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Research Letter

Prenatal diagnosis of partial trisomy 16p (16p12.2→pter) and partial monosomy 22q (22q13.31→qter) associated with increased nuchal translucency and abnormal maternal serum biochemistry in the first trimester

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A 33-year-old, gravida 4, para 1, woman underwent first-trimester screening for chromosome abnormalities using ultrasound and maternal serum biochemistry at 13 weeks of gestation. The fetal nuchal translucency (NT) measured 3.62 mm (Fig. 1). The levels of free beta-human chorionic gonadotrophin (free β-hCG) and pregnancy-associated plasma protein A (PAPP-A) were 0.686 multiples of median (MoM) and 0.272 MoM, respectively. The woman screened positive for trisomy 21 (risk of 1/11), trisomy 18 (risk of 1/33), and trisomy 13 (risk of 1/20). Chorionic villus sampling was performed. The fetal karyotype was 46,XX,der(22)t(16;22)(p12.2;q13.31) (Fig. 2). Cytogenetic analysis of the parents revealed a karyotype of 46,XY in the father and a karyotype of 46,XX,t(16;22)(p12.2;q13.31) in the mother (Fig. 3). The mother had experienced spontaneous abortions twice before and had a healthy 5-year-old son. The family did not had a history of congenital malformations. The woman had not been aware of her translocation status prior to this pregnancy.

Prenatal ultrasound at 15 weeks of gestation revealed a singleton fetus with nuchal edema and fetal biometry equivalent to 13 weeks. The pregnancy was subsequently terminated, and a 94-g edematous fetus was delivered with a round face, hypertelorism, prominent glabella, bulbous nose, full cheeks, anteverted nares, long philtrum, thin lips, micrognathia, low-set ears, and short neck (Fig. 4). Cytogenetic analysis of the fetal tissues confirmed the prenatal diagnosis. Oligonucleotide-based array comparative genomic hybridization (aCGH) using CytoChip Oligo Array (BlueGnome, Cambridge, UK) detected a 20.91-Mb duplication at chromosome 16p13.3−p12.2 and a 3.58-Mb deletion at chromosome 22q13.31−q13.33, or arr cgh 16p13.3p12.2 (36,796 − 20,949,861)×3, 22q13.31q13.33 (45,988,973 − 49,565,846)×1 (NCBI build 36, March 2006) (Fig. 5).

The present case provides evidence that fetuses with partial trisomy 16 p may present increased NT thickness in the first trimester. Digilio et al [1] suggested that 16 p subtelomeric duplication causes susceptibility to vascular anomalies. Abnormalities of the heart and great arteries have been proposed to be associated with increased fetal NT thickness [2]. Partial trisomy 16 p has been described to be associated with fetal ascites, hydrops fetalis, and/or cystic hygroma.

Chen et al [3] previously reported a fetus with partial trisomy 16 p (16p12.2→pter) and partial monosomy 22q (22q13.31→qter) presenting with fetal ascites and ventriculomegaly in the second trimester. The present case has an unbalanced reciprocal translocation similar to that of the case

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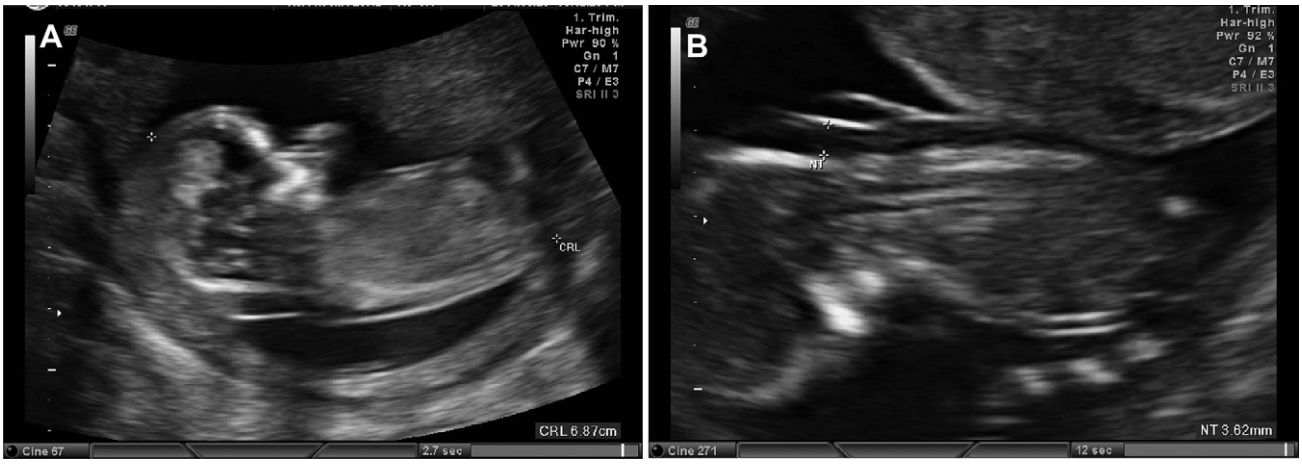

Fig. 1. Prenatal ultrasound at 13 weeks of gestation shows an increased thickness of nuchal translucency.

described by Chen et al [3], and manifested increased NT in the first trimester and nuchal edema in the second trimester. The family in the present case and the family in the case reported by Chen et al [3] are not related, although the breakpoints of familial translocation in these two families are very similar.

Chen et al [4] reported fetal ascites, oligohydramnios, and renal agenesis in a fetus with partial trisomy 16 p (16p13.2→pter) and partial trisomy 13q (13q12.3→qter). Martin et al [5] reported hydrops fetalis and cystic hygroma in a fetus with a terminal 16 p duplication. Fetuses with uncommon aneuploidies can manifest increased NT in the first trimester [6,7].

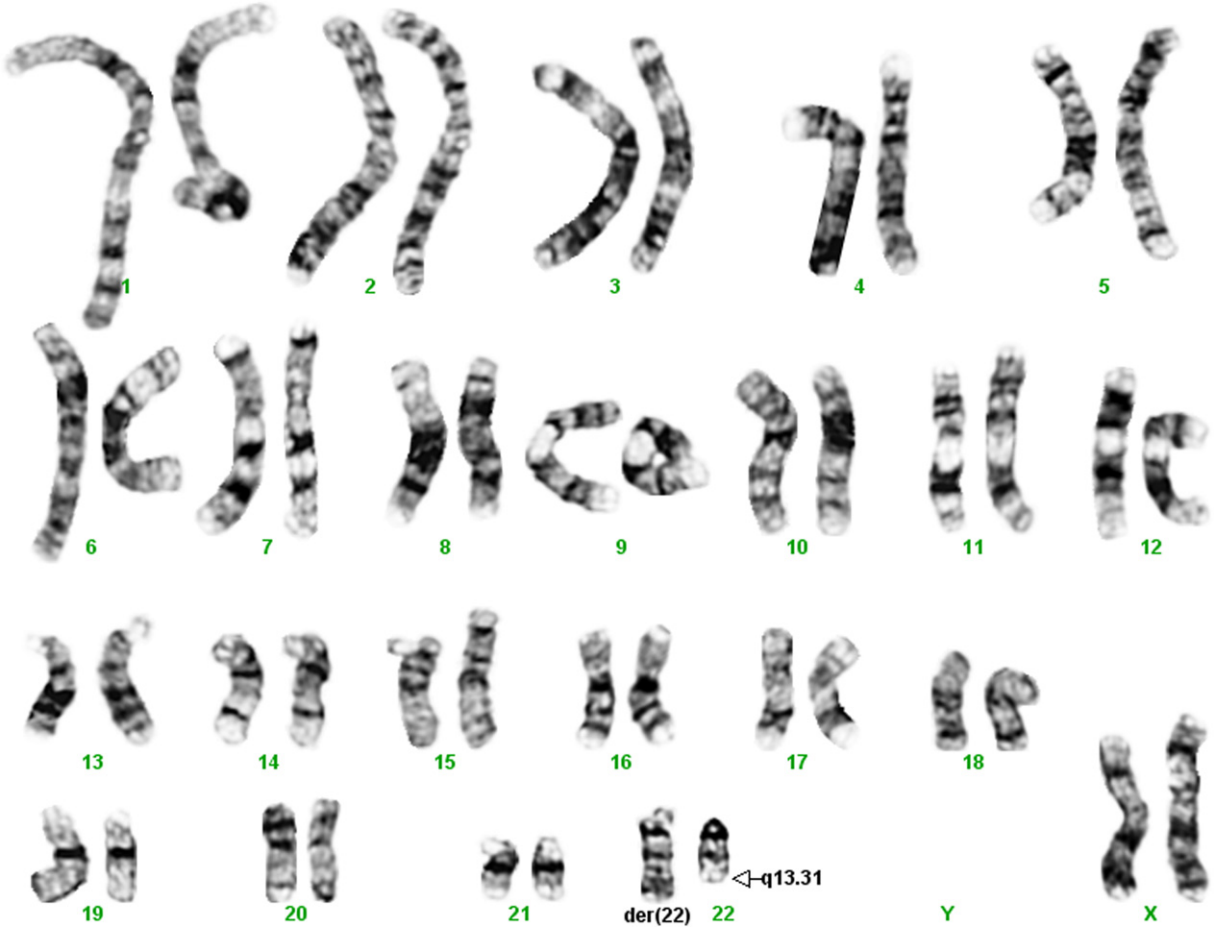

Fig. 2. G-banded karyotype of the fetus shows a derivative chromosome 22, or der(22). The fetal karyotype is 46,XX,der(22)t(16;22)(p12.2;q13.31). The arrow indicates the breakpoint.

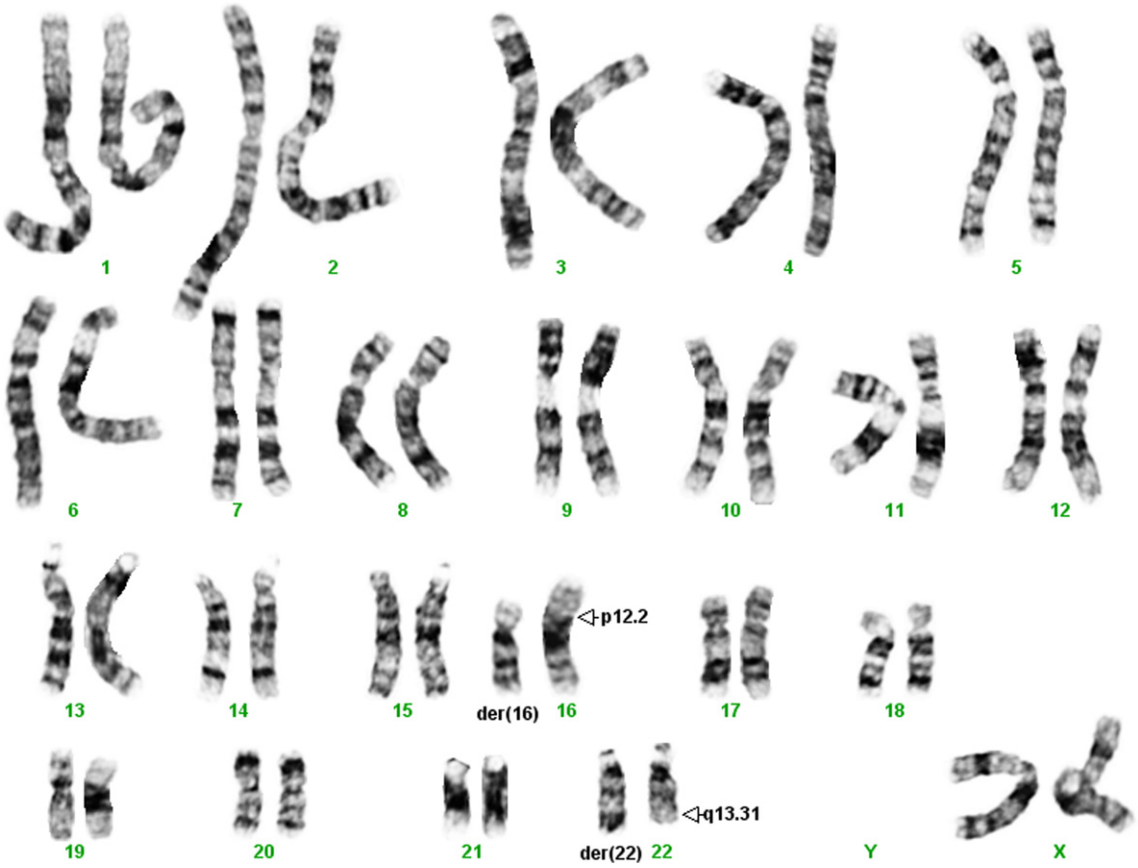

Fig. 3. G-banded karyotype of the mother shows a der(16) and a der(22). The maternal karyotype is 46,XX,t(16;22)(p12.2;q13.31). The arrows indicate the breakpoints.

Increased NT may be a first-trimester ultrasound marker of fetal partial trisomy 16 p.

The present case also provides evidence that fetuses with partial monosomy 22q may present low levels of free β-hCG and PAPP-A in first-trimester screening. The present patient had abnormally low levels of maternal free β-hCG and PAPP-A in the first trimester. Koç et al [8] reported a prenatal diagnosis of mosaic ring 22 duplication/deletion with terminal 22q13 deletion due to the abnormal first-trimester screening results of 1.01 MoM of free β-hCG and 0.31 MoM of PAPP-A. It has also been noted that trisomy 22 pregnancies are associated with a distinctive first-trimester maternal serum screening pattern of an extremely high level of β-hCG and a low level of PAPP-A [9]. A low level of PAPP-A in the first-trimester maternal serum biochemistry may be a distinctive feature in pregnancies with fetal chromosome 22 abnormalities.

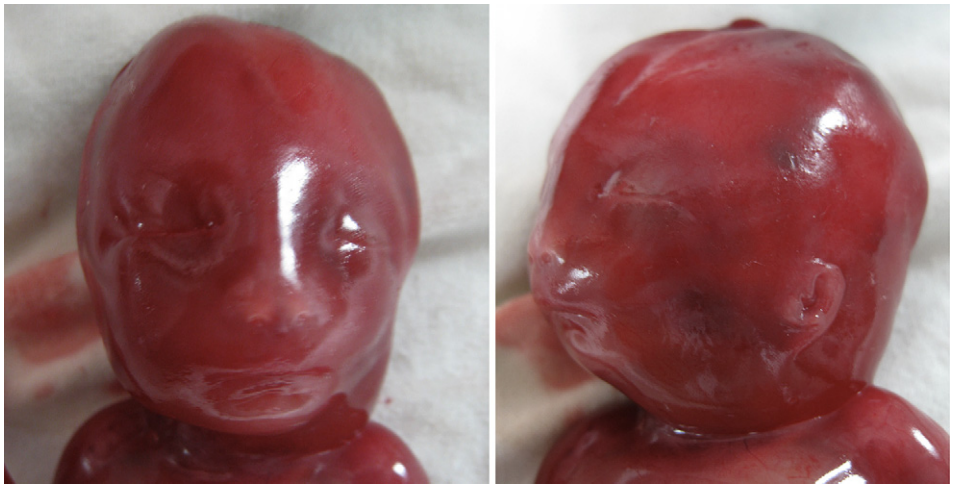

Fig. 4. Craniofacial appearance of the fetus at birth.

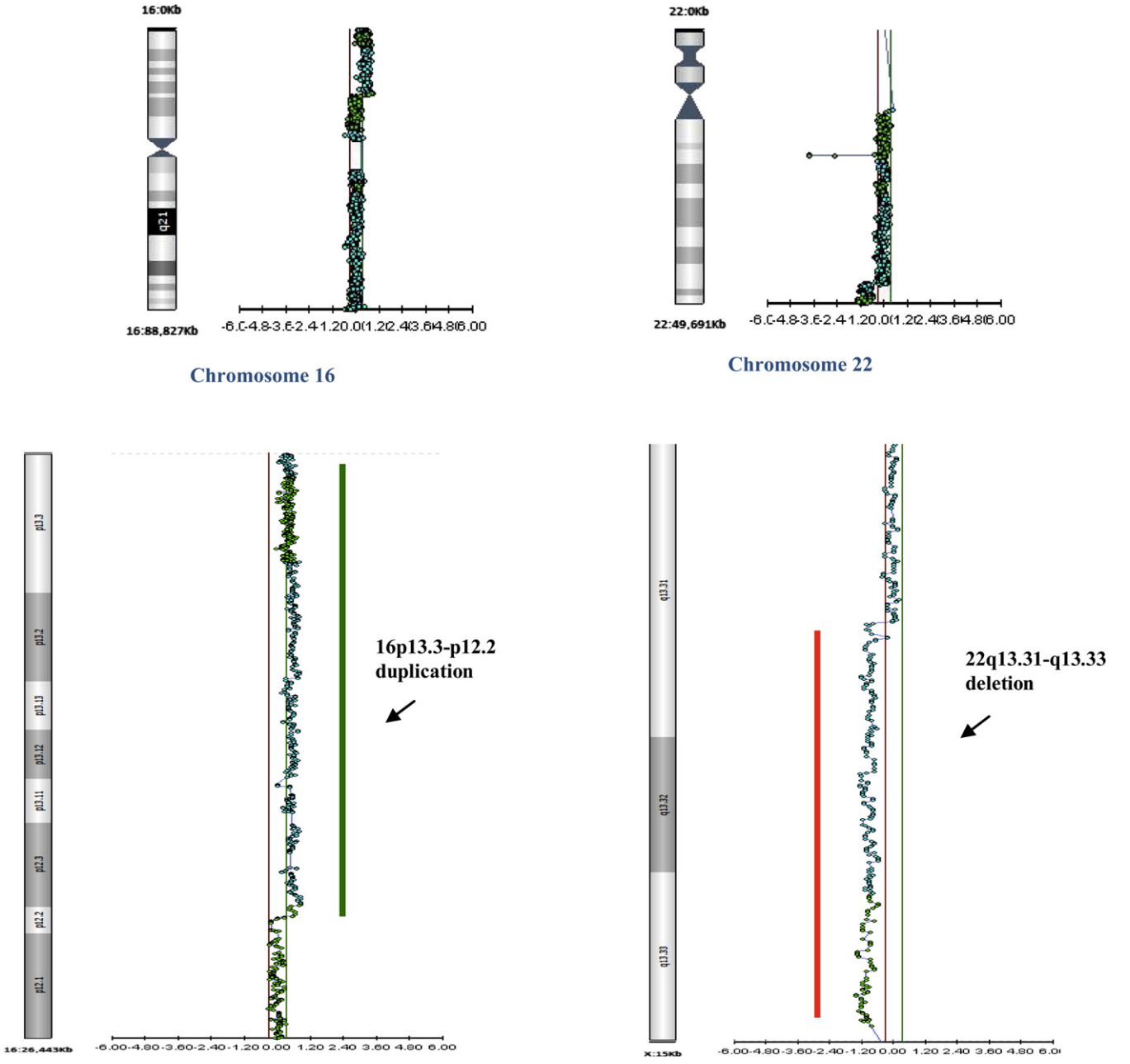

Fig. 5. Oligonucleotide-based array comparative genomic hybridization shows a 20.91-Mb duplication at chromosome 16p13.3−p12.2 and a 3.58-Mb deletion at chromosome 22q13.31−q13.33.

Acknowledgments

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