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Intertwin anastomoses in monochorionic placentas after fetoscopic laser coagulation for twin-to-twin transfusion syndrome: Is there more than meets the eye?

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Objective: This study was undertaken to detect missed anastomoses on the chorionic surface as well as hidden connections in the depth of the cotyledons in placentas after laser coagulation for twin-to-twin transfusion syndrome (TTTS) and to correlate these findings to clinical outcome.
Study design: All cord vessels were injected with dyed barium sulphate. A digital photograph of the chorionic surface angioarchitecture and single-shot digital X-ray (Rx) angiograms were made. The presence and diameter of any missed anastomoses on the chorionic surface and of any hidden angiographic connections were determined.
Results: Fifty placentas were analyzed, 7 of double intrauterine fetal death (IUFD) and 43 of double survivors. In 9 of 43 (21%) cases with double survival and in all 7 cases of double IUFD, missed anastomoses were identified that should have been ablated by laser coagulation ($P < .001$). There appeared to be a correlation between the type and diameter of missed anastomoses on the chorionic surface and the clinical outcome. Placentas with missed large arteriovenous/venoarterial anastomoses (AV/VA) (N = 8) were from cases with recurrent TTTS or double IUFD (unless compensated by a large arterioarterial anastomosis [AA]). Next, missed small AV/VA (N = 4) without AA resulted in isolated (ie, without TTTS) discordant hemoglobin levels requiring intrauterine transfusion. Finally, when there were no missed anastomoses (N = 34), TTTS had resolved in all cases and outcome was good, although 1 case had discordant hemoglobin values treated with a single intrauterine transfusion and 4 others had discordant hemoglobin at birth. On Rx angiography, potential hidden connections were present, all but 1 case.
Conclusion: Coagulation of all anastomoses visible on the chorionic surface seems adequate to treat TTTS. However, hidden connections in the depth of the cotyledon could not be excluded and may be involved in lesser degrees of intertwin transfusion.

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Monochorionic twins share a single placenta and in almost all cases vascular anastomoses connect the 2 fetal circulations.[1] Intertwin transfusion is thus a constant and usually balanced phenomenon. However, in about 10% to 15% of monochorionic twins, a chronic imbalance in net flow occurs leading to the twin-to-twin transfusion syndrome (TTTS). TTTS is a sonographic diagnosis based on the presence of polyhydramnios in the polyuric recipient's sac and oligohydramnios in the oliguric donor's sac.[2] The pathophysiology of the disease is usually explained on an angioarchitectural basis. Placental anastomoses can be arterioarterial (AA), arteriovenous/venoarterial (AV or VA), and venovenous (VV). AA and VV are typically superficial and bidirectional anastomoses on the chorionic surface, forming direct communications between the arteries and veins of the 2 fetal circulations, respectively. AV or VA are unidirectional anastomoses, which occur at a capillary level deep within the cotyledon. However, the supplying artery and draining vein of an AV anastomosis can be visualized on the placental surface, piercing the chorionic plate next to each other.[3] It has been clear for more than a century that TTTS is caused by the relative excess of unidirectional AV anastomoses, which create an imbalanced interfetal transfusion leading to TTTS, unless compensated by reverse transfusion through other (superficial or deep) anastomoses. Both postnatal injection studies[1] and in vivo fetoscopic observations[4,5] indicate the presence of at least 1 such unidirectional AV-anastomosis as the anatomic prerequisite for the development of TTTS.

Untreated, severe midgestational TTTS carries a mortality rate of nearly 70%.[6] Over the years, several methods to treat TTTS have been proposed.[2] However, at present fetoscopic laser coagulation of the vascular anastomoses appears to be the best first-line treatment.[7] Provided that all anastomoses can be visualized on the chorionic surface, laser coagulation will treat the cause of the disease by disconnecting the 2 fetal circulations. However, a recent vascular cast study of monochorionic placentas suggested the existence of hidden anastomoses that cannot be visualized on the chorionic surface and that would invariably be missed during laser therapy.[8]

We studied the placental angioarchitecture in relation to the clinical outcome in TTTS cases treated with laser and resulting in either double survival or double intrauterine fetal death (IUFD). Indeed, cases with only 1 survivor are not suitable for placental examination because of postmortem changes. In addition to inspection of the chorionic surface, X-ray (Rx) angiography was used to detect potential, hidden anastomoses that were not visible on the chorionic surface.

Material and methods

Collection of placentas

The placentas originated from the participating centers within the Eurofoetus project, which were invited to send intact placentas from cases treated with fetoscopic laser coagulation for severe midgestational TTTS with either optimal outcome, ie, double survival into the third trimester or suspected surgical failure, such as double IUFD, recurrent TTTS, or isolated (ie, without TTTS) discordant hemoglobin levels. Fresh placentas were sent in a watertight container without any fixation. The interval between placental delivery and analysis depended on the day of the week and the distance between the centers and our laboratory. The placentas were stored in a refrigerator (4°C) until analysis. Manipulation of the placentas was performed by 2 investigators (L.L. and J.J.). This study covered a 19-month period between September 2003 and March 2005.

Technique of laser coagulation

TTTS was diagnosed according to the internationally accepted sonographic criteria adopted by the Eurofoetus project: a monochorionic twin pregnancy with polyhydramnios of 8 cm or more deepest vertical pocket in the recipient less than 20 weeks' gestational age (GA) ($\geq$10 cm from 20 weeks' GA onward) and oligohydramnios of 2 cm or less deepest vertical pocket in the donor, with distended bladder in the recipient and collapsed bladder in the donor(s) during most of the examination. Laser coagulation was performed according to the method described in detail elsewhere.[9] Briefly, a 3.3-mm trocar was inserted percutaneously under ultrasound guidance into the sac of the recipient. The vascular equator was identified with the fetoscope, and all visible anastomoses were coagulated with Nd/YAG or diode laser energy. We also coagulated vessels with uncertain course, where it was impossible to determine whether they did anastomose or not because of the position of the intertwin septum, fetus, or placenta. The operators from the participating centers are experienced with the procedure, performing it for at least 5 years with a minimum caseload of 40 cases per year.

Most patients were kept in the hospital for 48 hours after the procedure, with daily ultrasound scans. If double IUFD was diagnosed, labor was induced shortly thereafter. Ultrasound surveillance in ongoing pregnancies consisted of at least biweekly growth assessment and Doppler studies of umbilical artery, ductus venosus, and middle cerebral artery (MCA). Further interventions (such as intrauterine transfusions) were performed if necessary.[10] Data related to GA at intervention, placental location, interval from procedure to fetal death or delivery, other intrauterine interventions, GA at birth, and neonatal characteristics such as birth weight