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Single umbilical artery – marker for chromosomal abnormalities: report of two postnatal cases

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Abstract

Single umbilical artery (SUA) is one of the most common umbilical abnormalities. SUA is believed to be caused by agenesis of one of the umbilical arteries, atrophy of a previously normal artery, or presence of the original artery of the body stalk. SUA may occur either isolated or in conjecture with additional fetal and chromosomal abnormalities. Here we present two cases with prenatally diagnosed SUA, both associated with chromosomal abnormalities, and a short review of the literature. We emphasize the necessity of fetal karyotype assessment for patients with nonisolated SUA, those with abnormal genetic screening results and those with intrauterine growth restriction.

Keywords: *single umbilical artery, chromosomal abnormalities, prenatal marker*

Introduction

Normally, the umbilical cord contains two arteries and one vein, an obliterated allantois duct, all surrounded by Wharton's jelly and contained within an outer layer of amnion[1]. The rudimentary umbilical cord is formed during the 4th to 8th weeks of gestation and the blood flow is established by the end of the 5th week of gestation[1].

Multiple abnormalities of the umbilical cord were described: anomalies of the cord length and diameter, distorsionalabnormalities, vascular anomalies, abnormal cord insertion, solid and cystic lesions.

Single umbilical artery (SUA) is one of the most common congenital malformations[2] and may occur in association with additional anomalies or, as in many cases,can be an isolated feature. There are three hypotheses for pathogenic mechanism of SUA: a) primary agenesis of one umbilical artery; b) secondary atrophy or atresia of a previously normal umbilical artery; c) persistence of the original allantoic artery of the body stalk[3].

According to clinical studies the reported incidence of SUA is found in about 0.5% - 2.5% of pregnancies[4,5,6] going up to 4.8% in some studies[3]. Postnatal figures showed an incidence of 0.2%-0.4% infants born with SUA[7,8]. A statistical analysis on autopsy cases established an incidence of 1% individuals with SUA[9].

SUA has been associated with fetal abnormalities such as structural malformations, chromosomal anomalies, intrauterine growth restriction, preterm birth[10,11,12]. SUA does increase the risk for the baby having cardiac, skeletal, intestinal or renal complications.

The evaluation of the umbilical cord is usually made by routine obstetric ultrasound examination. Color Doppler ultrasound can be used to assess the number of umbilical cord vessels in prenatal period[13].

Neonates with SUA and isolated SUA had increased rates of prematurity, growth restriction and adverse neonatal outcome[14].

Case reports

We present two cases referred to our Genetics Department for complex congenital anomalies.

Patient 1

The baby, a male, has been evaluated in Mother and Child Care Institute "Prof.dr.Alfred Rusescu" from Bucharest for the first time at age of 5 months. He was the first child of a nonconsanguineous family, his mother was 30 years old and father 37 years old. The pregnancy was apparently normal, the only abnormal prenatal sign was single umbilical artery, with birth at term, by vaginal delivery, cranial presentation, APGAR score 6. At birth, weight was 3150g (P25), length was 51 cm (P75) andoccipito-frontal circumference (OFC) was 37,7cm (P90).

Abdominal ultrasonography and ophthalmological evaluation were normal.The transfontanelar ultrasound showed borderline ventriculomegaly and the cardiac echography revealed a persistent ductusarteriosus.

At age of 5 months 2 weeks, morphometric parameters were: weight=7620g (P90), length=69cm (P95), head circumference=44cm(P90). Clinical picture was characterized by dysmorphic features, with plagiocephaly, frontal boses, posteriorlyrotated ears with bilateral narrow external auditory canal, hypoplastic ear lobes, high vaulted palate, hypoplastic scrotum, cryptorchidia, axial hypotonia, congenital stridor, spot skin hypopigmentation on the right side of the abdomen.

Conventional cytogenetic evaluation was performed. Peripheral blood from the patient was harvested on heparin anticoagulant and was prepared for culturing. Metaphases were obtained after 72h incubation of two

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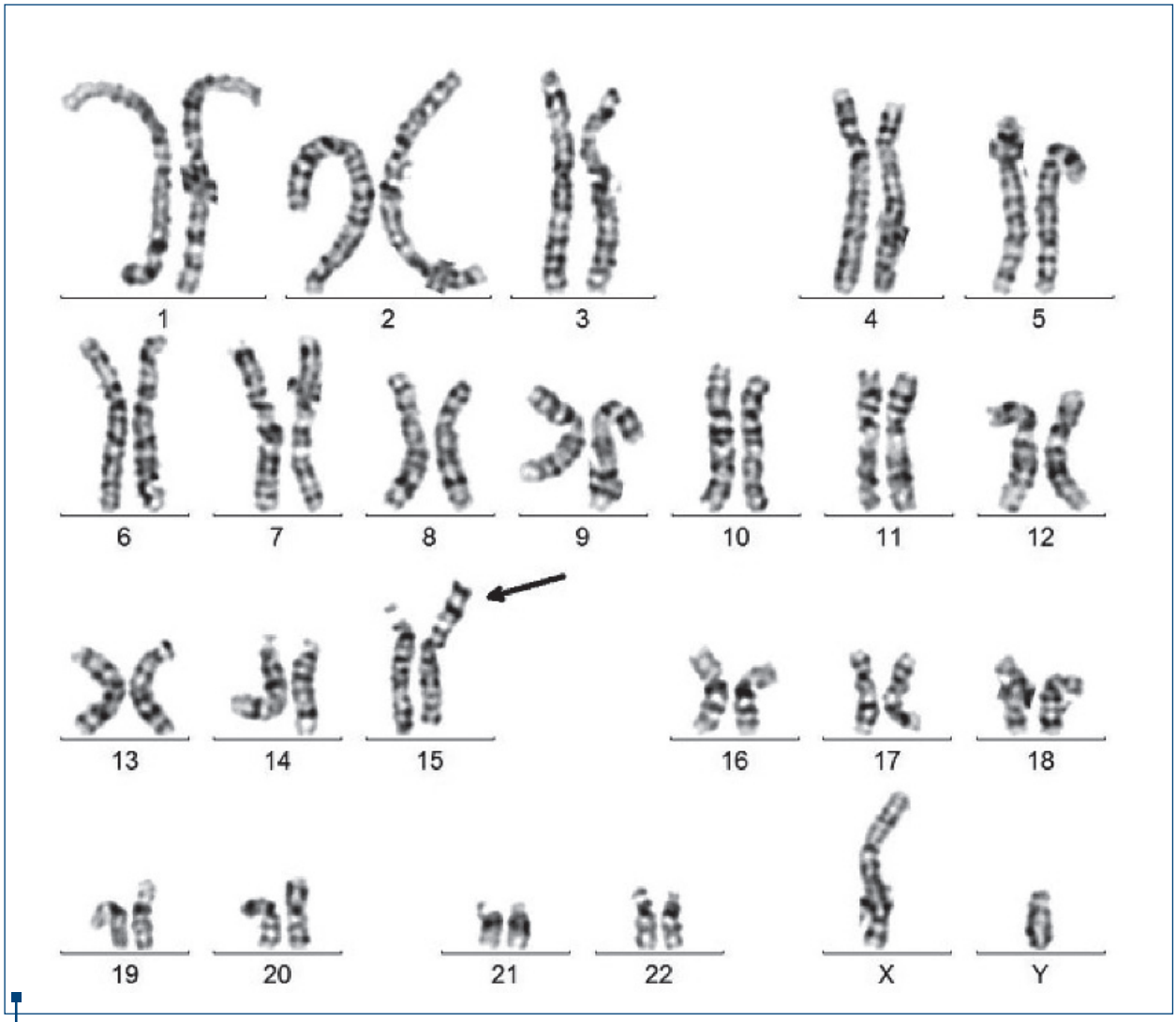

Figure 1. Karyotype of the patient 1 46,XY,der(15)(?::15p11.1→qter)

different lymphocyte cultures, and chromosomes were analyzed after GTG banding.

Standard karyotypeshowed an abnormal result, with a derivative chromosome 15, orginating from the addition of supplementary genetic material of unknown origin on the short arm of chromosome 15: 46,XY,der(15)(?::15p11.1→qter)[15](Figure 1). The cytogenetic testingfor the parents found a balanced translocation involving chromosomes 1 and 15 for the mother (Figure 2).

Patient 2

This girl is the second child of a young family. The brother of the patient was healthy.

Prenatal evaluation showed oligoamnios and intrauterine growth retardation observed at age of 29 weeks. Review of her prenatal medical record revealed the presence of SUA. Maternal biochemical screening by triple test was normal.

She was prematureborn at gestational age of 33 weeks, by cesarean delivery, and APGAR score 7. At birth, her weight was 1200 g, length=38 cm, OFC=29 cm, with intracranial hemorrhage degree 2, absorbed afterwards.

At age of 3 months results of her physical evaluation showed dysmorphic features, hypotonia, psychomotor delay and severe postnatal growth retardation, with her weight=2890g (<P5). Postnatal investigations showed persistent ductusarteriosus, thalamic microcalcifications on transfontanelar ultrasound and a partial duplication of the left kidney.

Her karyotype resultfrom peripheral blood cell culture(Figure 3)showed a derivative chromosome 15, with an insertion of genetic material of unknown origin at the long arm of chromosome 15: 46,XX,ins(15;?)(pter-q22::?::q22-qter). Parental karyotypes were normal. In addition to karyotyping, microarray single nucleotide polymorphism (SNP) analysis was performed. This method is used for the identification of DNA polymorphisms and dosage changes (such as copy number gains and losses). Microarray SNP analysisfor the patient identified a duplication of chromosome 15 (q21.2 to q24.1). This de novo

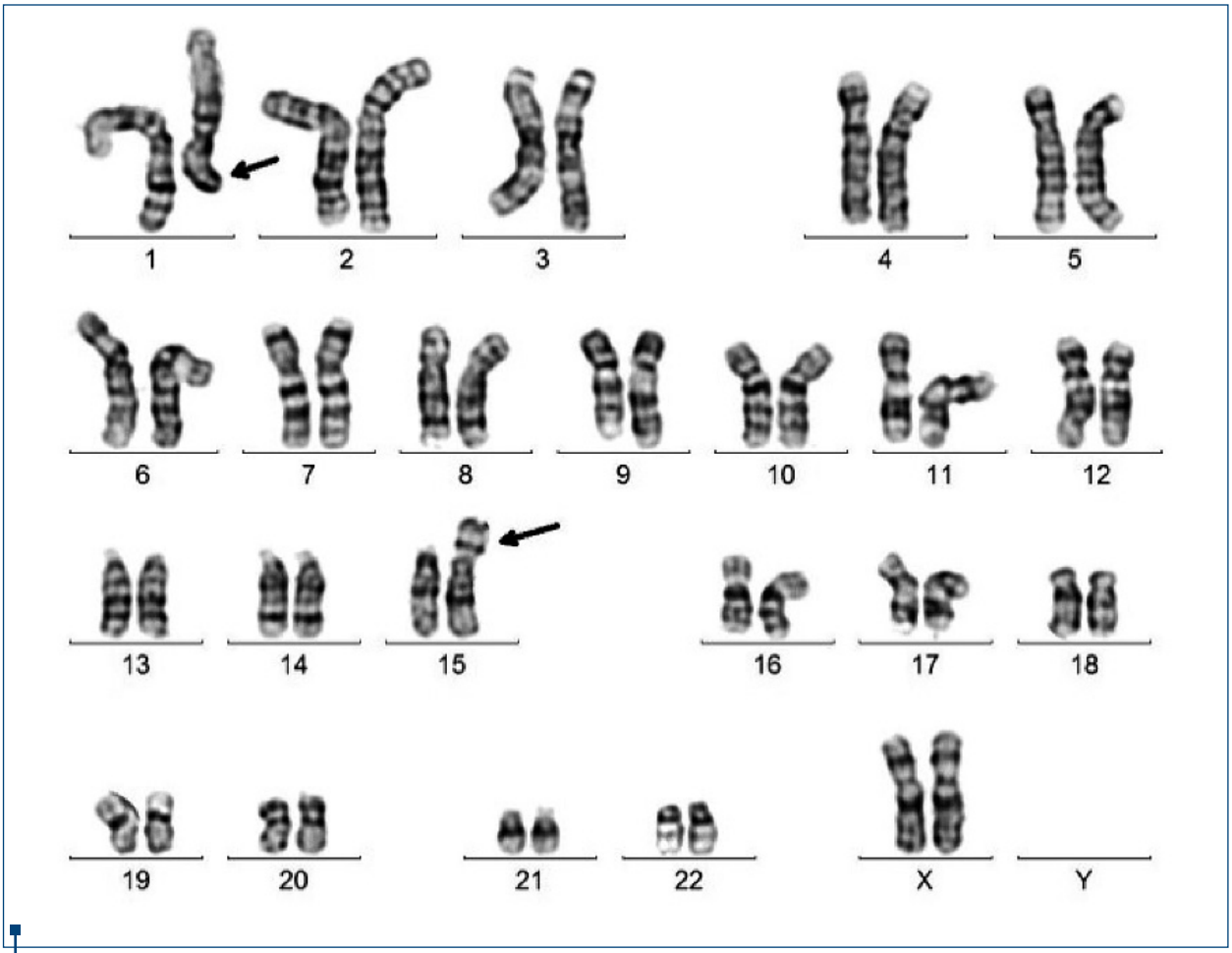

Figure 2. Karyotype of the patient's mother 46,XX,t(1;15)(q32;p11.2)

(not present in neither of her parents) chromosome 15 duplication explains the phenotype of the girl.

Discussion

Different studies synthesized possibilities of associated minor and major prenatal abnormalities with SUA: oligohydramnios, intrauterine growth retardation, renal agenesis, fetal ascites, diaphragmatic hernia, hydrocephalus, meningomyelocele[15,16], cleft palate, esophageal atresia[5], skeletal dysplasia, holoprosencephaly, enlarged cisterna magna, hydrothorax, omphalocele, cardiac defects[17].

In unselected obstetric population, many researchers indicated an increased risk for fetal aneuploidy in cases with SUA and major fetal anomalies[18].Various chromosomal abnormalities, such as trisomies involving 13, 18, 21, X chromosomes, monosomy X and other chromosomal defects were identified in different groups[18,19]. There were no chromosome abnormalities in fetuses with an isolated single umbilical artery[3]and this relatively common finding suggests only a modest increase in risk for fetal aneuploidy[20].

According to a study performed in Nova Scotia, Canada, SUA fetuses and neonates had a 6.77 times greater risk of congenital anomalies and a 15.33 times greater risk of chromosomal abnormalities[14]. The most common congenital anomalies found in chromosomally normal fetuses and neonates in this study were genitourinary (6.48%), cardiovascular (6.25%) and musculoskeletal (5.41%). Neonates with SUA and isolated SUA had increased rates of prematurity, growth retardation and adverse neonatal outcome[14].

Our selected cases presented single umbilical artery associated with other fetal echographic signs and isolated SUA, confirmed postnatally by specific investigations. First case showed only SUA in the prenatal period, without other obvious abnormalities, increasing the difficulty to make an early diagnosis of the chromosomal anomaly identified later. Our second case was marked by important abnormal fetal findings in association with SUA, all very suggestive of a chromosomal anomaly: intrauterine growth retardation and oligoamnios. For both cases prenatal genetic testing was not performed.

Conclusions

Identification of SUA is important for prenatal diagnosis of congenital and chromosomal anomalies. The

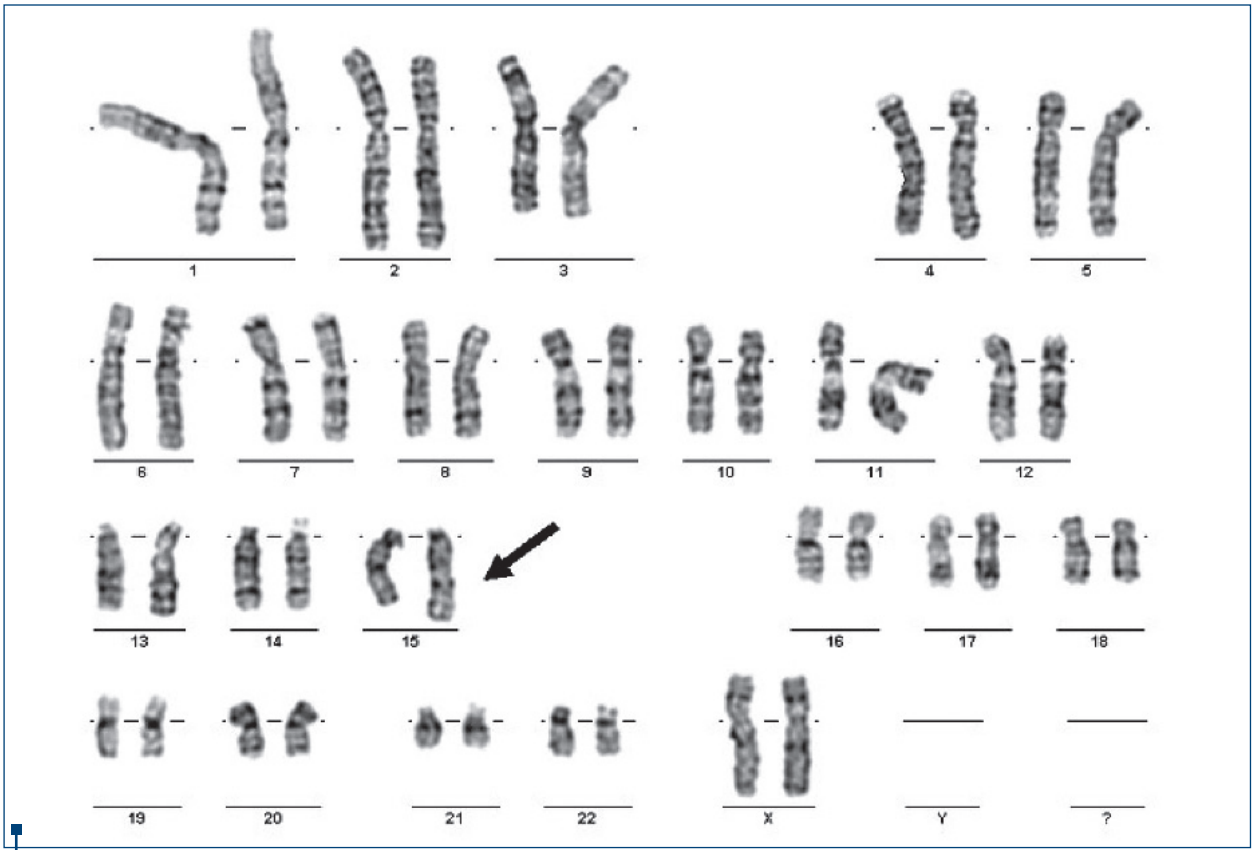

Figure 3. Karyotype of the patient 2 46,XX,ins(15;?)(pter-q22::?::q22-qter)

presence of single umbilical artery requires a detailed prenatal and postnatal ultrasonographic examination to rule out associated abnormalities. Special attention should be accorded to the cardiac, genitourinary, gastrointestinal, and central nervous systems. Pregnancies identified as having fetuses with associated structural anomalies should be offered amniocentesis. Pregnancies with isolated SUA should be carefully monitored for fetal growth restriction.

Also, we recommend further evaluation and genetic counseling especially in cases with identified additional anatomical defects. ■

References

1. Spurway J, Logan P, Pak S. The development, structure and blood flow within the umbilical cord with particular reference to the venous system. AJUM 2012, 15(3), 97-102.
2. Geipel A, Germer U, Welp T, Schwinger E, Gembruch U. Prenatal diagnosis of single umbilical artery: determination of the absent side, associated anomalies, Doppler findings and perinatal outcome. Ultrasound Obstet Gynecol 2000, 15(2), 114-117.
3. Lubusky M, Dhaifalah I, Prochazka M, Hyjanek J, Mickova I, Vomackova K, Santavy J. Single umbilical artery and its siding in the second trimester of pregnancy: relation to chromosomal defects. Prenat Diagn 2007, Vol. 27(4), 327-31.
4. Defigueiredo D, Dagklis T, Zidere V, Allan L, Nicolaides KH. Isolated single umbilical artery: need for specialist fetal echocardiography? Ultrasound Obstet Gynecol. 2010, 36(5), 553-5.
5. Dane B, Dane C, Kiray M, Cetin A, Yayla M. Fetuses with single umbilical artery: analysis of 45 cases. Clin Exp Obstet Gynecol. . 2009, 36(2), 116-9.
6. Agata W, Aleksander I, Małgorzata OA, Dorota KP, Wojciech C, Patrycja B, Marcin S, Adrian L, Krzysztof S. Single umbilical artery: what does it mean for the fetus? Ginekol Pol. 2007, 78(11), 869-72.
7. Leung AK, Robson WL. Single umbilical artery. A report of 159 cases. Am J Dis Child. 1989, Vol. 143, 1, pp. 108-11.
8. Deshpande SA, Jog S, Watson H, Gornall A. Do babies with isolated single umbilical artery need routine postnatal renal ultrasonography? Arch Dis Child Fetal Neonatal Ed. 2009, 94(4), 265-7.
9. Heifetz SA. Single umbilical artery. A statistical analysis of 237 autopsy cases and review of the literature. Perspect Pediatr Pathol 1984, 8(4), 345-78.
10. Martinez-Payo C, Gaitero A, Tamarit I, Garcia-Espantaleon M, Goy EI. Perinatal results following the prenatal ultrasound diagnosis of single umbilical artery. Acta Obstet Gynecol Scand 2005, 84, 1068-74.
11. Ferreira V, Vaz I, Reis AP, Mendes MJ, Maria do Céu R. Antenatal detection of single umbilical artery: what does it mean? Nascer e Crescer. 2013, 22(3), 140-4.
12. Rinehart BK, Terrone DA, Taylor CW, Isler CM, Elaine Larmon J, William Roberts E. Single umbilical artery is associated with an increased incidence of structural and chromosomal anomalies and growth restriction. Am J Perinatol 2000, 17(5), 229-32.
13. Ulm B, Ulm MR, Deutinger J, Bernaschek G. Umbilical artery Doppler velocimetry in fetuses with a single umbilical artery. Obstet Gynecol 1997, 90(2), 205-9.
14. Murphy-Kaulbeck L, Dodds L, Joseph KS, VAn den Hof M. Single umbilical artery risk facttors and pregnancy outcomes. Obstet. Gynecol. 2010, 4(116), 843-50.
15. Shaffer LG, McGowan-Jordan J, Schmid M. International System of Cytogenetic Nomenclature, ISCN, [ed.] Karger. 2013.
16. Sener T, Ozalp S, Hassa H, Zeytinoglu S, Basaran N, Durak B. Ultrasonographic detection of single umbilical artery: a simple marker of fetal anomaly. Int J Gynaecol Obstet 1997, 58(2), 217-21.
17. Nyberg DA, Mahony BS, Luthy D, Kapur R. Single umbilical artery. Prenatal detection of concurrent anomalies. J Ultrasound Med 1991, 10(5), 247-53.
18. Granese R, Coco C, Jeanty P. The value of single umbilical artery in the prediction of fetal aneuploidy: findings in 12,672 pregnant women. Ultrasound Q 2007, 23(2), 117-21.
19. Khong TY, George K. Chromosomal abnormalities associated with a single umbilical artery. Prenat Diagn 1992, 12(11), 965-8.
20. Aubrey Milunski, Jeff M. Milunski. Genetic disorders and the fetus: diagnosis, prevention and treatment. s.l. Wiley-Blackwell, 2010.