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A case of hand-foot-and-mouth disease in a systemic lupus erythematosus patient presenting as late complication onychomadesis

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Abstract

Hand, foot and mouth disease (HFMD) is a common childhood viral disease, characterized frequently by flu-like illness with fever, myalgia and typical vesicular lesions on the palms, soles, buttocks and oral cavity. Although HFMD primarily occurs in children, it can also be seen in immunocompromised adults. This report describes a laboratory-confirmed clinical case of Echovirus-7 hand, foot and mouth disease, presented with typical clinical features and late complication onychomadesis in an immunocompromised patient with systemic lupus erythematosus in Greece.

Keywords: Diseases; Fever; Case.

Introduction

Hand, foot, and mouth disease (HFMD) Is a relatively common viral infection that predominantly affects young children, usually during the spring and fall months [1]. It is caused by members of the human enterovirus (HEV) Genus that belong to the Picornaviridae family, specifically human enteroviruses and coxsackieviruses [2]. The most often involved serotypes are enterovirus 71 (EV71) And coxsackievirus A16 (CVA16), Which both belong to the HEV-A species. However, other HEV-A serotypes, as well as some HEV-B, have also been associated with flares of the disease [3,4]. Echovirus-7 (Echo-7) Belongs to the species HEV-B of the genus Enterovirus. Echo-7 usually infects neonate and older children and sporadically, may causes mild clinical manifestation of hand foot mouth disease (HMFD) Up to a more severe form of aseptic meningitis and meningoencephalomyelitis [5,6]. HFMD is characterized by a brief flu-like illness with fever, myalgia, runny nose and erythematous, typical vesicular lesions on the palms, soles, buttocks and oral cavity [3]. In the majority of cases flares are sporadic, but epidemics may also occur. Severe form of HFMD is characterized as a case involving the central nervous system (CNS) That can progress into neurological

complications such us aseptic meningitis, encephalitis, and acute flaccid paralysis [7]. Onychomadesis is the shedding of the nails beginning at the proximal end, probably caused by the temporary arrest of the nail matrix. It is a painless, reversible non-inflammatory condition that generally resolves without complications. Recently, onychomadesis has been described as a sporadic, late complication of HFMD in children [8,10] and in adults [11]. In childhood, nail abnormalities are generally rare and can manifest either in the context of inherited diseases, or because of systemic illnesses, trauma, or drug uptake. Additionally, many cases are considered idiopathic [9]. Although HFMD primarily occurs in children, it can also be seen in immunocompromised adults [1,12].

In Greece, there are several studies regarding enterovirus surveillance although data for Echovirus are scarce. Indeed, most data are provided by the testing of specimens from aseptic meningitis outbreaks or acute flaccid paralysis cases. Enteroviruses are also among the most important emerging waterborne pathogens. Echovirus 7 has been isolated from sewage samples in Greece, indicating its broad circulation [13]. As the Hellenic Polioviruses/Enteroviruses Reference Laboratory (HPERL) we routinely receive samples from patients suspected for enterovirus infection and we present here for the first time in Greece a HFMD caused by Echovirus-7.

Case Study

We report here a case of a 43 years old female diagnosed with SLE and glomerulonephritis, under immunosuppressive medication (mycofenolate mofetil 3 x 500 mg and hydroxychloroquine 200 mg daily), Who presented in late autumn with typical clinical features HFMD. The initial symptoms started with a general sense of feeling unwell and erythematous vesicular lesions on the palms of her hands, that progressed afterwards to the dorsum and soles of the feet (Figure 1). Her 5-years-old daughter had been recently diagnosed with HFMD, presenting with mild red spots on the palms 5-6 days before the onset of the patient's clinical features. Patient reported rash, itching and slight pain on the hand and soles of the feet with no episode of fever. There were no signs of spots on the tongue and inside the mouth.

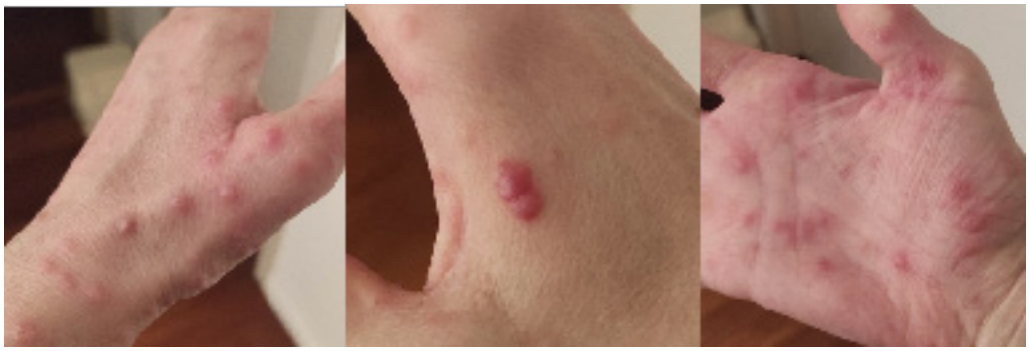

Figure 1: Drawings in 6 to 9 months after UCBC therapy.

Laboratory results two days after the initiation of symptoms showed typical findings of viral infection and no sign of an SLE flare (Table 1). Specifically, there were elevated large mononuclear cells (Mono) – 12%, elevated ESR - 29 and elevated CRP - 1.35 (Table 1). Whole blood cells (WBC) Were 5750, while lymphocytes were 13%, typically low for this patient. Complement C3 and complement C4 were within normal limit.

Table 1: Laboratory findings two days after initiation of the clinical symptoms.

Pertinent laboratory markers	Value	Pertinent laboratory markers	Value
WBC (10^3/μl)	5.7	Phosphorus (mg/dL)	3.4
RBC (10^3/μl)	4.9	Calcium (mg/dL)	9.1
Hgb (g/dL)	14.2	Iron (mg/dL)	32
Hct(L/L)	42.8	Ferritin (ng/mL)	66.1
Plt Count (10^3/μl)	319	Total protein (g/dL)	7.3
Neutr %	72	Albumin (g/dL)	52.9
Lymp %	13	a1-globulins (g/dL)	3.9
Mono %	12	a2-globulins (g/dL)	11.7
ESR (mm/hr)	29	β1-globulins (g/dL)	4,6
C-reactive protein (mg/dL)	1.35	β2-globulins (g/dL)	3,4
Glucose (mg/dl)	78	γ-globulins (g/dL)	23.5
Creatinine (mg/dL)	0.83	Complement C3 (mg/dl)	121
AST (IU/L)	19	Complement C4 (mg/dl)	23.4
ALT (IU/L)	12	Anti-DNA-ds antibodies (1:10)	Neg
γ-GT (IU/L)	39	Anti-ANA antibodies (1:320)	+/-
Alkaline Phosphatase (IU/L)	58	Urine proteins 24h (mg/24h)	455.10
CPK (IU/L)	119	BMI (kg/m^2)	19.2

The diagnosis of HFMD was made based on typical clinical findings and molecular analysis of whole blood and nasal swab. Extraction of viral RNA from blood and swab sample was performed, as previously described [14], and real time PCR targeting the 5'UTR region of enterovirus genus was applied [14]. Positive results for the presence of enteroviral RNA were obtained, with a higher viral load in blood sample compared to nasal swab.

The clinical symptoms have peaked 3-4 days after onset of the disease with extensive presence of blisters in hands and foot presenting rash and pain (Figure 2). Upon clinical evaluation and laboratory results, the patient stopped her SLE medication for ten days and received supporting therapy with paracetamol 500mg and betamethasone valerate 0.1% w/w cream upon irritation from the symptoms.

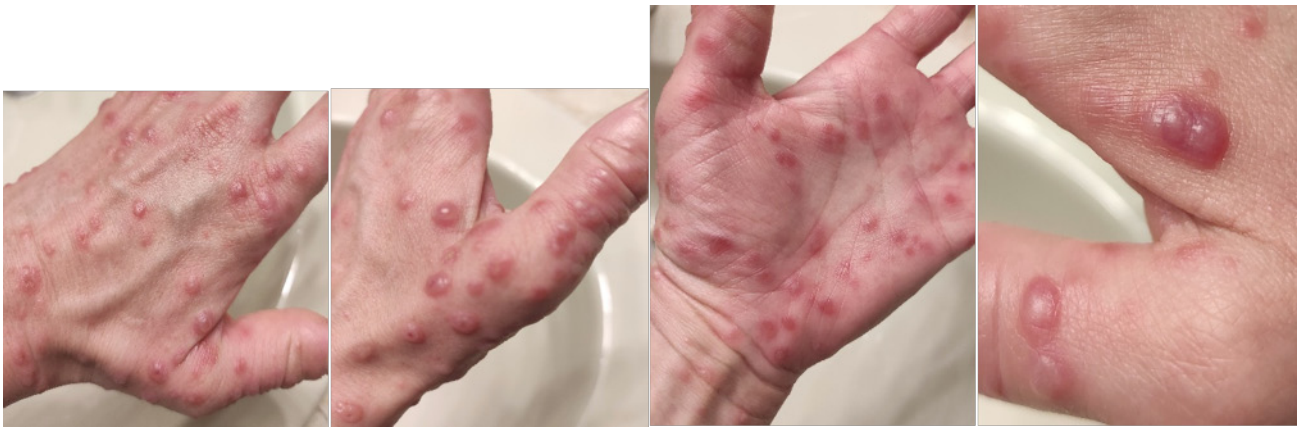

Figure 2: Photographs from the erythematous vesicular lesions on the backs and palms of the hands that peaked on day 3-4 after infection.

After recovering from the HFMD, 5-6 weeks later, the patient developed onychomadesis involving both hand and feet (Figure 3) as a late complication of HFMD that persisted for more than 5 months.

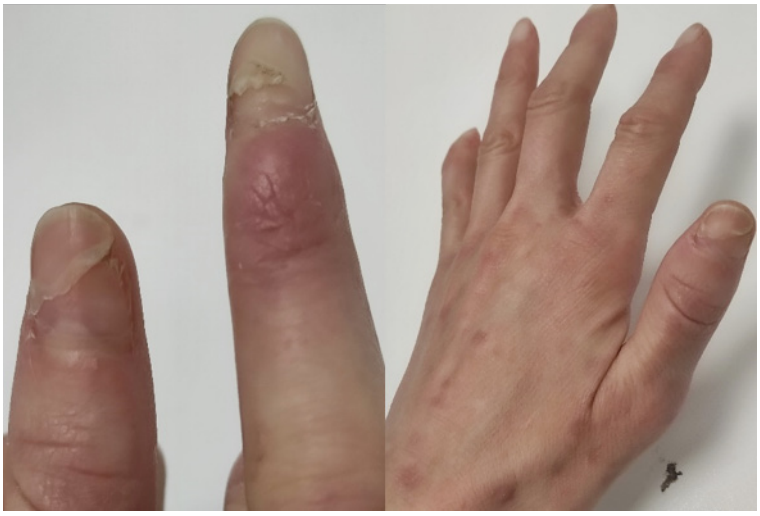

Figure 3: A. Onychomadesis in hand nails persisting 3 months after infection with Echo7, **B.** erythematous vesicular lesions on the hands had almost resolved at the same timepoint.

Genotypic identification of enterovirus strain was performed by seminested RT-PCR amplification of the VP1 region, as previously described [14]. Enterovirus Echo7 was identified in both the blood and swab samples of the patient. To better understand the molecular epidemiology of this Echo7 strain [Echo7strain/GR/2022], phylogenetic analysis, using MEGA 5 program [15], was conducted based on the VP1 sequence of the global Echo7 strains. All Echo7 strains are classified into three groups (A, B, and C), With at least 13.7 % VP1 nucleotide diversity between each subgroup [6]. Echo7strain/GR/2022 has clustered with the prototype strain Wallace isolate in 2001 with 100% identity, showing that there has been no significant evolutionary effect taking place related to VP1 region.

Discussion/Conclusions

HFMD is a highly infectious syndrome mainly caused by members of the HEV genus from the Picornaviridae family. Initial clinical manifestations are characterized by typical erythematous vesicular lesions on the palms, soles, buttocks and oral cavity. Other clinical symptoms comprised flu-like illness with fever, myalgia and abdominal pain. HFMD lesions usually resolve spontaneously without complications within 7 to 10 day. Onychomadesis is a nails disorder that has been described as a complication of HFMD mainly in children [8-10]. But has been also reported in adults. This clinical manifestation is usually self-limited and requires no medication.

In the current study, we describe a case of onychomadesis following HFMD in an immunocompromised patient diagnosed with SLE associated with Echo-7 infection. The diagnosis of HFMD was made on the basis of typical clinical findings and molecular analysis of the viral pathogen. The immunocompromised background of the patient set the basis for prolonged symptoms of Echo-7 infection and late recession.

Circulation of different EVs in common throughout Greece and two peaks of EV positivity rates have been observed, during April-August and during November-December [16], that is in line with the period

the patient presented with symptoms. According to surveillance studies performed by the HPERL, Enterovirus B species are the most frequently amplified among hospitalized patients. E30, CVB5 and E9 are the most frequent serotypes of Enterovirus B species identified in Greece [16]. There are no reports on the emergence of Echo7 in Greece in hospitalized patients or patients presenting complications. However, there is evidence for its circulation in the country from the data obtained from studies conducted in sewage samples [13]. It is the first time that a severe Echo 7 case is described in Greece relating to an immunocompromised patient.

Declarations

Informed Consent: The patient provided written informed consent for images to be published.

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