Neonatal Hypoxic Brain Injury

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Contents

- HIE
  - Preterm
  - Term
- Germinal matrix haemorrhage
- Perinatal stroke

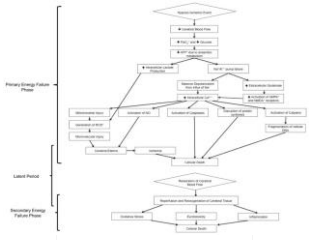
Modalities

- Ultrasound
  - Lower cost, quick, no radiation, non-invasive
  - Good at detecting IVH, PVL and hydrocephalus
  - Can't see everything, parenchymal abnormalities may be non-specific
- CT
  - Quick but requires patient transfer, radiation exposure
  - Not sensitive, essentially used for in extremis infants not safe to go in the magnet
- MRI
  - Most sensitive and specific, visualising all areas of the brain
  - Requires transport

Hypoxic-ischaemic encephalopathy

- Neonatal encephalopathy caused by systemic hypoxaemia and/or reduced cerebral blood flow resulting from an acute peripartum or intrapartum event.
- Intrapartum events include
  - Uterine rupture, placental abruption, cord prolapse, amniotic fluid embolism, exsanguination or massive feto-maternal haemorrhage.
- Fetal / neonatal factors
  - Arrhythmia, thrombosis, surfactant deficiency, meconium aspiration, congenital heart disease
- Maternal factors
  - Pre-eclampsia, maternal hypoxia (asthma, PE, pneumonia, CO, severe anaemia)

Pathophysiology



Pathogenesis

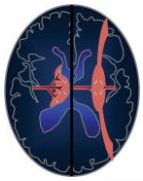
- Depends on
  - Brain maturation
  - Severity of event
  - Length of event – > 10 minutes required for parenchymal injury
- 36 weeks typical pre-term to term cut-off
- Delayed injury due to programmed apoptosis

Pathogenesis

- Degree of maturation dictates the configuration of the vascular supply and the state of the regional metabolism
- Most metabolically active tissues
  - Pre-term – deep grey matter, thalami and brainstem
  - Term – lateral thalami, GP, putamina, hippocampi, brainstem and sensorimotor cortex
- Vascular supply
  - Pre-term – ventriculopetal penetrating arteries
  - Term – intervascular border zone

Vascular watershed zones

Pre-term



Term

Patterns of Injury

	Pre-term	Term
Mild-moderate	• Periventricular leukomalacia / WMIP • Germinal matrix haemorrhage	• Watershed zone infarcts
Severe	• Thalami, brainstem • Germinal matrix haemorrhage	• Thalami, putamina, hippocampi, brainstem, corticospinal tracts and sensorimotor cortex

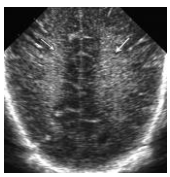
Clinical diagnosis

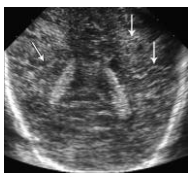
- Clear history – or not e.g. intrauterine arrhythmia
- Depressed baby (APGAR scores)
- Disturbed neurological function
  - Difficulty with respiration
  - Depression of tone and reflexes
- Sarnat criteria
- Abnormal EEG

Pre-term HIE – Mild-moderate

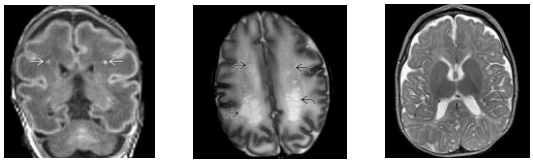
- PVL / WMIP
  - Initially start as areas of increased echogenicity
    - May be confluent or heterogeneous
  - Cavitate over 2-6 weeks
  - Ventricular enlargement
  - Focal - macrocystic (>1-2 mm) vs. microcystic (not perceivable on imaging)
  - Diffuse - hypomyelination and volume loss
- MRI with DWI most sensitive examination acutely
- US underestimates non-haemorrhagic / non-cavitary lesions

Pre-term HIE – Mild-moderate

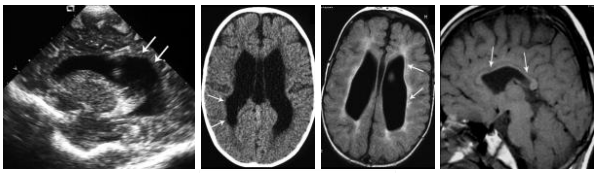




Pre-term HIE – Mild-moderate



Pre-term HIE – Mild-moderate

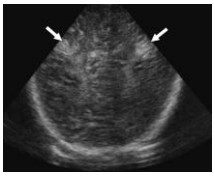


Pre-term HIE - Severe

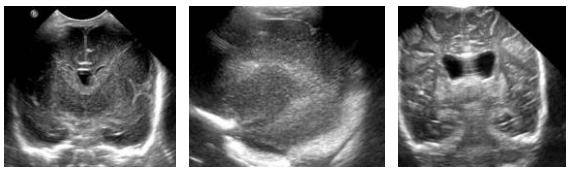
- Thalami, brainstem, cerebellum
- Often intracranial haemorrhage will dominate

Term HIE – Mild-moderate Injury

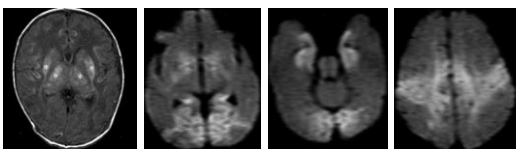
- Mild or partial
  - Peripheral pattern of cortical injury / watershed
  - Cortex and subcortical white matter – hard to see on US



Term HIE – Severe Injury



Term HIE – Severe Injury



Prognosis

- Term injury
  - Mild-moderate – 20% mortality, 25% significant neurological sequelae (spastic quadraparesis
  - Severe – high mortality rate, survivors develop extra-pyramidal (dystonic) quadraparesis)
- Pre-term injury
  - Fare worse

Multi-system disease

- Redistribution of blood:
  - To brain, heart and adrenal glands
    - Cerebral and adrenal gland haemorrhages
  - Away form kidneys, bowel and skin
    - Renal failure
    - Ischaemic colitis
    - Skin necrosis

Treatments

- Therapeutic hypothermia (33.5 degrees C for 72 hours)
  - Short window of 2-6 hours – importance of early identification
- Adequate ventilation and fluid support
- Seizure control
- Other neuroprotective agents e.g. calcium channel blockers, nitric oxide inhibitors etc. under investigation

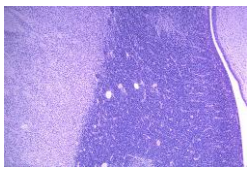
Germinal Matrix Haemorrhage

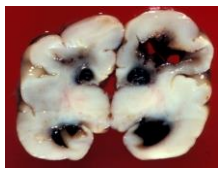
- Most common intracranial haemorrhage in premature neonates, 90% in the first week of life
- Glial and neuronal differentiation site
- Highly vascular, with friable blood vessels
- Neonatal stress causes fluctuations in cerebral blood flow
- Lack of appropriate cerebral autoregulation in preterm neonates
- Present in caudothalamic groove, thickest at 25-26 weeks and involutes at 35-36 weeks + cerebellum

Germinal matrix haemorrhage – risk factors

- Low gestational age / SGA
- Maternal infection / chorioamnionitis
- Early sepsis
- Hypotension
- Hypoxaemia / hypercarbia
  - Lung haemorrhage, lack of steroids

Germinal Matrix Haemorrhage





Germinal matrix haemorrhage - Grading

Grade	Description	Prognosis
Papile (1978)		
1	Confined to caudothalamic groove	< 1% mortality
2	Extension into the ventricle	< 2 % mortality
3	Complicated by hydrocephalus	~ 20% mortality
4	Complicated by parenchymal venous infarct	~ 90% mortality
Neurodevelopmental significance of grade I-II haemorrhages not well understood		
Low grade haemorrhages associated with white matter lesions on MRI		
Volumetric MRI studies have shown reduced cortical volume in patients with low grade GMH		
White matter lesions probably more important with respect to cerebral palsy		

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Germinal matrix haemorrhage

- Poor interobserver agreement between grade I and grade II
  - Can confuse choroid for haemorrhage, or vice versa
  - Kappa 0.2-0.26
  - Look for ependymal thickening and blood layering in the occipital horn (mastoid / posterior fontanelle)

Echogenicity anterior to groove is haemorrhage, choroid terminates at groove

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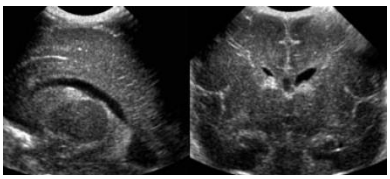
Grade 1



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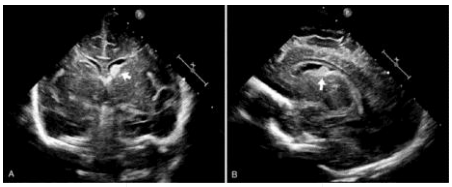
Grade 2



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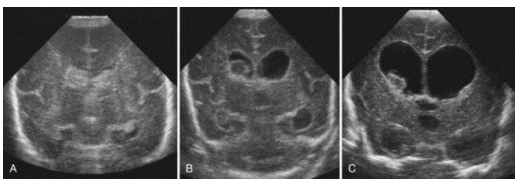
Grade 3



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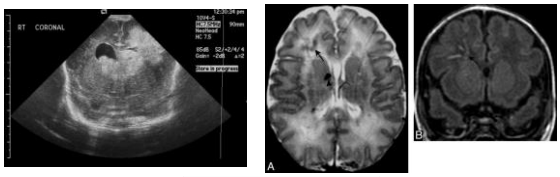
Grade 4



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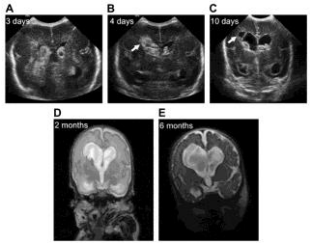
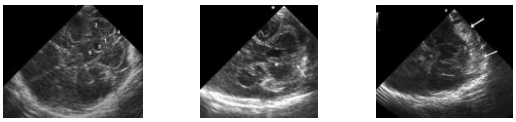
Follow-up



Cerebellar haemorrhages

- Matrix in hemispheres and vermis (floor of fourth ventricle)



Choroidal haemorrhage

- Choroid is source of origin
- Can be bound by choroid or rupture into ventricle
- Good prognosis if no hydrocephalus
- Can be impossible to distinguish

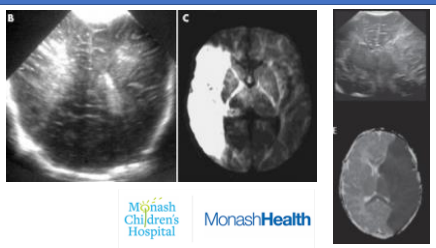
Hydrocephalus

- Two mechanisms
  - Communicating - blockage of arachnoid villi by blood products / post-haemorrhagic arachnoiditis
  - Obstructive – clot physically blocking the ventricular system, such as at the aqueduct
- May require shunt
- Outcome relates to severity of initial insult, delay to treatment, effect of shunt complications etc.

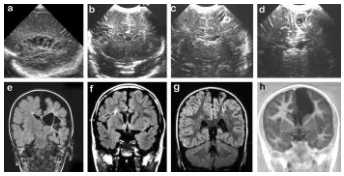
Neonatal stroke

- Ultrasound will not detect hyperacute infarcts
- When the infarcted tissue starts to become oedematous ultrasound will show focal parenchymal swelling and echogenicity
- Arterial strokes conform to vascular territories

Neonatal stroke



Neonatal stroke



References

- Neonatal Hypoxic-Ischemic Encephalopathy: Multimodality Imaging Finding RadioGraphics Oct 2006 26 suppl 1
- Imaging Findings in Neonatal Hypoxia: A Practical Review AJR:192 Jan 2009