Uniparental isodisomy for paternal 2p and maternal 2q in a phenotypically normal female with two isochromosomes, i(2p) and i(2q)

EDITOR—Recently, Bernasconi *et al*¹ and Shaffer *et al*² described carriers of isochromosomes 2p (i(2p)) and 2q (i(2q)). In both patients maternal uniparental disomy (UPD) (2), the exceptional inheritance of both chromosomes 2 from the mother, was detected. Isochromosome formation of both the short and the long arms of a chromosome in one carrier is a rare event. In addition to isochromosomes 2, there exist single reports on two isochromosomes 4p and 4q,³ isochromosomes 7p and 7q,⁴ and isochromosomes 9p and 9q.⁵ In these cases, the parental origin was determined and was mostly maternal.

The phenotypes of the carriers of i(2p) and i(2q) and maternal UPD(2) are rather inconsistent. Bernasconi *et al*¹ reported a healthy woman with a history of five spontaneous abortions. In contrast, the patient of Shaffer *et al*² showed features similar to those of three maternal UPD(2) patients ascertained because of confined placental mosaicism (CPM) for trisomy 2.⁶⁻⁸ In all these four patients, severe intrauterine growth retardation with oligohydramnios or anhydramnios and postnatal growth retardation were observed, with additional findings including hypospadias and pulmonary dysplasia or hypoplasia. Three patients showed good motor and intellectual development⁶⁻⁷ and the fourth patient died of severe pulmonary hypoplasia shortly after birth. The phenotypically normal girl published by Heide *et al*,⁹ who shows maternal UPD(2) and a normal chromosomal complement supports the observations that maternal UPD(2) has no clinical effects.

Up to now, partial or complete paternal UPD(2) has never been reported. Here we describe a healthy carrier of i(2p) and i(2q), in whom molecular studies showed a paternal UPD(2p) and a maternal UPD(2q).

The healthy, 36 year old woman was referred for chromosomal analysis because all of her six pregnancies had resulted in spontaneous abortion during the first trimester. She had normal physical and mental development. She went through normal puberty and her final height is 176 cm (+2 SD). She is of normal intelligence and works as a nurse.

GTG banded chromosome analysis on lymphocyte cultures of the proband showed a non-mosaic, 46,XX,i(2)(p10),i(2)(q10) chromosome complement. Cytogenetic analyses of the proband's parents showed normal 46,XX and 46,XY karyotypes.

Table 1 Results of STR typing in the UPD(2) family. Data from markers other than chromosome 2 are not shown; the order and localisation of markers correspond to those published by Gyapay *et al*¹⁰

STR	Localisation	Father	Mother	Proband	Informativity
D2S319	2pter	1-2	2-2	1-1	Paternal UPiD
D2S168	2pter-qter	1-4	2-3	4-4	Paternal UPiD
D2S131	2p22-p25	2-2	1-3	2-2	Paternal UPD
D2S160	2p13-q14	1-1	1-1	1-1	—
	Cen				
D2S121	2q12-q13	1-1	2-2	2-2	Maternal UPD
D2S118	2q32	1-2	3-4	3-3	Maternal UPiD
D2S117	2qter-qter	1-1	1-1	1-1	—
D2S116	2q32	2-2	1-1	1-1	Maternal UPD
D2S325	2qter-qter	1-1	2-3	2-2	Maternal UPiD
D2S125	2qter-qter	1-1	2-2	2-2	Maternal UPD
	2qter				

For molecular studies, DNA was isolated from peripheral lymphocytes from the proband and her parents. UPD(2) was determined by short tandem repeat typing (STR). Primers and map location were obtained from the chromosome 2 linkage map published by Gyapay *et al*.¹⁰ Typing of four markers on chromosomes other than chromosome 2 was carried out to confirm normal maternal and paternal contributions.

The results of STR typing are shown in table 1. In three out of four 2p markers, only one paternal allele could be identified; the fourth STR was not informative. On 2q, we detected only one maternal allele in five out of six markers with the sixth not being informative. Therefore, paternal uniparental isodisomy (UPiD)(2p) and a maternal UPiD(2q) is present. A similar condition has been described formerly for chromosome 7⁴; in a postnatally growth retarded girl, a paternal isochromosome 7p and a maternal isochromosome 7q were detected. The following mechanism of formation can be postulated. An incomplete mitotic recombination occurred in a zygote primarily biparental for chromosome 2, followed by the loss of paternal 2q and maternal 2p without the centromere, and centromeric misdivision of the rearranged chromosomes.

To the best of our knowledge, paternal UPD(2) has not previously been described. The finding of a paternal UPD(2p) in a phenotypically normal person indicates that this condition does not seem to have any phenotypic effect. It can be speculated that no paternally imprinted genes are located on the short arm of chromosome 2. Of course, based on only one case, the possibility of the existence of a paternally imprinted gene in 2p cannot be excluded with certainty.

Additionally, maternal UPD(2q) in our proband provides further evidence that there are no imprinted genes on the long arm of chromosome 2, corresponding to the results of Bernasconi *et al*¹ and Heide *et al*.⁹ Therefore, our data support the hypothesis that maternal UPD(2) does not influence the phenotype. The clinical findings in the patients with maternal UPD(2) showing abnormalities can probably be attributed to placental dysfunction owing to CPM or to possible mosaicism for trisomy 2. In the case of the phenotypically affected carrier of i(2p) and i(2q),² the most probable method is formation of the zygote with biparental disomy 2, subsequent centromeric misdivision resulting in maternal i(2p) and i(2q), and loss of paternal chromosome 2. This mechanism is compatible with CPM for trisomy 2. Thus, this might be the cause of the clinical findings in this patient.

Except for the possibility of homozygosity for recessive mutations, neither paternal UPD(2p) nor maternal UPD(2q) appears to have any adverse effect on the phenotype. There is no evidence for paternally imprinted genes on 2q or maternally imprinted genes on 2p.

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1 Bernasconi F, Kargüzel A, Celep F, Keser I, Lüleci G, Dutly F, Schinzel AA. Normal phenotype with maternal isodisomy in a female with two isochromosomes i(2p) and i(2q). *Am J Hum Genet* 1996;59:1114-18.