Case Report

Acute Flaccid Paralysis in Single Upper Limb with HFMD from Enterovirus71 Infection: Case Report and Review of the Literature

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Background: Human enterovirus71 [EV71] infection caused hand-foot-mouth disease [HFMD]. Although most of the symptoms are mild with fever and painful vesicular lesions on the hands, mouth, and oral mucosa, some patients developed serious neurological complications including acute brain stem encephalitis, aseptic meningitis, acute flaccid paralysis [AFP] mimicking paralytic poliomyelitis, Guillain-Barre syndrome, transverse myelitis, and cerebellar ataxia. The worldwide eradication of poliomyelitis, EV71 is the one of important causes of AFP.

Objective: To report a 1-year-old male patient who developed AFP in upper limb two days after the onset of HFMD.

Case Report: EV71 was isolated from a stool specimen after two days onset of AFP. The spinal magnetic resonance imaging [MRI] indicated that there was long strip high signal on T2WI and low signal on T1WI in cervical spinal cord at the level of C3 to C6 levels on sagittal images and low signal on T1WI and high signal on T2WI in unilateral anterior horn. He was treated with vitamin B1-6-12 and physical rehabilitation and still had residual motor weakness on proximal muscle at one-year follow-up.

Conclusion: EV71 infection was related to acute flaccid poliomyelitis-like. MRI showed the damage at anterior horn of the spinal cord with clinical correlation. Prognosis was poor because there was no established anti-viral treatments or ancillary treatments available for EV71, resulting in persistent motor weakness at long-term follow-up. Multi-limb paralysis and limbs weakness distribution with both upper and lower limbs weakness is the clinical predictive prognosis.

Keywords: Enterovirus71, Acute flaccid paralysis, Hand-foot-mouth disease, Neurological complication

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Hand-foot-mouth disease [HFMD] is an epidemic disease occurring around the world. The typical skin lesions develop after two to three days of febrile illness characterized by multiple fluid-filled blisters appearing on the hands, feet, and inside the mouth. Enterovirus71 [EV71] is a common cause of HFMD[1-8] and associated with serious clinical manifestations characterized by acute brain stem encephalitis, aseptic meningitis, acute flaccid poliomyelitis-like paralysis, Guillain-Barre syndrome, transverse myelitis, and cerebellar ataxia[9-21]. Since the worldwide eradication of poliomyelitis, EV71 has been one of the important causes of acute flaccid paralysis [AFP][22]. Sixty-five cases were detected and reported AFP associated with EV71 infection from eleven outbreaks between 1973 and 2012.

We are reporting a one-year-old male patient who developed AFP in single upper limb two days after the onset of HFMD. We did a literature review of the pathogenesis, clinical presentation, diagnostic assessment, outcome measure, and clinical predictive prognosis.

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Case Report

A one-year-old, Thai male patient experienced acute onset of the right arm flaccid paralysis following 2-day period of prodromal with fever and HFMD. The motor power of right deltoid, biceps, and hand grip were graded 0 and absent deep tendon reflexes. His consciousness was preserved and the brainstem was also intact. At the onset of acute paralysis, he still had high grade fever and skin lesions.

He was referred and admitted at Naresuan University Hospital on day 5 of AFP. He was afebrile and had normal consciousness. The muscle strength of right wrist and hand grip were forth level on the Medical Research Council [MRC] scale and the right deltoid and the right bicep were second and third level,

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respectively. Right bicep and triceps tendon reflexes were diminished. Other neurological examinations were normal. Due to gradually clinical improvement, her parents asked to delay the appointment for lumbar puncture and magnetic resonance imaging [MRI] as scheduled.

The cerebrospinal fluid [CSF] was obtained due to the persistent weakness as well as MRI, both were performed at 1 month after ictus. CSF glucose and CSF protein were 62 mg/dl and 23.5 mg/dl, respectively, with traumatic tab (RBC 1,000 cells/cumm, WBC 3 cells/cumm with neutrophil 1 cell and lymphocyte 2 cells). The spinal MRI (Figure 1) indicated long strip high signal on T2-weighted image [T2WI] and low signal on T1-weighted image [T1WI] in cervical spinal cord at the level of C3 to C6 levels, and on sagittal images with low signal on T1WI and high signal on T2WI in unilateral anterior horn. The contrast-enhanced T1WIs did not show enhancement of the anterior horn cell lesions. EV71 was isolated from a stool specimen after two days onset of AFP. The stool was repeatedly cultured on day 4 after AFP and CFS polymerase chain reaction [PCR] for enterovirus was performed, which the results were both negative. He was treated with vitamin B1-6-12 and physical rehabilitation.

After one-year following-up, he was full recovered in distal muscle strength and muscle tone but still had residual motor weakness of proximal limb to strengthen II-III level.

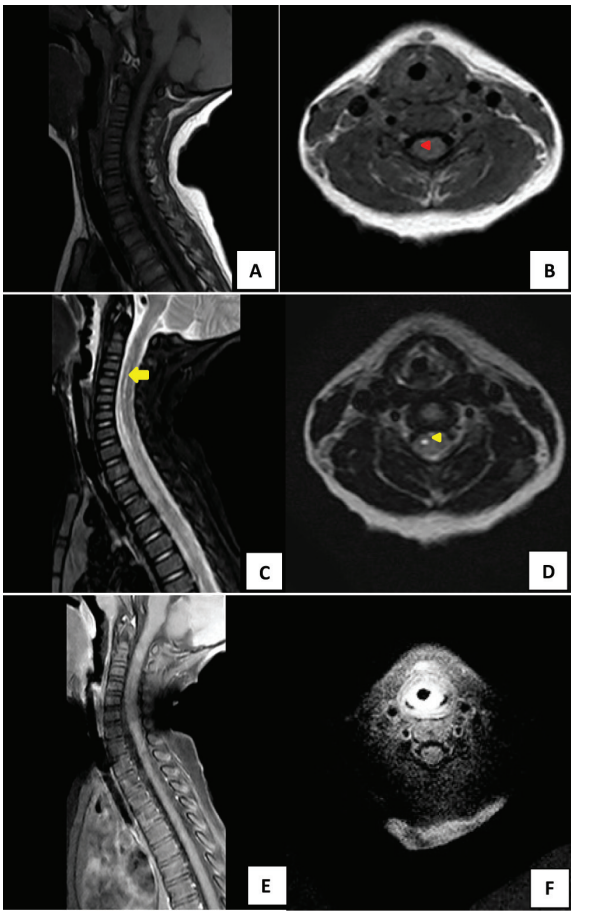

Figure 1. Persistent weakness of right upper limb 1 months after EV71 infection. A, B) Unenhanced saggittal and axial T1-weighted image shows hypointense lesions in the anterior horn cells of spinal cord at C5 level (arrowhead). C) Sagittal fast spin-echo T2-weighted (STIR) image shows a long-segment hyperintense lesion extending from C3 to C6 levels in the right anterior horn region (arrow). D) Axial fast spin-echo T2-weighted image at the same level as in B shows a hyperintense lesion in the right anterior horn region (arrowhead). E, F) Contrast-enhanced T1-weighted images do not show enhancement of the anterior horn cell lesions.

Discussion

HFMD is an epidemic disease that occurs around the world. Several enterovirus under the family Piconarviridae cause HFMD including human EV71, coxackievirus, and ECHO virus[1-8]. Age related to infection is identified as 4-years-old or younger children[8,9,23-26] and the fatality rate is highest in infants at the age between 7 and 12 months old[18]. Epidemic EV71 infection is associated with variety of symptoms from mild fever, herpangina, HFMD to serious neurological complication such as acute brainstem encephalitis, aseptic meningitis, GBS, acute transverse myelitis, acute cerebellar ataxia, and AFP[11-14,18,22,26-29]. Most of the children with rhombencephalitis experience cardiopulmonary complication associated with high mortality rate[2,4,8,11,19,26,33-37].

AFP is defined as the acute onset of flaccid limbs and absent tendon reflexes. EV71 related to AFP in HFMD is often seen in child less than three years old and has become one of the causes of AFP since the poliomyelitis has been eradicated through immunization[22,38]. The incidence rate of AFP with EV71 related to HFMD reported in 1973 in Japan outbreak was 2%[39,40], in 1975 in Bulgaria was 7.4%[41,42], in 1977 in New York was 17%[38], in 1978 in Hungary was 4%[43], between 1988 and 1990 in Brazil was 58%[28], in 1998 in Taiwan was 10%[12,27,29], in 1999 in Western Australia was 1%[30], between 2003 and 2005 in Denver was 31%[31], and between 2008 and 2012 in China was 12.5%[32].

In 2011, an outbreak of HFMD affected 17,562

children in Thailand. Of these, six patients died and EV71 was recovered from two fatal rhombencephalitis cases[45]. Recent study, in 2012 by Jiratchaya et al showed 704 cases of HFMD where EV71 was identified in 62 HFMD patients (8.8%)[1]. Extremely high infection rate was observed in 1-year-old infant and higher incidence rate was found in the fall season, possibly attributable to contaminated water and environment[45]. However, no patients having AFP with EV71 related HFMD had been reported in Thailand. In the present review, we reported a 1-year-old male patient who developed AFP in single upper limb two days after the onset of HFMD.

Previously, few studies reported on EV71 related with AFP (Table 1). Between 1973 and 2012, 65 cases of AFP associated with EV71 infection were detected and reported. About 90% of patients presented at less than two years of age. Cutaneous findings included multiple ulcers in the throat and soft palate, accompanied by rash or small vesicles on palms and soles (41 cases), oral ulcers (4 cases), erythema (1 case) and no skin lesion (6 cases). The symptoms of AFP can develop in 2- to 4-day period of prodromal illness with fever and skin lesion. Depending on the site of infection, acute onset of flaccid paralysis could be involved with one or more limbs in both upper and lower extremities. The unilateral weakness was often associated with upper limbs and the bilateral weakness usually involving lower limbs. Acute evolving flaccid quadriparesis was observed in six cases associated with acute brain stem encephalitis.

For diagnoses, mild CSF lymphocytic pleocytosis of 10 to 100 cells per μL is typical, but occasionally there may be none. The CSF protein and glucose concentration in CSF to plasma ratio is generally normal[37]. Enterovirus is more common isolates from stool/rectum, throat and vesicle fluid. Viral shedding from gastrointestinal tract can be detected in the throat and stool up to 2 and 11 weeks after recover from HFMD or herpangina, respectively[42,46-48]. EV71-RNA in stool is significantly more frequent in severe cases[36]. Serum EV71-RNA is detected positive in 60% of severe cases and in 84.25% of uncomplicated cases, but in only 0% to 5% of CSF samples from patients with neurological diseases that are identified as virulent pathogen by culture or PCR[12,36,43,48]. The amplicon PCR assay is more sensitive than viral culture and is independent of the delay between the onset of symptoms and CSF collection, whereas the viral cultures are all negative in the sample collected more than 24 hours after the onset of symptoms in patients with enteroviral meningitis[49]. MRI is currently the preferred diagnostic modality for neurologic complications in children with EV71-infected HFMD characterize by hypo-intensity on T1WI and hyper-intensity on T2WI predominantly involve anterior horn regions of spinal cord. In severe cases, the lesions may undergo cavity change[41,50-52].

The pathological changes and pathogenesis in AFP of EV71 related HFMD were reviewed. The pathology showed EV71 infection had specific involvement in the same region as polio virus including dorsal nucleus of vagus nerve, medial longitudinal fasciculus, nucleus tractus solitary in dorsal medulla, abdocens nerve nucleus in dorsal pons, red nucleus, substantianigra, nucleus of trochlear nerve in the middle part of midbrain, putamen, thalamus, and anterior horn cell of spinal cord[11,53,54]. These affected mainly in the gray matter and inflammatory responses were demonstrated in autopsy[37]. EV71 neuropathogenesis is still not fully understood[55]. The EV71 virus is transmitted via the fecal-oral route of infection and causes persistent viremia and direct movement through the blood-brain-barrier. The rapid progression to neurological and cardiopulmonary complications within 3 to 5 days after the onset of EV71 infection and the positive staining of enteroviral antigens and nucleic acids in neurons of fatal cases suggested that viral replication and direct cytopathic effects of the virus on the host cells[19,37,56]. Degeneration and necrosis is one mechanism of neuronal damage. Another mechanism is explained by occlusive vasculitis from the inflammatory cells infiltration that leads to nucleus in grey matter ischemic change[57,58]. Recent studies suggested that EV71 infection increased the enhanced expression of IL-1, IL-6, IL-10, IL-13, IFN-γ, and TNF and associated with life-threatening complications[4,10,59-61]. To decrease the mortality rate in case of severe EV71 infection such as brain stem encephalitis, the expression of IFN-γ-inducible protein 10 [IP-10] to enhance viral clearance, increase IFN-γ expression and boost the infiltration of CD8 T cells are found in the plasma and CSF with kinetics similar to viral titers in the blood and brain[4]. Recent transgenic animal model studies demonstrated the specific viral receptor, Human Scavenger receptor B2 [SCARB2][62-65] and P-selectin glycoprotein ligand-1 [PSGL-1][69-71], related to neurological diseases in vivo and may induce the local production of proinflammatory cytokines such as IP-10, MCP-1, IL-6, IL-8, and G-CSF levels, which had much higher levels in CSF than in plasma from patients with neurological damage[69-71].

Table 1. Previously reported prevalence of acute flaccid paralysis in infants and young children with enterovirus71 [EV71] infection

	Age (month)	Skin lesion	Neurological complication/ AFP	MRI	CSF parameter: WBC (cells/mm^3) RBC (cells/mm^3) Protein (mg/dL) Glucose (mg/dL)	Positive EV71 specimens	Treatment/outcome	Reference
Japan 1973 (2 cases)	NA	HFMD	Both monoparesis lower extremities	NA	NA	NA	Both patients recovered in 40 days	39
Bulgaria 1975-1976 (8 cases)	NA	NA	NA	NA	NA	All feces	All recovered	41
New York 1977 (2 cases)	F/2	No skin rash	Aseptic meningitis, RLL paralysis	NA	WBC 165 L87% Protein 26 Glucose 100	Feces, throat viral culture	Fully recovered at 4 months followed-up	38
	F/16	No skin rash	Meningoencephalitis, urinary incontinence, RLL paralysis	NA	WBC 30 L50% Protein 16 Glucose 64	Serology/paired serum antibodies	Fully recovered in 1 week	
Hong Kong 1985 (5 cases)	81	Oral ulceration	RUL	NA	WBC 0	Serology/paired serum antibodies	Recovered	44
	9	HFMD	RUL	NA	WBC 500 L55%	Serology/paired serum antibodies	Recovered	
	17	HFMD	LUL	NA		Serology/paired serum antibodies	C5,6,7 signs persist	
	5	HFMD	LUL	NA	WBC 67 L32%	Serology/paired serum antibodies	C5,6,7 signs persist	
	4	Erythema	RUL	NA	WBC 25 L71%	Serology/paired serum antibodies	Recovered	
Australia 1987 (1 case)	NA	NA	NA	NA	NA	NA	NA	30
Brasil** 1988-1990 (5 case)	NA	NA	NA	NA	NA	Paired serum/ seroconversion	One with residual motor deficiency	28
Malasia 1997 (5 cases)	1 case report M/22	NA	LUL with brain stem encephalitis	NA	NA	NA	Death	4,58
Taiwan 1998 (7 cases)	F/16	HFMD	Fever, vomiting, lethargy, RLL weakness, tachycardia	Normal	WBC 33 Protein 22 Glucose 65	Feces	Recovered	13,29,34, 50,71
	F/18	HFMD	Fever, myoclonus, tremor, lethargy, tachypnea, tachycardia, LUL weakness	Enhancement of L anterior horn region of cord and ventral root, L2-4	WBC 83 Protein 43 Glucose 56	Feces	Recovered	
	M/6	HFMD,	Fever, myoclonus, tremor, lethargy, tachypnea, tachycardia, LUL weakness	T2 high signal intensity lesion in the L anterior horn region of the cervical cord, C3-6	WBC 80 Protein 49 Glucose 70	Feces	Recovered	
	M/30	Herpangina	Vomiting, fever, myoclonus, ataxia, bilateral lower limbs paralysis, transient neurogenic bladder	Contrast enhancement of bilateral ventral roots and T2 HS lesions in bilateral anterior horn, T8 to conus	WBC 41 Protein 85 Glucose64	Throat, feces	Improved, mild L leg weakness	
	F/16	HFMD,	RLL weakness	Long slit cavity lesion in the R anterior horn of cord from T10 to conus	WBC 44 Protein 43 Glucose 60	Feces	Improved, mild R leg weakness	
	M/5	HFMD	LUL weakness	T2 high signal intensity lesion in the L anterior horn region of cervical cord from C3-6	WBC 240 Protein 82 Glucose61	Throat	Recovered	
	M/1	HFMD	Bilateral lower limbs weakness	Bilateral anterior horn T2 high signal intensity lesions, lumbosacral cord	NA	Feces	Improved with sequelae	
Western Australia 1999 (1 case)	F/40	No rash	Meningitis, LUL (C5-6) monoplegia	NA	WBC 900 Protein 40	Feces, throat	Fully recovered within 2 weeks	27

AFP = acute flaccid paralysis; MRI = magnetic resonance imaging; CSF = cerebrospinal fluid; WBC = white blood cell; RBC = red blood cell; NA = not available; M = male; F = female; HFMD = hand-foot-mouth disease; RLL = right lower limb; RUL = right upper limb; LLL = left lower limb; LUL = left upper limb; IVIG = intravenous immunoglobulin

Table 1. Continued

	Age (month)	Skin lesion	Neurological complication/ AFP	MRI	CSF parameter: WBC (cells/mm^3) RBC (cells/mm^3) Protein (mg/dL) Glucose (mg/dL)	Positive EV71 specimens	Treatment/outcome	Reference
Denver 2003-2005 (5 cases)	M/6	Mouth ulcer	Meningoencephalitis, monoparesis	NA	WBC 228 RBC 43 Glucose 71 Protein 52	Rectal swab, throat,nasal,urine	Monoparesis	31
	F/7	Mouth ulcer	Monoparesis	NA	Not determined because of CSF being grossly bloody	Throat and nasal swab	Monoparesis	
	M/60	No rash	Brainstem encephalitis quadriplegia	NA	WBC 76 RBC 8 Glucose 126 Protein 56	Rectal, nasal swab	Paralyzed, depend on mechanical ventilation	
	M/24	No rash	Meningoencephalitis, monoparesis	NA	WBC 55 RBC 95 Glucose 68 Protein 39	Throat, rectal swab	Recovered	
	F/24	No rash	Meninigitis, monoparesis	NA	WBC 11 RBC 0 Glucose 51 Protein 44	Throat	Monoparesis	
China August 2008-November 2010 (9 case)	NA	HFMD	LUL grade II	C2-5 left anterior horn cell	NA	NA	LUL grade IV	52
	NA	HFMD	Encephalitis, LUL grade IV LLL grade III	C4-7, T8-L1 left anterior horn cell	NA	NA	LUL grade V LLL grade V	
	NA	HFMD	LUL & LLL grade III	C2-5 left anterior horn cell	NA	NA	LUL grade IV LLL grade V	
	NA	HFMD	Encephalitis, RUL grade III LUL grade II	C1-7 bilateral anterior horn cell	NA	NA	Both upper grade IV	
	NA	HFMD	Encephalitis, Both upper grade III RLL grade II LLL grade III	C3-4, T11-L1 bilateral anterior horn cell	NA	NA	Dead	
	NA	HFMD	Both upper grade I Both lower grade IV	T10-L1 right anterior horn cell	NA	NA	Both upper LLL grade V RLL grade IV	
	NA	HFMD	Both upper grade III RLL grade II LLL grade III	C2-5 bilateral anterior horn cell	NA	NA	RUL grade III RLL grade V	
	NA	HFMD	Encephalitis, Both upper grade 0 Both lower grade IV	C2-5 bilateral anterior horn cell	NA	NA	Both upper grade I Both lower grade V	
	NA	HFMD	RUL grade 0 LUL grade I Both lower grade III	C2-5 bilateral anterior horn cell	NA	NA	Loss follow-up	
China 2008-2012 (7 cases)	F/6	HFMD	Brainstem encephalitis, grade 0 all limbs paralysis	Contrast enhancement of the anterior horn roots in the whole spinal cord	NA	Feces	Dead	32
	M/7	HFMD	Brainstem encephalitis, all limbs paralysis - grade I upper limbs - grade II lower limbs	Partial contrast enhancement of the anterior roots and anterior horns of the whole spinal cord	NA	Throat	Slightly high arch feet (2- year follow-up)	
	M/22	HFMD	Brain encephalitis, grade II both upper limbs	Bilateral abnormalities of anterior horn cells at C1-4	NA	Throat	Mild limb weakness	
	M/12	HFMD	Grade II in both lower limbs	Bilateral abnormalities of anterior horn cells at T10-L1	NA	CSF	Normal	

AFP = acute flaccid paralysis; MRI = magnetic resonance imaging; CSF = cerebrospinal fluid; WBC = white blood cell; RBC = red blood cell; NA = not available; M = male; F = female; HFMD = hand-foot-mouth disease; RLL = right lower limb; RUL = right upper limb; LLL = left lower limb; LUL = left upper limb; IVIG = intravenous immunoglobulin

Table 1. Continued

	Age (month)	Skin lesion	Neurological complication/ AFP	MRI	CSF parameter: WBC (cells/mm^3) RBC (cells/mm^3) Protein (mg/dL) Glucose (mg/dL)	Positive EV71 specimens	Treatment/outcome	Reference
	M/12	HFMD	Grade I-II in both lower limbs	Bilateral abnormalities of anterior horn cells at T9-L, bilateral contrast enhancement of the anterior roots	NA	Feces	Normal	
	M/24	HFMD	Grade 0 in RUL	Bilateral abnormalities of anterior horn cells at C4-7	NA	Throat	Mild upper limb weakness	
	F/24	HFMD	Grade I in LLL	Left-sided abnormalities of anterior horn cells at T9-L1	NA	CSF	Normal	
China May-August 2011 (16 cases)	F/60	HFMD	Both lower limbs grade II	ventral horn T10-L1	WBC 18	NA	IVIG/recovery	51
	M/13	HFMD	LLL grade IV RLL grade II	Right side T10-12	WBC 16	NA	IVIG/recovery	
	M/48	HFMD	LLL grade 0 RLL grade III	Left side T10-L1	WBC 2	NA	Weakness grade III	
	M/16	HFMD	Both upper & lower grade IV	C2-5	WBC 10	NA	IVIG/mild weakness	
	M/18	HFMD	Brainstem encephalitis Both upper grade IV Both lowet grade III	Ventral horn C1-3	WBC 3	NA	IVIG/recovery	
	F/8	HFMD	Brainstem encephalitis, Both upper grade IV LLL grade III	Left lateral and ventral horn T10-11	WBC 12	NA	IVIG/weakness grade III+	
	M/12	HFMD	LLL grade 0 RLL grade IV	Left side T10-11	WBC 10	NA	Weakness grade III+	
	M/18	HFMD	Both lower grade III	Anterior horn cells C1-5	WBC 30	NA	IVIG/recovery	
	F/16	HFMD	LUL grade 0 RUL & LLL & RLL grade IV	Left side&venrtral hornl C5-7	WBC 15	NA	Weakness grade II	
	M/17	HFMD	Brainstem encephalitis LUL grade III RUL & LLL & RLL grade I	Anterior horn cells at C1-7	WBC 12	NA	IVIG/mild weakness	
	F/20	HFMD	LLL grade III	Left side T11-12	WBC 30	NA	Recovery	
	M/6	HFMD	LLL grade 0 RLL grade III	Left side T10-L1	WBC 15	NA	IVIG/weakness grade III	
	F/16	HFMD	LUL grade 0 RUL grade III RLL grade III	Not done	WBC 110	NA	IVIG/weakness grade II	
	F/18	HFMD	LLL grade 0 RLL grade III	Left side T11-L1	WBC 10	NA	IVIG/weakness grade III	
	M/9	HFMD	Brainstem encephalitis RUL grade 0	Right side C2-7	WBC 6	NA	IVIG/weakness grade II	
	M36	HFMD	LLL grade IV RLL grade II	Right side T11-12	WBC 17	NA	IVIG/mild weakness	
This study	M/12	HFMD	Grade 0 in RUL	Right -sided abnormalities of anterior horn cells at C3-6	WBC 3 (N1,L2) RBC 1,000 (traumatic tab) Protein 23.5 Glucose 62	Feces	Residual proximal right upper limb weakness	

AFP = acute flaccid paralysis; MRI = magnetic resonance imaging; CSF = cerebrospinal fluid; WBC = white blood cell; RBC = red blood cell; NA = not available; M = male; F = female; HFMD = hand-foot-mouth disease; RLL = right lower limb; RUL = right upper limb; LLL = left lower limb; LUL = left upper limb; IVIG = intravenous immunoglobulin

In contrast to poliovirus-related AFP, EV71-related AFP has better prognosis in long-term follow-up[71]. Treatment with Intravenous immunoglobulin [IVIG] did not significantly improve the clinical outcome[51]. There were no significant associations between CSF virus isolation and mortality as well as clinical features associated with poor prognosis. Most of the patients had complete recovery or persistent mild weakness, except three fatal cases of AFP associated with acute brainstem encephalitis[3,52,54,58]. In this review, the

clinical predictive prognosis was analyzed by t-test and Chi-square test with SPSS 17.0 (Table 2). Sex, age less than one year, brain involvement, and skin lesion were not significantly different in the children that fully recovered when compared to the children with neurologic sequel whereas multi-limb paralysis and limbs weakness distribution with both upper and lower limbs weakness were the worse prognosis clinical outcome. Chen et al mentioned the patients' recovery order begun with distal limbs and slowly recovered in proximal muscle strengthen and muscle tone[32]. The follow-up findings in previous studies showed reversible depended on the size of the lesion and severity of the disease, and bilateral anterior horn lesions may have a less favorable outcome.

Conclusion

Since routine poliovirus immunization systems was initiated and poliomyelitis was eradicated, EV71 has been viewed as the main cause of AFP related HFMD. Even though many clinical trials for antiviral strategies against EV71 and EVs immunization have been developed, but they are still not available. These might lead to sequel of limb dysfunction and worse prognosis. The EV71-associated HFMD is an epidemic disease transmitted via the fecal-oral route and attributable to contaminated water and environment. Therefore, good sanitation and clean environment, especially drinking boiled water and regular hand washing, should be strongly emphasized for prevention of EV71 infection in epidemic area.

Table 2. Clinical predictive prognosis of acute flaccid paralysis in infants and young children with enterovirus71 infection

Clinical predictive prognosis	Outcome		*p*-value
	Fully recovery n (%)	Neurological sequale n (%)	
Sex (n = 40)			0.361
Male	9 (22.5)	15 (37.5)	
Female	8 (20.0)	8 (20.0)	
Age (n = 45)			0.787
≤1 year	8 (17.8)	11 (24.4)	
>1 year	12 (26.7)	14 (31.1)	
Number of limbs weakness (n = 55)			0.024*
Monoplegia	15 (27.3)	11 (20.0)	
Multi-limb paralysis	8 (14.5)	21 (38.2)	
Upper vs. lower limb involvement (n = 51)			0.081
Upper limbs	7 (13.7)	8 (15.7)	
Lower limbs	12 (23.5)	9 (17.6)	
Both upper and lower limbs	3 (5.9)	12 (23.5)	
Limbs weakness distribution (n = 51)			0.031*
Only upper or lower limbs weakness	19 (37.3)	17 (33.3)	
Both upper and lower limbs	3 (5.9)	12 (23.5)	
Brain involvement (n = 55)			0.832
Brain involvement	10 (18.2)	13 (23.6)	
No brain involvement	13 (23.6)	19 (34.5)	
Skin lesion (n = 55)			0.361
Skin lesion	18 (32.7)	28 (50.9)	
No skin lesion	5 (9.1)	4 (7.3)	

* $p<0.05$

What is already known on this topic?

HFMD is an epidemic disease and associates with serious clinical manifestations characterized by acute brain stem encephalitis, aseptic meningitis, acute flaccid poliomyelitis-like paralysis, Guillain-Barre syndrome, transverse myelitis, and cerebellar ataxia.

What this study adds?

No case of EV71-related AFP has been reported in Thailand. In this study, EV71-related AFP might be leading to sequel of limb dysfunction and worse prognosis. According to the articles reviewed, multi-limb paralysis and limbs weakness distribution with both upper and lower limbs weakness are significant clinical predictive prognosis. As EV- immunization is still not available, personal hygiene is very important and should be strongly emphasized for protection against EV71 infection in epidemic area.

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Potential conflicts of interest

The authors declare no conflict of interest.

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