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Short communication

Enterovirus D68 disease and molecular epidemiology in Australia

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ABSTRACT

Background: Enterovirus D68 (EV-D68) has received considerable recent attention as a cause of widespread respiratory illness. Neurological syndromes such as acute flaccid paralysis following EV-D68 infection have also been reported in a small number of cases.
Objectives: To summarize the clinical and epidemiological characteristics of laboratory confirmed EV-D68 cases in Australia.
Study design: We combined EV-D68 data acquired through laboratory surveillance in Western Australia with cases from national *enterovirus* surveillance and regional acute flaccid paralysis (AFP) surveillance. Clinical data was obtained for EV-D68 cases and capsid protein sequences were used for phylogenetic analysis.
Results: Sporadic cases of EV-D68 were recorded in Australia since 2008, with peaks in activity during 2011 and 2013. EV-D68 was primarily associated with respiratory disease, but was also detected in cerebrospinal fluid of one patient and faeces of two patients presenting with AFP.
Conclusions: EV-D68 has been circulating in Western Australia and is likely to have also been present in the wider region for a number of years, causing primarily respiratory disease. Detection of EV-D68 in cerebrospinal fluid of one patient and in faeces of two AFP cases reinforces the association between EV-D68 and neurological disease.

1. Background

Enterovirus D68 (EV-D68) has emerged as a common cause of respiratory illness worldwide [1–5]. Recent outbreaks have caused numerous cases of respiratory disease [6,7], with acute flaccid paralysis (AFP) or other neurological syndromes following infection in a small minority of cases [8–11].

2. Objectives

EV-D68 data from surveillance networks in Australia was pooled in order to describe the epidemiology of EV-D68 in the region, including clinical presentations, seasonality and distribution patterns. Capsid protein sequences were used to compare the Australian EV-D68 strains to those from other regions.

3. Study design

In Western Australia (WA) 55 EV-D68 cases have been identified since 2007 as part of routine *enterovirus* screening at PathWest Laboratory Medicine WA. A further three cases were identified through regional AFP and national *enterovirus* surveillance by the

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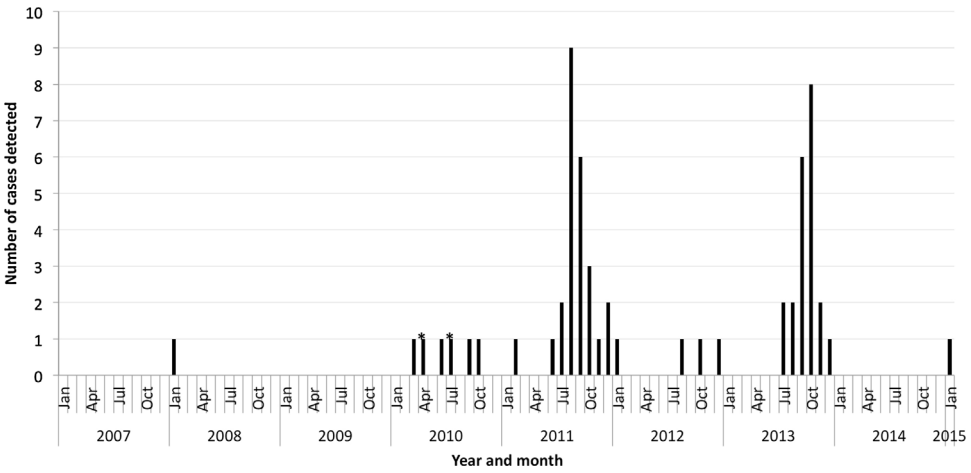

Fig. 1. Temporal distribution of EV-D68 in Australia 2007–2014. *Denotes the two AFP cases.

National *enterovirus* Reference Laboratory. As *enterovirus* screening of respiratory samples from community patients is uncommonly performed in WA, the majority of the WA EV-D68 cases (85%) were from hospitalised patients. *Enteroviruses* were detected by RT-PCR [12] and genotypes identified by sequencing a portion of the 5′ non-translated region. Where possible a portion of the capsid protein VP1 was sequenced [13] and used for phylogenetic analysis.

4. Results

The first EV-D68 case in WA was identified early in 2008 and there were two periods of heightened EV-D68 activity from July–October (winter–spring) of 2011 and 2013 (Fig. 1). These peaks coincided with the WA influenza seasons of 2011 and 2013, and did not coincide with peaks in rhinovirus activity (data not shown).

The majority of the EV-D68 cases (52; 90%) were detected from respiratory samples, of which 46 were upper respiratory samples. Five patients, including two AFP cases, had faeces or rectal swabs collected. There was one case where EV-D68 was detected in cerebrospinal fluid (CSF) from a patient without other samples collected for *enterovirus* testing. Multiple samples from three patients demonstrated EV-D68 persistence for 12, 19 and 22 days. All three patients were immunosuppressed and were aged 21 years, 9 months and 2 years, respectively. A further five patients had enteroviral co-infections; with coxsackievirus A, echovirus 3, rhinovirus B and two patients with rhinovirus A.

The mean age of patients with EV-D68 was 8.5 years (range 10 days–81 years) with 49% (27 cases) in children aged between 6 months and five years, 27% (15 cases) in children aged 5–15 years and 13% (7 cases) in adults (Table 1). The male to female ratio of EV-D68 cases was 1.9:1, with significantly ($p = 0.0146$) less fever recorded in the males. Respiratory symptoms were most frequently reported following EV-D68 infection in WA, with 29 cases (53%) of lower airway disease (Table 1) including 21 cases (38%) where asthma or wheeze was reported and 6 cases of bronchiolitis (11%). There were eight cases of pneumonia (14%) and five patients had upper respiratory tract infections (9%). Fever was reported in only 12 cases (22%), headache or malaise in 3 cases (5%) and rash in one case (2%). EV-D68 was detected in CSF from a 25 year old male patient who presented with meningism as part of a febrile illness but self-discharged after several hours. There was no pleocytosis and protein levels in CSF were normal. EV-D68 was detected in faeces of two AFP cases, both of which occurred in 2010: the first a 22 month old child from New South Wales, diagnosed with spinal cord ischaemia. The second a six-year-old from the Solomon Islands who presented with right leg paralysis. EV-D68 was also identified in ileostomy fluid of an 11-year-old Victorian child experiencing abdominal pain and lethargy with acute frank blood loss from the ileostomy. None of the patients died as a result of EV-D68 infection. Sixteen of the patients identified in WA (29%) were immunosuppressed (cancer therapy 11; transplant recipient 2; neutropaenic 1; HIV 1; multiple congenital abnormalities 1) when infected, with similar presentations to those not immunosuppressed, except lower airway disease which was less common in the immunosuppressed patients ($p < 0.0001$).

Table 1
Demographic and clinical characteristics of EV-D68 cases identified in Western Australia.

Parameter	Number of cases (%)	Fever (%)	Upper respiratory symptoms/cough (%)	Lower respiratory airways disease (%)[a]	Pneumonia (%)
Age					
<6 months	6 (11)	0	1 (17)	3 (50)	1 (17)
6 months–5 years	27 (49)	5 (19)	1 (4)	19 (70)	3 (11)
5–15 years	15 (27)	5 (33)	1 (7)	6 (40)	2 (13)
>15 years	7 (13)	2 (29)	2 (29)	1 (14)	2 (29)
Immunosuppression					
Yes	16 (29)	6 (38)	3 (19)	1 (6)	3 (19)
No	39 (71)	6 (15)	2 (5)	28 (72)	5 (13)
Sex					
Female	19 (34)	8 (42)	1 (5)	9 (47)	2 (10)
Male	36 (65)	4 (11)	4 (11)	20 (56)	6 (17)

[a] Asthma, wheeze, bronchiolitis.