

INTRODUCTION

Tetrasomy 9p is a rare chromosomal imbalance defined by the presence of a supernumerary chromosome, either an isochromosome or an isodicentric chromosome derived from the short arm of chromosome 9. The most recurrent breakpoints being 9p10, 9q12 and 9q13¹.

Tetrasomy 9p has been reported in some cases in prenatal diagnosis. On ultrasound, it usually presents with intrauterine growth restriction (IUGR), abnormal facial profile, ventriculomegaly, cardiac and renal/pelvis alterations^{1,2,3}. However, few reports establish a correlation between fetal features and the size of isochromosome or the presence of isodicentric 9^{1,4}.

METHODS

We report the clinical case of a 32-year-old pregnant woman, G2P1, underwent amniocentesis at 13 weeks of gestation with fetal increased nuchal translucency (7mm). The fetus also presented IUGR, cystic hygroma, generalized subcutaneous edema, cardiac malformations, abnormal facial profile and fetal death. The karyotype was performed by standard *in situ* methods. Fluorescence *in situ* hybridization (FISH) was performed using centromeric probe CEP9.

RESULTS

Conventional cytogenetic and FISH analyses revealed a supernumerary chromosome idic(9)(q12) in all cells examined.

After counseling the couple opted for termination of pregnancy. The *post-mortem* analysis revealed a macerate fetus, a single umbilical arteria, IUGR, cervical cystic hygroma, facial dysmorphism with cleft lip and palate, hypertelorism and low set ears (Table I, columns A and B).

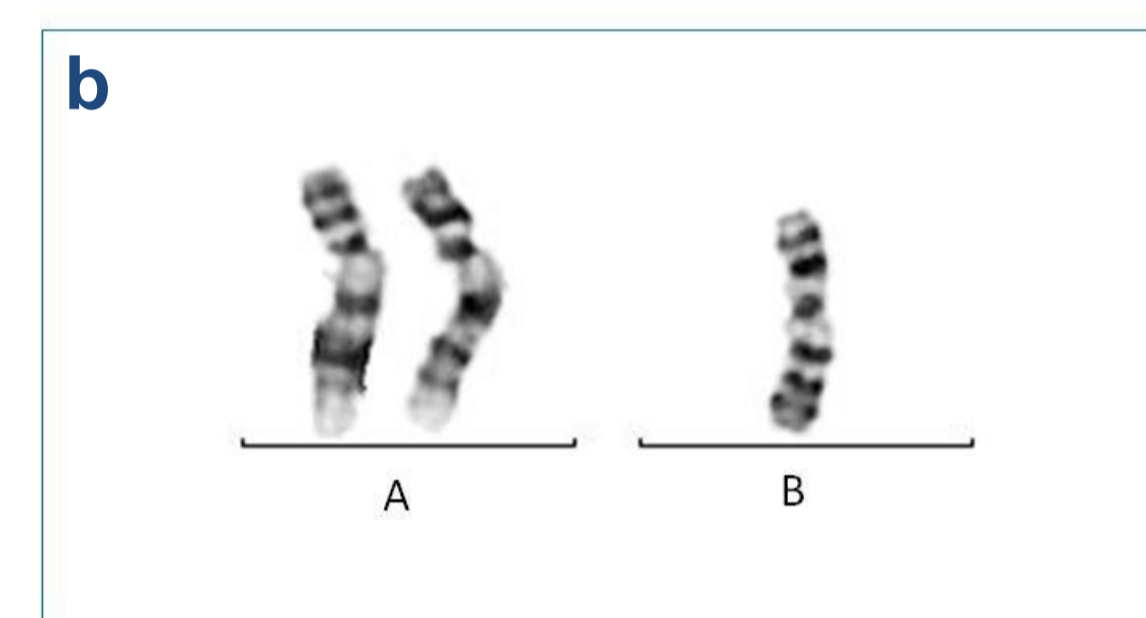
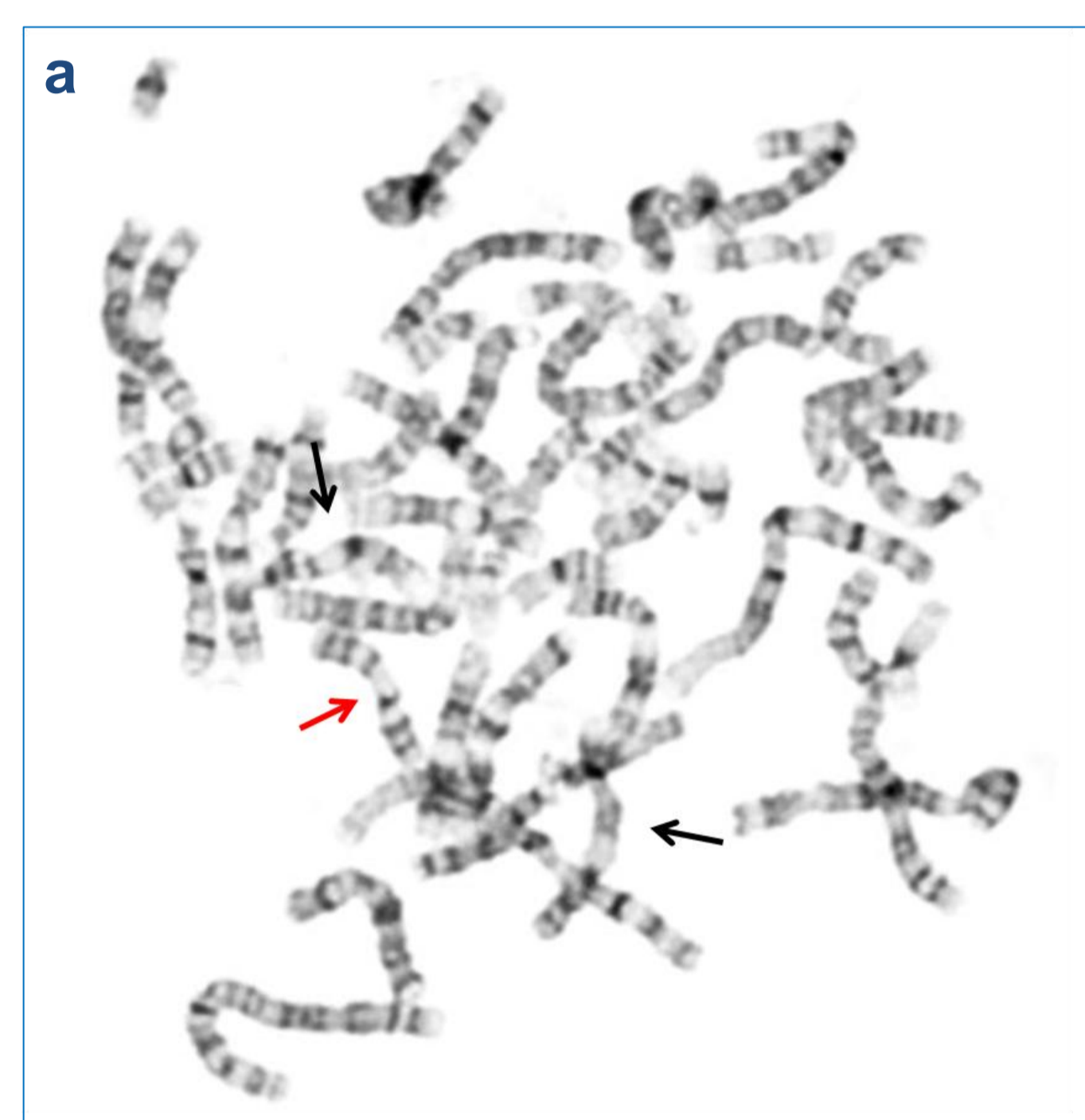


Figure 1. (a) Metaphase showing the two normal chromosomes 9 (black arrows →) and the chromosome idic(9) (red arrow →); **(b)** The two chromosomes 9 (A) and the idic(9) (B).

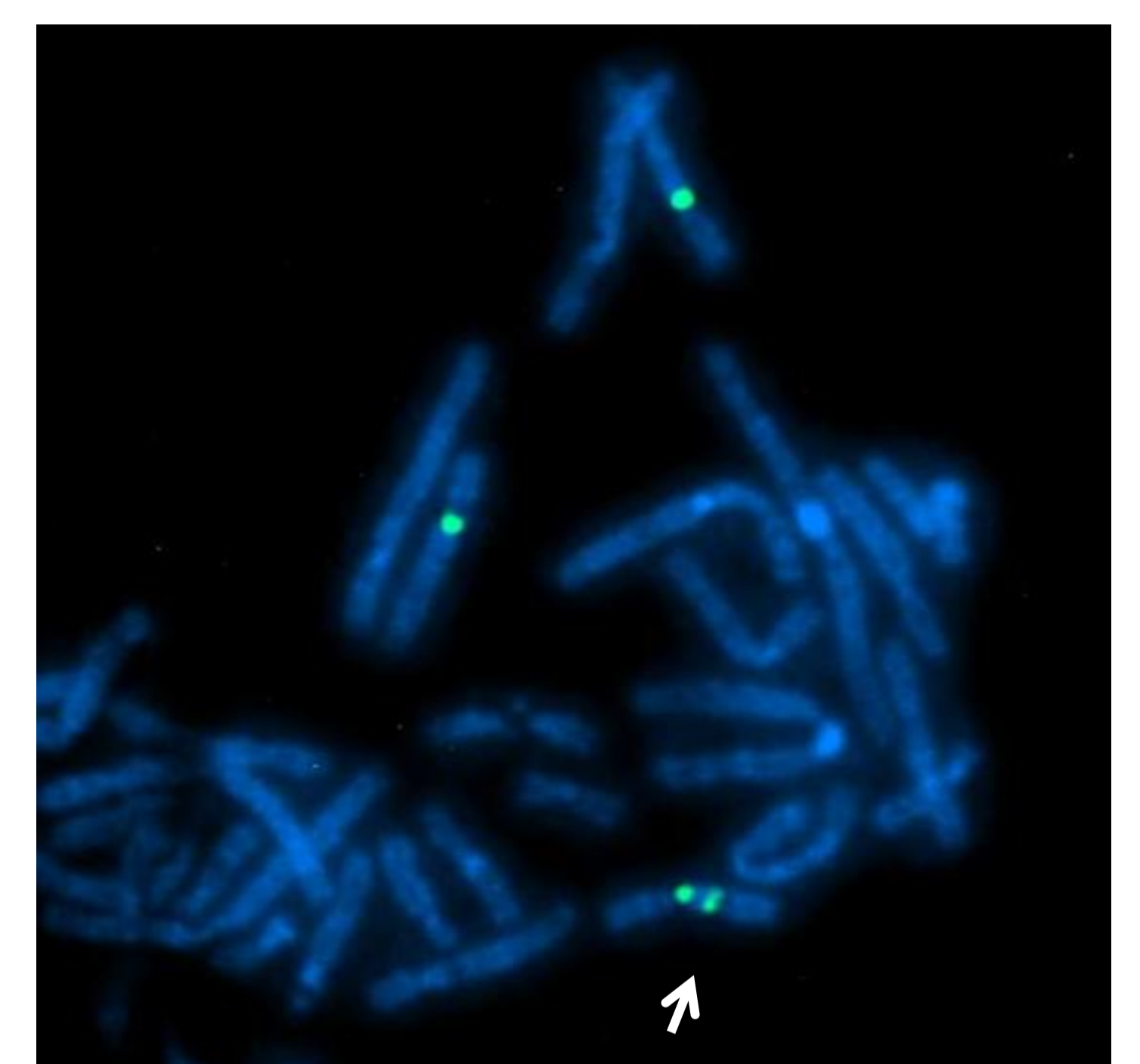


Figure 2. Partial metaphase showing centromeric probe signal (green) on both chromosomes 9 and in chromosome idic(9) (arrow).

Table I – Prenatal ultrasonography (USS)/TOP clinical findings (+ - present; Av - abnormal value; A- Absence;) presents in tetrasomy 9p cases

Reference/ cases	A	B	C	D	E	F	G	H	I	J	K	L
Breakpoints	q12	q21	p10	mos q21	q12	i(9)	p11	q13	p10	q12	q21.1	i(9p)
USS weeks	13	1stT	22	19	11	16	13	12	2T	12	19	17; 24
Fetal death/TOP		13	13	23			22	?	30	30	TOP	Fd
Nuch Trans. 7 th 1 st tri- (mm)	7.3		Av					2.9		Av		
Nasal bone			A				A					
Fetal Size/IUGR		+	N	+	+	+			+			+
Single umbilical arteria		+	+	+		+						
Edema subcutaneo	+	+					+					
Cystic hygroma	+	+							+			
Fetal ascites/Hydropsis F.				+							+	
Hydrocephalus						+						
Oligohydramnios												+
Open Metopic suture							+					
Micrognathia				+		+						
Agnesis corpus callosum				+		+						+
Ventriculomegaly				+		+			+			+
Dandy-Walker				+		+	+			+	+	+
Cerebellum anomaly								+	+			
Abnormal facial profile/ Facial dysmorphism	+	+		+				+				+
Hypertelorism		+							+			
Bilateral cleft Lip/ palate			+	+			+		+			
Mandibular hypoplasia			+									
Retrognathism							+					
Low set ears			+	+		+						+
Short neck				+								
Cardiac malformation	+	+		+		+			+			
Common mesentery				+								
Pulmonary hypoplasia				+								+
Lung anomalies												+
Kidneys/pelvis alterations			+	+			+	+	+	+	+	+
Diaphragmatic hernia												+
Cervical abnormalitie	+					+						
Bilateral palmar creases				+								
Short and large thumbs				+								
Hypoplastic nails				+								
Abnormal hands position				+								
Brachydactyly									+			
Rock-bottom club foot				+		+	+		+			

A - Present study ; B - El Khattabi, 2015 (patient 10); C - El Khattabi, 2015 (patient 11); D - Chen, 2014; E - Lazebnik, 2015; F - Podolsky, 2011; G - Nakamura-Pereira, 2009; H - di Vera, 2008; I - Henriques, 2005; J - Deurloo, 2004; K - Dhandha, 2002 (case 3); L - McDowall, 1989.

DISCUSSION

✓The symptoms of tetrasomy 9 may vary in range and severity from case to case⁵. The prenatal findings and the *post-mortem* analysis are summarized on Table I, as well as data from other reports^{1,2,3,4,6,7,8,9,10,11}. In generally, the findings of present case are in accordance with most reports.

✓Nevertheless, an early detection of a cardiac anomaly is uncommon and such the hypertelorism is not commonly described. Additionally the fetal death occurred early than in the most cases described in the literature.

✓The most relevant facts in this case are the earlier USS detection of relevant fetal features, and the earlier fetal death. Cerebral malformations and visceral abnormalities were not possible to clearly identify because of the fetus macerated condition.

✓The influence of breakpoints position (p10, q12, q13, q21 or q22) on the severity of the phenotype is controversial^{1,4}. In most cases breakpoints on p10, on q12 or on q13 show a similar phenotype with no significant variation between cases i(9) and idic(9) or psu idic(9). However, involvement of 9q region appears to be more often associated with cardiac malformations, intellectual deficiency and death¹. In generally, the prognosis of tetrasomy 9p is poor^{1,9}.

✓In summary, a recognizable phenotype for tetrasomy 9p is emerging and common findings on prenatal ultrasound include IUGR, ventriculomegaly, cleft lip or palat, and renal anomalies. The exact extent of the isochromosomes does not seem to predict severity, but mosaic cases are less severe, or at least have a greater probability of survival^{4,12,13}.

✓This case aims to be a contribute to a better karyotype-phenotype correlation in cases with tetrasomy 9p and isodicentric chromosomes idic(9).

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