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Placental vascular recruitment after single intrauterine demise: a newly diagnosed phenomenon unique to monochorionic pregnancies

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Conflict of interest statement

All authors have read and approved the manuscript and have no conflict of interest to declare.

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Data sharing statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement

In compliance with the Belgian legislation and GDPR no approval of the ethics committee was sought for this study, since the main object is biological material. Personal data of the patients was collected for an ongoing study on placental sharing, therefore additional informed consent was not necessary.

Bulleted statements

What's already known about this topic?

If one twin dies during pregnancy, its placental part degenerates as it is no longer perfused.

What does this report add?

In monochorionic twin pregnancies, the surviving twin may recruit the placental share of its demised co-twin through a large arterio-arterial and veno-venous anastomosis.

Monochorionic (MC) twin pregnancies are at high-risk of fetal demise, which occurs in about 11% of diamniotic and 18% of monoamniotic twin pregnancies ¹⁻². This excessive mortality is largely caused by the shared circulation, which can lead to acute or chronic intertwin transfusion imbalances. Such imbalances probably also account for the high incidence of congenital anomalies, occurring in up to 6% of diamniotic ¹ and 23% ² of monoamniotic pairs and usually affecting only one twin. In places where termination is legally permitted, coagulation of the umbilical cord can be offered to selectively reduce the anomalous twin ³. If one of a twin pair dies during pregnancy, either spontaneously or after selective reduction, its placental part is no longer perfused and degenerates ⁴.

In our hospital, we routinely inject all MC twin placentas that resulted in 2 livebirths with contrast dye for research purposes. We usually do not inject placentas with intrauterine demise remote from birth, as due to maceration the angio-architecture can no longer be examined. We report on three placentas with intrauterine demise of one twin, one spontaneous demise in a monoamniotic pair and two after cord coagulation in a diamniotic setting, where the placental share of the demised twin did not degenerate but was entirely recruited by the surviving co-twin.

Our technique for placental injection has been described elsewhere ⁵. In these cases, we injected the cord vessels of the surviving twin with coloured barium sulphate (Micropaque®, Guerbet group, Paris, France). We took a digital photograph of the placental surface as well as an X-ray angiogram. The initial vascular equator was estimated and delineated on the photograph and the share of each twin was measured using ImageJ software (<https://imagej.nih.gov/ij/download.html>). Afterwards, the placentas were sent for pathology.

The first placenta was from a MC monoamniotic twin pregnancy in a 32-year-old para 4 gravida 6. She was diagnosed with gestational diabetes, which was well-controlled by dietary

measures only. The pregnancy was uneventful until 28 weeks, when an unexpected demise of one twin was diagnosed. The surviving twin had no signs of anemia and 3 weeks later neurosonography and MRI did not show any ischemic-hypoxic brain lesions. Because of extensive cord entanglement and the risk of subsequent double demise, the patient consented to a fetoscopic cord transection, which was performed at 31 weeks without complications. Further ultrasound scans showed good fetal well-being with normal Doppler findings of the umbilical artery, ductus venosus and middle cerebral artery. Estimated weight was at the 59th centile before the surgery and continued to follow this centile for the remainder of pregnancy. At 35 weeks, a boy was born vaginally in good condition with a birth weight of 2534g (39th centile). He was admitted to the neonatal unit for respiratory support with continuous positive airway pressure (CPAP). A brain MRI on day 8 was normal. Macroscopic evaluation of the placenta showed proximate cord insertions in the middle of the placenta (*Figure 1A*). Placental territories were estimated to be 37% for the demised twin and 63% for the surviving co-twin. An X-ray angiogram showed contrast in all cotyledons (*Figure 1B*). Microscopic examination showed autolysis of the demised twin's cord, absence of maceration and similar maturation in the biopsies taken in different parts of placenta.

The second placenta was from a MC diamniotic twin pregnancy in a 31-year-old primigravida. At 15 weeks, one twin was diagnosed with sacral agenesis. The patient opted for a cord coagulation in the third trimester to reduce the risk of miscarriage and extreme preterm birth. The procedure was performed uneventfully at 32 weeks. Day one post-surgery, the surviving twin had normal Doppler measurements, and these remained normal throughout pregnancy. Estimated weight increased from the 53rd centile at the time of surgery to the 81st centile prior to birth. At 38 weeks, a healthy boy was born vaginally with a birthweight of 3380 grams (60th centile). The baby was shortly admitted to the neonatal unit because of hyperbilirubinemia. Cranial ultrasound on day 21 was normal. Macroscopic evaluation of the

placenta after birth showed both cords inserting eccentrically. The placenta looked equally divided between the twins. It was estimated that 52% belonged to the demised twin and 48% to the surviving co-twin (*Figure 1C*). X-ray angiogram confirmed the presence of contrast in the whole placental territory (*Figure 1D*). Pathology showed autolysis of the demised twin's cord and a similar mature aspect of the parenchyma in both parts.

The third placenta was from a MC diamniotic twin pregnancy in a 24-year-old primigravida. At 16 weeks, amyoplasia was diagnosed in one twin. The patient also opted for an elective cord coagulation in the 3rd trimester. At 20 weeks, a partial mono-amniotic pregnancy was diagnosed ⁶ as both twins were noted to be in the same sac, whereas the septum had been visualised previously and no invasive testing had been done. At 29 weeks, we performed a bipolar coagulation and laser transection of the cord of the affected twin. Day one, the healthy twin had minimal prefrontal oedema and ascites, which resolved by day five, while Doppler studies remained normal. Growth evolved from the 20th to the 50th centile. At 32 weeks, the patient presented with ruptured membranes, and labour ensued. A girl was born in good condition with a birth weight of 1740g (29th centile). The baby was admitted to the neonatal unit and required one day of CPAP. Cranial ultrasound on the estimated due date was normal. In this case, the cords inserted side-by-side. The demised twin had about 61% of the placenta, whereas 39% belonged to the surviving co-twin (*Figure 1E*). Here as well, X-ray angiogram showed radio-opacity in the entire placenta (*Figure 1F*). Pathology was similar as in the other cases, confirming the autolytic cord of the demised twin and a similar maturation of the parenchyma in both shares.

The possibility that the surviving twin may recruit the placental vascular territory of its demised co-twin has never been described in the literature thus far. Normally, the share of the demised twin degenerates as it is no longer perfused. The underlying mechanism of this placental recruitment appears to be the presence of an arterio-arterial and veno-venous

anastomosis. After the demise of one twin, the surviving twin pumped its deoxygenated blood into the placental share of its demised co-twin through the arterio-arterial anastomosis, whereas oxygenated blood returned from the demised twin's share through the veno-venous anastomosis. The presence of such anastomoses is also the underlying mechanism of a twin-reversed arterial perfusion sequence. If one of a MC pair dies in the first trimester, the surviving twin (also called pump twin) may pump blood into the placental share and body of its demised co-twin (also called acardiac twin) if a large arterio-arterial anastomosis is present. Deoxygenated blood will then flow in the opposite direction into the umbilical cord of the acardiac twin, hence the name twin reversed arterial perfusion. The acardiac twin will continue to grow, which can lead to high-output cardiac failure in the pump twin ⁷. In all our cases, the demise occurred in the third trimester and in 2 cases the cord was coagulated precluding the occurrence of a twin reversed arterial perfusion sequence.

Even though placental sharing was assessed three to seven weeks after the demise and may not be entirely the same as prior to the intervention, all placentas appeared to be equally shared. As a result, the surviving twins nearly doubled their placental surface, which did not seem to impact the Doppler examinations. Because of the sudden increase in placental surface, we had expected a decrease in resistance in the umbilical artery blood flow. In our third case, the surviving twin showed signs of a transient, mild hydrops. Such transient hydrops has been described before in donor twins after successful laser surgery for twin-to-twin transfusion syndrome, where it is presumably related to a sudden increase in volume load ⁸. Typically, umbilical venous volume flow also increases in the donor twin after laser surgery ^{9,10}. It might be that the surviving twin also experiences an increase in umbilical venous blood flow after placental recruitment.

The exact incidence and implications of placental recruitment are currently unknown and warrant further investigation. An arterio-arterial in combination with a veno-venous

anastomosis is present in about 1 in 4 diamniotic ¹¹ and nearly half of the monoamniotic placentas ¹². If the cords insert side-by-side, as in 2 of our cases, 80% of the placentas have an arterio-arterial and veno-venous anastomosis ¹³ and in the event of a single demise, the surviving co-twin may recruit additional vascular territory of its demised co-twin. Only a large prospective series of MC pregnancies undergoing selective reduction by umbilical cord coagulation may further elucidate its incidence and relevance. Such a prospective study may consist of umbilical venous volume flow measurements, fetoscopic mapping of the anastomoses, dye injection of the placentas and neurodevelopmental follow-up of the surviving twins.

References

1. Lewi L, Jani J, Blickstein I, et al. The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study. *Am J Obstet Gynecol.* 2008;199(5):514.e1-514.e8.
2. Van Mieghem T, De Heus R, Lewi L, et al. Prenatal management of monoamniotic twin pregnancies. *Obstet Gynecol.* 2014;124(3):498-506.
3. Lewi L, Gratacos E, Ortibus E, et al. Pregnancy and infant outcome of 80 consecutive cord coagulations in complicated monochorionic multiple pregnancies. *Am J Obstet Gynecol.* 2006;194(3):782-9.
4. Jauniaux E, Elkazen N, Leroy F, et al. Clinical and morphologic aspects of the vanishing twin phenomenon. *Obstet Gynecol.* 1988 Oct;72(4):577–81.
5. Lewi L, Deprest J, Hecher K. The vascular anastomoses in monochorionic twin pregnancies and their clinical consequences. *Am J Obstet Gynecol.* 2013; 208(1):19–30.
6. Galjaard S, Moerman P, Corveleyn A, et al. Partial monochorionic and monoamniotic twin pregnancies: a report of two cases. *Ultrasound Obstet Gynecol.* 2014; 44(6):722–4.
7. Moore TR, Gale S, Benirschke K. Perinatal outcome of forty-nine pregnancies complicated by acardiac twinning. *Am J Obstet Gynecol.* 1990 Sep;163(3):907–12.
8. Gratacós E, Van Schoubroeck D, Carreras E, et al. Transient hydropic signs in the donor fetus after fetoscopic laser coagulation in severe twin-twin transfusion syndrome: incidence and clinical relevance. Vol. 19, *Ultrasound Obstet Gynecol.* 2002; 19: 449–453.
9. Gratacós E, Van Schoubroeck D, Carreras E, et al. Impact of laser coagulation in severe

- twin-twin transfusion syndrome on fetal Doppler indices and venous blood flow volume. *Ultrasound Obstet Gynecol.* 2002 Aug 1; 20(2):125–30.
10. Baschat AA, Gungor S, Glosemeyer P, et al. Changes in umbilical venous volume flow after fetoscopic laser occlusion of placental vascular anastomoses in twin-to-twin transfusion syndrome. *Am J Obstet Gynecol.* 2010 Nov 1; 203(5):479.e1-479.e6.
11. Lewi L, Cannie M, Blickstein I, Jani J, Huber A, Hecher K, Dymarkowski S, Gratacós E, Lewi P, Deprest J. Placental sharing, birthweight discordance, and vascular anastomoses in monochorionic diamniotic twin placentas. *Am J Obstet Gynecol.* 2007;197(6):587.e1-8.
12. Hack KE, van Gemert MJ, Lopriore E, Schaap AH, Eggink AJ, Elias SG, van den Wijngaard JP, Vandenbussche FP, Derks JB, Visser GH, Nikkels PG. Placental characteristics of monoamniotic twin pregnancies in relation to perinatal outcome. *Placenta.* 2009;30(1):62-5.
13. Zhao DP, Peeters SH, Middeldorp JM, Klumper FJ, Duan T, Oepkes D, Lopriore E. Monochorionic placentas with proximate umbilical cord insertions: definition, prevalence and angio-architecture. *Placenta.* 2015;36(2):221-5.

Figure 1:

(A) Monochorionic mono-amniotic twin placenta after cord transection at 31 weeks after single intra-uterine death at 28 weeks. The cord of the deceased twin is marked with 2 clamps. Injection of the umbilical arteries of the surviving twin with barium sulphate and ink (blue) and of its umbilical vein with barium sulphate and eosin (red) shows filling of the entire placental vasculature through a large arterio-arterial anastomosis (white star) and veno-venous anastomosis (grey star). The presumed equator is delineated by a white dotted line. (B) Placental X-ray angiogram after injection of both arteries and vein showed radio-opacity of the entire vasculature confirming placental recruitment of the placental share of the demised twin by its healthy co-twin. The arterio-arterial anastomosis is marked with a white star, the veno-venous anastomosis with a grey star.

(C) Monochorionic twin placenta after cordocclusion for sacral agenesis at 32 weeks and delivery at 38 weeks. The cord of the healthy twin is marked with 2 clamps. Injection of the umbilical arteries of the surviving twin with barium sulphate (white) and of its umbilical vein with barium sulphate and eosin (red) show filling of the entire placental vasculature through a large arterio-arterial anastomosis (white star) and veno-venous anastomosis (grey star). The presumed equator is delineated by a white dotted line. (D) Placental X-ray angiogram after injection of both arteries and vein showed radio-opacity of the entire vasculature confirming

placental recruitment of the placental share of the demised twin by its healthy co-twin. The arterio-arterial anastomosis is marked with a white star, the veno-venous anastomosis with a grey star.

(E) Monochorionic twin placenta after cordocclusion for amyoplasia at 29 weeks and delivery at 32 weeks. The cord of the surviving twin is marked with 1 clamp. Injection of the umbilical arteries of the surviving twin with barium sulphate and ink (blue) and of its umbilical vein with barium sulphate (white) show filling of the entire placental vasculature through a large arterio-arterial anastomosis (white star) and veno-venous anastomosis (grey star) between the side-by-side cord insertions. The presumed equator is marked by a white dotted line. (F) Placental X-ray angiogram after injection of the umbilical vein of the healthy twin showed radio-opacity of the entire venous vascular bed through the large veno-venous anastomosis (grey star) confirming complete placental recruitment by the surviving co-twin.