Brazilian Dental Science
Ciência Odontológica Brasileira
unesp
UNIVERSIDADEESTADUALPAULISTA "JÚLIO DE MESQUITA FILHO"
Instituto de Ciência e Tecnologia
Campus de São José dos Campos

CASE REPORT

doi: 10.14295/bds.2016.v19i4.1261

# Report of a rare case of hand-foot-mouth disease in an adult woman with systemic arthritis

Relato de um caso raro de doença das mãos pés e boca em uma mulher adulta

**Luciana Eloísa da Silva Castro NÓBREGA[1], Viviane Alves de OLIVEIRA[1], Patrícia Teixeira de OLIVEIRA[1], Éricka Janine Dantas da SILVEIRA[1], Ana Miryam Costa de MEDEIROS[1]**

1 – Post-Graduation Program of Oral Pathology – Department of Oral Pathology – Federal University of Rio Grande do Norte – Natal – RN – Brazil.

## ABSTRACT

Hand-foot-mouth disease (HFMD) is a highly infectious disease, rare in adults which usually presents a painfull stomatitis. We describe a rare case of HFMD in a 34-year-old woman with medical history of recent intestinal infection and systemic arthritis with only oral and hands involvement. Additionally, we discuss diagnosis and treatment of this disease and reinforce the importance of the correct diagnosis because delayed diagnosis can cause spread of the disease.

## KEYWORDS

Adult; Arthritis; Mouth diseases.

## RESUMO

A doença das mãos, pés e boca (DMPB) é altamente infecciosa, incomum em adultos e geralmente se apresenta com uma estomatite dolorosa. Nós descrevemos um caso raro de DMPB em uma mulher de 34 anos de idade, com história clínica de infecção intestinal recente e artrite sistêmica com manifestação oral e em mãos. Além disso, discutimos o diagnóstico e tratamento desta doença reforçando a importância do diagnóstico correto, uma vez que o diagnóstico tardio pode ocasionar a propagação da doença.

## PALAVRAS-CHAVE

Adulta; Artrite; Doença da boca.

## LITERATURE REVIEW

Hand, foot and mouth disease (HFMD) is an acute self-limiting, febrile infection that clinically characterized by erythematous papules on oral mucosal, palms of hands and soles of the feet. It considered to highly contagious disease, transmitted through fecal-oral route or contact with skin lesions and oral secretions. Coxsackievirus A16 and enterovirus 71 are the most commons virus causing HFMD disease, but other enterovirus serotypes have also been associated with the disease [1-4].

This disease occurs mainly in infant, less than 10 years old and when present in adults, it usually occurs in immunocompromised patients [3,5]. The treatment used in milder cases is symptomatic and supportive, since lesions regress spontaneously within one to two weeks [1,3].

Microbiological viral research by RT-PCR of the vesicular fluid aspirated from the lesions may be used as aid in diagnosis, although it can be made only based on clinical presentation [6].

We report a rare case of HFMD in a woman adult and discuss the clinical characteristics, diagnosis and treatment of this disease. Additionally, we reinforce the importance of

knowledge about patient's habits because it could help in faster diagnosis, once this disease can progress to severe form and spread easily to other people.

## CASE REPORT

In August 2012, a 34-year-old female caregiver on a nursery school was referred to our department complaining diarrhea and painful mouth ulcers with 4 days of duration. Her medical history includes recent intestinal infection and treatment for rheumatoid arthritis. With two days after of the appearance of the lesions, she had presented to clinician who prescribed dexamethasone 5 ml (IM) for treatment of injuries to her hands and mouth. The patient reported that had close physical contact with several children at daycare center with similar lesions diagnosed with HFMD. She denied any prodromal or accompanying symptoms such as fever or anorexia. Physical examination revealed numerous vesicles, erythema and ulcers with 2 - 4mm in diameter on the trunk, palms of the hands and fingers (Figures A and B), oropharynx and oral mucosa, located on the lower lip, retromolar region, hard palate and tongue (Figures C, D and E). At this moment, the body temperature was 37.5 degrees Celsius. As basis in the clinical information with the appearance of skin and oral lesions, medical history, we performed the diagnosis of hand, foot and mouth disease, eliminating the possibility of treating other possible diseases with similar clinical feature such as herpangina, aphthous stomatitis, varicella, secondary syphilis, measles and other rash illnesses. The patient was treated symptomatically with Benzitrat® mouthwash - an anti-inflammatory and analgesic solution – 3 rinses a day with 15ml of pure mouthwash and was oriented to stay away from her professional activities until the lesions complete regression. Fifteen days after the first consultation, the patient returned free of lesions, no nail changes were observed. The treatment was suspended and she was released to return to work.

## DISCUSSION

Hand, foot and mouth disease (HFMD) is viral infection caused by enteroviruses that is most common in children aged less than or equal to two years, in the summer, although rare cases may be seen in immunocompromised adults [7]. It´s more common in some countries of world as China, but it can be found all over the world [8,9]. A search of the English-language literature in the Pubmed and Medline database regarding HFMD in immunocompetent adult in the past 11 years (2003 through 2014) yield only 6 cases in adults (Table I). Concerning to Shin et al. [1], this is a primarily children´s disease, but some cases can be seen in adult, mainly in immunocompromised. Shea et al. [7] and Flor de Lima et al. [10] reported a case in men immunocompetent adults.

The first evidence of EV71 infection (major viruses that cause HFMD) in Brazil was associated with cases of acute flaccid paralysis occurred in the Federal District and the states of Piauí, Goiás and Bahia [14]. Here, we report a rare case of the HFMD in adult from a region of northeastern Brazil tropical climate, which had prior contact with younger children in your workplace with similar lesions.

In adult, skin symptoms are more severe than in children, and yet the treatment is usually not necessary [13]. An adult patient, reported by Toya et al. [13], had also associated with systemic rheumatoid arthritis, but did not have any complications, similar to what we observed in our case.

We suggest that the treatment used by our patient for rheumatoid arthritis with corticosteroids and the history of intestinal infection associated by contact with children in her work have contributed to the development of this disease, since the transmission of viruses that cause HFMD occurs from one person to another from oropharyngeal secretions or feces to the mouth, nose or eyes, transferred through the hands or fomites.

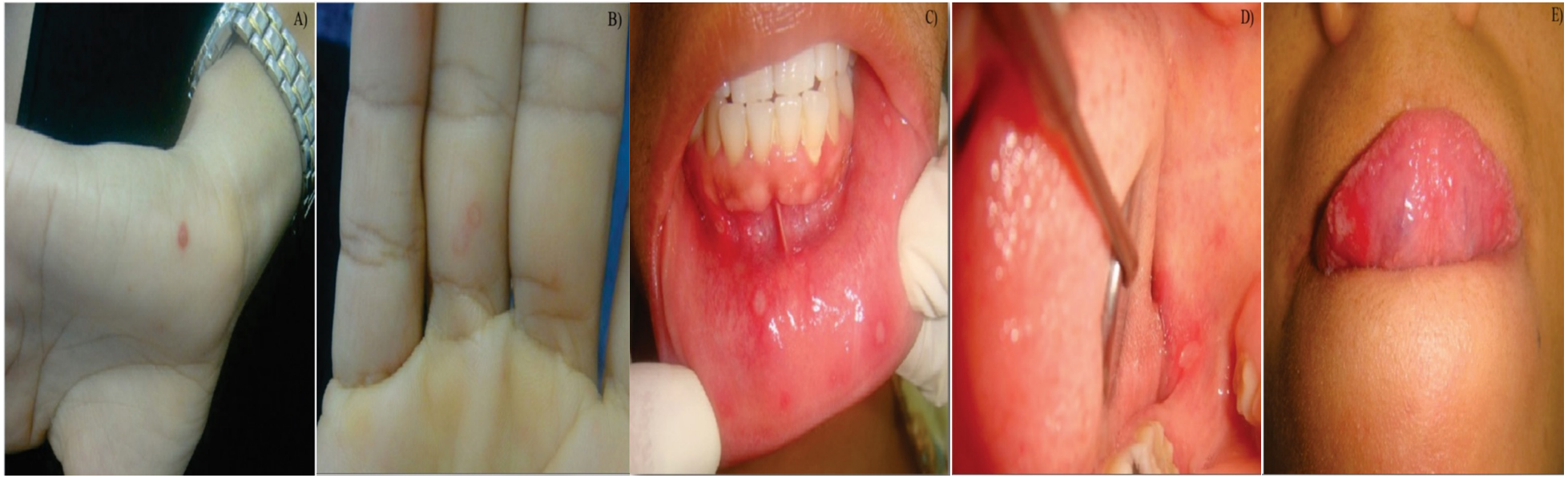


**Figure 1** - a) Ulcerated lesion in the palmar region. b) Ulcerated lesion in the fingers region. c) Multiple ulcerations in lower lip. d) Ulceration in the retromolar region of the oral cavity. e) Ulcerated lesion in ventral surface of the tongue.

Thus, our patient was advised to withdraw temporarily from her professional activities due the fact that the same work in direct contact with children has this orientation even more significant, since children are more susceptible to this disease involvement. Thereby, actions of hygiene and social distancing measures have been recommended as control and disease prevention. However, empirical evidences support these control measures are limited to a few studies [15].

Shea et al. [7] reported that the initial presentation of the HFMD lesions includes erythematous papules on the palms, feet, and in the oral cavity, accompanied by prodromal symptoms such as myalgia, mild fever, and abdominal pain. The lesions usually involve into vesicles and then spontaneously resolve within 1 or 2 weeks. They are usually asymptomatic, but in some cases, pressure and touch can provoke pain. In our case, the patient had just initial characteristic symptoms of the disease with small lesions spread in oral mucosa and hands.

Shin et al. [1] reported that oral lesions usually appear simultaneously with or precede cutaneous lesions, but the simultaneous occurrence of lesions on the hands, feet and in the oral cavity in adults in infrequent.

**Table I** - Cases of HFMD reported in adults over the past decade

| Reference | Location | Cases, n | Mean age, years | Gender | Oral Lesions |
|---|---|---|---|---|---|
| Faulkner et al. [5] | Australia | 01 | 27 | male | no |
| Hamaguchi et al. [11] | Japan | 01 | 37 | woman | no |
| Shin et al. [1] | Korea | 01 | 35 | male | no |
| Shea et al. [7] | China | 01 | 37 | male | yes |
| Flor de Lima et al. [10] | Portugal | 01 | 35 | male | yes |
| Akkoyunlu et al. [12] | Istambul | 01 | 43 | male | yes |
| Toya et al. [13] | Japan | 01 | 35 | male | yes |

Additionally, these authors commented that in an immunocompromised adult the HFMD may occurs without oral lesions. In the present case, the patient exhibited simultaneous lesions in oral mucosa and hands, but not in feet.

The diagnosis of HFM disease was made based on history, as well as typical clinical findings, including distribution of skin lesions, same we made in present case, but the microbiological diagnosis, made by RT-PCR of the vesicular fluid aspirated from the skin lesion and naso/oro-pharyngeal swabs can be performed as a diagnostic aid. Serological diagnosis depends on demonstrating a 4-fold increase in neutralizing antibody titer 10 to 14 days after the onset of illness [7]. Additionally, when the performed biopsy, the histopathological characteristics include reticular and ballooning degeneration of the epidermis with no inclusion bodies or multinucleated giant cells [1]. The low prevalence of this disease in adults may be because the diagnosis may be overlooked when the lesions do not typically come in three locations. But, concerning to Faulkner et al. [5], the oral lesions may also occur in isolation without cutaneous lesions.

The literature agrees that the treatment is symptomatic once the disease resolves spontaneously without complications within 7 to 10 days, like described in our case which it used only the supportive and symptomatic treatment with Benzitrat® (benzidamida hydrochloride) that contains anti-inflammatory and analgesic, widely used in the treatment of disorders that have common factor pain and swelling, exercising local anesthetic action, stimulating and accelerating the healing process of recovery injured tissues. However, there are rare reports of serious complications such as pneumonia, cardiomyopathies, aseptic meningitis, like others, and in these cases there is no effective clinical treatments or drugs, and the progression is faster [16].

Some authors report that acyclovir is the most antiviral drug used in the world for treat diseases caused by herpes simplex, herpes zoster and Epstein-Barr [6]. To exert its therapeutic effect, acyclovir needs to be activated by thymidine

kinase present in viruses such as herpes simplex, herpes zoster, and Epstein–Barr virus [18]. This enzyme results in the monophosphorylation of acyclovir that must then undergo biphosphorylation and triphosphorylation by cellular enzymes. This triphosphylated form of acyclovir inhibits viral DNA, which results in complete and irreversible inhibition of further viral DNA synthesis. Enteroviruses, however, lack thymidine kinase and in vitro studies have failed to show any inhibitory effect on these viruses by acyclovir [17,20]. Since the Coxsackie A16 virus causing hand-foot-and-mouth disease lacks this enzyme, the beneficial therapeutic effect must be explained on other grounds, possibly due to enhancement of the antiviral effect of the patient's own interferon [17].

However, Shelley et al. [17] demonstrated a beneficial therapeutic effect in the treatment of HFMD with oral acyclovir (200-300 mg five times daily for five days) in twelve children and one adult. Symptomatic relief and significant involution of lesions were observed within twenty-four hours of starting acyclovir. As mentioned in our patient, treatment with oral acyclovir was not recommended because presentation of the disease was mild. Faulkner et al. [5] cited that in other situations the use of oral acyclovir may be considered as in infants who generally have a more severe course and in severely symptomatic patients.

The development of an effective vaccine against enteroviruses HFMD's causative is so important to prevent and control the disease due the epidemics recurrent nature and the lack of effective anti-viral therapy. At least three vaccines were produced in China and Taiwan which are in testing phase [20]. Selection of the target population is essential for the development of future vaccines and immunization strategies [16].

The HFMD is usually self-limiting disease, but often severe manifestations can be observed, mainly in adults immunocompromised. However, health professionals should be aware of these disease typical manifestations, in order to recognize it and treat it properly. In this report, we discussed diagnosis and treatment of this disease and reinforce the importance of the correct diagnosis because delayed diagnosis can cause spread of the disease.

## REFERENCES

1. Shin JU, Oh SH, Lee JH. A case of hand-foot-mouth disease in a immunocompetent adult. Ann Dermatol. 2010 May;22(2):216-8. doi: 10.5021/ad.2010.22.2.216.
2. Rabenau HF, Richter M, Doerr HW. Hand, foot and mouth disease: seroprevalence of Coxsackie A16 and Enterovirus 71 in Germany. Med Microbiol Immunol. 2010 Feb;199(1):45-51. doi: 10.1007/s00430-009-0133-6.
3. Wong SSY, Yip CCY, Lau SKP, Yuen KY. Human enterovirus 71 and hand, foot and mouth disease. Epidemiol Infect. 2010 Aug;138(8):1071-89. doi: 10.1017/S0950268809991555.
4. Onozuka D, Hashizume M. The influence of temperature and humidity on the incidence of hand, foot and mouth disease in Japan. Sci Total Environ. 2011 Dec 1;410-411:119-25. doi: 10.1016/j.scitotenv.2011.09.055.
5. Faulkner CF, Godbolt AM, DeAmbrois B, Triscott J. Hand, foot and mouth disease in an immunocompromised adult treated with aciclovir. Australas J Dermatol. 2003 Aug;44(3):203-6.
6. Lott JP, Liu K, Landry ML, Nix WA, Oberste MS, Bolognia J, et al. Atypical hand-foot-and-mouth disease associated with coxsackievirus A6 infection. J Am Acad Dermatol. 2013 Nov;69(5):736-41. doi: 10.1016/j.jaad.2013.07.024.
7. Shea YF, Chan CY, Hung IFN, Chan KH. Hand, foot and mouth disease in an immunocompetent adult due to Coxsackievirus A6. Hong Kong Med J. 2013 Jun;19(3):262-4. doi: 10.12809/hkmj133692.
8. Wang Y, Feng Z, Yang Y, Self S, Gao Y, Longini IM, et al. Hand, foot and mouth disease in China: Patterns of spread and transmissibility during 2008-2009. Epidemiology. 2011 Nov;22(6):781-92. doi: 10.1097/EDE.0b013e318231d67a.
9. Li W, Yi L, Su J, Lu J, Ke C, Zeng H, et al. Seroprevalence of Human Enterovirus 71 and Coxsackievirus A16 in Guangdong, China, in pre- and post-2010 HFMD epidemic period. PLoS One. 2013 Dec 4;8(12):e80515. doi: 10.1371/journal.pone.0080515.
10. Flor de Lima B, Silva J, Rodrigues AC, Grilo A, Riso N, Riscado MV. Hand, foot, and mouth syndrome in an immunocompetent adult: a case report. BMC Res Notes. 2013 Nov 3;6:441. doi: 10.1186/1756-0500-6-441.
11. Hamaguchi T, Fujisawa H, Sakai K, Okino S, Kurosaki N, Nishimura Y, et al. Acute encephalitis caused by intrafamilial transmission of enterovirus 71 in adult. Emerg Infect Dis. 2008 May;14(5):828-30. doi: 10.3201/eid1405.071121.
12. Akkoyunlu Y, Ceylan B, Aslan T. Hand, foot, and mouth disease in an adult. Braz J Infect Dis. 2014 Mar-Apr;18(2):227-8. doi: 10.1016/j.bjid.2013.11.004.
13. Toya M, Endo Y, Fujisawa A, Tanioka M, Miyachi Y. An adult case of severe hand-foot-mouth disease accompanying persistent feverand systemic arthrit. Dermatol Online J. 2012 Aug 15;18(8):14.
14. Castro CMO, Cruz ACR, da Silva EE, Gomes MLC. Molecular and seroepidemiologic studies of Enterovirus 71 infection in the State of Pará, Brazil. Rev Inst Med Trop São Paulo. 2005;47(2):65-71.

15. Ruan F, Yang T, Ma H, Jin Y, Song S, Fontaine RE, et al. Risk factors for hand, foot, and mouth disease and herpangina and the preventive effect of hand-washing. Pediatrics. 2011 Apr;127(4):e898-904. doi: 10.1542/peds.2010-1497.

16. Zhu FC, Liang ZL, Meng FY, Zeng Y, Mao Q, Chu K, et al. Restrospective study of the incidence of HFMD and seroepidemiology of antibodies against EV71 and CoxA16 in prenatal women and their infants. PLoS One. 2012;7(5):e37206. doi: 10.1371/journal.pone.0037206.

17. Shelley WB, Hashim M, Shelley ED. Acyclovir in the treatment of hand-foot-and-mouth disease. Cutis. 1996 Apr;57(4):232-4.

18. Elion GB. Acyclovir: discovery, mechanism of action, and selectivity. J Med Virol. 1993;Suppl 1:2-6.

19. Gilbert GL, Dickson KE, Waters M, Kennett ML, Land SA, Sneddon M. Outbreak of enterovirus 71 infection in Victoria, Australia, with a high incidence of neurologic involvement. Pediatr Infect Dis J. 1988 Jul;7(7):484-8.

20. Liang Z, Mao Q, Gao Q, Li X, Dong C, Yu X, et al. Establishing China's national standards of antigen content and neutralizing antibody for evaluation of enterovirus 71 (EV71) vaccines. Vaccine. 2011 Dec 6;29(52):9668-74. doi: 10.1016/j.vaccine.2011.10.018.

**Luciana Eloísa da Silva Castro Nóbrega**
**(Corresponding address)**
Federal University of Rio Grande do Norte, Department of Oral Pathology,
Senador Salgado Filho Ave., 1787, Lagoa Nova, Natal, RN, Brazil,
CEP 59056-000.
E-mail address: luelocastro@gmail.com

Date submitted: 2016 Mar 22

Accept submission: 2016 Dec 07