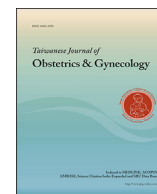


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## Case Report

### Prenatal diagnosis and molecular cytogenetic characterization of $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)(\text{p}11.2\text{q}26.3)$ in a fetus associated with paternal pericentric inversion



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## ABSTRACT

**Objective:** We present prenatal diagnosis and molecular cytogenetic characterization of a recombinant chromosome 10 in a fetus associated with a paternal pericentric inversion.

**Case Report:** A 35-year-old woman underwent amniocentesis at 18 weeks of gestation because of an advanced maternal age. Amniocentesis revealed a karyotype of  $46,XY,\text{der}(10)\text{del}(10)(\text{q}26.3)\text{dup}(10)(\text{p}11.2\text{p}15)$ . She underwent repeat amniocentesis at 21 weeks of gestation and array comparative genomic hybridization revealed a 31.65-Mb duplication of chromosome 10p15.3–p11.22 and a 3.07-Mb deletion of chromosome 10q26.3. Prenatal ultrasound findings were unremarkable. She was referred for genetic counseling and cytogenetic analysis revealed a karyotype of  $46,XY,\text{inv}(10)(\text{p}11.2\text{q}26.3)$  in the father and a karyotype of  $46,XX$  in the mother. The pregnancy was subsequently terminated, and a fetus was delivered with prominent facial dysmorphism. Postnatal cytogenetic analysis of the placenta revealed a karyotype of  $46,XY,\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)(\text{p}11.2\text{q}26.3)$ . Fluorescence *in situ* hybridization analysis revealed a duplication of terminal 10p and a deletion of terminal 10q in the recombinant chromosome 10. Array comparative genomic hybridization analysis of the cord blood and umbilical cord confirmed the prenatal diagnosis.

**Conclusion:** Prenatal diagnosis of a recombinant chromosome because of an advanced maternal age should alert the possibility of a paternal pericentric inversion.

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## Introduction

Prenatal diagnosis of a 10p–10q rearrangement with a duplication/deletion event involving 10p distal duplication and

10q terminal deletion due to parental pericentric inversion has not previously been reported. The recombinant chromosome 10 with 10p duplication/10q deletion can be the result of a meiotic recombination event in a parent carrying a pericentric inversion of chromosome 10 [1,2]. The estimates of frequency of inversions in the population range from 0.12% to 0.7% for pericentric inversions and from 0.1% to 0.5% for paracentric inversions [3]. In case of one of the parents with a chromosome inversion, there is

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about 5% recurrence risk for the recombinant chromosome in the offspring [4]. Parents with larger inversion size may lead to production of unbalanced gametes and carry a higher risk for unbalanced offspring with chromosomal duplication/deletion [5,6].

Here, we present our experience of prenatal diagnosis and molecular cytogenetic characterization of  $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)(\text{p}11.2\text{q}26.3)$  in a fetus associated with a paternal chromosome 10 pericentric inversion which was detected after genetic counseling.

### Case Presentation

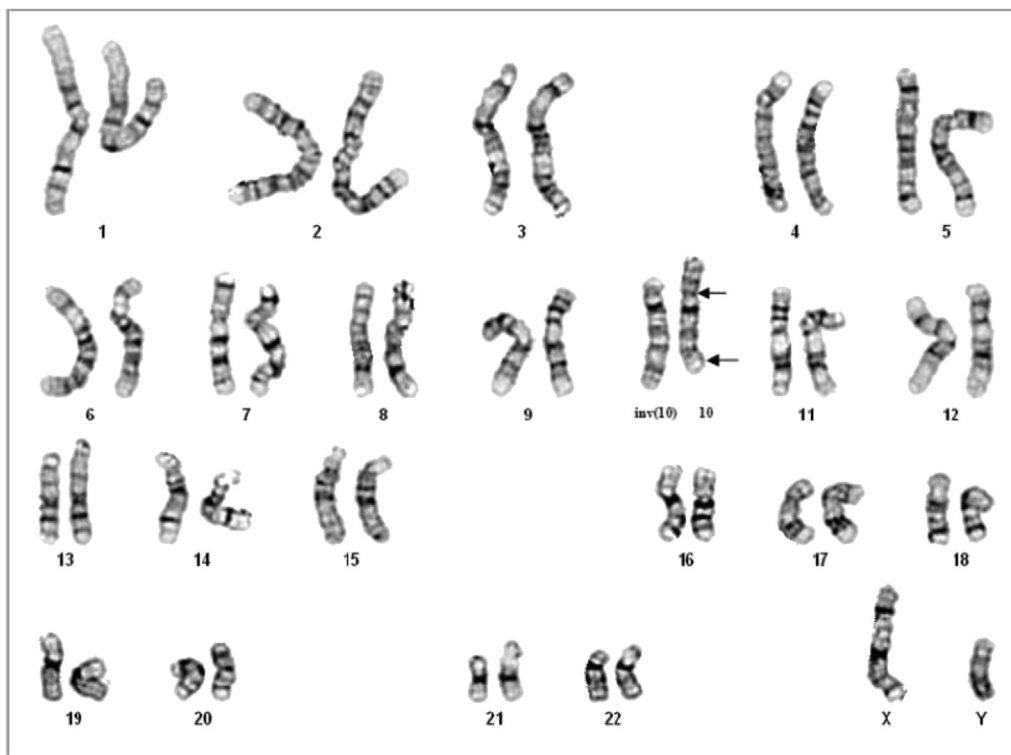
A 35-year-old, gravida 2, para 1, woman underwent amniocentesis at 18 weeks of gestation because of an advanced maternal age. Her husband was aged 35 years. The couple had a 2-year-old healthy daughter with a karyotype of 46,XX, and there was no family history of congenital malformations. Amniocentesis revealed a karyotype of 46,XY, $\text{der}(10)\text{del}(10)(\text{q}26.3)\text{dup}(10)(\text{p}11.2\text{p}15)$ . She underwent repeat amniocentesis at 21 weeks of gestation and array comparative genomic hybridization (aCGH) revealed a 31.65-Mb duplication of chromosome 10p15.3–p11.22 and a 3.07-Mb deletion of chromosome 10q26.3. Prenatal ultrasound findings were unremarkable. She was referred for genetic counseling and cytogenetic analysis of the parents revealed a karyotype of 46,XY, $\text{inv}(10)(\text{p}11.2\text{q}26.3)$  (Figure 1) in the father and a karyotype of 46,XX in the mother. The pregnancy was subsequently terminated, and a 518-g male fetus was delivered at 23 weeks of gestation with facial dysmorphism of hypertelorism, large low-set ears, a broad and long nasal bridge, a long face, and micrognathia. Postnatal cytogenetic analysis of the placental tissues revealed a karyotype of 46,XY, $\text{rec}(10)$

$\text{dup}(10\text{p})\text{inv}(10)(\text{p}11.2\text{q}26.3)$  (Figure 2). Fluorescence *in situ* hybridization (FISH) analysis of cultured trophoblasts confirmed a duplication of distal 10p and a deletion of terminal 10q in the recombinant chromosome 10 (Figure 3). aCGH analysis of cord blood and umbilical cord confirmed the prenatal diagnosis. The aCGH analysis of the umbilical cord revealed a 31.65-Mb duplication of 10p15.3p11.22 (136,391–31,782,515) [GRCh37 (hg19)] including 108 OMIM genes and a 3.07-Mb deletion of 10q26.3 (132,365,431–135,434,149) including 18 OMIM genes. The aCGH result was  $\text{arr } 10\text{p}15.3\text{p}11.22 (136,391-31,782,515) \times 3.0, 10\text{q}26.3 (132,365,431-135,434,149) \times 1.0$  (Figure 4). Polymorphic DNA marker analysis using the DNAs extracted from the umbilical cord and parental peripheral bloods confirmed a paternal origin of the chromosome aberration (Table 1).

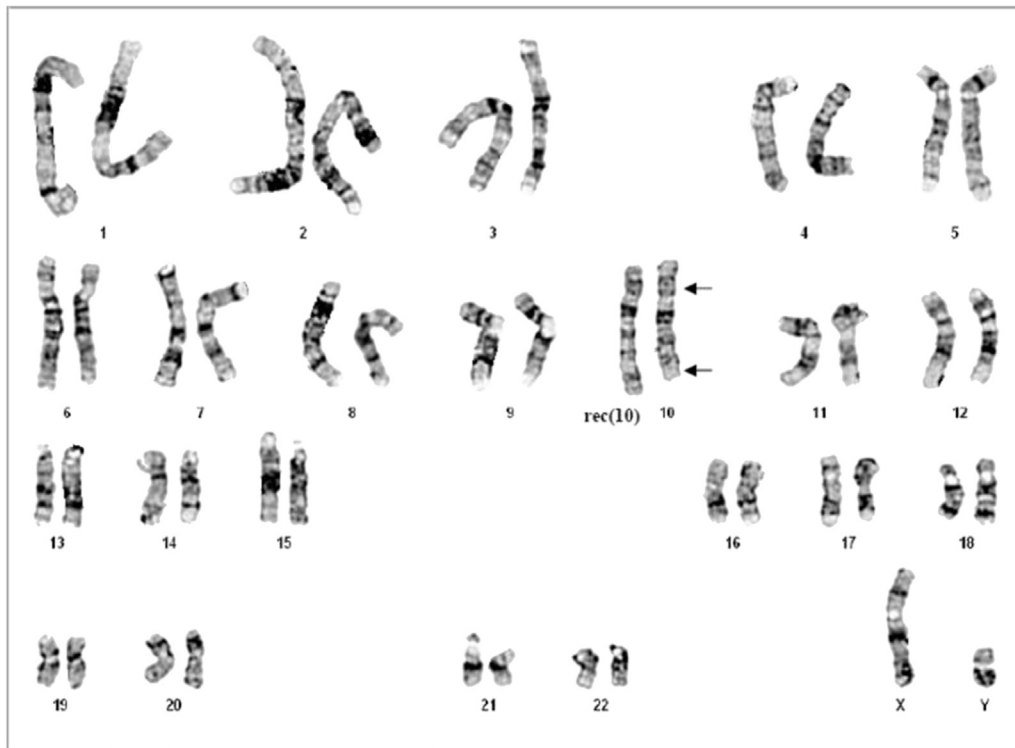
### Discussion

To date, at least eight reports of  $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)$  with partial 10p duplication/10q deletion [1,2,7–12] and two reports of  $\text{rec}(10)\text{dup}(10\text{q})\text{inv}(10)$  with partial 10q duplication/10p deletion [13,14] resulting from paternal or maternal pericentric inversions have been published.

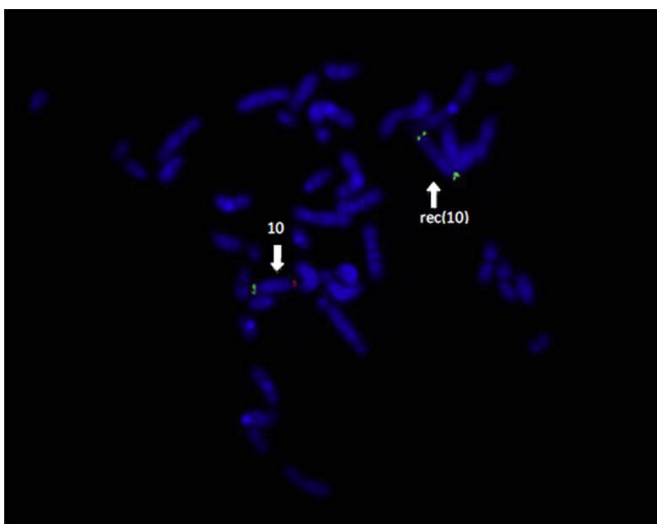
In the reported cases with  $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)$ , most patients involved a 10p breakpoint closer to chromosome 10 centromere and a 10q breakpoint closer to 10q telomere. Therefore, the patients with  $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)$  are likely to manifest severe 10p duplication syndrome and mild 10q deletion syndrome. Lansky-Shafer et al [7] reported an infant with features of trisomy 10p syndrome and a karyotype of 46,XY, $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)(\text{p}11\text{q}26)\text{mat}$ . Yunis and Torres de Caballero [1] reported an affected 10-year-old boy with a karyotype of 46,XY, $\text{rec}(10)\text{dup}(10\text{p})\text{inv}(10)(\text{p}11\text{q}25)\text{mat}$ . Roberts et al [8] reported a family with a brother and sister with



**Figure 1.** A karyotype of 46,XY, $\text{inv}(10)(\text{p}11.2\text{q}26.3)$  in the father. The arrows indicate the breakpoints.  $\text{inv}$  = inversion.



**Figure 2.** A karyotype of 46,XY,rec(10)dup(10p)inv(10)(p11.2q26.3) in the fetus. The arrows indicate the breakpoints. dup = duplication, inv = inversion; rec = recombinant.



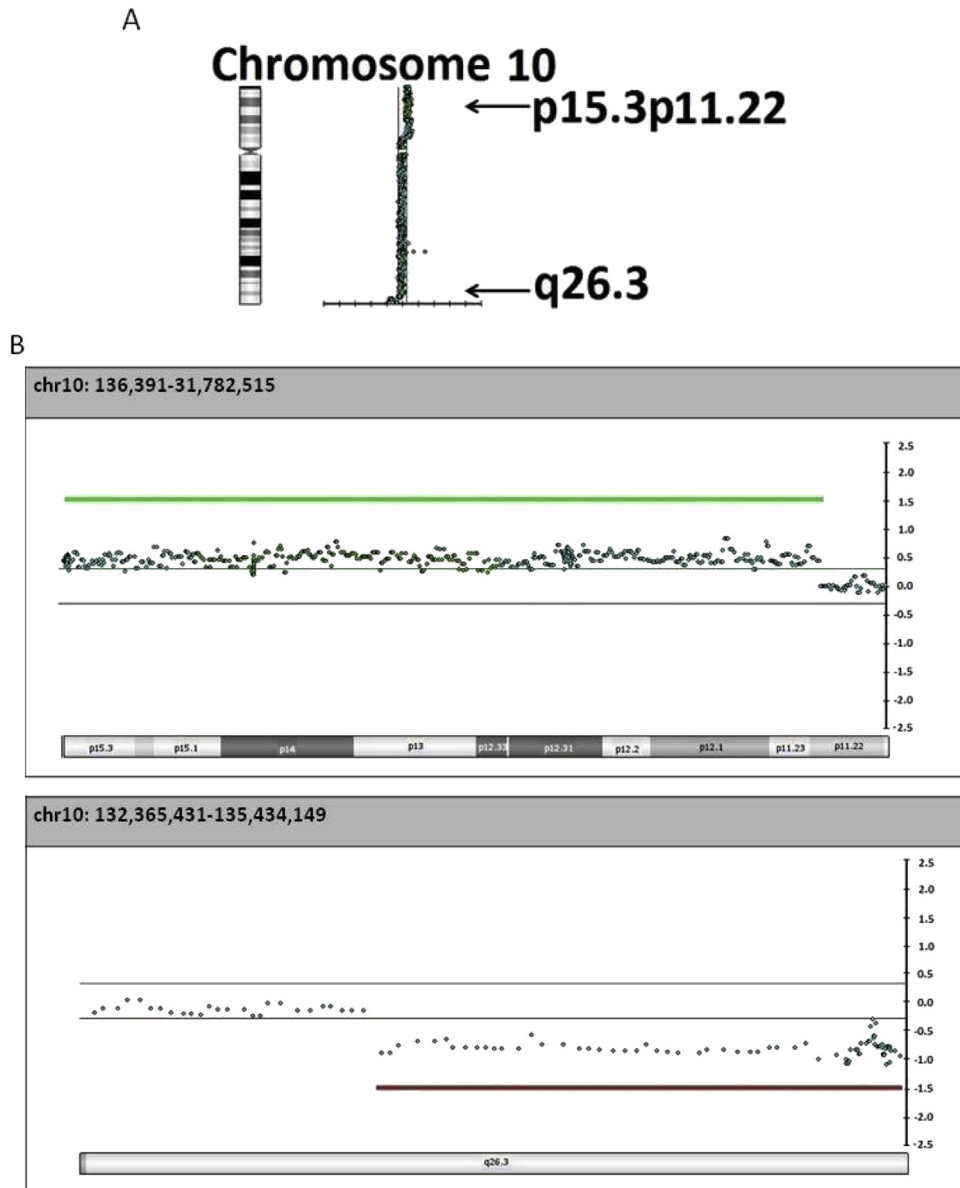
**Figure 3.** Fluorescence *in situ* hybridization analysis using the bacterial artificial chromosome probes of RP11-959L8 (chromosome 10p15.2; 3,018,257–3,203,607; dye: FITC, green) and RP11-91E2 (chromosome 10q26.3; 133,448,055–133,598,823; dye: Texas Red, red) shows one green signal and one red signal in the chromosome 10 and two green signals but no red signal in the recombinant chromosome 10 [rec(10)].

developmental delay and multiple minor dysmorphic features and the karyotypes of 46,XY,rec(10)dup(10p)inv(10)(p15.1q25.2)pat and 46,XX,rec(10)dup(10p)inv(10)(p15.1q25.2)pat, respectively. Ohba et al [9] reported a female infant with specific characteristics of duplication of 10p and a karyotype of 46,XX,rec(10)dup(10p)inv(10)(p11.2q25.2)mat. Kulharya et al [10] reported an infant with learning disability, facial dysmorphism, and developmental delay

with a karyotype of 46,XY,rec(10)dup(10p)inv(10)(p11.2q26)mat and a malformed boy in another family with the karyotype of 46,XY,rec(10)dup(10p)inv(10)(p11q26)mat and a stillborn female of the same family with Potter sequence and multicystic renal dysplasia with the karyotype of 46,XX,rec(10)dup(10p)inv(10)(p11q26). Kozma and Meck [11] reported two relatives with 10p trisomy, 10q monosomy and facial dysmorphism with a karyotypic abnormality of rec(10)dup(10p)inv(10)(p11.2q26)mat. Mihçi et al [12] reported one female infant with facial dysmorphism, developmental delay, clinodactyly, and a karyotype of 46,XX,rec(10)dup(10p)inv(10)(p13q26)mat. Ciuladaite et al [2] reported two relatives with a chromosome constitution of 46,XX,rec(10)dup(10p)inv(10)(p15.1q26.12)mat in a 13-year-old girl with facial dysmorphism, profound hypotonia, bilateral clubfeet, and psychomotor and language developmental delay, and an opposite chromosome constitution of 46,XX,rec(10)dup(10q)inv(10)(p15.1q26.12) with facial dysmorphism and developmental delay in her 28-year-old maternal aunt.

The peculiar aspect of the present case is the detection of paternal pericentric inversion following genetic counseling. The indication of prenatal diagnosis in this case was because of an advanced maternal age. However, the recombinant chromosome 10 of the fetus was found to be resulted from a paternal pericentric inversion. In the present case, the paternal inversion was detected only after genetic counseling of prenatally detected chromosomal abnormality and the acquired information of a familial pericentric inversion is very important in the subsequent pregnancies.

In summary, we present prenatal diagnosis and molecular cytogenetic characterization of rec(10)dup(10p)inv(10)(p11.2q26.3) in a fetus associated with a paternal pericentric inversion. We suggest that prenatal diagnosis of a recombinant chromosome



**Figure 4.** Array comparative genomic hybridization of umbilical cord using CytoChip ISCA Array (Illumina, San Diego, CA, USA) shows a 31.65-Mb duplication of 10p15.3-p11.22 and a 3.07-Mb deletion of 10q26.3 or arr 10p15.3p11.22 (136,391–31,782,515)  $\times$  3.0, 10q26.3 (132,365,431–135,434,149)  $\times$  1.0. (A, B) Chromosome zoom-in view.

**Table 1**

Genotypic information of the proband and the parents at short tandem repeat markers specific for chromosome 10p obtained by quantitative fluorescent polymerase chain reaction assays.<sup>a</sup>

Markers	Locus	Father	Mother	Proband
D10S2479	10p15.3	116, 120	124, 124	116, 116, 124
D10S2483	10p15.3	124, 128	120, 128	124, 124, 128
D10S2474	10p12.31	112, 112	108, 108	108, 112, 112
D10S675	10p11.22	76, 84	84, 92	76, 92

<sup>a</sup> Alleles (size in base pairs) are listed below each individual.

because of an advanced maternal age should alert the possibility of a paternal pericentric inversion.

#### Conflict of interest

The authors have no conflicts of interest relevant to this article.

#### Acknowledgments

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