

Characterization of Cutaneous Findings in the Enterovirus Outbreak of 2011-2012

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Introduction

- Most outbreaks of hand, foot and mouth disease (HFMD) in North America are caused by Coxsackie A16.
- Beginning in November 2011, there were an increasing number of reports of atypical HFMD many of which were associated with Coxsackie A6 (CVA6), a virus uncommonly seen in the US.
- There have been international reports of CVA6 outbreaks in Finland, Taiwan, Japan and Singapore starting as early as 2008.
- The rash associated with CVA6 has been described as “more severe,” but has not been well characterized.
- Our aim was to characterize the cutaneous findings of this exanthem that diverge from typical HFMD.

Methods

Study Design

- Multi-institutional, retrospective, case series of a convenience sample of patients evaluated by pediatric dermatologists with atypical presentations of HFMD.

Inclusion Criteria

- Viral confirmation of CVA6 or met the clinical case criteria (see below).

Exclusion Criteria

- Presentation could be explained by another named illness
- Presentation consistent with classic HFMD with <5% body surface area (BSA) involved.

Clinical Case Criteria

- **Definite case:** CVA6 confirmed via rtPCR in oropharynx, skin, blood, or stool
- **Probable case:** At least 1 criterion from group 1, and at least 1 from group 2

Group 1 (Features suggestive of HFMD)

- Enterovirus PCR positive
- Exanthem characteristic of coxsackie infection
- Exanthem with some vesicles classic for Coxsackie infection
- History of exposure to HFMD 2-14 days prior to disease onset

Group 2 (Unusual Morphology or Extent)

- Exanthem more extensive than classic HFMD (>5% BSA)
- Erosions, vesicles and bullae with acrofacial accentuation
- Purpuric/petechial/hemorrhagic lesions
- Gianotti-Crosti-like eruption
- Large bullae

Viral Testing

When ordered by the clinician, enterovirus typing was performed using rtPCR by the Centers for Disease Control or the California Department of Public Health.

Statistical Analysis

- Data was collected and analyzed using Excel

Results

Table 1. Demographics (N=64)

Age	Mean	2.9 years (SD 3.7)
	Median	1.4 years
	Range	4 months - 16 years
Gender	Male	30 (47%)
	Female	34 (53%)
Race/ethnicity	White	35 (55%)
	African American	13 (20%)
	Hispanic/Latino	7 (11%)
	Asian	7 (11%)
Pre-existing skin condition (N = 62)	Atopic dermatitis	37 (58%)
	Sunburn	2 (3%)
	Diaper dermatitis	2 (3%)
	Seborrheic dermatitis	1 (1.5%)
	Tinea pedis	1 (1.5%)

Results

Table 2. Cutaneous features: location and morphology [# positive/# reported (%)].

Location	Palms/soles	51 /64 (80%)
	Extremities	63/63 (100%)
	Face	52/64 (81%)
	Torso	35/64 (55%)
	Buttocks, groin, perineum	45/57 (79%)
	Oropharyngeal erosions/ulcers	29/61 (48%)
	Nail Changes	7/29 (24%)
Lesional morphology	Vesicles	55/60 (92%)
	Bullae	6/47 (13%)
	Erosions	55/61 (90%)
	Papules	61/62 (98%)
Other morphologic features	Eczema herpeticum-like	36/64 (56%)
	Other <i>locus minoris</i>	13/60 (22%)
	Gianotti-Crosti-like	21/60 (35%)
	Hemorrhagic/purpuric/petechial	11/62 (18%)

Figure 1. Two toddlers with erosions localized to areas of atopic dermatitis. (a) CVA6 positive.



Figure 2. (a) 13 yo with facial erosions and vesicles and acral hemorrhagic lesions. CVA6 positive. (b) 7 yo with OP erosions and acral purpuric papules.



Figure 3. A toddler with vesicles in a sunburned area; CVA6 positive.



Figure 4. Prominent periorificial involvement.



Figure 5. Tongue erosions. CVA6 positive.



Figure 6. Acral vesicles and bullae. CVA6 positive.



Figure 7. 4 mo infant with large acral bullae. CVA6 isolated from bulla fluid.



Results

Figure 8.

Body Surface Area Affected

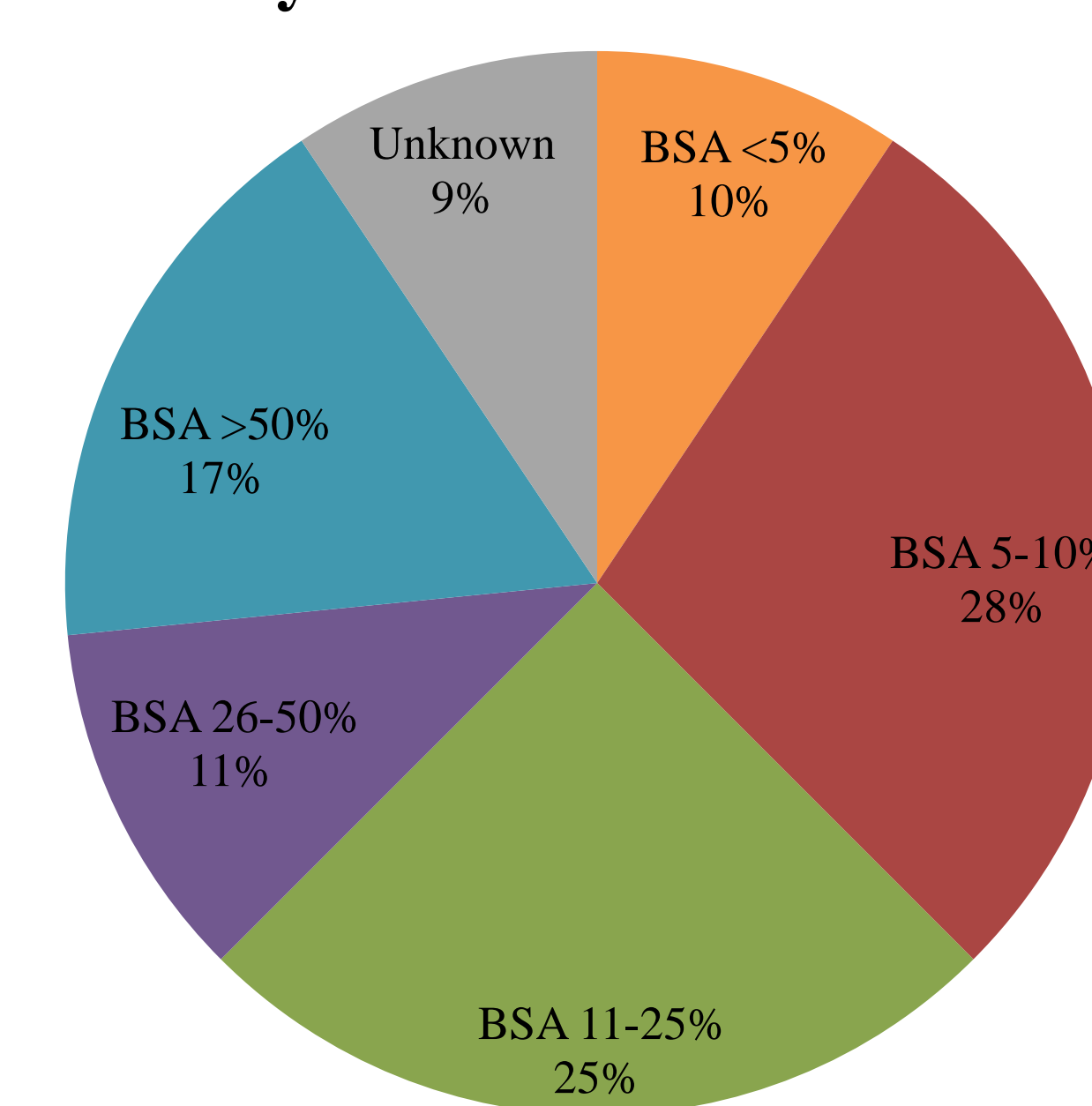


Figure 9.

Number of Atypical Enterovirus Cases by Month of Presentation

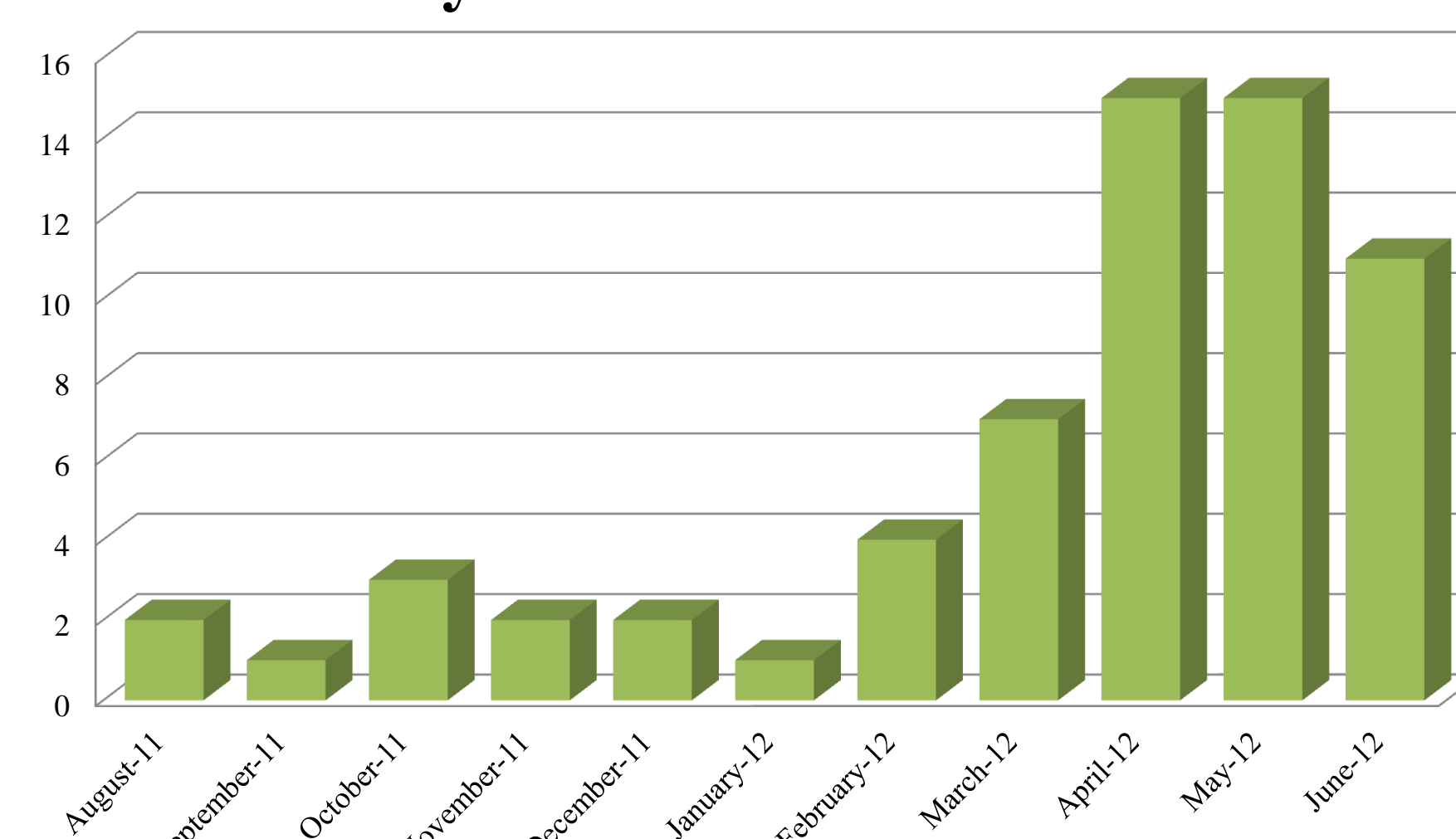


Table 3. Clinical features [# positive/# reported (%)].

Symptoms	Fever	42 (66%)
	Sore throat/mouth	21 (33%)
	Vomiting	5/54 (9%)
	Diarrhea	6 /58 (10%)
	Cough	8 /50 (16%)
	Dehydration	5/49 (10%)
	Headache	1/37 (3%)
	Breathing difficulty	1/45 (2%)
	Stiff neck	0/35 (0%)
Exposures (N=64)	Family	9 (14%)
	Daycare/school	22 (34%)
	Other	3 (5%)

Table 4. Diagnostic tests performed

Diagnostic Test	#Positive	#Sent
Enterovirus PCR	18	19
Coxsackie A6 PCR	14 (2 pending)	16
Viral culture	0	13
HSV (DFA, Cx, PCR)	0	18
VZV (DFA, PCR)	0	2
Bacterial culture (MRSA, MSSA)		9
Skin biopsy	*	4

*Skin histopathology results: (1) Acute spongiotic dermatitis; (2) Focal interface dermatitis with mild spongiosis consistent with viral exanthem; (3) Spongiosis, papillary dermal edema, superficial and deep perivascular and periadnexal lymphocytic infiltrate; (4) Dermal inflammatory infiltrate with prominent neutrophils and focal exostosis. DIF negative

Conclusions

- The exanthem associated with the enterovirus outbreak of 2011-2012 has an atypical presentation that in many cases has been proven to be due to a unique serotype, CVA6.
- The atypical features of this outbreak are:
 - Large BSA involvement – the majority have >10% BSA.
 - Frequent “eczema coxsackicum,” i.e. eczema herpeticum-like presentation
 - Accentuation in areas of skin injury or irritation (*locus minoris*)
 - Prominent facial involvement
 - Less oropharyngeal involvement than classic HFMD
- Onychomadesis has been reported to be a common feature following CVA6 infection, but we could not fully assess nail changes because of short follow-up time.
- Associated systemic symptoms do not appear to be more severe than in typical HFMD.
- Clinicians should be aware of this atypical presentation that mimics vasculitis, eczema herpeticum, and primary bullous disorders to avoid misdiagnosis and unnecessary interventions.
- Enterovirus PCR of skin, oropharynx, perirectum, or blood can be diagnostic. Viral culture is not recommended as CVA6 does not grow well in culture.

References

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