Unknown	+	-	Unknown	-
Congenital heart disease	-	+	-	+	+	Unknown	+, 4 VSDs and a PFO
Finger abnormalities	-	+(thumb adduction)	+(clinodactyly)	-	+(hexadactyly)	+(thumb anomalies)	+slightly widened bulbar fingers
Renal abnormalities	-	+(absent Lt kidney)	-	+	-	+(multi cystic dysplasia(Lt))	+hypospadias
Facial asymmetry	+	-	+	+	-	Unknown	Unknown
Vertebral anomalies	-	+	+	+	+	Unknown	+, scoliosis

+, present; -, absent; \*, terminated.

Abbreviations: VSD, ventricular septal defect, PFO, patent foramen ovale.

patient included the entire short arm (26.06 Mb) of chromosome 20, which is not related to the long arm of chromosome 20 or to other chromosomes. In addition, no mosaicism was detected. The effects of the sSMC on phenotype depend on euchromatin size (> 1 Mb) and the level of mosaicism (average 68%) [5].

The clinical findings of the present case were similar to those of previously reported pure trisomy 20p cases (Table 1). The patient reported by Sidwell, *et al.* [7] grew normally (approximately 10th percentile) and achieved improvement through speech therapy and physiotherapy. Our patient showed no skeletal abnormalities till date and is able to walk on her own. She is evaluated regularly at our clinic and is under careful observation. Some studies have reported that sSMC also increases the risk of uniparental disomy (UPD)[5, 10]. Therefore, the limitation of our study is that the UPD testing was not performed.

Majority of patients with trisomy 20p syndrome seem to have normal weight at birth and survive through adulthood, which may delay diagnosis similar to that in our patient. Therefore, early detection of trisomy 20p is important in diagnosis and proper genetic counseling. Our case is the first report of a pure trisomy 20p from sSMC in Korea.

## AUTHOR CONTRIBUTIONS

Drafting of the manuscript: JC, JAK. Review of patients' clinical information: BLE. Critical revision of the manuscript: BGP, SY, JAK. Interpretation of genetic data: MK, JAK.

## CONFLICTS OF INTEREST

None declared.

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