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Newsletter

The contribution of placental histopathology in investigating adverse pregnancy outcome

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2nd Quarter 2018

Why does adverse pregnancy outcome often remain unexplained?

- There may be poor correlation between maternal indicators of infection and placental findings.
- Placental causes of foetal and perinatal death may be clinically silent, e.g. delayed villous maturation or foetal vascular malperfusion (FVM).
- Intrauterine growth restriction has a multifactorial aetiology related to foetal, maternal and placental pathology.

Causes of intrauterine growth restriction (IUGR)

- *Infections:* Viral, parasitic
- *Multiple gestation*
- *Maternal vascular malperfusion:* Maternal diseases, e.g. hypertension, diabetes, auto-immune disease, smoking, recreational drugs
- *Foetal vascular malperfusion:* Maternal thrombophilia, abnormal cord insertion
- *Chromosomal:* Placental mosaicism, aneuploidy (Trisomy 21)
- *Other:* e.g. maternal floor infarction/massive perivillous fibrin deposition (see Figure 1), villitis of unknown aetiology (VUE)

Figure 1. Maternal floor infarction/massive perivillous fibrin deposition. The maternal surface is replaced by a thick white "rind" of fibrin. This entity is associated with IUGR, a very high rate of recurrence in subsequent pregnancies, and a significant risk of neurologic handicap.

How can placental histopathology contribute?

- Determine the pathophysiology of an adverse pregnancy outcome
- Contribute to the management of the mother and neonate in the acute and longer term
- Contribute to the management of subsequent pregnancies, and recurrence risk
- Determination of timing of events may assist in medicolegal assessment of cases
- Contribute to defining health policies and allocation of resources

Cerebral palsy (CP)

Cerebral palsy occurs in 1.5 to 2.5 cases per 1 000 live births, and around 50% of cases occur in term infants in low risk pregnancies. There has not been a decrease in the prevalence of cerebral palsy in the last three decades, despite several advances in foetal monitoring and neonatal ICU care.

Only 8 – 10% of CP cases at term can be attributed to intrapartum hypoxia. The remainder may be related to remote antenatal processes. Most children with CP demonstrated no evidence of "foetal distress" intrapartum. Neuroradiologic studies, however, reveal injury consistent with an insult within hours of delivery.

Hypothesis

- Placental lesions decrease the threshold for brain injury so that relatively minor intrapartum insults cause severe neurological injury.
- Although placentas possess between 33 – 50% excess capacity, placentas with decreased reserve may function adequately, but be unable to cope with the stress associated with labour.
- Multiple early and recent insults act together to increase the risk of brain injury at birth, i.e. perinatal asphyxia may be the CONSEQUENCE, rather than cause of neurologic impairment.

Risk factors for cerebral palsy

- IUGR
- Cerebral defects
- Maternal infection
- Placental infection
- Family history of CP/neurological disorder

Prenatal factors associated with cerebral palsy and other neurological defects

Preterm

Placental lesions may modulate the risk; may not usually be the sole cause – CNS damage may be due to immaturity

- Chorioamnionitis with severe foetal inflammatory response (FIR)
- Severe maternal vascular malperfusion
- Diffuse villous oedema
- Multiple placental lesions

Term
Often accompanied by basal ganglia injury due to inflammatory placental lesions

Placental pathology relevant to cerebral palsy

- *Sentinel lesions*
  - Abruptio placentae/uterine rupture
  - Foetal haemorrhage
  - Umbilical cord occlusion/constriction
- *Thrombotic or inflammatory lesions of foetal circulation*
  - Foetal vascular malperfusion (thrombotic vasculopathy)
  - Severe chronic villitis with destruction of villi
  - Meconium-associated vascular necrosis of foetal vessels
  - Chorioamnionitis with severe foetal vasculitis
- *Decreased placental reserve*
  - Maternal vascular malperfusion (uteroplacental insufficiency)
  - Diffuse chronic villitis
  - Chronic abruption
  - Chronic foetal vascular malperfusion (obstruction)
  - Massive perivillous fibrin deposition
- *Adaptive responses in the placenta*
  - Increased nucleated red blood cells
  - Villous chorangiosis
  - Distal villous immaturity

The global childbirth litigation industry

Most experts in litigation in this area have highlighted three focal points:

- Failure to identify clinically important placental lesions
- Failure to detail in the record the significance of these lesions
- Failure to communicate to the parents the cause-and-effect relationship

Placental pathology can:

- Identify processes that directly cause or contribute to neurological damage or impairment
- Identify placental pathological processes that cause decreased placental reserve, placing the foetus at risk when entering labour
- Indicate an abnormal intrauterine environment which was present prior to onset of labour

Indications for requesting placental histopathology

The following indications for placental histopathology are currently used in South Africa:

1. All unexplained stillbirths after 24 weeks gestation or birthweight $\geqslant$ 500 g
2. Indications of asphyxia in a viable baby. This group consists of all neonates who required resuscitation, unless clearly due to abruptio placentae or cord prolapse
3. Second or higher order mid-trimester loss
4. Idiopathic preterm labour (gestational age < 34 weeks or birth weight < 1800 g)
5. Suspected clinical chorioamnionitis
6. Suspected maternal TB or maternal TB on treatment for less than 2 months
7. Cases of severe intrauterine growth restriction
8. All multiple pregnancies with uncertain chorionicity at the time of birth
9. Cases of severe pre-eclampsia

How to request placental pathology

- The placenta should be submitted in 10% buffered formalin in a plastic container of sufficient size that it does not distort the placenta.
- The following clinical information should be supplied on the request form:
  - Gestational age
  - Live birth or stillbirth
  - Relevant maternal history and diseases
  - History of recurrent pregnancy losses
- Based on the findings by the histopathologist, PCR testing for specific infectious diseases, e.g. *Toxoplasma gondii,* CMV, and *Listeria monocytogenes* (see Figure 2) can also be performed on the formalin-fixed placental tissue.

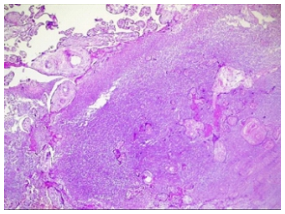

Figure 2. *Listeria monocytogenes* causes microabscesses in the placental parenchyma.

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design done and printed by: ELECTRONIC LABORATORY SERVICES (PTY) LTD PRINT BUREAU ITEM CODE: N00182
corporate branding/newsletters/south africa/2018/N00182 The contribution of placental histopathology in investigating adverse pregnancy outcome A4 Eng Duplex 170gsm Leo Mar2018.cdr | rev000