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Identical twins – yet unequal

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Title figure:
De Wikkelkinderen (source: www.commons.wikimedia.org)

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After spontaneous conception a monochorionic-diamniotic (MC-DA) twin pregnancy was diagnosed. The pregnancy was complicated in the 24th week of gestation by twin-to-twin transfusion syndrom (TTTS) with oligohydramnios and growth restriction of the suspected donor. Laser coagulation of the underlying anastomosis was performed in a tertiary hospital at 24 2/7 weeks of gestation. The peri-interventional course was favorable and the twins displayed symmetric growth with equal amounts of amniotic fluid.

Two and a half weeks later, the mother was admitted to a private maternity clinic for tocolysis due to premature contractions. She received a short course of antibiotics for a suspected urinary tract infection.

When tocolysis failed and rupture of membranes of twin B occurred, the mother was transferred to our hospital and an urgent Caesarian section was performed at 29 3/7 weeks of gestation.

Twin A, the suspected acceptor, had a birth weight of 1205 g. Due to insufficient respiratory effort, he was intubated in the delivery room and extubated to CPAP on the following day. Subsequently, CPAP was discontinued after 8 days and supplemental oxygen was provided up to a corrected gestational age of 33 4/7 weeks. Twin B, the suspected donor, had a birth weight of 1100 g. Compared to his brother, he had

milder respiratory problems and required CPAP for 8 days and supplemental oxygen for only 1 day. However, on day of life 4, routine cerebral ultrasound examination of twin B demonstrated bilateral, huge parenchymal cysts across the entire cortex (Fig. 1–3). The cysts did not change over time and were thought to have been acquired prenatally. Cerebral ultrasound examination of twin A was normal.

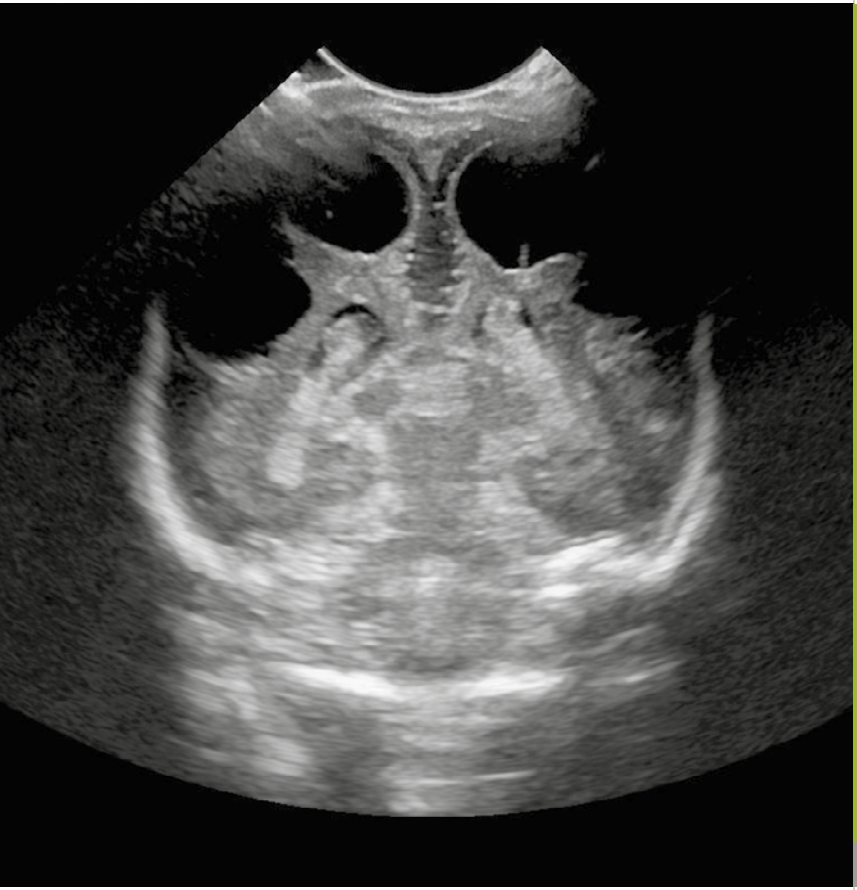

Fig. 1

Cranial ultrasound (coronal view) on DOL 4: extensive symmetric cystic encephalomalacia of the whole cortex.

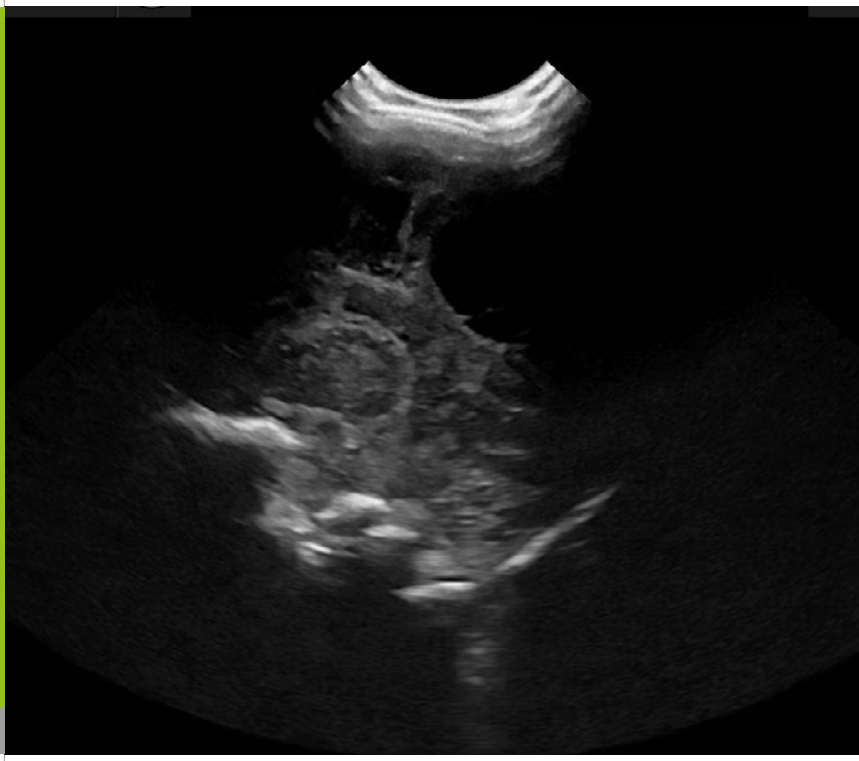

Fig. 2

Cranial ultrasound (sagittal view) on DOL 4: extensive symmetric cystic encephalomalacia of the whole cortex.

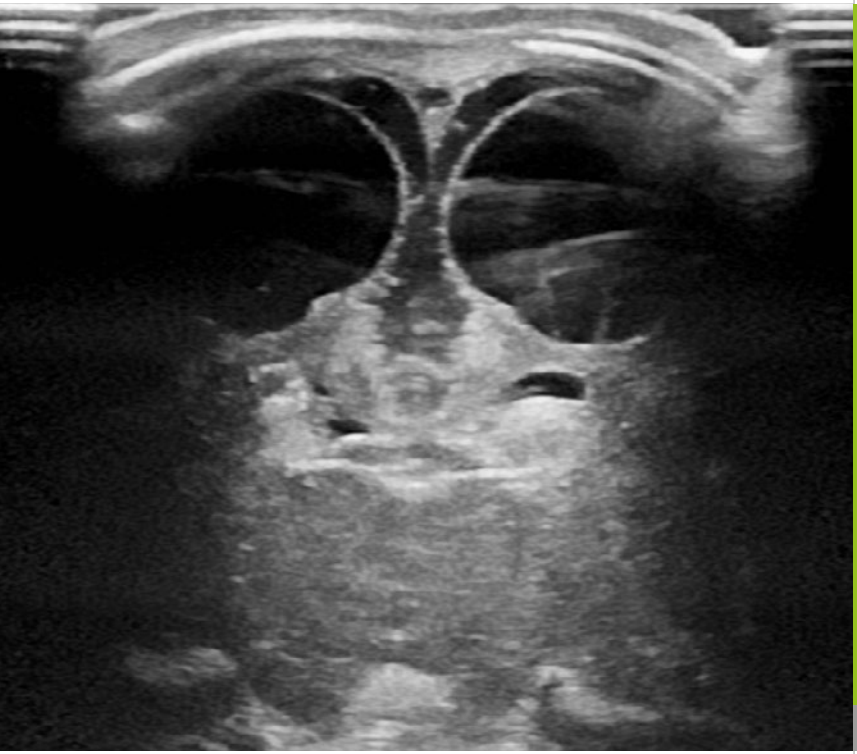

Fig. 3

Cranial ultrasound (coronal view) on DOL 4: extensive symmetric cystic encephalomalacia of the whole cortex.

Near term, the infants were discharged home with twin B showing signs of spasticity and poor motor function. An MRI confirmed mainly parietooccipital encephalomalacia (Fig, 4), suspected to have arisen as a consequence of TTTS at an early stage of pregnancy.

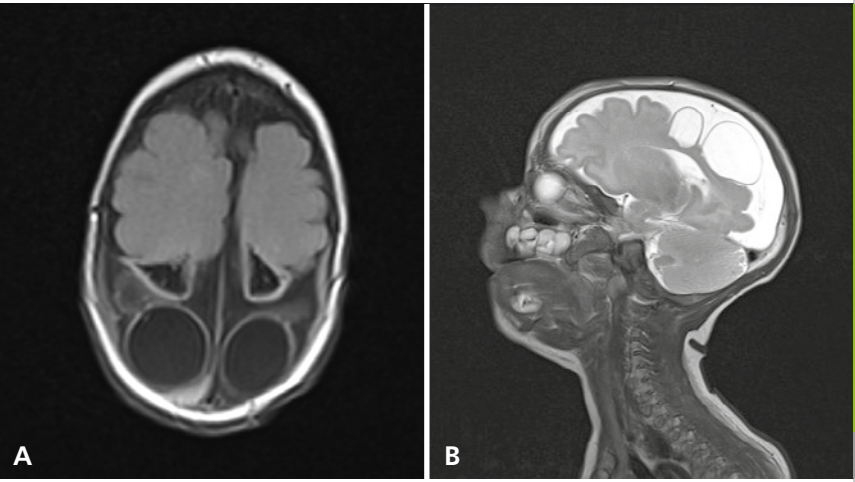

Fig. 4

Cerebral MRI (A: T1-weighted, B: T2-weighted) on DOL 52 at a corrected gestational age of 42 2/7 weeks: symmetrical, mainly parietooccipital cystic encephalomalacia and cerebral atrophy.

Since discharge, twin B has been seen at multiple follow-up visits. He has developed increasing spasticity requiring analgesics and spasmolytics, as well as feeding difficulties and failure to thrive. At 6 months of age, percutaneous endoscopic gastrostomy (PEG) was performed. Head growth was well below the 3rd percentile.

Pregnancies in women of advanced age has become increasingly common, and, together with assisted reproductive techniques (ART), has led to a steadily increasing incidence of multiple pregnancies in high income countries over the last few decades. ART surveillance in the US in 2015 indicated that 35 % of ART-conceived pregnancies led to multiple-births (1). In Switzerland, currently 1 out of 50 infants are born following ART, but only 15 – 20 % of ART pregnancies result in multiples (1, 2).

Twinning is not only associated with increased risks for intrauterine and perinatal complications with unfavorable outcomes for children and mothers, but also with a higher incidence of birth defects. The main risks are miscarriage, preeclampsia, antepartum bleeding, postpartum hemorrhage, IUGR, preterm delivery, asphyxia, seizures and neurodevelopmental delay. The overall mortality in twin pregnancies was reported to be four times higher compared to singleton pregnancies and is highest among monochorionic-monoamniotic (MC-MA), followed by monochorionic-diamniotic (MC-DA) twins. These complications are often the result of placental or cord disorders that are mainly associated with monochorionic (MC) twins (3).

After the third day of fertilization, the trophoblast loses its ability separate, and the resulting MC placenta has to supply multiple fetuses, who are

either di- (DA) or monoamniotic (MA). As a consequence, in approximately 25 % of twin pregnancies the fetuses share a single placenta, potentially leading to unequal distribution of placental territories or an imbalance of intra-placental and inter-fetal vascular shunts. Most of these pathologies can be diagnosed by ultrasound.

Nearly all MC placentas have vascular anastomoses between the umbilico-placental circulations that are either arterio-arterial (aa), arterio-venous (av) or veno-venous (vv). The unidirectional av-anastomoses seem to play an important role in the pathophysiology of TTTS, twin anemia-polycythemia sequence and severe growth disorders if the blood flow is unbalanced and not sufficiently counter-regulated by the remaining vascular connections (4 – 7).

The pathophysiology and adaptive processes in an unbalanced circulation are due to the anastomoses that lead to an uncontrolled transfer of fluid and vasoactive mediators. This results in volume depletion and vasoconstriction of the donor twin and fluid overload and congestive heart failure in the recipient twin. The cardiac alterations in the acceptor twin typically consist of diastolic dysfunction and AV valve regurgitation. Due to cardiac stretch the cardiomyocytes of the acceptor twin secrete natriuretic peptide leading to an increase in glomerular filtration rate, polyuria and polyhydramnios. In contrast, the donor twin

suffers from hyperdynamic cardiac dysfunction and global hypoperfusion; the resulting oligohydramnios is the product of renal hypoperfusion and an upregulation of the renin-angiotensin-aldosterone system (RAAS), that initially leads to a stabilization of blood pressure through vasoconstriction and water reabsorption (4, 6).

Historically, TTTS was associated with an almost universal perinatal mortality, and, in the rare case of survival, there was a high incidence of disability.

The first academic description of TTTS dates back to 1886, when Schatz described vascular anastomoses between normal and acardiac twins (8). Earlier, non-medical descriptions can be found in the book of Genesis with the birth of Esau and Jacob, or in art with the painting «De Wikkelkinderen» that depicts two swaddled twin boys, one of them being pink and the other one appearing pale (see title figure) (9).

In the 1990s, therapeutic amnioreduction became the treatment of choice for severe TTTS with serial drainage of amniotic fluid. The goal of reducing the amniotic fluid volume was to decrease the risk of preterm labor, as well as to improve balancing blood flow through vv collaterals by reducing intra-amniotic pressure. This treatment changed the outcome and improved survival rates to 50 – 65 %.

Maternal digoxin to improve fetal cardiac function, or indomethacin to reduce polyhydramnios had some effect but are no longer recommended as a first line treatment. Finally, other treatment options, such as selective feticide or inter-amniotic septostomy also did not find their way into clinical routine.

In the late 1990s, non-selective laser coagulation of chorionic vessels crossing the inter-twin membranes showed similar results as sequential amnioreduction with overall survival rates of 55 – 69 % and single-twin survival rates of 73 – 82 %. This technique was followed by selective laser coagulation after initial identification and mapping of anastomoses and serial occlusion.

Nowadays, the treatment of choice is a combination of the two laser methods, the so-called Solomon technique, with first selective laser coagulation, followed by superficial coagulation of microvasculature on the chorionic plate leading to a separation of the two fetal vascular territories. This technique has been associated with an improved double-twin survival rate of 86 % (10).

With improving survival rates, long-term morbidity, mainly due to cerebral injury, has become more important. Overall, the incidence of antenatally acquired severe cerebral lesions (PIVH grade III & IV, PVL grade II or greater, porencephalic cysts, ventricular dila-

tation, cerebral atrophy and arterial infarction) in MC twins without TTTS is 2 %, compared to 10 % in MC twins treated by fetoscopic laser coagulation. In twins treated by serial amnioreduction, the incidence of cerebral lesions is even higher. TTTS twins treated with amnioreduction have an incidence of severe neurological impairment (CP, severe motor and/or cognitive development delay, bilateral blindness, deafness requiring amplification with hearing devices) of about 20 %, whereas the incidence in the laser group is more favorable with 10 % (11). Minor neurologic deficits (strabism, mild speech and/or motor delay) are seen in 7 – 11 % (12, 13).

Interestingly, there is no difference in the incidence of severe cerebral lesions in donor and acceptor twins. The exact mechanism is not fully understood but is probably the result of hemodynamic imbalance that leads to hypoxic-ischemic insult in donors and hyperviscosity in recipients. It remains unclear whether these lesions happen before, during or after the fetoscopic laser surgery (14).

See also: COTM 08/2001:
Surviving twin with encephalomalacia

See also: COTM 08/2016:
Prognosis for the co-twin following intrauterine

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