

Clinical and Demographic Analysis of Patients with Hand, Foot and Mouth Disease Diagnosis

El, Ayak, Ağız Hastalığı Tanısı Alan Hastaların Klinik ve Demografik Olarak Analizi

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Abstract

Objectives: Hand, foot and mouth disease is a viral infection which is characterized by fever, vesicular lesions in palm, sole, and mouth, and is frequent observed in children. We aimed to investigate the clinical characteristics of 33 patients admitted to the Clinic of Dermatology in Ankara Atatürk Training and Research Hospital between 2015 and 2017.

Materials and Methods: Thirty-three patients were evaluated for the presence of symptoms such as fever, pain, burning, pruritus, age, sex, localization of lesions, family and atopy history.

Results: The median age of the 33 patients studied was 12.21±9.45 years (min-max: 1-36), there were 23 children and 10 adults. The mean duration of illness was calculated as 3,9±1,9 days (min-max: 1-7). 36.36% of the patients (n = 12) were male. 26 (78.78%) patients had fever history. There were atopy histories in 5 patients (15.15%), and medical history in the family and close encountered persons of 9 patients (27.27%). Eight patients (24.24%) complained of sore throat, 7 patients (21.21%) of itching. Vesicular lesions were monitored in the palms and soles of 31 patients (93.93%) and in the mouths of 24 patients (72.72%). The most frequent involvement site was hand palm (96.96%). Only 2 patients (6.06%) developed onychomadesis after the disease.

Conclusion: We have observed a female gender dominance unlike other studies. It should not be forgotten that; although more common in children, the disease can be observed also in young adults, it can involve body parts other than hand-foot-mouth, and long follow-ups are important in the severe form of the disease.

Key words: Hand foot and mouth disease, infection, viral

Öz

Giriş: El ayak ağız hastalığı; ateş, el içi, ayak tabanı ve ağızda veziküler lezyonlar ile karakterize, sıklıkla çocuklarda görülen viral bir enfeksiyondur. Biz de; 2015-2017 tarihleri arasında Atatürk Eğitim ve Araştırma Hastanesi Dermatoloji Polikliniği'ne başvuran ve el ayak ağız hastalığı tanısı alan 33 hastanın klinik özelliklerini retrospektif olarak araştırmayı amaçladık.

Materyal ve Metot: Dermatoloji polikliniğine başvuran ve klinik olarak el ayak ağız hastalığı tanısı konulan 33 hasta yaş, cins, ateş, ağrı, yanma, kaşıntı gibi semptomların varlığı, lezyonların lokalizasyonu, aile ve atopi öyküsü açısından değerlendirildi.

Bulgular: Çalışmaya alınan 33 hastanın yaş ortalaması 12,21±9,45 yıl (min-maks: 1-36) idi, 16 yaşından küçük 23 çocuk hasta ve 16 yaşından büyük 10 erişkin hasta vardı. Hastalık süresi ortalama 3,9±1,9 (min-maks: 1-7) olarak hesaplandı. Hastaların %36,36'sı (n=12) erkek idi. 26 (%78,78) hastada ateş öyküsü olup, 24'ünde (%72,72) subfebril bir ateş (37,5) varken, 2' sinde (%6,06) 39 derece idi. 5 hastada (%15,15) atopi öyküsü, 9 hastada (%27,27) ailede ve yakın temasta olduğu kişilerde hastalık öyküsü vardı. Sekiz hasta boğaz ağrısı (%24,24), 7 hasta (%21,21) kaşıntıdan şikayetçi idi. 31 hastada (%93,93) el içi ve ayak tabanı, 24 hastada (%72,72) ağız içinde veziküler lezyonlar izlendi. En sık tutulan bölge el içi idi (%96,96). Hastalık sonrası sadece 2 hastada (%6,06) onikomadesis geliştiği görüldü.

Sonuç: Yapılan diğer araştırmalardan farklı olarak çalışmamızda; el ayak ağız hastalığında kadın cinsiyet hakimiyeti gözlemledik. Çocuklarda daha sık olmasına rağmen özellikle genç erişkinlerde de hastalığın görülebileceği, el-ayak-ağız haricindeki vücut bölgelerini de tutabileceği, şiddetli formunda uzun takiplerin önemli olduğu unutulmamalıdır.

Anahtar kelimeler: El ayak ağız hastalığı, enfeksiyon, viral

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Introduction

Hand-Foot-Mouth Disease (HFMD) is a contagious viral infection, caused mainly by Enterovirus 71 (EV71) and Coxsackie virus A16 (CVA16), and is mostly seen in children.^{1,4} It can be transmitted by direct contact with environmental factors such as infected individuals or pool water, by oral fecal route or through inhalation.^{2,3,5} The disease, which is usually mild and self-limiting, can be more severe, especially with enterovirus 71, and can cause epidemics and rarely fatal complications such as encephalitis, meningitis, myocarditis, pulmonary edema, and paralysis.^{1,5-7} The diagnosis is clinical, but the type identification of enteroviruses may be required in severe forms.^{1,5} Lesions in hand palm, foot sole, and mouth are the characteristic features. Following the 3 to 7 day incubation period, the lesions begin as a 3-7 mm erythematous maculae and rapidly turn into oval shaped vesicles, surrounded by a red halo. The long axis of the lesions is parallel to skin lines, lesions fade in a few days and degrades within nearly 1-2 weeks without leaving any scar or scab. The lesions start in the mouth at first, then spread into the hand palm and foot sole. Lesions may not always involve these 3 typical body parts, they may be seen in other parts of the body as well.^{1,3,7}

In Asia, major outbreaks have been reported in recent years, where severe cases have been observed.⁸⁻¹⁰ The increasing frequency of this infection, which is observed more mildly in our country, led us to monitor the clinical features of HFMD-diagnosed cases in our polyclinic.

Materials and Methods

Between 2015 and 2017, 33 patients who were clinically admitted to Ankara Atatürk Training and Research Hospital, Clinic of Dermatology with a diagnosis of HFMD were included to the study. The study was approved by Yıldırım Beyazıt University, Yenimahalle Training and Research Hospital Clinical Research Ethics Committee (Decision no and date: 2017/10/04, 21/11/2017) and complied with the requirements of the Declaration of Helsinki. The patient files were retrospectively assessed. The age, gender, location of the lesions; the presence of symptoms such as fever, pain, burning, itching, sore throat; the duration of the illness, the month applied, HFMD story of a member of the family or a close encountered person; complications such as accompanying diseases or onychomadesis were all recorded. The results of 11 patients whose laboratory tests were examined were also evaluated.

Statistical analysis was performed using SPSS software, Version 18 (SPSS Inc., Chicago IL, USA) based on the acquired retrospective data. Frequencies were calculated for variables

related to demographic and clinical patient characteristics. Qualitative variables were expressed as percentage. Quantitative variables were expressed as mean, standard deviation, median (min-max). Fisher's exact test was used to compare gender distribution. A p value of less than 0.05 was accepted as statistically significant.

Results

The mean age of the 33 patients studied was 12.21 ± 9.45 years (min-max: 1-36), there were 23 children (69.69%) under 16 years of age and 10 adults (30.30%) over 16 years of age. Nineteen patients (57.57%) were found under 10 years of age and 11 patients (33.33%) were under 5 years of age. The mean duration of illness was calculated as 3.9 ± 1.9 days (min-max: 1-7). Females were 63.63% of the patients (n=21). Fourteen out of 23 children (60.86%) and seven out of 10 adult patients (70%) were female. There was no statistically significant gender difference between children and adult patients ($p=0.710$). Twenty-six (78.78%) patients had fever history, while 24 (72.72%) had a subfebrile fever (37.5°C) and 2 (6.06%) had 39°C fever. The complaints of these two patients with 39°C fever developed after the pool. There was atopy history in 5 patients (15.15%), and medical history in the family and close encountered persons of 9 patients (27.27%). Eight patients (24.24%) were complaining of sore throat, 7 patients (21.21%) of itching, 4 patients (12.12%) of pain and burning. A pool history was detected in three patients (9.09%). Vesicular lesions were monitored in the hand palms and foot soles of 31 patients (93.93%) and in-mouth of 24 patients (72.72%). The most frequent site of lesion was the hand palm (96.96%), lesions involved only hand palm in one patient (3.03%). Soft palate, gingiva, tonsils, buccal mucosa, labial mucosa and tongue were the locations where intraoral lesions were involved. Papulovesicular and maculopapular lesions were observed in the extremities (thigh, leg, arm, knee, elbow) of 5 patients (15.15%), facial regions (perioral region, nose end, forehead, chin) of 7 patients (21.22%), mammary and inframammary regions in 3 patients (9.09%), genital regions of 2 patients (6.06%), and gluteal region of one patient (3.03%). Only 2 patients (6.06%) developed onychomadesis after the disease. The general condition of the patients was good, blood examination was requested from 11 patients. Mild CRP elevation was observed in three and 2 had mild thrombocytopenia (142,000 and 127,000 $\text{K}/\mu\text{L}$). White blood cell and liver function tests were normal. One patient had type I diabetes and one patient was found to be hepatitis B carrier.

Twelve patients (36.36%) applied in September 6 (18.18%) in October, and 4 (12.12%) in November. Three patients were observed in each of August and May, 2 in July, and one in each of December, February, and April.

Clinical and demographic characteristics of the patients are shown in Table 1. Hand, foot and mouth lesions are shown in Figures 1-3.

Table 1. The characteristic features of the patients

Patient No	Gender	Age	Disease duration	Localization	History of illness in family and close contact person	Fever	Pruritis	Atopy	Sore throat	Pain	Burning	Pool history
1	M	3 y	3 days	Palmar, plantar, palate, around the mouth, thigh and leg, forearm	Kindergarten +	+	-					-
2	M	5 y	4 days	Palmar, plantar	-	+	-	-	-	-	-	-
3	M	22 y	2 days	Scalp, palmar, plantar and chest	Sibling +	+(39°C)	+	-	-	+	+	+
4	M	10 y	4 days	Chin, forehead, palmar, plantar, soft palate	-	+(39°C)	-	-	-	+	+	+
5	M	22 y	5 days	The inside and outside of the nose, gingiva, palmar, plantar	-	+	-	-	+	+	+	-
6	F	1 y	1 day	Palmar, plantar, genital area, thigh	-	+	+	+	-	-	-	-
7	F	17 y	3 days	Palmar, plantar, soft palate	Classmate +	+	-	-	+	-	-	-
8	F	4 y	2 days	Palmar, plantar, tongue and buccal mucosa	-	-	-	-	-	-	-	-
9	F	14 y	7 days	Palmar, plantar	Sibling +	+	-	-	-	-	-	-
10	M	28 y	2 days	Perioral area, soft palate, palmar, plantar	-	+	+	-	+	+	-	-
11	M	15 y	3 days	Palmar	-	+	+	+	-	-	-	-
12	F	7 y	3 days	Palmar, plantar, tongue and soft palate	-	-	+	-	-	-	-	-
13	M	3 y	3 days	Palmar, plantar, chin (After a month onychomadesis in fingernails)	-	+	+	-	-	-	-	-
14	F	10 y	4 days	Palmar, plantar	-	-	+	-	-	-	-	-
15	F	7 y	2 days	Palmar, plantar	-	+	-	-	-	-	-	-
16	F	8 y	2 days	Palmar, plantar, around the lip, tonsils	-	+	-	-	+	-	-	-
17	F	13 y	5 days	Palmar, plantar, dorsum of foot, inframammary area, soft palate	-	+	-	-	-	-	-	+
18	M	8 y	3 days	Palmar, plantar, soft palate	-	+	-	-	-	-	-	-
19	F	5 y	2 days	Palmar, plantar, soft palate	-	-	-	-	-	-	-	-
20	F	5 y	1 day	Palmar, plantar, soft palate	Kindergarten +	+	-	-	-	-	-	-
21	M	2 y	6 days	Palmar, plantar, buccal mucosa	-	+	-	-	-	-	-	-
22	F	2 y	7 days	Palmar, plantar, soft palate	-	+	-	-	-	-	-	-
23	M	9 y	7 days	Palmar, plantar, labial mucosa	-	-	-	-	-	-	-	-
24	M	4 y	7 days	Palmar, plantar, knees, elbows	-	-	-	-	-	-	-	-
25	F	17 y	3 days	Plantar, gluteal area, elbows, soft palate	-	+	-	-	-	-	-	-
26	F	34 y	3 days	Palmar, plantar, perioral area	-	+	-	-	-	-	-	-
27	F	12 y	7 days	Palmar, plantar, soft palate	Sibling +	+	-	-	+	-	-	-
28	F	8 y	5 days	Palmar, plantar, soft palate	Sibling +	+	-	-	+	-	-	-
29	F	21 y	5 days	Palmar, plantar, soft palate	Sibling +	+	-	-	+	-	-	-
30	F	4 y	2 days	Palmar, plantar, hand dorsum, dorsum of foot, arms	-	+	-	+	-	-	-	-
31	F	24 y	4 days	Palmar, plantar (Two months after lesions; onychomadesis in fingernails)	-	-	-	-	-	-	-	-
32	F	36 y	5 days	Palmar, plantar, genital area and breasts (hepatitis B carrier)	-	-	-	+	-	-	-	-
33	F	23 y	7 days	Palmar, plantar, pharynx (Diabet)	Uncle and nephew +	-	-	+	-	-	-	-



Figure 1. Palmar hand lesions



Figure 2. Plantar lesions



Figure 3. Lesions on soft palate and around the mouth

Discussion

The disease was first reported in New Zealand and Canada in 1957, then in North America, Australia, and Europe, and in 1997 and beyond, it has become a major health problem that has been fatal, threatening especially the Asia Pacific countries.^{5,11}

It is stated that the incidence of this disease which can be observed all over the world is increasing and causing great epidemics in Malaysia, Taiwan, Singapore, Thailand, Vietnam, Korea, China and Japan.^{2,5,6,11,12} It is suggested that the subtropical Monsoon climate, where heavy rainfall and moisture is seen, facilitates the growth and spread of enteroviruses, and that the ecology of enteroviruses is an important factor in the emergence of HFMD outbreaks.¹² It is reported that in China, the incidence increases between April and August, and peaks twice in June and November.⁶ It has also been reported that it is observed more frequently in summer and autumn in our country.¹⁷ We observed in our study that; this disease is more frequent in the autumn months, especially in September.

Pathogenic agents may also differ from season to season. Zhiuang et al. stated that EV71 was isolated more in cases seen in June, and CVA16 in cases in November. In recent years, it has been claimed that the rate of infection with these two pathogenic agents is decreasing and pathogens such as CVA 6, ECHO virus 30 and CVA 10 are becoming more prevalent. Two or three pathogens can also cause infection together.⁶ CVA6, CVA16, CVB5 have been identified as pathogenic agents in cases serotyped and reported from our country.⁵ None of our patients had virus isolation.

Geographical differences and climate, as well as the population density, low socio-economic level, low education, rural settlement are other factors that affect the incidence.⁴

HFMD mostly affects children under five years of age. In our study, 11 patients (33.33%) were equal to or under five years of age, while Topkarcı, Karadağ and Uğraş et al. have reported this rate respectively as 52.30%, 79%, and 87.40%.^{1,5,13} The low rate in our study may be due to the inclusion of adults. Bucak et al. reported the rate of patients under five years old as 92.30%, and under one year old as 15.30%. It is stated that lower the age of the children, higher the severity of the disease.^{7, 14} We had one patient at the age of one, two at the age of two, and the disease was mild. Gui et al. indicated that 53% of the 454.339 cases reported in China between 2008 and 2012 constituted children between the ages of 0-5, while children under 5 were the most susceptible age group to HFMD.¹² Lui et al., from China reported the rate of children under 5 years of age as 92.90%.² It has been reported that 97.50% of the cases in Thailand were under the age of 6, and 78.80% of the cases in Singapore were under 4 years.¹⁵⁻¹⁶ The severity of the disease as well as the complications in children under 5 years of age were reported to be higher.¹⁵ Ghosh et al. reported that 61.10 % of 62 patients aged between 9 months and 20 years were below 12 years of age, 16.10% of them had family history, and the most frequent involvement site was the hand palm.¹⁷

Fever was present in 78.78% of our patients, comparable with the results of Topkarcı et al (76.20 %).¹³ Bucak encountered fever in 82.10%, Karadag in 66.66%, and Uğraş in 61.40% of the patients.

While the hand palm and foot sole were involved together in 93.93% of the patients, the most frequent lesions were observed in the hand palm (96.96%), and 72.72% of the patients had vesicular lesions in the mouth. The lesions in the mouth were most commonly in the soft palate (39.39%). Apart from the hand, foot and mouth; knee, elbow, gluteal region and facial involvement may also be present.¹³ Eighteen (54.54%) patients had lesions out of the hand, foot or mouth.

While there was usually a male dominance in other studies, we found a female dominance (63.63%).^{15,18} Topkarcı et al. reported a gluteal involvement of 80.90% and more frequently at younger ages, but we encountered gluteal lesion only in one patient.¹³

Onychomadesis, Beau's lines and desquamation are delayed dermal findings and can occur in 3-6 weeks.¹⁹ In our 2 patients (6.06%), onychomadesis developed, all fingernails were affected and appeared at about 6th week.

In general, diagnosis can be made in the clinical setting, in case of severe complications, laboratory studies may be performed and type identification may be needed.

Symptoms of mild HFMD are fever, papulovesicular rash in the hand, foot, mouth, gluteal region, rarely anorexia and cough.² As the diagnosis, the severity of the lesions is often determined on the bases of symptoms. High fever (over 39 degrees), long duration of fever over three days, absence of skin lesions, absence of oral lesions, young age, diarrhea, dyspnea, seizures, hyperglycaemia, tachycardia, vomiting, lethargy and leukocytosis should suggest severe forms.^{7,11} In severe cases, fatal complications such as interstitial pneumonia, meningitis, encephalitis, pulmonary edema, myocarditis may develop.¹¹ We had one patient with type I diabetes and 2 patients with fever of 39 degrees, but their lesions were mild. Early diagnosis of serious cases reduces mortality. Therefore, the follow-up of patients is important. Specifically, children without oral lesions should be followed closely.¹¹

Serious case reports are extremely rare in our country, and no fatal infection has been reported.⁵ However, in the last years, large number of migrants coming to our country and the climate changes caused by global warming may have affected the course of the disease. For this reason, one should be careful in patients in terms of risk factors, long follow-ups should be done in terms of complications.

Treatment of this highly contagious disease is symptomatic and it is important to take protective measures. As the disease may cause spontaneous abortion and growth deficiency, care must be taken to protect the pregnant from the disease, especially in the first trimester. Direct contact with infected person and goods should be avoided, contaminated goods should be disinfected, drinking water and pools should be chlorinated, and hands should be washed frequently.^{1,13}

We have observed female gender dominance in HFMD in our study. The mean age was also higher. The low rate in our study may be due to the inclusion of adults. Low number

of patients in single-centered studies may be a reason for this. This is a restriction in our study. The studies are usually carried out either in pediatrics or dermatology out-patient clinics. There is a need for collaborative work in this area. It should be noted that especially young adults are under risk although it is more prevalent in children, the disease may also involve body parts other than hand-foot-mouth, and atypical vesicular lesions should remind the disease. The symptoms should be well interrogated in terms of severe form, and long follow ups should be done.

There is a need for multicenter studies involving rural areas, in which dermatologists as well as infectious diseases physicians, pediatricians and primary care physicians work together to fully elucidate the incidence of HFMD.

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