Fetofetal transfusion in triplets

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Abstract

A case of fetofetal transfusion syndrome (FFTS) in a monochorionic triplet pregnancy, in which all three fetuses shared a common circulation, is reported. All babies were born alive, although two died within two days of delivery. This case highlights the problem of FFTS with accompanying high perinatal morbidity and mortality in naturally occurring monochorionic triplet gestations.

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Fetofetal transfusion syndrome (FFTS) is a serious complication of monochorionic multiple gestations, due to the presence of placental vascular anastomoses,^{1,2} and is a well described cause of significant morbidity and mortality in twin gestations.^{1–5} Interfetal vascular anastomoses can also occur in monochorionic triplets and monochorionic twins in triplet sets, but FFTS in triplets has only been reported in two published cases where placental injection studies were done.^{6,7} In both reports two fetuses in each set participated in FFTS and all four affected fetuses were still-born. We report a case of FFTS in a monochorionic triamniotic triplet pregnancy in which all three fetuses shared a common circulation and were all born alive, although two died within two days of delivery.

Case report

A healthy 27 year old woman who conceived naturally was found to have triplets on routine ultrasound examination at eight weeks. Follow up ultrasound examinations were normal until 21 weeks' gestation when the presence of a

shared circulation between two fetuses was suspected on the basis of oligohydramnios (maximum vertical pocket of amniotic fluid (MVPAF) = <2 cm) and smaller size in one (triplet A), and hydramnios (MVPAF = 8.9 cm) and larger size in the other (triplet B). Because of progression of the hydramnios over the next week in triplet B (MVPAF = 12.5 cm), and fear that the rapid uterine distension would lead to preterm labour or rupture of membranes, indomethacin (50 mg orally every 6 hours) was begun in the hope of reducing the amniotic fluid volume (fig 1). Indomethacin was given despite the presence of severe oligohydramnios in triplet A. Over the next two weeks (22–23 weeks), progression of the suspected fetofetal transfusion (FFT) was evidenced by lack of growth, persistently small bladder, and oligohydramnios in triplet A, and by the development of ascites, skin oedema, and worsened hydramnios in triplet B. Five reduction amniocenteses (750 ml, 950 ml, 625 ml, 1250 ml, 1120 ml) were performed on the sac of triplet B between 23 and 26 weeks, to reduce the substantial uterine distension (fig 1). Triplet B also developed an enlarged heart and ultrasound evidence of intraventricular haemorrhage (IVH) with enlarged lateral ventricles (fig 2A). Triplet A had severe oligohydramnios and the urinary bladder could no longer be visualised. Triplet C was thought to be unaffected ('innocent bystander') by the FFT. At 27 weeks, spontaneous labour began and three girls were delivered by emergency caesarean section. Clinical characteristics at birth are shown in the table.

Further postnatal course

TRIPLET A

The donor baby, had hypovolaemic circulatory collapse, severe hyaline membrane disease, renal failure, severe grade IV IVH, with cystic changes in periventricular areas indicating that the damage had a prenatal onset (fig 2B). She died at 2 days of life.

TRIPLET B

The recipient baby was hydropic and plethoric with clinical and echocardiographic evidence of congestive cardiac failure. She developed severe hyaline membrane disease. Grade III IVH, which had been identified in utero, was confirmed postnatally (fig 2A). She died on the first day of life despite partial exchange transfusion immediately following delivery and maximum cardiorespiratory support.

TRIPLET C

A probable participant in the shared circulation, she had a stormy neonatal course and

Figure 1 Amniotic fluid volume in relation to gestational age and therapeutic interventions (*amniocentesis).

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Figure 2 (A) Triplet B: antenatal ultrasound scan showing IVH with enlarged ventricles. (B) Triplet A: ultrasound scan on day 1 of life showing grade IV IVH with cystic changes in periventricular areas.

required ventilatory support for 50 days due to hyaline membrane disease and bronchopulmonary dysplasia. She had a patent ductus arteriosus which required two courses of indomethacin for closure. She also had grade IV IVH with evidence of parenchymal cystic changes on one side. She had numerous other complications of prematurity but with supportive care was ultimately discharged home at 45 weeks' postconceptional age. Follow up examination at 6½ months (corrected for prematurity) showed appropriate developmental progress with normal adaptive, social, and motor skills, and normal vision and hearing.

There was one placenta and examination showed it to be monochorionic triamniotic. Disc weight was 825 g with dimensions of 25×21×3 cm. Disc colour was plethoric in the part apportioned to triplet B and pale in the part apportioned to triplet A. The rest of the disc was of normal colour. Placental vessel injection studies with colour contrast and radiographic studies revealed surface anastomoses between triplet A and C, but none between A and B or C and B. Deep anastomoses between placental vessels of triplet A and B were identified.

Discussion

The only certain way to prove that there had been FFT from triplet A into triplet B would have been to inject a marker – by means of cordocentesis – into the circulation of triplet A and then sometime later detect it again by cordocentesis in the circulation of triplet B. Although this was not done, the accumulated evidence of FFT from A to B is compelling.

The placenta was monochorionic – plethoric adjacent to B and pale adjacent to A. Injection studies after birth revealed deep communications between A and B. While in utero, the typical features of severe FFT, the so-called

'stuck twin' phenomenon, were observed (fig 3). Fetus A was growth retarded, presumably hypovolaemic with a small heart, had a persistently small and later non-visualisable urinary bladder, initially decreased and subsequently absent amniotic fluid volume, and much reduced mobility as a consequence of its amniotic membrane pushed against its body by the hydramnios in triplet B's sac. Fetus B was well grown, presumably hypervolaemic, had a dilated heart, developed ascites and skin oedema, had a persistently full bladder and had gross hydramnios which persisted despite attempts to reduce it pharmacologically with indomethacin and mechanically with repeated reduction amniocenteses (total 4.7 litres removed over three weeks). Fetus B also developed ultrasonographic findings of grade III IVH in utero. At birth there was a clear discrepancy in size (690 g *v* 1000 g) and in haemoglobin (107 g/l *v* 197 g/l). The antenatal prediction that fetus A would have postnatal renal failure and that fetus B would be in congestive cardiac failure at birth was confirmed postnatally. Indeed, antenatally the prognosis for A and B was considered so grim that the whole thrust of management was to forestall labour long enough for C, presumed to be an 'innocent bystander', to have a reasonable chance of survival. As it was, C's small size and anaemia at birth, as well as the presence of placental surface anastomoses with fetus A, suggested that she, too, had participated somewhat in the shared circulation.

The shunting of blood from one fetus to another is a possibility in any multiple pregnancy with a monochorionic placenta. In monochorionic placentae vascular anastomoses are almost always present^{1 2}; they are very rare in dichorionic placentae.² An imbalance in the net flow of blood across the placental vascular communications from one

Clinical characteristics at birth

Triplet	Weight (g)	Length (cm)	Head circumference (cm)	Apgar scores at 1 and 5 minute	Cord pH		Haemoglobin (g/l)	Clinical status
					Venous	Arterial		
A	690	31	23	5, 9	7.36	7.30	107	Hypovolaemic, circulatory collapse
B	1000	36	24.5	1, 4	7.31	7.24	197	Congestive cardiac failure
C	690	32	23.5	5, 6	–	7.28	105	Relatively stable

Figure 3 Antenatal ultrasound scan demonstrating 'stuck twin' phenomenon: gross hydramnios in sac of triplet B (white arrow) pushing amniotic membrane against triplet A (black arrow) who is stuck between amnion and the body of uterus.

fetus to the other results in fetofetal transfusion syndrome. This occurs in about 15% of monozygotic twin pregnancies but its prevalence in triplet gestations is not known. Including the present case, there are only three reports describing the phenomenon in triplet pregnancies.^{6,7} Collectively, seven out of nine fetuses in these three reports died perinatally. Fetal deaths are much more common in monochorionic twins than in dichorionic twins,^{5,8} and one would assume this to be the same for triplets. Indeed, although fetal losses have been reported in monochorionic,^{6,9} dichorionic,⁷ and trichorionic^{9,10} triplet gestations, the most consistent finding associated with fetal death is monochorionic placentation.^{1,9} This reinforces the possible contribution of FFTS to the outcome of monochorionic gestations. One reason why improved outcome has been reported¹¹ in recent series of triplet pregnancies is that they comprise largely artificially conceived multi-zygotic gestations, in which FFT is not a risk. Our case highlights the continuing problem of FFTS, with accompanying high perinatal morbidity and mortality, in naturally occurring monochorionic triplet gestations.

In the past twin-twin transfusion syndrome has been made postnatally or diagnosed at necropsy after careful examination of the placenta. The accuracy of the traditional standard neonatal diagnostic criteria based on birthweight and haemoglobin differences among the participating twins has been questioned.¹² Moreover, the neonatal diagnostic criteria may not be applicable antenatally.⁶ Based on ultrasonography, Doppler velocimetry, and cordocentesis, composite fetal diagnostic criteria have been proposed.¹³ But as pointed out earlier, marker injection studies using cordocentesis antenatally, confirm the presence of unequivocal FFTS.

Neonates who have participated in FFTS are a considerable management challenge. They present not only the usual problems associated with prematurity, but also the sequelae of chronic uteroplacental insufficiency, hypoxaemia, anaemia, hypovolaemia, and oligohydramnios in the donor fetus; and

hypervolaemia, increased blood viscosity, congestive heart failure, hydrops, and polyhydramnios in the recipient fetus. There may be significant long term morbidity associated with antenatal visceral infarcts in surviving infants.³ There is evidence that even at long term follow up the cardiac function of the recipient twin may be compromised.¹⁴ Although expeditious management by trained staff will certainly improve the outcome of the affected neonates, it is important to realise that the visceral damage observed in association with FFTS may have already occurred before delivery. Based on current understanding of the pathophysiology of the damage to the surviving infants, it is obvious that the genesis of problems associated with twin-twin transfusion syndrome is in utero. This underlines the importance of antenatal diagnosis and possible antenatal therapeutic intervention, to improve the survival and lower the morbidity associated with FFTS. Although considerable progress has been made in the past decade, the antenatal therapeutic intervention is complicated by moral, ethical, legal, and technical complexities. It is hoped that the early promise shown by some novel therapeutic approaches will evolve into some effective therapeutic strategies.¹⁵ Some of the severe complications of FFTS that occur in utero and the pathophysiology of the fetal/neonatal brain injury that occurs in some of these cases is discussed in the Current Topic published in this issue (see pp 48–50).

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