Clinical cases in virology

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Viruses in May, 2013
2 year old Vietnamese boy

- Previously well

- April: unwell 4 days with fever and unsteady walking

- Presented shocked, tachycardic + tachypnoeic to Canterbury Hospital and transferred to PICU at CHW

- Intubated and ventilated
History

- Travel: Visit to Vietnam and Cambodia in February (6 weeks prior to illness)

- F.H. No siblings, but uncle admitted to Canterbury Hospital with pharyngitis
Examination

- On ventilator, muscle relaxed, on maximal inotropes
- Cold peripheries, tachycardic, normal heart sounds
- No hepatosomegaly
Investigations

- Hb 115, WCC 7.1 (N 4.5, L 2.6), Plat 244
- U + E, creatinine, liver function normal
- CRP 13, procalcitonin >10
- Troponin 960
- Creatine kinase 1053 (N 18-150)
- Chest X-ray: increased shadowing, no cardiomegaly
Diagnosis?
ID consult

- Referred as presumed myocarditis
- Not clinically in heart failure
- Echocardiogram: no LV dysfunction
- ICU nurse said had to keep suctioning mouth for frothy secretions (not endotracheal tube)
- Any thoughts?
Further history

- Uncle 3 years old

- Myoclonic jerks in sleep at home
Clinical diagnosis

- Brainstem encephalitis
Progress

- Enterovirus in stool and nasopharyngeal aspirate
- Treated with methylprednisolone x 5 days
- IVIG
- Doing very poorly
Baby IK

- Baby IK (DOB 24/10/12)

7-day old girl transferred from Blacktown nursery:

- IUGR
- Petechial rash
- Hepatosplenomegaly
- Thrombocytopenia:
  - Ix with BM aspirate
• Increased signal: T2 tegmentum, posterior medulla and pons, extending into the anterior cervical cord

• Findings in keeping with features of encephalitis due to enterovirus

• No evidence of leptomeningeal enhancement to suggest meningitis
Antenatal History

- Mother 18 year old primigravida
  - One UTI infection during pregnancy – treated
  - No other complications
  - No regular medications
  - Morphology scan @ 20/40 normal
  - Growth U/S @ 36/40, EFW=1880g (<1st %ile)
  - Plan for induction
Perinatal

- Born at 37/40 @ Blacktown Hospital

- Induction of labour → Emergency LSCS
  - Failure to progress, meconium liquor, fetal distress

- GBS status unknown:
  - Mother given IV benzylpenicillin prior to delivery
  - No prolonged ROM
  - Baby given 5 days IV penicillin and gentamicin
  - Blood cultures were negative at 48h
Birth

- APGAR scores 9 + 9
- No resuscitation needed
- Arterial Gas
  - pH 7.29
  - Lactate 3.9
  - Base Excess 1.8
- Birth weight = 1980g (<1<sup>st</sup> %ile)
- HC = 31cm (<10<sup>th</sup> %ile)

- Transfer to Blacktown SCN: for IUGR
<table>
<thead>
<tr>
<th>TORCH screen</th>
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</thead>
<tbody>
<tr>
<td><strong>Rubella IgG</strong></td>
<td>Negative</td>
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<tr>
<td><strong>HSV</strong></td>
<td>Negative</td>
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<tr>
<td><strong>HIV Antigen / Ab</strong></td>
<td>Negative</td>
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<tr>
<td><strong>CMV IgM</strong></td>
<td>Weak positive</td>
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<tr>
<td><strong>CMV PCR</strong></td>
<td>Pending</td>
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<tr>
<td><strong>Urine CMV PCR</strong></td>
<td>Pending</td>
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<tr>
<td><strong>Toxoplasmosis IgM</strong></td>
<td>Positive</td>
</tr>
<tr>
<td><strong>Placental tests</strong></td>
<td>Pending</td>
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</tbody>
</table>
More antenatal history...

- No pet cats at home
- Owns dogs
- No consumption of unpasteurised milk / dairy during pregnancy
- No raw meat
Maternal Serology

- **29/03/2012** – (1st trimester)
  - CMV IgG +ve
  - CMV IgM –ve
  - Rubella IgG titre low, ?needs booster
  - Hep B/C, HIV, syphilis negative

- **30/10/12** (1 week postnatal)
  - CMV IgG +ve
  - CMV IgM –ve
  - Toxoplasmosis IgG and IgM -ve
Thrombocytopenia

- Petechial rash on face and forehead
- No bruising or bleeding
- Vitamin K given
- Thrombocytopenia:
  - Platelets 38 x 10⁶/L (Day 0)
  - 30 x 10⁶/L (Day 1)
  - Platelet transfusion 10ml/kg
Neonatal alloimmune thrombocytopenia?

- **Head U/S (day 2)**
  - No intracranial bleeding
  - Asymmetrical lateral ventricle
  - Bilateral choroid plexus cysts (incidental finding)

- **NAIT screening:**
  - Maternal serology: negative (day 4)
  - Paternal serology: refused test
Persistent thrombocytopenia:
- Back down to 20 (day 5)

Transfer to CHW Grace HDU for BM aspirate (day 8)
Results:

- Megakaryocytes present
- Reassuring that resolution of thrombocytopenia imminent
Other issues so far:

- **Hypernatraemia**
  - Na 151
  - Increased fluids to 150ml/kg/day and resolved

- **Abnormal LFTs**

- **Prolonged APTT**
  - Gastro consulted – watch and wait
  - Resolved without intervention
More test results available

- In the meantime....

- Baby IK's results:
  - Urine and blood PCR CMV +ve

- Congenital or acquired CMV?
Congenital or acquired CMV?

- CMV is a herpesvirus

- Herpesviruses are forever

- Detection of virus in first week of life: congenital, thereafter can be either congenital or acquired

- IgM: congenital or acquired, unless in first week of life
Tests for baby with congenital CMV?

- **Head ultrasound:**
  - Repeated (day 9)
    - Ventricular and choroidal cysts
    - Lenticulostriate vasculopathy consistent with congenital toxoplasmosis?

- **Skull X-rays:**
  - No calcification

- **Ophthalmological:**
  - Normal clear media, disc, macula

- **Hearing:**
  - **SWISH test:** normal bilaterally
    - Review 3 monthly until 1 year, then 6 monthly until 3 years
Antiviral treatment?

- Should we treat congenital CMV infection?
  - All?
  - Selected?
  - Agent?
  - Duration?
  - Side effects?
  - Monitoring?
Literature review

- Results:
  - One RCT
  - Case series, reports
  - Pharmacokinetics
  - One ‘guideline’
RCT of ganciclovir in congenital CMV

- **Setting:** 1991-1999, 18 centres across USA

- **Population:**
  - Inclusion: 100 patients: <1m, symptomatic, urine CMV, CNS involvement (microcephaly, calcifications, abnormal CSF, chorioretinitis, hearing deficits)
  - Exclusion: <32w gestation, <1200g, HIV, palliative, renal dysfunction, antiviral or IVIG, hydranencephaly

- **Intervention:** IV ganciclovir 6mg/kg 12-hourly for 6 wk

- **Comparator:** no treatment

- **Outcome:** BSER at 6m
RCT

- **Results:**
  - 42 patients (25 intervention GCV, 17 control)
  - **Primary outcome:** BESR at age 6m
    - None of 25 patients’ hearing worse in GCV arm
    - Best ear (‘functional’) 7/17 (41%) worse in controls (P = 0.086)
    - Total ear (‘biological’) 15/36 (42%) worse in controls (P=0.011)
    - Results similar but less impressive at 12m
RCT

- **Adverse effects:**

  - Neutropenia: 63% in GCV arm, 21% controls (p<0.01)
    - 4 of 29 (13%) discontinued GCV, two given G-CSF
  
  - 3 patients with central line-associated bacteremia
  
  - 1 death in GCV arm – ‘complication of CMV’.
RCT: development

- Same study: developmental assessment as outcome

- Denver developmental assessments at 12 months: assessors not blinded.

- Follow-up achieved 75%
RCT

- **Primary outcome:**
  - Denver II assessment at 12m
  - 8.58 delays in GCV arm, 25.03 delays in control arm (P=0.005)
Pharmacokinetics

- PK study oral valganciclovir vs IV ganciclovir

- Equivalent 12hr AUC blood ganciclovir levels obtained with 16mg/kg dose valganciclovir cf. 6mg/kg dose IV ganciclovir
Summary

- Studies problematic

- **Efficacy for Symptomatic congenital CMV:**
  - Hearing impairment: less deterioration at 6m
  - Developmental Delay: less overall delays at 12m

- **Adverse effects:**
  - myelosuppression
  - CVL infections
  - Hospitalisation
Conclusion

- IV ganciclovir for 6 weeks
- Oral valganciclovir for some of duration
Baby IK

- IV Ganciclovir commenced age 14 days
  - Planned to treat with 5mg/kg BD for 6/52
  - Problems with venous access and adherence
  - Changed to oral valganciclovir after 2 weeks
Infant with rash and fever
Ella, 6 months old

- 12 hours after 3rd immunisation
- Previously well
- 2 weeks ago: in ED for 4hr with gastroenteritis, left
- Any questions?
Measles

Papular rash (palpable)

Morbilli = measles in Latin

Morbilliform = measles-like rash

HHV-6: morbilliform rash, but afebrile when appears
NSW outbreak

- 171 measles notifications in NSW in 2012 (the most since 1997)
- 169 notifications were linked to the one outbreak
- Outbreak was associated with travel to Thailand
- Transmission widespread in health care facilities, EDs and GPs
- Most cases in SW and Western Sydney
- Pacific Islander and Aboriginal persons disproportionately affected
- Most notifications in children <5 years old (n=58)
- 37 notifications in infants <1 year (too young to be vaccinated)
- 15 to 19 year olds also heavily involved in transmission (n=29)
- Average age 15 years (range: 4 months to 61 years), 52% male
- The majority of cases were unvaccinated
Figure 1: An approach to the patient with rash and fever

Features of rash

- Petechial/non-blanching
- Macular and/or papular
- Diffuse erythematous
- Vesicular/bullous

Clinical status

- Unwell
- Shocked
- Toxic

Possible diagnoses

- Meningococcal disease
- Dengue fever - take travel history
- Meningococcal disease (less likely)
  - Enterovirus infection
  - Rubella (unimmunised)
  - EBV
  - HSP
- Early meningococcal disease
  - Other rarer diagnoses – take travel history
- Measles (unimmunised)
  - Erythema infectiosum
  - Roseola infantum
  - Adenoviral infection
  - EBV
- Toxic shock syndrome
  - Invasive Group A streptococcal infection
  - Scarlet fever
  - Kawasaki disease
- Staphylococcal slapped cheek syndrome
  - Enterovirus infection
- Varicella zoster virus infection
  - Herpes simplex virus