Screening for enteroviral meningitis in infants and children - is it useful in clinical practice?

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BACKGROUND

Viral meningitis in children:

- Common cause of hospital admission especially during summer months[1]
- Differentiating viral meningitis from other infection can be difficult
- Most cases of enterovirus (EV) meningitis are benign/ self limiting[2]
- Lumbar Puncture relatively invasive for children
- Rapid diagnostic multiplex viral CSF PCR testing widely available
- Role of surrogate markers (e.g. CRP, WCC, CSF WCC count) uncertain
- A confirmed diagnosis has potential to improve outcome
  - e.g. length of stay (LOS), admission to HDU, need for/ duration of IV antibiotics

PURPOSE AND HYPOTHESIS

Purpose:

- Compare outcomes for infants and children (excluding SCBU) diagnosed with EV meningitis vs no virus detected on CSF samples

Hypothesis:

- Is there a role for additional laboratory markers and does CSF viral EV PCR testing impact on care pathway/ management/ prognosis?
- Can the care pathway be improved?

MATERIALS AND METHODS

- Infants and children admitted to Hospital between 2011 and 2017 where CSF viral PCR tests performed (n=215)
- PCR testing 2011-April 2015 by Bristol virology PHE laboratory using *in house* panel
- PCR testing May 2015-2017 by Torbay Hospital using *FTD* (Fast Track Diagnostics) *viral meningitis* panel
- 19 CSFs excluded (repeat sample, not admitted, taken post mortem)
- Reviewed remaining case notes (n=196)

Created clinical/pathological database combining lab data, PAS records and case notes

Age distribution analysis performed (Fig 1)

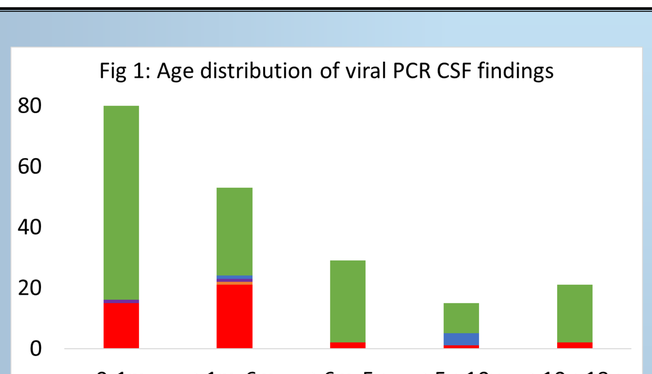
Compared EV CSF PCR +ve/ -ve results (excluding SCBU) (n=136) with data below:

- Adjusted CSF WCC based on RBC count using a 1(WCC):500(RBC) ratio (Fig 2)
- Peripheral WCC and CRP count (Figs 3a and 3b)
- Antibiotics given and antibiotic duration (Figs 4a and 4b)
- Whether admitted to HDU (Fig 5) and LOS (Fig 6)

LABORATORY ANALYSIS/ RESULTS

- 49/196 CSF samples were PCR +ve across all age ranges
- 41 (19.9%) +ve for EV
- HSV 1/2, VZV and HHV-6 detected in 2 (1.0%), 5 (2.6%) and 1 (0.51%), respectively
- Most EV cases amongst infants aged 1- 6m (21/39, 54%)
- Followed by infants aged <1m (15/39, 38%)
- Additional analysis done on infants (non SCBU) and children (n=136) (Figs 2-6)

Fig 1: Age distribution of viral PCR CSF findings



EV Lab markers (n=136)

Fig 2: Adjusted CSF WCC vs EV PCR result

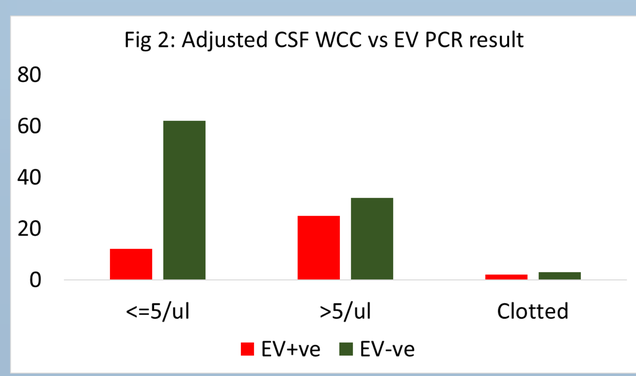


Fig 3a: First peripheral WCC count vs EV PCR result

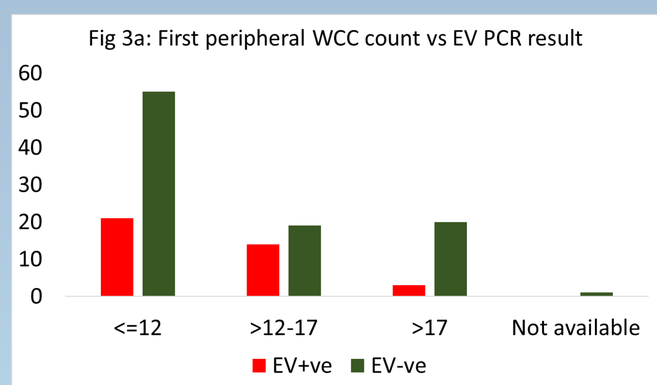
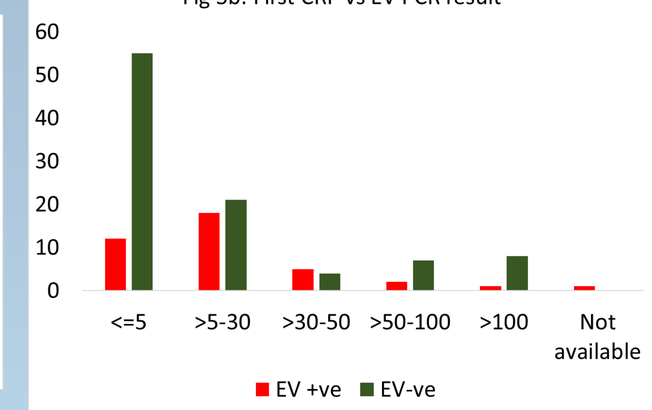


Fig 3b: First CRP vs EV PCR result



EV clinical outcomes (n=136)

Fig 4a: Were antibiotics given?

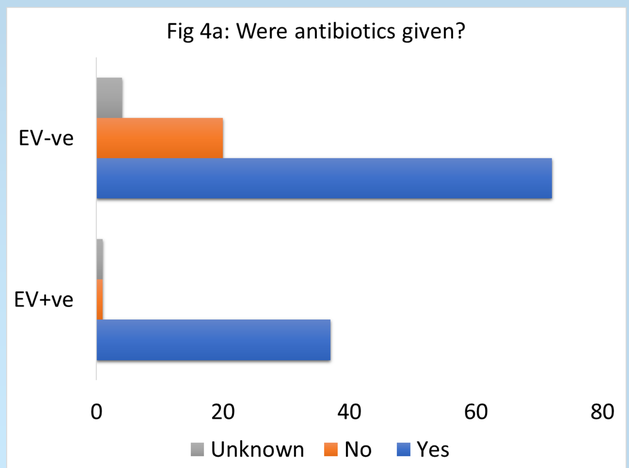


Fig 4b: EV PCR result vs antibiotic duration (days)

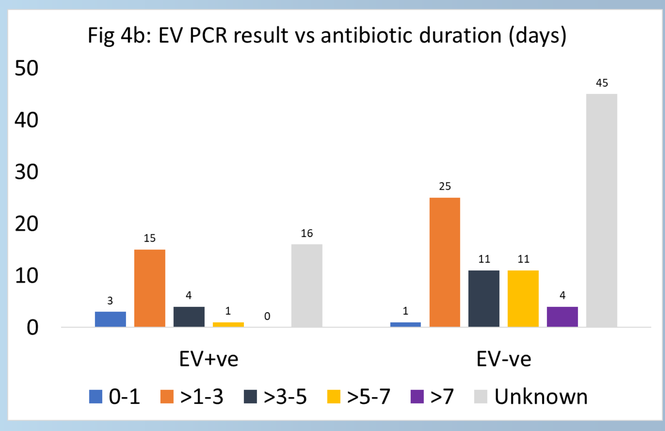


Fig 5: Admitted to HDU?

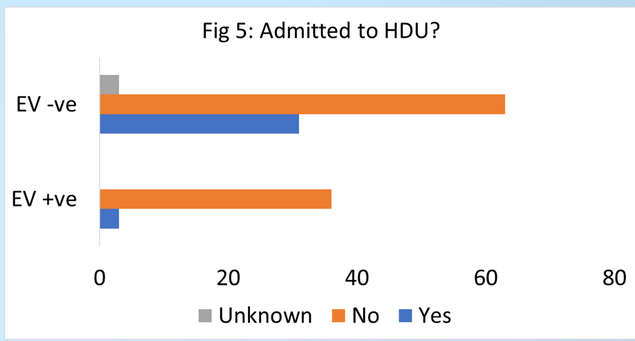
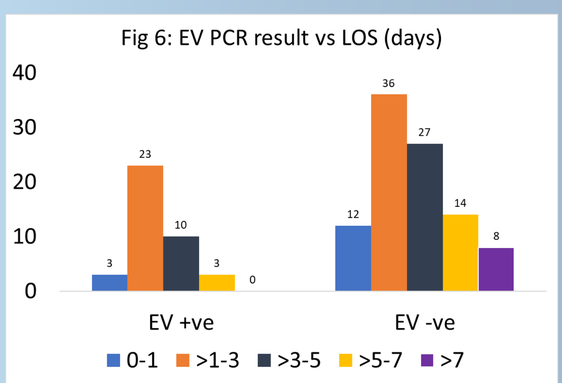


Fig 6: EV PCR result vs LOS (days)



DISCUSSION/ CONCLUSIONS

Retrospective study evaluated laboratory and clinical outcomes for EV meningitis in infants and children

- SCBU excluded as management different with relatively low numbers of positives (2/60 CSFs EV +ve, 3.3%)
- Most diagnosis aged <6m old (34/79 CSFs EV +ve if <6m)
- Relatively few >6m old (5/57 CSFs EV +ve if >6m) reflecting adult incidence[3]
- Most cases healthy infants with non-severe infection – need to be aware of changing epidemiology, outbreaks and/ or more pathogenic strains (e.g. EV D68/ 71)[4]

Focus needs to be on infants <6m old taking into account presentation including severity, past medical history and laboratory parameters below

Analysis of laboratory parameters (EBV PCR +ve vs PCR –ve):

- Adjusted CSF WCC (Fig 2) – cut off <5/µl would have missed 32% (12/37)
- CRP (Fig 3a) – cut off ≤50 mg/L would have detected 92.5% (37/39)
- Peripheral WCC (Fig 3b) – cut off <17/µl would have detected 92.3 % (36/39)

Analysis of clinical outcomes (EBV PCR +ve vs PCR –ve):

- Use of antibiotics (Fig 4a) greater with EV meningitis – 97% vs 78%
- Mean Duration reduced (Fig 4b) - 2.8 vs 3.9 days (excludes >7 days/ unknown)
- Requirement to admit to HDU reduced - 7.7% vs 33%
- Mean Length of Stay (LOS) - 3.3 vs 4.7 days (excludes >10 days)

Suggested guidance for suspected EV meningitis to improve care pathways:

- Focus on optimal age for viral PCR testing (<6m old)
- EV PCR irrespective of adjusted CSF WCC (<6m old)
- Review of antibiotics/ antivirals 24h as part of antimicrobial stewardship
- Promote earlier discharge if EV PCR +ve with safety netting
- Provide reassurance to the parents/carers concerning overall prognosis

BIBLIOGRAPHY

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4) Holm-Hansen CC, Midgley SE, Fischer TK. Global emergence of enterovirus D68: a systematic review. Lancet Infect Dis 2016; 16:e64.

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