Twin-to-twin transfusion syndrome for anesthesiologists
(and what Obstetricians and Neonatologists taught me)

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A.S. 1983, 27.01.2011

- Monochorionic diamniotic pregnancy
- Transferred from peripheral hospital on 27.01.2011 at 30 0/7 pregnancy weeks with premature contractions
- Tocolysis, pulmonary maturation
- Ultrasound status is normal, no feto-fetal transfusion, good hemodynamics in both fetus
- Inter-twin growth discrepancy 9.1%
- CTG-is reassuring
A.S. 1983, 27.01.2011

- Patient is seen by anesthesiologist on duty for routine premedication
February 9, 2011 09:28

• Patient stable, discussion about when to leave hospital with the obstetrician.
• Routine CTG at 09:28 is normal
• No more premature uterine contractions since 2 days
February 9, 2011, 22h18

- Routine CTG at ~22h00
- No more heart activity detected in fetus B
- Highly restricted heart activity with fetus A
February 9, 2011, 22h18

- Call from OB consultant for a crash c-section
- Patient intubated 22h25
- Incision 22h26
- Child A: delivered 22h27
- Child B: intrauterine death
Neonatology

• Child A delivered 22h27
• APGAR 0
• Child very pale
• Neonatal CPR started 22h27, intubation, placement of an umbilical catheter, adrenaline 60 mcg in 3 doses and volume is given
• The CPR ceases as post-mortem lividity appears at 22h39
• No CPR is attempted for child B

• Child A: 1740g, APGAR 0-0-0, pHA: 6.85, pHV: 7.22
• Child B: 2050g, APGAR 0-0-0, pHA: 6.79, pHV: 7.07
What happened?
**Diagnosis:**

*acute twin-twin transfusion syndrome stage V*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Both bladders are still visible</td>
</tr>
<tr>
<td></td>
<td>No Doppler anomalies</td>
</tr>
<tr>
<td>Stage II</td>
<td>The bladder is invisible in the donor twin</td>
</tr>
<tr>
<td></td>
<td>No Doppler anomalies</td>
</tr>
<tr>
<td>Stage III</td>
<td>Doppler anomalies in either twin:</td>
</tr>
<tr>
<td></td>
<td>AREDF in the UA</td>
</tr>
<tr>
<td></td>
<td>Absent or negative ‘a’ wave in the DV</td>
</tr>
<tr>
<td></td>
<td>Pulsatile flow in the UV</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Pleural effusion, pericardial effusion, ascitis or hydrops</td>
</tr>
<tr>
<td></td>
<td>in either twin</td>
</tr>
<tr>
<td>Stage V</td>
<td>Death of one twin</td>
</tr>
</tbody>
</table>

AREDF, absent/reversed end diastolic flow; UA, uterine artery; DV,; UV.
The obstetrician’s view: twin pregnancy

70%
The obstetrician’s view: twin pregnancy

30%

Monozygotic
(Monochorionic, Diamniotic)
The obstetrician’s view: twin pregnancy

1%

Monozygotic
(Monochorionic, Monoamniotic)
The obstetrician’s view: twin pregnancy

Cumulative lethality %

Monochorionic

Dichorionic

By courtesy of L. Raio
The obstetrician’s view: twin pregnancy

2 Assassins

Twin-twin transfusion syndrome

+ Umbilical cord entanglement

= classical problems of monochorionic pregnancies

By courtesy of L. Raio
The obstetrician’s view: inter-twin vascular anastomoses

• Almost all monochorionic twins share a single placenta with inter-twin anastomosis, allowing blood to transfer from one fetus to the other and vice-versa

• Unbalanced blood flow may lead to twin-twin transfusion syndrome

The obstetrician’s view: inter-twin vascular anastomoses

3 types of anastomosis:

- Artery to artery
- Vein to vein
- Arteriovenous

Superficial, bidirectional

Physiologic back-compensation of unidirectional flow

Unidirectional deep anastomosis, in 60% of monochorionic placentas, Small and high resistance

The obstetrician’s view: Distinct forms of TTTS concerning 10-20% of monochorionic diamniotic pregnancies

- **Acute TTTS:**
  during birth, rapid blood loss via superficial AA or AV anastomosis due to blood pressure differences associated with uterine contractions or fetal positions
  - Large differences in hemoglobin levels

- **Acute perimortem TTTS:**
  Acute exsanguination from the surviving twin into the low-pressure circulation of the dead co-twin
  - Co-twin death
  - Survival with cerebral impairment
  - Preterm delivery
The obstetrician’s view: Distinct forms of TTTS

Chronic TTTS: TOPS

– 95% of chronic TTTS, 9% of monochorionic twins

- **Donor**: Hypovolemia, oliguria oligohydramnion
- **Recipient**: Hypervolemia, polyuria, polyhydramnios, hyperosmolarity

**TOPS**=Twin oligo-polyhydramnios sequence
The obstetrician’s view: Distinct forms of TTTS
Chronic TTTS: TOPS

Quintero III, Laser 19. week: Evolution of amniotic liquid

By courtesy of L. Raio
The obstetrician’s view: Distinct forms of TTTS

Chronic TTTS: TOPS

Treatment: selective (sequential) laser coagulation of relevant anastomotic vessels
Selective laser treatment in Bern

By courtesy of L. Raio
Zusammenfassung Outcome nach Behandlung
(10 Studien [RCT, Metaanalysen])

<table>
<thead>
<tr>
<th>Resultate</th>
<th>Laser</th>
<th>serielle Amnionreduktion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kein Überleben (%)</td>
<td>13-25</td>
<td>9-49</td>
</tr>
<tr>
<td>Ein oder mehr Überlebende (%)</td>
<td>75-87</td>
<td>51-90</td>
</tr>
<tr>
<td>Neonatale Todesfälle (%)</td>
<td>4-12 (OR 0.24; CI 0.15-0.4)</td>
<td>14-39 (OR 0.20; CI 0.1-20.33)</td>
</tr>
<tr>
<td>Zerebrale Auffälligkeiten* (%)</td>
<td>13 (2-33)</td>
<td>29 (18-83)</td>
</tr>
</tbody>
</table>

*IVH, ischemic brain injury, PVL, andere radiologische Befunde


By courtesy of L. Raio
The neonatologists view: Morbidity

• CNS: Morbidity ~ 50% without treatment, 14% after laser
  – Donor: Anemia-Hypoxia: Leukomalacia and intraventricular bleeding from 24-34 weeks
  – Recipients: Hypertension and sludge: Stroke and intraventricular bleeding
    → Donor and recipients equally affected

• Cardiac: Congenital heart disease 12 times more frequent and mainly recipients affected
  – Donor: Hypovolemia with chronic heart insufficiency → hydrops
  – Recipients: Increased afterload and increased preload
    → Right ventricular outflow tract obstruction, biventricular hypertrophy
The neonatologists view: Morbidity

• Renal: Mainly donor affected
  – Donor: hypoxic-ischemic injury due to hypoperfusion. Acute renal failure, permanent tubular dysfunction possible. Activation of renin-angiotensin-aldosterone
  – Recipients: liquid overload leading to polyuria, augmentation of amniotic fluid

• Hematologic: frequently inter-twin hemoglobin difference >5g/dl
  – Donor: requiring blood transfusions in utero and at birth, thrombocytopenia, normoblastosis and reticulocytosis
  – Recipients: partial exchange transfusions

• Necrotizing enterocolitis, lower limb necrosis, amniotic band syndrome, hepatic infarction..
Vmax.sys A. cerebri media

Donor

IUT
Intraperitoneal
Hb 4g/l

Sectio

Akzeptor

By courtesy of L. Raio
The anesthesiologists view of fetal surgery
Bern University Hospital: ~ 15 interventions / year

• Every uterine manipulation increases the risk of preterm labour and preterm premature rupture of membranes

• Anesthetic requirements for the mother

• Anesthetic requirements of the fetus: amnesia, analgesia, immobility

• Preservation of gas exchange and cardiovascular stability

• Control of uterine tone, i.e. complete uterine relaxation
The anesthesiologists view of fetal surgery

• Minimally invasive and percutaneous procedures
  – Amniocentesis
  – Cordocentesis
  – Intrauterine blood transfusion
  – Needle aspiration of cysts
  – Shunt placement into fetal bladder or thorax
  – Laser surgery on placental vessels for TTTS

• Open fetal surgery/ in utero procedure

• Ex utero intrapartum procedures (EXIT)
# The anesthesiologists view of fetal surgery

<table>
<thead>
<tr>
<th>Condition</th>
<th>Open fetal surgery</th>
<th>Endoscopic fetal surgery</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twin-to-twin transfusion syndrome</td>
<td>No</td>
<td>Endoscopic laser ablation of placental vessels</td>
<td>(Senat et al., 2004); (Quintero et al., 2003); (Ahmed et al., 2009)</td>
</tr>
<tr>
<td>Congenital diaphragmatic hernia</td>
<td>No longer recommended</td>
<td>Fetal tracheal occlusion</td>
<td>(Harrison et al., 2003; Jani et al., 2009b)</td>
</tr>
<tr>
<td>Myelomeningocele</td>
<td>Benefit under review—MOMS trial</td>
<td>No&lt;sup&gt;a&lt;/sup&gt;</td>
<td>(Bruner et al., 2000b; Sutton and Adzick, 2004)</td>
</tr>
<tr>
<td>Large congenital pulmonary airway malformations</td>
<td>Sporadic cases</td>
<td>No&lt;sup&gt;a&lt;/sup&gt;</td>
<td>(Adzick et al., 1998; Bruner et al., 2000a; Crombleholme et al., 2002)</td>
</tr>
<tr>
<td>Acardiac twin/TRAP sequence</td>
<td>No</td>
<td>Sporadic cases</td>
<td>(Lee et al., 2007)</td>
</tr>
<tr>
<td>Amniotic band syndrome</td>
<td>No</td>
<td>Sporadic cases</td>
<td>(Quintero et al., 1997)</td>
</tr>
<tr>
<td>Sacrococcygeal teratoma</td>
<td>Sporadic cases</td>
<td>No</td>
<td>(Paek et al., 2001; Hedrick et al., 2004)</td>
</tr>
<tr>
<td>Hypoplastic left (and right) heart syndrome</td>
<td>No</td>
<td>Transcardiac balloon valvuloplasty</td>
<td>(Tworetzky et al., 2009)</td>
</tr>
<tr>
<td>Lower urinary tract obstruction</td>
<td>No longer recommended</td>
<td>Vesico-amniotic shunt</td>
<td>(Morris and Kilby, 2009)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>No</td>
<td>Pleuro-amniotic shunt</td>
<td>(Salomon et al., 2003)</td>
</tr>
<tr>
<td>Aquaductal stenosis</td>
<td>No</td>
<td>No longer recommended</td>
<td>(Clewell et al., 1981)</td>
</tr>
</tbody>
</table>

MOMS, Management of Myelomeningocele Study; TRAP, Twin Reversed Arterial Perfusion.

<sup>a</sup>Unsuccessful attempts at endoscopic treatment.

Anesthesia for minimally invasive and percutaneous procedures

• Local anesthetic infiltration of the abdominal wall is usually sufficient to reduce maternal discomfort
• Fetal immobility and analgesia via placental transfer
  – Low dose propofol
  – Continuous remifentanil
• In case of mini-laparotomy or multiple access ports for endoscopy
  – Neuraxial anesthesia preferred when no uterine exteriorization
  – General anesthesia preferred when exposure requires laparotomy or uterine exteriorization
Anesthesia for minimally invasive and percutaneous procedures

• Uncomplicated anterior placenta
  – Access to umbilical cord is easy, local or epidural anesthesia often sufficient

• Posterior placenta
  – Often requires more uterine manipulations, fetal movement with uterine manipulation increases difficulty of these cases
  – Good uterine relaxation & no fetal movement:
    ➔ General anesthesia
The anesthesiologists view of fetal surgery

• Epidural anesthesia:
  + Minimal effects on fetal hemodynamics
  + Minimal effects on uteroplacental blood flow
  + Minimal effect on postoperative uterine activity

- Lack of uterine relaxation
- Lack of fetal anesthesia
- Difficulty manipulating uterus and cord while fetus may be moving
The anesthesiologists view of fetal surgery

• General anesthesia
  – Balanced opiate-inhaled
    + Immobile-anesthetized fetus
    - Inability to fully relax the uterus
  – Deep inhaled (2-3 MAC)
    + Profound uterine relaxation
    - Fetal cardiac depression
    - Decreased utero-placental blood flow

→ Restrictive intraoperative iv fluids to minimize the risk of postoperative pulmonary edema associated with tocolytics
→ Effective postoperative analgesia may prevent preterm labour
Anesthesia for invasive procedures with hysterotomy

- General anesthesia with deep volatile technique
- Preoperative tocolysis and epidural catheter placement
- Increasing volatile anesthesia as long as the uterus is not flaccid, or supplemental nitroglycerin
- Fetal uptake of volatiles is slower than maternal uptake, but MAC is lower
- Direct fetal anesthesia with administration of fentanyl (10-25 µg/kg), verocuronium (0.2 mg/kg) and resucitation (atropine, adrenaline, crystalloids)
- Continuous assessment of fetal well-being (pulse oxymetry, fetal heart rate with ultrasonography or echocardiography)
Anesthesia for invasive procedures with hysterotomy

- At uterine closure administration of loading dose of magnesium sulfate (4-6 g/20min) followed by continuous infusion
- Activation of epidural anesthesia and stopping volatile anesthesia after uterine closure
- Close postoperative monitoring and tocolysis (magnesium, indomethacin, terbutaline, nifedipine)
- Postoperative evaluation of fetus with ultrasound and MRI to look for intracranial haemorrhage
Anesthesia for invasive procedures with hysterotomy: EXIT procedure

- Modified C-section: the child is delivered, but feto-placental circulation is maintained.
- Same anesthesiologic technique as for open fetal surgery
- Monitoring of fetus with pulse oxymeter and ultrasonography
- This technique may provide feto-maternal stability over several hours
- Once surgery completed the baby’s trachea is intubated, surfactant given, ventilation of the lungs is started.
- When the baby’s oxygen saturation is >90% the umbilical cord is clamped and the baby transferred to NICU
The anesthesiologists view of fetal surgery

General vs local anesthesia for the percutaneous laser treatment of twin-twin transfusion syndrome

A. Cristina Rossi, MD; Marc A. Kaufman, MD; Patricia W. Bornick, RN, MSN; Rubén A. Quintero, MD

• 266 consecutive patients
  – 10% general anesthesia: isoflurane/nitrous oxide
  – 38% general anesthesia: TIVA
  – 52% local anesthesia with sedation (fentanyl, midazolam and morphine)
The anesthesiologists view of fetal surgery

BP decreases in all 3 groups, but is more evident in the GenA group.

Fluctuations of BP in the perioperative period.

The anesthesiologists view of fetal surgery

### TABLE 4
Perinatal outcomes by type of anesthesia

<table>
<thead>
<tr>
<th></th>
<th>GenA</th>
<th>TIVA</th>
<th>LocA</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane detachment, n (%)</td>
<td>4 (15%)</td>
<td>4 (4%)</td>
<td>4 (3%)</td>
<td>.2398a</td>
</tr>
<tr>
<td>Leakage less than 21 d, n (%)</td>
<td>3 (11%)</td>
<td>8 (8%)</td>
<td>5 (3%)</td>
<td>.1200a</td>
</tr>
<tr>
<td>PROM less than 34 wks, n (%)</td>
<td>10 (37%)</td>
<td>48 (48%)</td>
<td>44 (31%)</td>
<td>.0370b</td>
</tr>
<tr>
<td>Miscarriage, n (%)</td>
<td>2 (7%)</td>
<td>1 (1%)</td>
<td>7 (5%)</td>
<td>.3395a</td>
</tr>
<tr>
<td>Delivery less than 34 wks, n (%)</td>
<td>12 (44%)</td>
<td>55 (55%)</td>
<td>55 (39%)</td>
<td>.0607b</td>
</tr>
<tr>
<td>GA at delivery (mean ± SD)</td>
<td>32.83 ± 3.85</td>
<td>32.43 ± 4.50</td>
<td>32.90 ± 3.49</td>
<td>.9039c</td>
</tr>
<tr>
<td>One or more survivors, n (%)</td>
<td>20 (74%)</td>
<td>90 (90%)</td>
<td>112 (80%)</td>
<td>.0590b</td>
</tr>
<tr>
<td>Stop surgery for bleeding, n (%)</td>
<td>0</td>
<td>1 (1%)</td>
<td>0</td>
<td>.4774a</td>
</tr>
<tr>
<td>Intraamniotic bleeding, n (%)</td>
<td>9 (33%)</td>
<td>13 (13%)</td>
<td>2 (1%)</td>
<td>&lt; .0001a</td>
</tr>
<tr>
<td>Blood transfusion, n (%)</td>
<td>0</td>
<td>1 (1%)</td>
<td>1 (0.7%)</td>
<td>1.00a</td>
</tr>
<tr>
<td>Pulmonary edema, n (%)</td>
<td>0</td>
<td>0</td>
<td>3 (2%)</td>
<td>.2487a</td>
</tr>
<tr>
<td>Operating time (mean ± SD)</td>
<td>50.22 ± 26.48</td>
<td>47.20 ± 18.35</td>
<td>46.58 ± 23.17</td>
<td>.5154c</td>
</tr>
<tr>
<td>Chorioamnionitis, n (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Switch from SLPVC to UCO, n (%)</td>
<td>2 (7%)</td>
<td>1 (1%)</td>
<td>0</td>
<td>.1075a</td>
</tr>
</tbody>
</table>

GA, gestational age; leakage, Leakage of amniotic fluid within 21 days after surgery; miscarriage, delivery before 24 weeks.

a Fisher exact test.

b $\chi^2$ for independence.

c Kruskal-Wallis (posttest: Dunn’s multiple comparisons).

Laser treatment for TTTS best done under local anesthesia with conscious sedation (LocA)

LocA associated with similar pregnancy outcomes than general anesthesia, but less maternal complications

LocA provides a constant hemodynamic status in the perioperative period, that optimizes adequate oxygenation and perfusion of mother and fetuses

Local anesthesia with sedation should be the technique of choice for percutaneous laser treatment of TTTS
Thanks' for huge help in preparing this presentation go to:

• Dr. Luigi Raio, Obstetrician
  Bern University Hospital

• Dr. Tom Riedel, Pediatric ICU
  Bern University Hospital
Questions?

Thank you!
The obstetrician’s view: inter-twinvascular anastomoses

**High risk:**

- one or more deep A-V anastomosis in combination with absent superficial A-A anastomosis
- Presence of superficial V-V anastomosis

**Table 2** Mortality of one or both children

<table>
<thead>
<tr>
<th></th>
<th>No A-A or V-V</th>
<th>A-A</th>
<th>V-V</th>
<th>A-A and V-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>20/52 = 39%</td>
<td>25/202 = 12%</td>
<td>5/8 = 63%</td>
<td>17/77 = 22%</td>
</tr>
</tbody>
</table>

A-A, arterio-arterial; V-V, veno-venous.

By courtesy of L. Raio
The obstetrician’s view: Distinct forms of TTTS
Chronic TTTS: TAPS

- Few and small AV anastomosis in absence of AA anastomosis
- Post-laser: 2-13%
- Spontaneous: 3-5%
- Absence of oligo-polyhydramnios, small but continuous blood flow from donor to recipient
- Hemodynamic compensatory mechanisms have time to take place:
  - Donor: High reticulocytes
- Treatment: Intrauterine blood transfusion

TAPS = Twin Anemia Polycythemia Syndrome
Selective laser treatment in Bern

By courtesy of L. Raio