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Research Letter

Prenatal diagnosis and molecular cytogenetic characterization of a mosaic derivative Y chromosome derived from a *de novo* unbalanced reciprocal Yq;13q translocation

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Prenatal diagnosis of a *de novo* unbalanced reciprocal translocation involving chromosomal segments with subtle difference in banding requires molecular cytogenetic technologies, such as spectral karyotyping (SKY), fluorescence *in situ* hybridization, and array-based comparative genomic hybridization, to characterize the nature of the aberrant chromosome [1]. Here, we report prenatal diagnosis and molecular cytogenetic characterization of *de novo* mosaic trisomy 13q (13q31.3→qter) in the second trimester.

A 36-year-old, primigravid woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. In 23 colonies of cultured amniocytes, 17 colonies had a derivative Y chromosome [der(Y)] with additional material at the end of the long arm of Y chromosome, whereas the remaining six colonies had a normal karyotype of 46,XY. The der(Y) was characterized by SKY using 24-color SKY probes (Applied Spectral Imaging, Carlsbad, CA, USA). The SKY analysis revealed that the der(Y) contained a segment of chromosome 13 in the distal end of the long arm of Y chromosome (Fig. 1). The parental karyotypes were normal. Level II ultrasound was unremarkable. The woman requested repeated amniocentesis at 22 weeks of gestation for confirmation. Using uncultured amniocytes, oligonucleotide-based array comparative genomic hybridization [SurePrint G3 Human CGH Microarray Kit 60K (Agilent Technologies, Santa Clara, CA, USA)] revealed a 20.3-Mb gene dosage increase encompassing the region of 13q31.3→q34 [arr cgh 13q31.3q34 (93,780,206–114,142,980)] (Fig. 2). Cultured amniocytes revealed a karyotype of 46,X,der(Y) t(Y;13)(q12;q31.3)[21]/46,XY[9] (Fig. 3). The parents opted to terminate the pregnancy, and an 832-g male fetus was delivered with hypertelorism, a depressed nasal bridge, a long philtrum, a thin upper lip, low-set ears, micrognathia, a small mandible, broad halluces, and a small penis, but had no polydactyly (Fig. 4). Cytogenetic analysis of the cord blood revealed a karyotype of 46,X,der(Y)t(Y;13)(q12;q31.3)[24]/46,XY[16].

The classical features of trisomy 13 syndrome or Patau syndrome on prenatal ultrasound include holoprosencephaly, Dandy-Walker malformation, ventriculomegaly, congenital heart defects, omphalocele, congenital diaphragmatic hernia, urinary tract abnormalities, megacystis, polydactyly, nuchal edema, cystic hygroma, and increased nuchal translucency thickness [2–4]. Partial trisomy 13q is usually caused by adjacent segregation of a parental translocation or unequal

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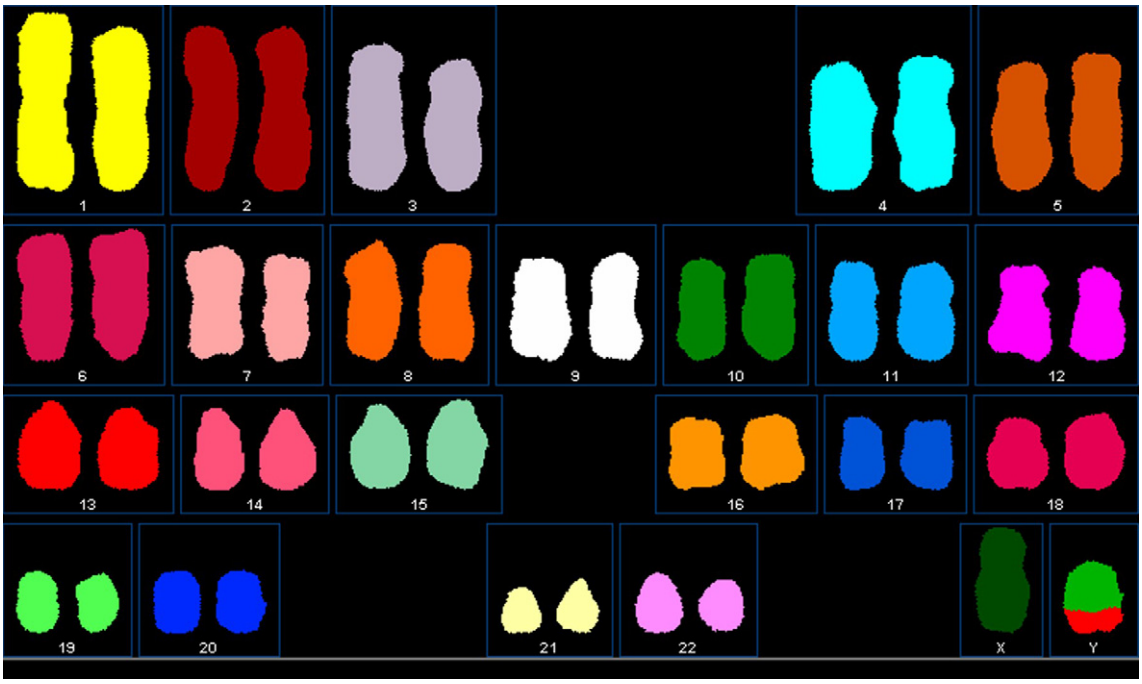

Fig. 1. Spectral karyotyping using 24-color probes shows that the der(Y) is caused by a translocation between chromosomes Y and 13.

crossing over of a parental pericentric inversion of chromosome 13, and it rarely occurs in a *de novo* event [5,6]. In the present case, both parents had normal karyotypes, confirming the *de novo* occurrence of the rearrangement, and the mosaic derivative Y chromosome resulting in partial trsiomy 13 was most likely caused by a postzygotic mitotic error.

To date, at least 10 patients with partial trisomy 13q (13q32→qter) have been described [7–15]. Trisomy of the distal part of the long arm of chromosome 13 (13q32→qter) has been shown to cause a distinctive mild phenotype resembling a part of the features of trisomy 13, such as growth retardation, trigonocephaly with metopic ridge, low-set ears,

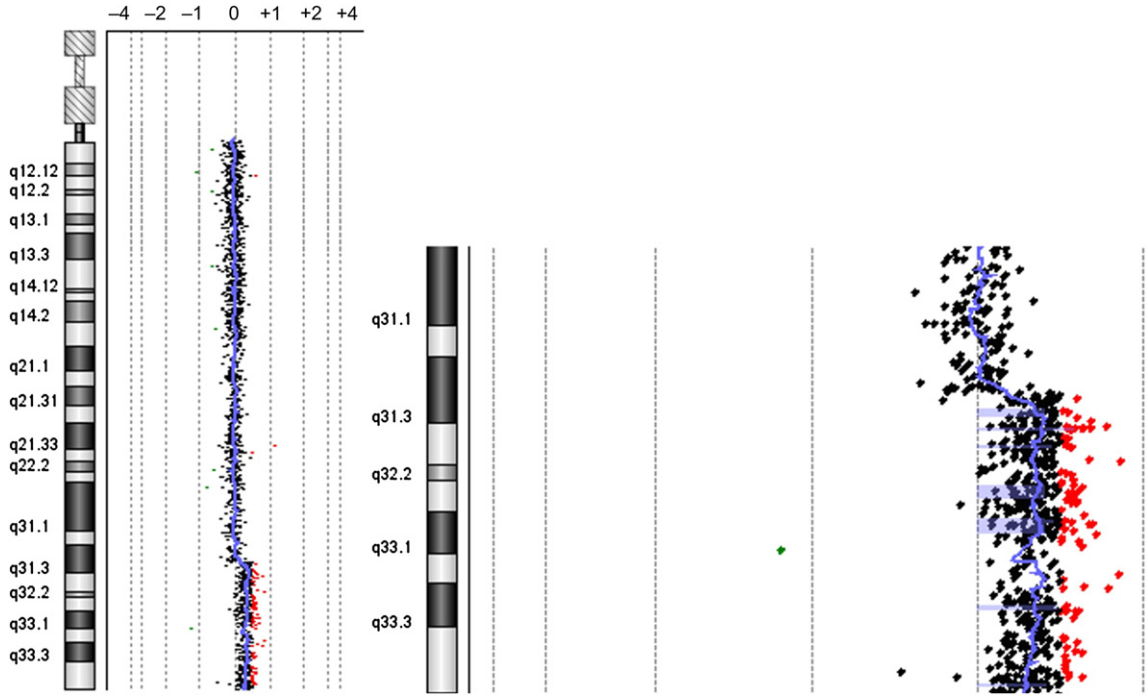

Fig. 2. Oligonucleotide-based array comparative genomic hybridization shows a 20.3-Mb gene dosage increase encompassing the region of 13q31.3→q34 (93,780,206–114,142,980).

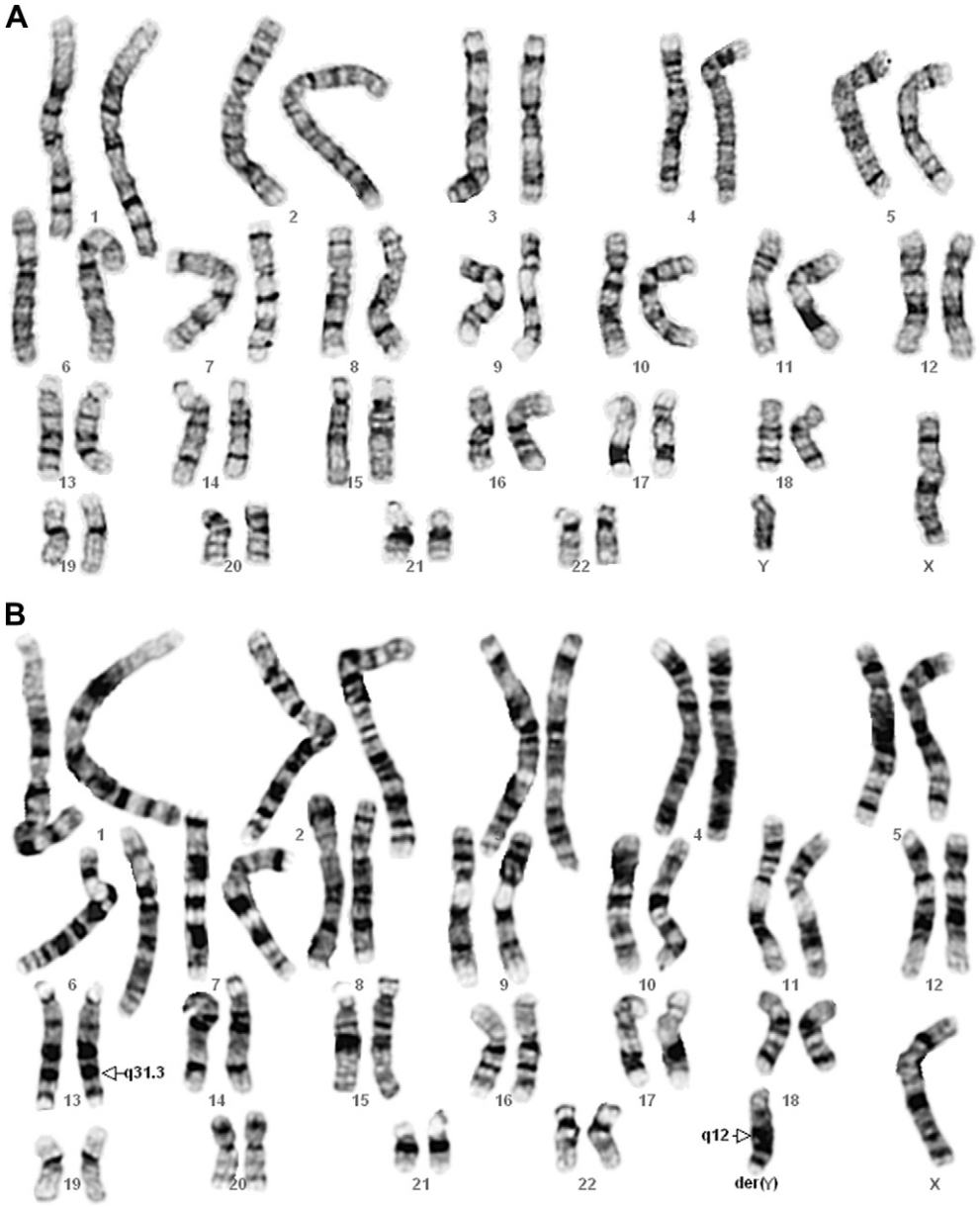

Fig. 3. (A) A karyotype of 46,XY and (B) a karyotype of 46,X,der(Y)t(Y;13)(q12;q31.3). Arrows indicate the breakpoints.

long and curved eyelashes, heavy eyebrows, small mandible, postaxial polydactyly, single palmar creases, and broad halluces [16]. The present case did not have characteristic polydactyly but had broad halluces. The region 13q32 has been suggested to contain genes associated with digital malformations, although specific genes at 13q32 involved in polydactyly have not yet been cloned [17,18]. Deletion of 13q32 may result in absent thumb and absent big toe [18,19], and duplication of 13q32 has been related to polydactyly [18,20]. Rao et al [12] reported a 19-month-old boy with dup(13)(q32→qter), del(1)(q42→qter), and severe phenotypic features of postaxial polydactyly, microphthalmia, tetralogy of Fallot, clubfeet, and sensorineural deafness. However, Helali et al [13] reported an 8-year-old boy with dup(13)(q32→qter) and del(18)(p11.32→pter), and mild phenotype of psychomotor retardation, tethered cord, fleshy ears, and normal facial features except for thin lips. Ioan et al [15] reported a 1-year-9-month-old girl with *de novo* dup(13)(q32→qter), hypotonia, bilateral postaxial polydactyly of the hands, a sheep-like cry, psychomotor retardation, a high and narrow forehead with temporal indentations, bushy eyebrows, long eyelashes, coloboma of the iris of the left eye, a short and upturned nose, low-set ears, a long and deep philtrum, a small mouth with everted lower lip, full cheeks, a small mandible, a high palate, a short neck, a narrow thorax, single palmar creases on both hand palms, broad thumbs and halluces, camptodactyly, and mild ventricular dilation. Maas et al [21] reported a 12.5-year-old girl with del(13)(q31.1→q31.3), dup(13)(q31.3→q33.2), mild to moderate mental retardation, growth retardation, seizures,

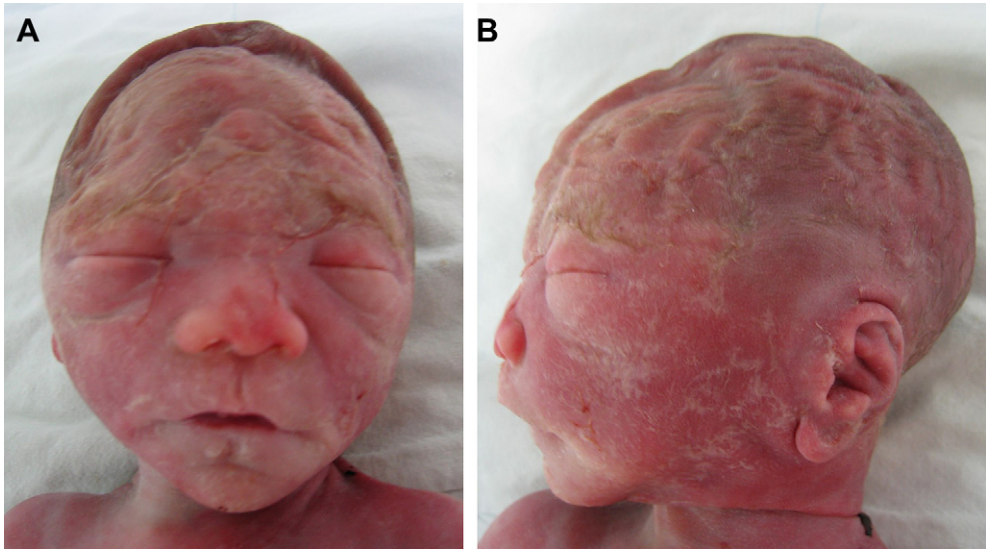

Fig. 4. The craniofacial appearance of the proband at birth.

facial asymmetry, cardiovascular anomalies, and adducted thumbs.

Unbalanced X;autosome or Y;autosome translocations involving chromosome 13q are very rare. Blennow and Sahlén [14] reported a female with partial trisomy of distal 13q (13q32→qter) and a karyotype of 46,X,der(X) t(X;13)(p21;q32) with short stature and repeated spontaneous miscarriages, but with normal intelligence and apparently no serious symptoms. In that case, the skewed X inactivation might have prevented abnormal symptoms. The woman had a healthy daughter inheriting the same unbalanced translocation. Cui et al [22] reported a 25-year-old man with azoospermia; slightly bilateral gynecomastia; multiple angiolipoma; a karyotype of 45,X,der(Y)t(Y;13)(q11.1;q12),-13 .ish der(Y)(SRY+, DYZ3+, wcp13+); and partial monosomy 13q(13pter→q12). Nikoliš et al [23] first reported a 10-month-old male infant with partial trisomy 13q(13q14→qter) and a karyotype of 46,X,der(Y) t(Y;13)(q12;q14)pat with congenital anomalies consistent with trisomy 13 syndrome, such as hemangiomas, polydactyly, congenital heart defects, microcephaly, partial fusion of the pelvis and scrotum, and facial dysmorphism. Ours is the second case report of an unbalanced Yq;13q translocation in association with partial trisomy 13q and adds to the literature of unbalanced Y;autosome translocations.

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