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Case Report

Partial monosomy 13q (13q21.32→qter) and partial trisomy 8p (8p12→pter) presenting with anencephaly and increased nuchal translucency: array comparative genomic hybridization characterization

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Abstract

Objective: To present array comparative genomic hybridization (aCGH) characterization of partial monosomy 13q (13q21.32→qter) and partial trisomy 8p (8p12→pter) presenting with anencephaly and increased nuchal translucency (NT).
Case Report: A 34-year-old primigravid woman was referred to the hospital at 12 weeks of gestation for termination of the pregnancy because of major structural abnormalities of the fetus. Prenatal ultrasound revealed a malformed fetus with anencephaly and an increased NT thickness of 5 mm at 12 weeks of gestation. Cytogenetic analysis of the fetus revealed a derivative chromosome 13. The mother was subsequently found to carry a balanced reciprocal translocation between 8p12 and 13q21. Bacterial artificial chromosome-based aCGH using fetal DNA demonstrated partial trisomy 8p and partial monosomy 13q [arr cgh 8p23.3p12 (RP11-1150M5→RP11-1145H12)×3, 13q21.32q34 (RP11-326B4→RP11-450H16)×1]. Oligonucleotide-based aCGH showed a 36.7-Mb duplication of distal 8p and a 48.4-Mb deletion of distal 13q. The fetal karyotype was 46,XY,der(13) t(8;13)(p12;q21.32)mat. The maternal karyotype was 46,XX,t(8;13)(p12;q21.32).
Conclusion: The 13q deletion syndrome can be associated with neural tube defects and increased NT in the first trimester. Prenatal sonographic detection of neural tube defects should alert chromosomal abnormalities and prompt cytogenetic investigation, which may lead to the identification of an unexpected parental translocation involving chromosomal segments associated with neural tube development.

Keywords: Chromosome 8; Chromosome 13; Monosomy 13q; Neural tube defects; Nuchal translucency; Trisomy 8p

Introduction

The 13q deletion syndrome, or 13q- syndrome, is a rare condition that presents with widely varying phenotypes, including moderate-to-severe mental retardation; developmental delay; and growth retardation; central nervous system anomalies, such as meningocele, encephalocele, anencephaly,

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Dandy-Walker malformation (DWM), corpus callosum agenesis, and holoprosencephaly (HPE); craniofacial abnormalities, such as microcephaly, brachycephaly, trigonocephaly, hypertelorism, microphthalmia, a broad nasal bridge, micrognathia, and facial cleft; hand and foot anomalies, such as thumb aplasia or hypoplasia, digital anomalies, and talipes; and other disorders, such as lung hypoplasia, intestinal malrotation, bowel atresia, and ambiguous genitalia [1–9]. We previously described the application of array comparative genomic hybridization (aCGH) in the prenatal diagnosis of aneuploidy [10,11]. Here, we report aCGH characterization of partial monosomy 13q (13q21.32→qter) and partial trisomy 8p (8p12→pter) presenting with anencephaly and increased nuchal translucency (NT) in the first trimester.

Case report

A 34-year-old primigravid woman was referred to the hospital at 12 weeks of gestation for termination of pregnancy because of major structural abnormalities of the fetus. The parents were nonconsanguineous and healthy. The father was aged 34 years. The mother reported no illness or recent infections. She neither had any history of prenatal exposure to teratogenic agents nor any family history of congenital malformations. Prenatal ultrasound at 12 weeks of gestation revealed a malformed fetus with anencephaly and an increased NT thickness of 5 mm. The pregnancy was subsequently terminated and a 6-g anencephalic fetus was delivered (Fig. 1). The external genitalia were ambiguous. Cytogenetic analysis of the fetal umbilical cord fibroblasts revealed a derivative chromosome 13 or der(13) (Fig. 2). Subsequent parental karyotyping revealed that the mother carried a balanced reciprocal translocation between 8p12 and 13q21 (Fig. 3). The paternal karyotype was normal. Bacterial artificial chromosome-based aCGH using fetal DNA demonstrated partial trisomy 8p and partial monosomy 13q [arr cgh 8p23.3p12 (RP11-1150M5→RP11-1145H12)×3, 13q21.32q34 (RP11-326B4→RP11-450H16)×1] (Fig. 4). Oligonucleotide-based aCGH showed a 36.7-Mb duplication of distal 8p and a 48.4-Mb deletion of distal 13q (Fig. 5). The maternal karyotype was 46,XX,t(8;13) (p12;q21.32). The fetal karyotype was 46,XY,der(13)t(8;13) (p12;q21.32)mat.

Discussion

The present case was associated with increased NT in the first trimester. The 13q deletion syndrome has been associated with increased NT [7], nuchal edema [12], and cystic hygroma [13]. Proposed mechanisms for the increase in NT thickness include altered composition of the extracellular matrix, abnormalities of the heart and great arteries, and disturbed or delayed lymphatic development [14]. The present case had haploinsufficiency of *COL4A1* and *COL4A2*, which are located on chromosome 13q34 and encode collagen type IV α-1 chain and α-2 chain, respectively. Collagen type IV is associated with laminin, entactin, and heparan sulfate proteoglycans to form the sheet-like basement membranes that separate epithelium from connective tissue. Increased NT is well known to be a first-trimester sonographic marker of trisomy 13 [15]. von Kaisenberg et al [16] suggested that increased NT in trisomy 13 fetuses is because of alteration in the composition of collagen type IV.

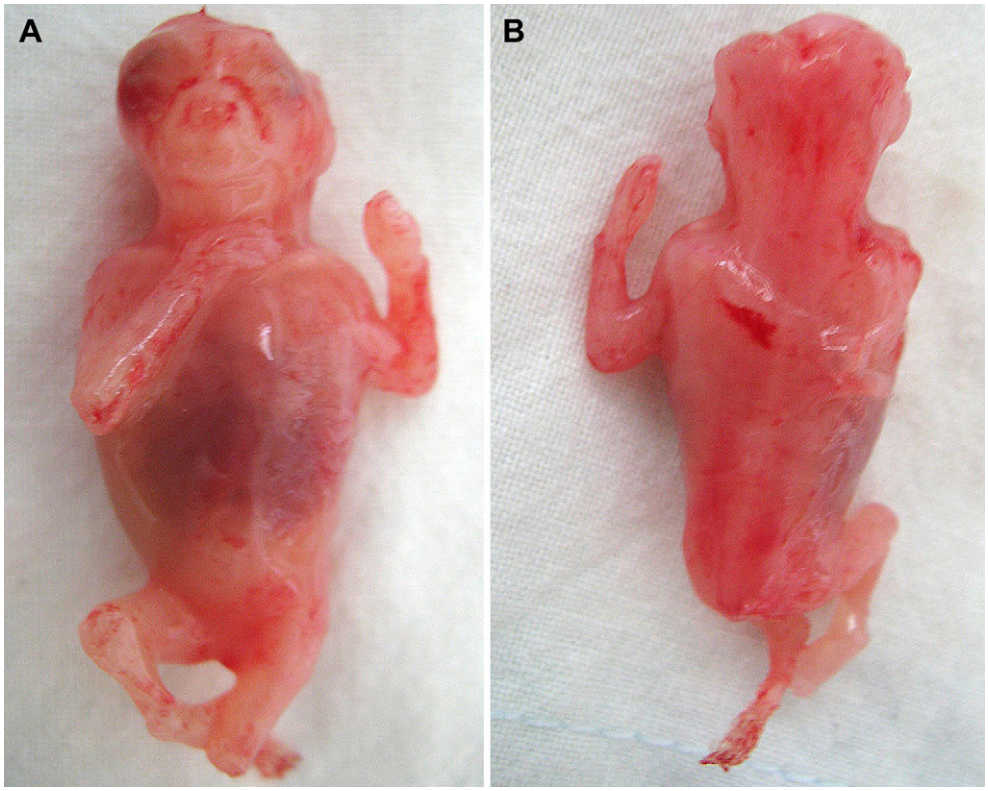

Fig. 1. (A) Anterior view and (B) posterior view of the fetus.