Fetal Anaemia and Intrauterine Transfusion

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South East Coast Regional Transfusion Committee Education Symposium
Wednesday 26 February 2020
Fetal Anaemia

• Clinical presentation:
  – Immune Fetal Hydrops
  – (Non-immune Fetal Hydrops)

• Management Fetal anaemia
  – MCA assessment
  – Fetal Blood sampling / Intrauterine Transfusion

• Case Studies
Clinical presentation – Fetal anaemia:

Fetal Hydrops:

• Immune and non-immune Fetal hydrops
• Abnormal fluid collection in at least two different fetal compartments:
  – Pericardial effusion
  – Pleural effusion
  – Ascites
  – Skin oedema (>5 mm)
  – Polyhydramnios
  – Thickened placenta (>6cm)
  – Cardiac failure
  – IUD
Immune Fetal Hydrops:

Result of circulating maternal AB against (fetal) red cell antigens (Red cell isoimmunization)

- >100 Red cell antigens, but isoimmunization associated with <30:
  - Typically:
    • anti-D, anti-C, anti-Kell, anti-E
  - Rarely:
    • anti-M, anti-N, anti-S
Red cell iso-immunization:

- 15% of Antenatal population Rh Negative
- Routine pregnancy AB screen – 12 and 28 week
- Rh negative patient – cfDNA for fetal genotype (IBGRL Bristol)
- If Rh positive fetus: Anti-D prophylaxis at 28 weeks (and after any sensitising event)
- cfDNA now available for Kell, C, e and C
Red cell iso-immunization: Assessment

Fig 1—Fetal haemoglobin concentration of 48 hydropic (○) and 106 non-hydropic (●) fetuses from red cell isoimmunised pregnancies at time of first fetal blood sampling.
Red cell iso-immunization: Assessment

- Fetal Anaemia - decreased blood viscosity
- Increased venous return + preload – increased cardiac output
- Increased arterial + venous blood flow velocities
- MCA-PSV useful method to assess anaemia
- Low false positive rate

Red cell isoimmunization: management

- None / Mild
- Maternal history
  - Fetal Rh group
    - Rh antibodies
      - <15 IU (or 1:128)
        - Expectant
      - >15 IU
        - MCA Doppler
          - PSV >2 SD’s
            - FBS / IUT
  - Severe
Red cell isoimmunization: management

- Fetal Blood sampling / Intra-uterine Transfusion:
  - Cordocentesis, Intrahepatic vein, intracardiac
  - Outpatient procedure – Fetal Medicine Unit
  - Consent - 1-2% procedure – related loss (PPROM/Fetal bradycardia)
  - Preoperative IV AB
  - Ultrasound guidance
  - Aseptic technique
  - Local Anaesthetic infiltration
  - 17 Gauge needle (1.4 mm diameter)
Red cell isoimmunization: management

- Intra-uterine Fetal Blood sample:
  - From 16 weeks of pregnancy
  - Transplacental or transamniotic
- Sample site:
  - Intrahepatic vein
  - Umbilical Cord insertion
  - Free loop
  - Intracardiac
- 1mL sample – immediate result in Fetal Medicine unit by Haematology team or Haemacue.
Red cell isoimmunization: management

- **Intrauterine Transfusion:**
  - Transfuse O Rh Negative, packed cells (HCT >85%), irradiated, CMV negative, Kell Negative
  - Rate – 10-15 ml/min
  - Monitor FH
  - Volume – dependent on HCT and fetal Hb:

<table>
<thead>
<tr>
<th>Gestational age:</th>
<th>Volume to transfuse:</th>
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<tbody>
<tr>
<td>16-18 weeks</td>
<td>5ml</td>
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<tr>
<td>20 weeks</td>
<td>20ml</td>
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<tr>
<td>&gt; 20 weeks</td>
<td>20mL + 10mL/week of gestation to a max of 100ml</td>
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- Repeat FBS post transfusion
- Paired samples to Haematology department for formal FBC.
Red cell isoimmunization: timing of subsequent transfusions

- Initial decision for IUT based on:
  - Hydrops
  - MCA PSV

- Timing of Subsequent IUT:
  - MCA predictive of severe anaemia for 2\textsuperscript{nd} (but not the 3\textsuperscript{rd} transfusion (for a DR of 95\%, MCA PSV): FPR
    - 1\textsuperscript{st} Transfusion 14\%
    - 2\textsuperscript{nd} Transfusion 37\%
    - 3\textsuperscript{rd} Transfusion 90\%
  - Anticipate rate of decrease of 0.4 g/dL/day
  - Empirically IUT every 2-3 weeks

Nicolaides et al. Prediction of severe fetal anemia in red blood cell alloimmunization after previous intrauterine transfusions
Red cell isoimmunization: timing and mode of delivery

• Aim to manage / resolve hydrops prior to delivery
• No contraindication to vaginal delivery (deliver on standard obstetric indications)
• Aim for delivery 34-36 weeks (based on good neonatal outcomes / limitations of MCA data)
Non-Immune Fetal Hydrops:

- **Structural abnormalities:**
  - Cardiac - HLHS, PA, arrhythmia (SVT, WPW)
  - Pulmonary – CCAM, CDH
- **Chromosomal abnormalities (X-, T13, T18, T21)**
- **Genetic syndromes**
  - Arthrogryposis, TS
- **Haematological disorders:**
  - Failure to manufacture Hb (a-thalassaemia)
  - Fetal haemorrhage (ICH)
  - Haemolysis (G6PD)
- **Infection:**
  - Bone marrow destruction (Parvovirus B19, CMV, Toxoplasmosis)
- **MCDA Twins - TTTS**
Non-Immune Fetal Hydrops:

• History:
  – FH of Metabolic disorders
  – Recent infection / exposure

• Investigations:
  – Maternal Blood:
    • Blood Group, Kleihauer and AB
    • FBC and electrophoresis
    • Viral screen – Toxoplasma, CMV, Rubella, Parvovirus
  – US/S (tertiary referral):
    • Detailed ultrasound scan
    • Fetal Echo
    • MCA Doppler
    • FBS (Fetal - FBC, Blood Group, karyotype, Viral screen)
  – Offer karyotype (10-20% risk of aneuploidy)
Non-Immune Fetal Hydrops:

• Management:
  – Dependent on aetiology
  – Cardiac malformation: very poor prognosis if hydrops secondary to structural (cardiac malformation). Offer TOP.
  – Cardiac arrhythmia: maternal therapy (Digoxin/Flecainide)
  – Fetal anaemia - IUT
  – Termination of pregnancy
  – Timing of delivery – may be associated with preterm delivery (secondary to polyhydramnios, or iatrogenic – PET).
  – Mode of delivery – optimal mode remains unclear. Aim for SVD.
  – Perinatal mortality rate – 40-90%
Case study #1:

- 36 year old
- G3 P2+0
- Admitted to DGH 29+6/40:
  - Oedema, hypertension, proteinuria – “feeling unwell”
  - Investigations:
    - Normal FBC, LFT and renal function
    - AB Rh positive – no atypical AB (at 28 weeks)
  - Management:
    - Admitted, routine Obs, CTG
    - US/S: Widespread hydrops, placentamegaly, pleural and pericardial effusions, skin oedema.
    - MCA 95 cm/s (> 1.5 MoM)
Case study #1:

- Further history – recent viral infection
- Diagnosis – Parvovirus B19 infection with maternal PET
- Management:
  - FBS/IUT
  - Initial Hb – 3.8 g/dL (Blood sent for TORCH, Karyotype)
  - Transfusion – 120 ml. Post procedure Hb – 9.5 g/dL
  - Planned repeat IUT
  - Returned to referring hospital
  - Abnormal CTG – Emergency LSCS. Neonatal admission
  - Confirmed Parvovirus
  - BW – 1980g.
Case study #2:

- 34 year old
- G1 Po
- Low risk first trimester Combined screening
- Routine anomaly scan (22 weeks):
  - Fetal Supraventricular Tachycardia
  - No evidence of hydrops
- Management:
  - Fetal Echo
  - Maternal ECG
  - Commenced on Digoxin 250μg TDS
Case study #2:

- Follow up scan – 24 weeks
  - Persistent SVT
  - Moderate Hydrops
  - (Normal MCA)
- Follow up scan – 27 weeks
  - Hydrops resolved
  - Normal SR (Rate 140 bpm)
- Continued on Maternal Digoxin
- Outcome:
  - IOL at 40 weeks (Maternal PET)
  - Normal SVD – Female infant 3572g (~50th centile)
  - Neonatal – Propranolol to 6 months of age.
Any Questions?
Fetal Anaemia Summary:

- **Immune Hydrops:**
  - Assess History, Maternal AB screen, Detailed US/S + MCA
  - FBS / IUT if MCA >1.5 MoM
  - FU: IUT 2 weeks

- **Non-immune Hydrops:**
  - Infection: Parvovirus B19, CMV, Toxoplasmosis.
  - MCDA Twins – TTTS
  - FBS / IUT if MCA >1.5 MoM
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