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Case Report

Anatomy Section

Isolated Single Umbilical Artery in Twin Pregnancies and its Adverse Pregnancy Outcomes - A Case Report and Review of Literature

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ABSTRACT

Single umbilical artery is the most common congenital abnormality of the umbilical cord and is seen in 4-11% of twin pregnancies. It is usually associated with intrauterine growth retardation, preterm labour, small-for-dates and other structural anomalies. There is no significant difference in the incidence between monochorionic and dichorionic twins. The left artery is usually absent more commonly than the right. The female co-twin was predominantly more affected than their male counterparts. Single umbilical artery is found twice more common in white women than in Afro-Asians and Americans. The hemodynamic disturbances occur early in the embryonic development, influence greatly in the development of single umbilical artery. Genetic and environmental factors also play a major role in the development of this anomaly. The pregnancies with single umbilical artery were classified as high risk group, because the overall perinatal mortality rate was estimated to be as high as 20%. There is a significant increase in the occurrence of single umbilical artery in pregnancies due to artificial reproductive technologies, as well as in spontaneous miscarriages. Prenatal ultrasonography is the principal diagnostic technique employed to identify single umbilical artery during 3rd trimester of pregnancy. The present case, reports the presence of a single umbilical artery in a monozygotic, monochorionic twin pregnancy, which is acardiac-acephalic fetus, small for dates, female sex, associated with other major structural anomalies, and was still born. Authors analyse its incidence, clinical presentations and pregnancy outcome and also review the pertinent literature.

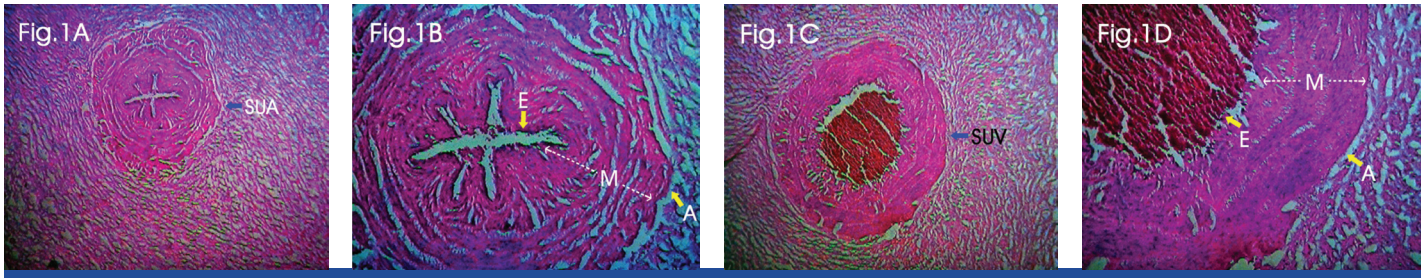
Keywords: Congenital malformation, Intrauterine growth retardation, Single umbilical artery, Twin pregnancies, Ultrasonography

CASE REPORT

A 28-year-old female, was admitted to a peripheral hospital, at 36 wk of gestation with labour pains. She was Gravida 4, Para 2 with a history of normal delivery on previous occasions. A prenatal ultrasonography diagnosed a twin gestation with monochorionic placenta. Since her normal progress of the labour was delayed, she had undergone a lower segment caesarean section. The first twin was a live healthy female singleton, with birth weight of 2.9 kg. The second twin was an acardiac-acephalic fetus, size 24 x 12 x 10 cm, weighing 1850 grams. Both twins share a common placenta, which was monochorionic and diamniotic, weighing 500 grams. Two umbilical cords were seen coming from the common placenta. The cord of the normal twin was long and edematous with a pair of umbilical arteries and one umbilical vein. The umbilical cord of the acardiac twin was short with a single umbilical artery and a single vein. A small piece of the cord was sliced, fixed in 10% formalin for 24 hours, processed, embedded in paraffin wax. It was sectioned with a rotary microtome under four micron thicknesses, and stained with regular H/E stain. Microscopic examination under both low and high magnification confirms the presence of SUA. The Hemotoxylin-eosin sections of umbilical cord was photographed by using Nikkon 7000-D with 16 megapixel camera and preserved for future reference [Table/Fig-1A-D].

DISCUSSION

Umbilical cord begins to form between 2nd and 6th wk after conception, acts as a conduit for two umbilical arteries and one umbilical vein [1]. The most common congenital abnormality of the umbilical cord is the single umbilical artery (SUA) and was seen in 0.2-1.1% of singleton and 4-11% in twin pregnancies [2]. It is usually associated with intrauterine growth retardation (IUGR), preterm labour, fetal and neonatal death, placental anomalies, abnormal umbilical cord insertions and other structural anomalies. The highest prevalence of intrauterine growth retardation (IUGR) in fetuses with SUA was mainly due to increase in the placental insufficiency [3]. The left artery was usually absent more commonly than the right. Even though the SUA abnormality can be detected as early as 13 wk of gestation, the diagnosis is confirmed only in the 3rd trimester of pregnancy by the sophisticated ultrasonography [4]. The etio-pathogenesis of SUA is still a matter of debate, but various theories have been put forward over the years to explain its occurrence. Genetic and environmental factors play a major role in the development of SUA in majority of the cases. Chromosomal abnormalities were reported in 8-11% of fetuses with SUA and were commonly seen in trisomies 13 and 18 but rarely in trisomy 21 and monosomy 45X [5]. The wide variations in the reported incidence of SUA, among spontaneous abortions, malformed fetuses, euploid and aneuploidy fetuses and the uncomplicated neonates are due to different methods employed to identify SUA, being lowest in ultrasound and in full term neonates and highest in abortuses and autopsies [6]. In the cases of singleton pregnancies, there is a gestational age-dependent change in the size of the single artery, with a sharp increase in its cross-sectional area starting around 26 wk of gestation. A significantly higher incidence of small-for-gestational age (SGA) neonates has been found when this adaptive dilation has not been observed [7]. The pregnancies with SUA were classified as a high risk group, because the overall perinatal mortality rate was estimated as 20% [6]. According to Delbaere et al., the SUA had been found more frequently in twins originating from assisted reproductive technologies (ART) [8]. Even though the reported incidence of SUA is as high as 11% from the pathological study series, there is little information available on the overall incidence and clinical importance of SUA in multiple gestations. The present study revealed a case report of SUA in a monozygotic, monochorionic twin pregnancy and tries to analyse its incidence, variable clinical presentations and adverse outcomes of cases of SUA in twin pregnancies.



[Table/Fig-1A]: Transverse section of the umbilical cord of the Acardiac-acephalic twin showing single umbilical artery (H/E stain - 4 X), SUA - Single umbilical artery **[Table/Fig-1B]:** Transverse section of the umbilical cord of the Acardiac-acephalic twin showing single umbilical artery (H/E stain - 10 X), A - Tunica Adventitia; M -Tunica Media; E - Endothelium of Tunica Intima **[Table/Fig-1C]:** Transverse section of the umbilical cord of the Acardiac-acephalic twin showing single umbilical vein (H/E stain - 4 X), SUV - Single umbilical vein **[Table/Fig-1D]:** Transverse section of the umbilical cord of the Acardiac-acephalic twin showing single umbilical vein (H/E stain - 10 X), A - Tunica Adventitia; M-Tunica Media; E - Endothelium of Tunica Intima

Types of SUA	Number and types of vessels in umbilical cord	Morphological anomalies	Incidence
Type I	Two vessels - one umbilical artery of allantoic origin from right/left common iliac artery and left umbilical vein	CNS anomalies, genito-urinary malformations, short umbilical cord and acardiac fetus	98%; Most common type
Type II	Two vessels - one umbilical artery of vitelline origin from superior mesenteric artery and left umbilical vein	Fetal malformations - sirenomelia, caudal regression and anal agenesis.	1.5%; Second common type
Type III	Three vessels - one umbilical artery of either allantoic/vitelline origin and left and anomalous right umbilical veins	Fetal anomalies - renal agenesis, unicornuate uterus, hydranencephaly and ipsilateral limb reduction.	Extremely rare with poor prognosis
Type IV	Two vessels - one umbilical artery (allantoic or vitelline) and the right umbilical vein.	Embryos undergo spontaneous abortion.	Very rare; incidence rate unknown

[Table/Fig-2]: Different types of SUA and its classical morphological features

The arterial system of the embryo begins to develop during 4-5th wk of embryonic period; the paired umbilical arteries carry the deoxygenated blood from embryos, traverse through connecting stalk, which later become the umbilical cord, and drains into the chorionic vessels of the placenta. The proximal part of umbilical arteries, become internal iliac and superior vesical arteries; distal parts obliterate to become medial umbilical ligaments [9]. The mechanism of development of SUA can be explained based on three theories, namely primary agenesis, secondary atresia of previously normal vessel and the persistence of the original allantoic artery of the body stalk. In the majority of cases of SUA, the left artery usually disappears, may be due to secondary atresia of the normal left umbilical artery and this was confirmed by histologically identifiable remnants of a second artery in many cases with SUA. So the second theory holds well in most of the cases [10]. Lacro et al., has observed asymmetry among the umbilical arteries, the right being larger than left and this asymmetry in size, may play a role in the pathogenesis of SUA, by favoring the larger right side over the left [11].

The majority of workers observed that the female co-twin was predominantly affected than their male counterparts, the ratio ranging from 1.2:1 to 1.4:1 [12]. The present case described here also belongs to the female sex. SUA is found twice as often in white women than in African, American and Asian women and was also found more frequently in young primiparous and older multiparous women. Pre-eclampsia, alcohol abuse, smoking, diabetes, chronic hypertension, obesity with BMI ≥ 30, epilepsy and poly/oligohydramnios also increase the risk of SUA significantly. Multiple gestations are at significantly higher risk for SUA than with their singleton counterparts [6,13,14].

Blackburn and Cooley described four types of SUA, based on the embryological development and was depicted in [Table/Fig-2] [15]. The hemodynamic disturbances which occur early in the embryonic development influence greatly in the development of feto-placental circulation as well as on the development of umbilical cord. Absence of Hyrtl anastomosis between the two umbilical arteries at the placental side of insertion may also be one of the causes of the discordant arteries. This theory of hemodynamic influences is mainly responsible for most cases of SUA in the twin to twin transfusion syndrome (TTTS) than in the rest of monochorionic twins, but this difference was not statistically significant [16]. The SUA is usually a part of the most acardiac-acephalic twins, in the twin reversed arterial perfusion sequence (TRAP). The present case report of SUA was observed in a case of acardiac-acephalic twin, which corresponds to the most extreme manifestation of TTTS. About 3/4th of the cases of acardiac twins described in the literature have a short umbilical cord with one umbilical artery and one umbilical vein, which indicates the persistence of transitory single artery phase, corresponds to Carnegie stage 12 [17]. The umbilical cord of the acardiac fetus presented here was also similar to the majority of cases with only one umbilical artery and one umbilical vein, suggested that the pathology might have occurred at or earlier than Carnegie stage 12.

The etio-pathogenesis of the SUA is even though complex can be discussed widely by various workers. The majority of authors postulate the role of genetic factors in the form of chromosomal anomalies as the cause of SUA, because it occurs as a part of many syndromes and aneuploidies. SUA was usually found associated with monozygous twinning, sirenomelia, VATER association, fetal hydantoin effects, Jarcho-Levin syndrome, Meckel-Gruber syndrome, multiple lentigines syndrome, autosomal trisomies 13 and 18 and Zellweger syndrome. It has also been reported in few cases of fetal trisomy 21 and monosomy 45X [5]. Environmental factors may also play a role in the development of SUA in addition to genetic factors alone. The intrauterine environment has an important influence on the outcome of the twins, and is frequently found associated with placental abnormalities and abnormal cord insertions, such as marginal and velamentous insertion [2]. Antoniou et al., examined the relative contributions of genetic and environmental determinants on umbilical cord morphology in over 10,000 twins and concluded that genetic and unique environmental factors play a substantial role in the development of single umbilical artery and other related anomalies of the cord [18].

Benirschke et al., have confirmed a greater frequency of SUA in multiple twin gestations [19]. Klatt et al., also observed that the incidence of SUA was greater in twin pregnancies than singletons; but there was no statistically significant difference between monochorionic and dichorionic twins [2]. But Bryan and Kohler on the other hand observed that the incidence of single umbilical artery in twin pregnancies was slightly less than in singletons [12]. In both studies the co-twin had three vessel cords. In the present case also the co-twin has a three vessel cord. SUA was found in approximately 5% of the cords in at least one twin, and it occurs more often in fetal demise than in live births. Among infants with SUA, over 20% have associated fetal anomalies - viz., cardiovascular, renal defects and multiple anomaly syndromes [4,6]. Due to intense competition

among twins, the monochorionic twins exhibit many complications in the form of increased perinatal mortality and discordant birth weight. So the presence of SUA is an indication to carry out karyotyping of new born at the earliest opportunity [20].

Victoria et al., observed that the prevalence of SUA was higher in the smaller fetus of severely discordant (≥25% discordance) mono/dichorionic twin pregnancies [21]. In analysing the case reports of SUA in twins, it is the lighter of the two that is affected in most cases. The development of small-for-dates infants with SUA may be due to an insult during the development of both umbilical artery and other organs or due to malnutrition, thus leading to IUGR [12]. Klatt et al., observed a higher incidence of small for gestational age (SGA) in twins with SUA [2]. About 40% of twin neonates with SUA had low birth weight - viz., below the 10th percentile for gestational age. The gestational age-dependent adaptive dilatation of the SUA in twin gestations was not as prominent as in singleton pregnancies. This failed dilatation of the SUA has been associated with growth developmental disorders in twins and also explains the higher frequency of small for gestational age in twins with SUA than in singleton pregnancies [7]. Stout et al., suggested that growth abnormalities are usually found associated with SUA, more in the case of twins than singleton pregnancies [13].

The twin fetus with SUA exhibited significant intrauterine growth retardation (IUGR). Preterm delivery was also slightly increased in twins complicated by SUA and was usually observed at ≤ 28-34 wk of gestation [13]. Raio et al., analysed 170 twin pregnancies to investigate the incidence and associated problems of SUA in twin pregnancies and concluded that the prevalence of IUGR, SGA and discordant birth weight was higher in the SUA group compared to the rest of the population; they further concluded twin pregnancies with at least one SUA are at higher risk for adverse outcome and local environmental factors are more important than genetic factors in the pathogenesis of SUA [22]. About 25% of the fetuses with SUA are born prematurely. Among SUA infants, low birth weight is of greater importance than prematurity as a factor in perinatal mortality [14].

In the present case report SUA was encountered in the lighter twin with gestational age of 29 wk & 5 d, weighing 1850 grams, while the normal co-twin was weighing 2900 grams and gestational age of 36 wk. The umbilical artery also shows narrowed tunica media with failure in adaptive dilatation. It belongs to monochorionic diamniotic twins with severe congenital anomalies and was stillborn. It is of the female sex. This was similar to small for gestational age (SGA) in the fetus in which the single umbilical artery carries the deoxygenated blood from normal pump twin to the parasitic malformed twin in a reversed direction through an artery to artery anastomosis on the fetal surface of the placenta, which is similar to Hyrtl anastomosis.

There is a significant increase in the occurrence of SUA in pregnancies due to ART, as well as in spontaneous miscarriages. This is against the earlier hypothesis of the development of SUA as an insult during early embryonic development [8]. Also vascular disturbances in the form of thrombo-embolic occlusions lead to a transient SUA situation in some of the monochorionic twins. There are conflicting reports which suggested a familial recurrence of SUA in multiple gestations mothers [23]. Detailed analysis of the malformations encountered in cases of SUA, suggested that there was no marked bias towards a particular organ or system, even though CNS defects, exomphalos and sirenomelia were too frequently found associated with SUA infants [12].

Prenatal ultrasonography is the principal diagnostic technique employed to identify SUA. Although SUA has been reliably diagnosed after 23 wk of gestation, few sporadic cases have been identified as early as 13 wk of gestation. The mean gestational age of discovery of SUA has been reported to be 29 wk [4]. Colour doppler imaging sometimes allows earlier and more confident diagnosis of SUA, but its efficacy is still not proved. Sonographic demonstration of the umbilical arteries in the fetal pelvis also provides supportive confirmation of SUA. Moreover the measurement of transverse intraluminal umbilical arterial diameter in SUA was always greater than that of arteries of three vessel cord, which indicate greater flow of blood through the vessel and to be useful in identification of SUA [4].

The perinatal mortality rate of pregnancies with SUA ranges from 8% to 60%, the mean mortality rate being 20%. This increased rate is accounted for exclusively by fetuses with accompanying malformations rather than fetuses with isolated SUA [14]. The reported incidence of SUA in twin pregnancies, in the literature varies from 0.8% to 11%. Multiple pregnancies have a 3-7 fold increased risk of SUA compared with singletons. SUA has been reported to occur in 4% of twin deliveries and 2% of all twin infants. The wide difference in the incidence is mainly due to the selection of the cases as well as observational errors; a higher incidence was noticed in pathological studies, while prospective and epidemiological studies show a lower incidence. The published incidences of SUA also vary based on mono/di chorionic pregnancies as well as a gross visual examination of umbilical cord, which give a high number of false-negative results [19]. Lamberty et al., used the gold standard placental histopathology in addition to standard ultrasound analysis in the second trimester and reported the sensitivity and specificity as 86% and 99% respectively [24]. Thus the potential advantage of our study is that we have a histopathological confirmation of SUA. So we advise microscopic histopathology of a cross section of umbilical cord be performed postnatally in addition to routine prenatal ultrasound analysis in all cases of SUA for exact postpartum diagnosis.

CONCLUSION

The authors conclude that SUA in one or both twins is a marker for various growth abnormalities, including IUGR, SGA and pre-term delivery compared to other twins. So we advise routine prenatal ultrasound assessments in all cases with SUA to find out decreased fetal growth and other associated anomalies. The present case report emphasizes the different aspects of SUA in twin gestations such as etio-pathogenesis, prenatal diagnosis and the recent advancements in management.

ABBREVIATIONS

SUA - Single umbilical artery.

IUGR - Intra uterine growth retardation.

SGA - Small-for-gestational age.

ART - Assisted reproductive technologies.

BMI - Body mass index.

TTTS - Twin-twin transfusion syndrome

TRAP - Twin reversed arterial perfusion.

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