Enterovirus Epidemiology in a UK Midlands Population: 2014-2016

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SUMMARY: We report a number of cases (n=102) of enterovirus (EV) infections in paediatric and adult patients, admitted with suspected sepsis or meningitis in UK Midlands during Jan 2014 to Dec 2016. Although clinically impossible to differentiate on admission, we show that Coxsackie B viruses appear to cause more severe infections than echoviruses, on the basis of laboratory parameter derangement. Serotyping also identified cases of EV D68 and EV 71, the two strains known to cause more severe neurological complications in children, though in these cases, fortunately, no such complications arose.

BACKGROUND: Enteroviruses are non-enveloped, single-stranded, positive-sense RNA viruses. They are members of the Picornavirus family and exhibit over 100 serotypes[1]. They cause a wide variety of paediatric and adult infections including neonatal sepsis, viral (aseptic) meningitis and other neurological disorders[2], and hand-foot-and-mouth-disease (HFMD)[3]. Here we present a 3-year (2014-2016) analysis of enteroviruses circulating in this UK Midlands population, using both clinical and viral serotyping data.

References: 1) Biologicals 1993;21:305-9; 2) Am J Epidemiol 1969;90:244-54; 3) Ped Infect Dis J 2016;35:e285-e300; 4) Lancet 2015;385:1662-71; 5) Kor J Ped 2016;59:395; 6) J Clin Virol 2015;64:92-6; 7) J Clin Virol 2015;69:172-5.

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MATERIAL/METHODS: All EV-positive cerebrospinal fluid (CSF) samples, which were tested as part of routine clinical work-up for paediatric sepsis or adult meningitis/encephalitis, were included during this 3-year retrospective study period. Clinical data was extracted for each of these patients and were compared between EV serotypes using the Fisher Exact or Mann-Whitney test as appropriate (Table 1). Enterovirus serotyping was performed at the UK national reference laboratory (Colindale PHE Enteric Virus Unit), using partial VP1 gene sequences.

RESULTS/ DISCUSSION: Of the 102 patients, 27 had Coxsackie A, 15 Coxsackie B and 60 echovirus; the most common EV serotypes detected were CA6, CB5, E18, E6 and E9 (Fig. 1). EV D68 was found in the respiratory swab of an ex-premature, now 5-month old baby with bronchiolitis, discharged home after a 5-day stay. EV 71 was found in a skin swab from a case of uncomplicated HFMD in a 2-year old child, discharged home on the same day of admission. Neither case had any neurological complications. Due to relatively little available clinical data for the patients with Coxsackie A infections, the statistical analysis was only performed for Coxsackie B viruses (CBVs) versus echoviruses. The results for this cohort showed that CBV was associated with increased length of stay (LOS), higher lymphocytosis, higher CSF protein and higher CSF lymphocytosis, but lower CRP (C-reactive protein), compared to echoviruses (Table 1). Although the clinical management is similar (in the absence of any specific antiviral treatment) for all EV serotypes, the availability of real-time serotyping may be useful to give clinical teams an indication of which cases may develop more severe disease, and therefore need closer monitoring – especially neonates.

Enterovirus surveillance, particularly in paediatric patients, is important to identify specific EV serotypes that can cause more severe disease, e.g. EV D68 and EV 71, which are currently relatively rare in this UK population. These serotypes are well-known to be a cause of hand-foot-mouth disease, but in particular, have been frequently reported to cause more serious neurological complications, including acute flaccid paralysis[4] and brainstem encephalitis[5]. Periodic, national surveillance will alert paediatricians to the presence of these viruses circulating in the community and prepare them to potentially manage more cases of severe respiratory and neurological disease in some patients, e.g. treatment with intravenous immunoglobulin (IVIG - though the benefits of this intervention are somewhat variable)[6,7].

CONCLUSIONS: In this mixed paediatric and adult UK Midlands population, presenting with sepsis or viral meningitis, multiple EV serotypes were identified in CSF samples. An analysis of the laboratory parameters from these patients showed evidence of more severe disease caused by Coxsackie B viruses compared to echoviruses. However, further larger studies are warranted to confirm this finding in other populations.

Fig. 1. Showing the distribution of EV serotypes in this UK Midlands population during a 3-year period (2014-2016, inclusive). CA–Coxsackie A; CB–Coxsackie B; E–echovirus; EV–enterovirus (numbered strains).

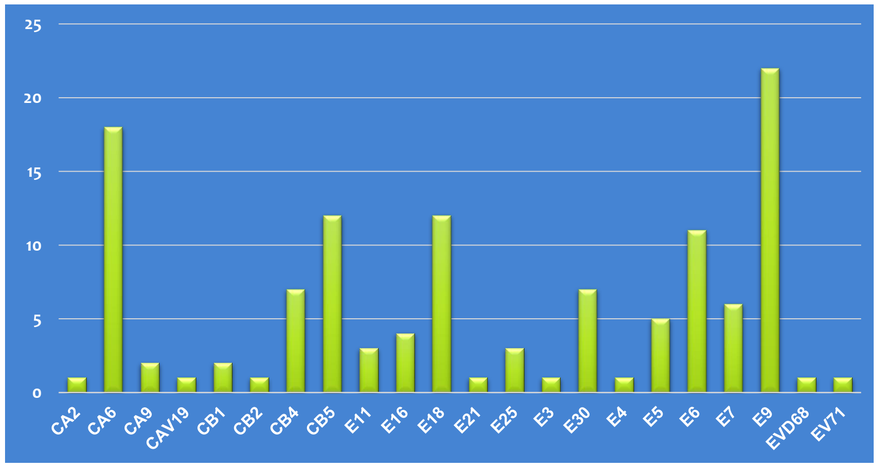

Table 1. Clinical parameters analysed to compare the severity of illness in patients infected with Coxsackie B vs. echoviruses. LOS-length of stay; CRP-C-reactive protein; CSF-cerebrospinal fluid; WCC-white cell count.

Parameters		Coxscakie B Virus		Echovirus	p-value
Age (year)	n	median (Q1-Q3) or %	n	median (Q1-Q3) or %	
0-1	12/15	80%	31/60	52%	0.1412
2-19	0/15	0%	6/60	10%	
20-68	3/15	20%	23/60	38%	
LOS (days)	15	4 (3-6)	60	3 (2-4)	0.0325
CRP	15	5 (3-9)	59	14 (3-28)	0.0195
Lymphocytes (blood)	15	5.44 (2.44-7.51)	57	2.36 (1.23-3.9)	0.0105
CSF protein	15	0.64 (0.43-0.98)	58	0.435 (0.38-0.59)	0.0283
CSF WCC	15	103 (75-417)	57	29 (4-97)	0.0085